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REVIEW

SESQUITERPENE LACTONES AND SYSTEMATICS OF THE GENUS *ARTEMISIA*

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Key Word Index—*Artemisia*; Asteraceae; sesquiterpene lactones; systematics; phylogeny; taxonomy.

Abstract—The sesquiterpene lactones isolated from species in the genus *Artemisia* have been reviewed in an attempt to better understand the phylogeny and systematics of the four sections (subgenera), *Abrotanum*, *Absinthium*, *Dracunculus* and *Seriphidium*, proposed by Besser in 1829. The absence of hair on the receptacle is the only morphological characteristic separating species of *Abrotanum* from the species of *Absinthium*. There are no chemical characteristics segregating the species in these two subgenera since both produce eudesmanolides and guaianolides that are identical or biosynthetically similar. This suggests that the two subgenera could be combined into one (*Artemisia*) as proposed by Poljakov. The subgenus *Seriphidium* is composed of two geographical groups, one in the Old World and the other in the New World. The Old World species almost exclusively produce sesquiterpene lactones in the eudesmanolide class whereas the New World species (section *Tridentatae*) produce eudesmanolides and guaianolides, many of the latter being identical or structurally related to the sesquiterpene lactones in New World *Abrotanum* species. The chemical data in conjunction with geographic distributions suggest that the subgenus *Seriphidium* is polyphyletic and that the section *Tridentatae* originated from *Abrotanum*. Consequently, the *Tridentate* should be recognized as a subgenus separate and distinct from the Old World *Seriphidium*. There was insufficient information from the subgenus *Dracunculus* for interpretation.

INTRODUCTION

The genus *Artemisia* L. is one of the largest and most widely distributed of approximately 60 genera in the tribe Anthemideae of the Asteraceae (Compositae). This genus, with nearly 300 species, is found predominantly in the northern temperate regions of the world (North America, Europe, Asia and North Africa), in the 0–50 cm precipitation zone, with southward extensions toward the tropics [1].

The first rational and natural arrangement of the genus was given by Besser [2], but was uncompleted at his death. Major portions of his work were included in the texts of de Candolle [3] and Hooker [4]. Besser [2] divided the genus into four sections based on fundamental differences in floral structure (Table 1).

Phylogenetically, *Abrotanum* and *Absinthium* represent the more primitive sections, while *Dracunculus* and *Seriphidium* are the more advanced [5]. Since Besser's sections were natural, they have remained the basic divisions within the genus, although some taxonomists have elevated them to the subgenus level [6, 7] and reduced the subgenera to three by combining *Abrotanum* with *Absinthium* to form the subgenus *Artemisia* [7].

Table 1. Besser's division of *Artemisia*

Morphological characters	Section
1. Heads heterogamous, the marginal flowers pistillate	
2. Central flowers fertile, with normally developed achenes	
3. Receptacle not hairy	1. *Abrotanum*
3. Receptacle long hairy	2. *Absinthium*
2. Central flowers sterile, their achenes aborted	3. *Dracunculus*
1. Heads homogamous, marginal flowers absent	4. *Seriphidium*

The shrubby members of the subgenus *Seriphidium* endemic to North America were recognized as being closely related by Rydberg [6] and he grouped them together in the section *Tridentatae* of the subgenus *Seriphidium*. This subdivision was not accepted by Hall and Clements [5] or Ward [8] but was later followed by Beetle [9]. McArthur and Plummer [10] have argued that the New World *Tridentatae* and the rest of the (Old World) *Seriphidium* should be recognized as separate taxonomic entities based on present and past geographic distribution, karyotypes, chemistry and shrubby habits.

Similarly, Keck [11] recognized a close relationship among several species in the section *Abrotanum* and grouped them together in the subsection *Vulgares*. The species in this subsection are not restricted to the New World, although the American species probably originated here [11]. The sesquiterpene lactones have been examined in many of the American *Vulgares* and this information may provide some insight into their phytogenetic relationships.

Until recently, the general consensus has placed the origin of the genus in Central Asia with subsequent migration to North America through the Bering land Bridge [5, 9, 10, 12, 13]. Beetle, originally an advocate of Old World genesis [9], has since revised his thoughts and now suggests *Artemisia* may have originated in the Americas [14]. The biological evidence, however, points to Eurasia as the center of origin. Approximately 200

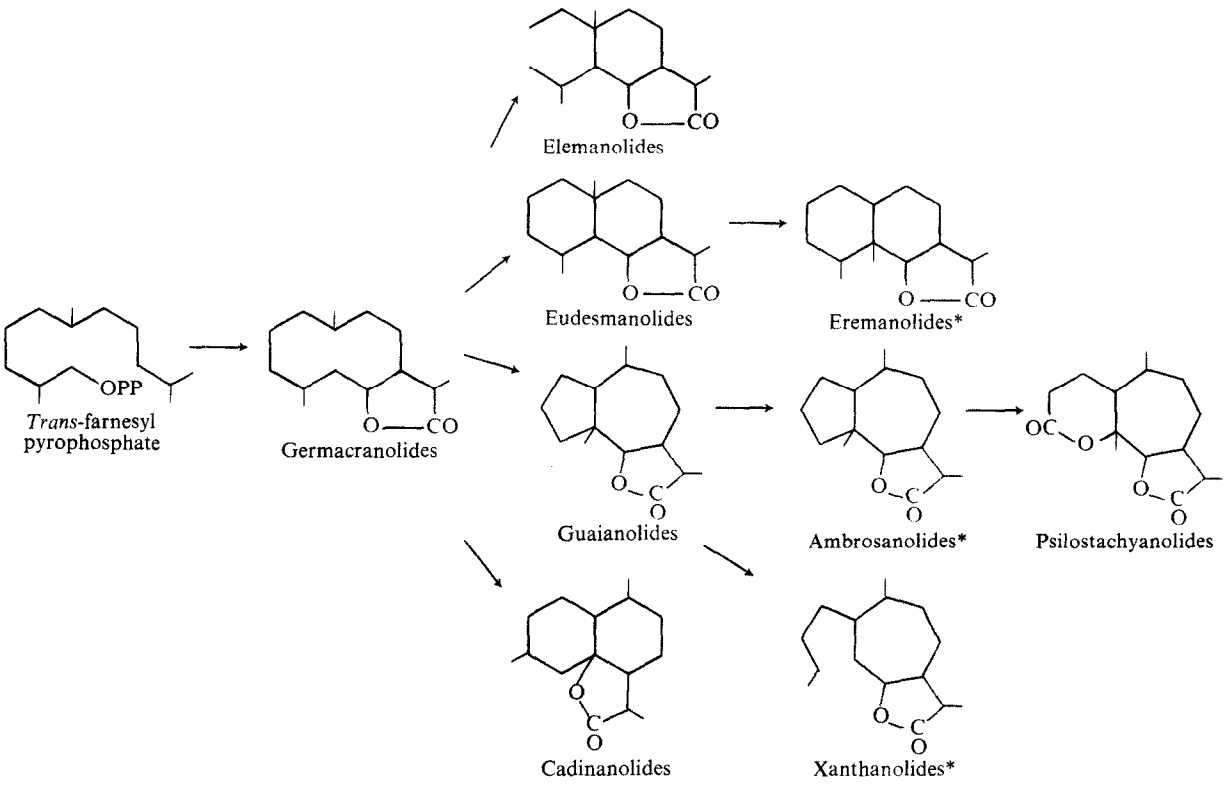


Fig. 1. The proposed biosynthetic pathways for the various structural classes of sesquiterpene lactones found in the genus *Artemisia* (classes marked with an asterisk have not yet been discovered in this genus).

species are present in the Old World compared to about 50 in North America. The two genera *Chrysanthemum* and *Tanacetum*, the nearest and least-specialized relatives of *Artemisia* [12] as well as other genera in the tribe *Anthemideae*, grow predominantly in Eurasia and Africa [13]. Furthermore, there is little paleobotanical evidence of *Artemisia* species in the early North American floras [15, 16]. *Artemisia* species may have migrated from the Old World throughout most of the late tertiary and periodically during the Pleistocene when the Bering land bridge was present [17], thus providing sufficient time for the origin and dispersal of the present *Tridentatae* in North America.

This then raises the question of how the *Tridentatae* originated. Currently, only three subgenera, *Abrotanum*, *Absinthium* and *Dracunculus*, transect Beringia [18, 19]. Members of the *Seriphidium* are found predominantly in Eurasia and northern Africa [7, 10], but not in eastern Russia or North America. Conversely, the *Tridentatae* occupy the environments of western North America with no representatives in the northern latitudes of Canada, Alaska or eastern Siberia [9, 19]. This provides the foundation for McArthur and Plummer's [10] argument that the shrubby *Tridentatae* on the North American continent originated separately from the Old World *Seriphidium*, from herbaceous ancestors in the subgenus *Artemisia* (Poljakov's [7] combination of *Abrotanum* and *Absinthium*).

The sesquiterpene lactone data for the *Artemisia* have been compiled and reviewed categorically by subgenera (sections) in an attempt to use these chemical characteristics to better understand the phylogeny and systematics of the genus. More specifically, these data may be useful or help provide answers to the following systematic questions:

(a) Are the species in the subsection *Vulgares*, as proposed by Keck [11], a closely related group that is distinct from other species in the section (subgenus) *Abrotanum*?;

(b) What is the origin of the section *Tridentatae* and its relationship to the subgenera *Seriphidium* and *Artemisia*?;

(c) Do the sesquiterpene lactones preclude or support any of the previous taxonomic arrangements?

Before examining the sesquiterpene lactones in this genus, it should be emphasized that the germacranolides represent the simplest biosynthetic class. These are then biosynthetically transformed into the more advanced classes (Fig. 1) by cyclization, rearrangements and oxidation [20–23].

SESQUITERPENE LACTONES OF THE SUBGENERA ABROTANUM

Species in the subgenus *Abrotanum* produce the most structurally diversified and biosynthetically advanced sesquiterpene lactones in the genus (Tables 2 and 3, Figs. 2 and 3) with the greatest variety of structural types in plants from the Old World.

Table 2. Classification of *Artemisia* species by sesquiterpene lactone structural classes*

Subgenera	Sesquiterpene lactone structural classes†						
	Germacranolides	Eudesmanolides	Guaianolides	Elemanolides	Cadinanolides	Modified cadinanolides	Psilostachyanolides
Abrotanum	2	9	8		1	1	1
Absinthium	2	3	8				
Dracunculus		1	1				
Seriphidium	1	26	3	1			
Tridentatae	2	6	5				

* Each species was placed into a class based on the most biosynthetically advanced compound isolated from it. If a germacranolide and a guaianolide were extracted from the same plant collection, then the species was tallied only as a guaianolide producer. If separate collections of the same species contained structurally different compounds, germacranolides in one and guaianolides in another, then the species was tallied under both headings. Each species was counted only once within a class, without regard for the subspecies, or the number of different compounds produced belonging to that class. The only species with exceptions were *A. douglasiana* and *A. nova*. *Artemisia douglasiana* was listed under both eudesmanolides and guaianolides because it produced the former compounds in the spring and the latter compounds in the fall. *Artemisia nova* was listed only under guaianolides although both eudesmanolides and guaianolides were isolated from it, the latter class was more frequent. This is the only species in which both these structural classes occurred simultaneously.

† See Fig. 1. No ambrosanolides, eremanolides or xanthanolides are present in *Artemisia* species.

Table 3. Sesquiterpene lactones isolated from the genus *Artemisia*

Species	Location	Compounds	References
		ABROTANUM (ARTEMISIA [7])	
A. annua L.	Belgrade, Yugoslavia	Arteannuin-B (**3**), C* $C_{15}H_{20}O_3$, mp 152°, $[\alpha]_D^{20}$ −6°	[25]
	Peoples Republic of China	Qing hau sau (**4**), mc	[26]
A. californica Less.	Malibu, Los Angeles Co., California, U.S.A.	Artecalin (**32**), Eu, $C_{15}H_{20}O_4$, mp 225–227°, $[\alpha]_D^{23}$ +45°	[52]
A. camphorata Vill.	Iran	Santonin (**11**), Eu	[37]
A. carruthii Wood	Graham Mountain, Graham Co., Arizona, U.S.A.	Matricin (**31**), Gu, $C_{17}H_{22}O_5$, mp 152–156°, $[\alpha]_D^{30}$ −122° ($CHCl_3$)	[51]
	NA†, North America	Ludartin (**29**), Gu, $C_{15}H_{18}O_3$ 11,13-Dihydroludartin (**30**), Gu, $C_{15}H_{20}O_3$	[50]
A. douglasiana Bess.	West Los Angeles, California, U.S.A.	Spring growth: Arglanine (**16**), Eu, $C_{15}H_{18}O_4$, mp 207°, $[\alpha]_D^{24}$ +111° Douglanine (**17**), Eu, $C_{15}H_{20}O_3$, mp 115–117°, $[\alpha]_D^{24}$ +133° Ludovicin-B (**22**), Eu, $C_{15}H_{20}O_4$, mp 152°, $[\alpha]_D^{25}$ +138° Fall growth: Arteglasin-A (**27**), Gu, $C_{17}H_{20}O_5$, mp 207–208°, $[\alpha]_D^{25}$ +110° (*c* 0.8) Arteglasin-B (**28**), Gu, $C_{17}H_{20}O_6$, mp 192–194°, $[\alpha]_D^{25}$ +150° (*c* 0.5)	[47–49]
A. franserioides Greene	Greer, Apache Co., Arizona, U.S.A.	Artefransin (**33**), Gu, $C_{17}H_{20}O_6$, mp 197–198°, $[\alpha]_D^{25}$ +33° (*c* 0.6, Py)	[53]
A. incana L.	Endemic to Caucasus, U.S.S.R.	Deacetylmatricarin (**5**), Gu, $C_{15}H_{18}O_4 \cdot H_2O$, mp 150–151.5°, $[\alpha]_D^0$ +13.63° (EtOH; *c* 3.68)	[27, 90]
A. judaica L.	Egypt	Tauremisin (vulgarin, judaicin) (**9**), Eu, $C_{15}H_{20}O_4$, mp 176–177°, $[\alpha]_D^{20}$ +42.7° ($CHCl_3$; *c* 6.8)	[33–35, 113]
A. klotzchiana Bess.	San Roberto, Nuevo Leon, Mexico	Deacetylmatricarin (**5**), Gu Achillin (**25**), Gu, $C_{15}H_{18}O_3$, mp 144–145°, $[\alpha]_D^{26}$ +151° ($CHCl_3$; *c* 0.995)	[45, 165]
	Actopan, Hildago, Mexico	Deactymatricarin (**5**), Gu Chrysartemin-A (**15**), Gu, $C_{15}H_{18}O_5$, mp 250°, $[\alpha]_D$ +51° Matricarin (**26**), Gu, $C_{17}H_{20}O_5$, mp 190–191°, $[\alpha]_D^{23}$ +23.5° ($CHCl_3$; *c* 0.65)	[41, 46]
A. ludoviciana Nutt.	Punta de la Loma, Nuevo Leon, Mexico	Deacetylmatricarin (**5**), Gu Achillin (**25**), Gu	[45]

Table 3.—*Continued*

Species	Location	Compounds	References
A. ludoviciana ssp. *albula* (Woot.) Keck	NA, North America	Ludalbin (**24**), Eu, $C_{17}H_{22}O_5$, mp 169–171°, $[\alpha]_D^{27}$ + 227.6° ($CHCl_3$; *c* 1.0)	[44]
A. ludoviciana ssp. *mexicana* (Willd.) Keck	Eagar, Apache Co., Arizona, U.S.A.	Douglanine (**17**), Eu Ludovicin-A (**21**), Eu, $C_{15}H_{20}O_4$, mp 215°, $[\alpha]_D^{25}$ +128° Ludovicin-B (**22**), Eu Ludovicin-C (**23**), $C_{15}H_{18}O_4$, mp 193–195°, $[\alpha]_D^{25}$ +95°	[43]
A. mexicana Willd. (syn. *A. ludoviciana* ssp. *mexicana* (Willd.) Keck)	Mexico City, Mexico, 1960	Estafiatin (**14**), Gu, $C_{15}H_{18}O_3$, mp 104–106°, $[\alpha]_D$ −9.9°	[40]
	Mexico City, Mexico, 1967	Estafiatin (**14**), Gu Chrysartemin-A (**15**), Gu	[41]
	Mexico City, Mexico, 1968	Arglanine (**16**), Eu Douglanine (**17**), Eu	[41]
	Mexico City, Mexico, 1970	Artemorin (**6**), Gr, $C_{15}H_{20}O_3$, mp 115–117°	[42]
	Mexico City, Mexico, 1971	Armexine (**18**), Eu, $C_{15}H_{20}O_4$	[42]
	New Mexico, U.S.A.	Santonin‡ (**11**), Eu	[54]
A. mexicana var. *angustifolia*	Actopan, Hildago, Mexico, 1974	Tulipinolide (**13**), Gr, $C_{17}H_{22}O_4$, mp 181°, $[\alpha]_D^{25}$ +249° ($CHCl_3$; *c* 4.8)	[39]
	Actopan, Hildago, Mexico, 1975	Arglanine (**16**), Eu Artemexifolin (**19**), Eu, $C_{17}H_{20}O_6$, mp 260°, $[\alpha]_D^{22}$ +156° ($CHCl_3$) Armexifolin (**20**), Eu, $C_{15}H_{18}O_4$, mp 207–208°	[39]
A. neo-mexicana Woot. (syn. *A. ludoviciana* ssp. *mexicana* (Willd.) Keck)	New Mexico, U.S.A.	Santonin‡ (**11**), Eu	[54]
A. princeps Pamp.	Northern Honshu, Japan	Yomogin (**10**), Eu, $C_{15}H_{16}O_3$, mp 201–202°, $[\alpha]_D^{20}$ −88° ($CHCl_3$; *c* 0.11)	[36]
A. stelleriana Bess.§	NA	1,2-Dihydrosantonin (**12**), Eu, $C_{15}H_{20}O_3$	[38]
A. tilesii Ledeb.	Unalakleet, Bering Straits, Alaska, U.S.A.	Deacetylmatricarin (**5**), Gu Matricarin (**26**), Gu	[46]
	Palmer, Cook Inlet, Alaska, U.S.A.	Matricarin (**26**), Gu	[46]
A. verlotorum Lamotte	Milbertshofen, Germany and Tessin Region of south-eastern Switzerland	Artemorin (**6**), Gr Verlotorin (**7**), Gr, $C_{15}H_{20}O_4$, mp 130–132° Anhydroverlotorin (**8**), Gr, $C_{15}H_{18}O_3$, mp 123–124°	[28–31]
	Nunawading, Australia (naturalized)	Tauremisin (**9**), Eu	[30, 32]
A. vulgaris L.	Belgrade, Yugoslavia	Psilostachyin (**1**), P, $C_{15}H_{20}O_5$, mp 210–212°, $[\alpha]_D^{20}$ −100° ($CHCl_3$; *c* 0.294) Psilostachyin-C (**2**), P, $C_{15}H_{20}O_4$, mp 223–225°, $[\alpha]_D^{20}$ −82° ($CHCl_3$; *c* 0.602)	[24]
A. wrightii Gray (syn. *A. carruthii* Wood)	New Mexico, U.S.A.	Santonin‡ (**11**), Eu	[54]
		ABSINTHIUM (*ARTEMISIA* [7])	
A. absinthium L.	NA, Eurasia	Artabsin (**34**), Gu, $C_{15}H_{20}O_3$, mp 133–135°, $[\alpha]_D^{20}$ −49° ($CHCl_3$; *c* 1.56) Absinthin (**35**), Gu dimer, $C_{30}H_{40}O_6$, mp 179–180°, $[\alpha]_D^{20}$ +180° ($CHCl_3$; *c* 1.9) Anabsinthin (**36**), Gu dimer, $C_{30}H_{40}O_6$, mp 210°, $[\alpha]_D^{20}$ +111° (MeOH; *c* 2.05)	[55–57, 59, 66, 166]
	Pullman, Whitman Co., Washington, U.S.A. (naturalized)	Artabsin (**34**), Gu	[58]
	Tashkent Oblast, Uzbek SSR, U.S.S.R.	Artabsin (**34**), Gu	[61]

Table 3.— *Continued*

Species	Location	Compounds	References
	Tashkent Oblast, Uzbek SSR, U.S.S.R.	Artabin (**37**), Gr, $C_{15}H_{22}O_3$, mp 162–164 , $[\alpha]_D^{20}$ +220° Arabsin (**38**), Eu, $C_{15}H_{22}O_4$, mp 188–189°, $[\alpha]_D^{23}$ +89° (EtOH; *c* 2.71)	[62–64]
	NA, Eurasia	Ketopelenolide-A (**39**), Gr, $C_{15}H_{22}O_3$, mp 112–114°, $[\alpha]_D^{20}$ −277° Ketopelenolide-B (**40**), Gr, $C_{15}H_{22}O_3$, mp 172°, $[\alpha]_D^{20}$ +213° Hydroxypelenolide (**41**), Gr, $C_{15}H_{24}O_3$, mp 108°, $[\alpha]_D^{20}$ −14°	[67, 83]
	Golubac, Yugoslavia	Ketopelenolide-A (**39**), Gr	[65]
A. anethifolia Web.	Tuva ASSR, Russian SFSR, U.S.S.R.	Ketopelenolide-B (**40**), Gr	[68]
A. arborescens L.	NA	Arborescin (**45**), Gu, $C_{15}H_{20}O_3$, mp 145°, $[\alpha]_D^{20}$ +63° ($CHCl_3$)	[57, 75–77]
A. ashurbajevii Winki	Chonkemine, Kirghiz SSR, U.S.S.R.	Hanphyllin (**51**), Gr, $C_{15}H_{20}O_3$, mp 189° Granilin (**52**), Eu, $C_{15}H_{20}O_4$, mp 195–197°	[85]
A. austriaca Jacq.	Poltava, Poltava Oblast, Ukrainian SSR, U.S.S.R.	Deacetylmatricarin (**5**), Gu	[78, 79]
	Dzhezkazgan Oblast, Kazakh SSR, U.S.S.R.	Santonin (**11**), Eu	[80]
A. canariensis Lee	Isla de Tenerife, Canary Islands	Tauremisin (**9**), Eu Tabarin (**53**), Eu, $C_{17}H_{22}O_6$, mp 213–215°, $[\alpha]_D$ +10°	[86]
A. caucasica Willd.	Gelendzhik, Krasnodar Oblast, Russian SFSR, U.S.S.R.	Grossmizin (**46**), Gu, $C_{15}H_{18}O_4 \cdot H_2O$, mp 120–135° crystallizes again and remelts at 156–158 , $[\alpha]_D^{20}$ +115.26° (EtOH; *c* 1.2) Canin (**47**), Gu, $C_{15}H_{18}O_5$, mp 244–246°, $[\alpha]_D^{25}$ −35° (Py; *c* 1.0)	[81, 83, 141, 142]
A. jacutica Drob.	Ytyk-Kel, Alekseev region of Yakut ASSR, Russian SFSR, U.S.S.R.	Ketopelenolide-B (**40**), Gr Sieversinin (**42**), Gu, $C_{15}H_{20}O_3$, mp 141–142°, $[\alpha]_D^{20}$ +57°	[69, 70]
A. lanata Willd.	Algora, Guadalajara Province, Spain	Achillin (**25**), Gu 8α-Hydroxyachillin (**48**), Gu, $C_{15}H_{18}O_4$ 1,10-Epoxyachillin (**49**), Gu, $C_{15}H_{18}O_4$, mp 236–238°, $[\alpha]_D$ +102° ($CHCl_3$; *c* 0.18) 1,10-Epoxy-8α-hydroxyachillin (**50**), Gu, $C_{15}H_{18}O_5$	[84]
*A. rutifolia**** Steph. et Spreng.	Central Asia, region of the Turkestan Range, U.S.S.R.	Canin (**47**), Gu	[81, 83, 141, 142]
A. sieversiana Willd.	NA, U.S.S.R.	Artabsin (**34**), Gu Absinthin (**35**), Gu dimer	[71]
	NA, U.S.S.R.	Sieversinin (**42**), Gu	[70]
	Talas, Talas Oblast, Kirgiz, U.S.S.R.	Sieversin (**43**), Gu, $C_{17}H_{22}O_5$, mp 128–131° Globicin (**44**), Gu	[72–74]
		DRANCUNCULUS	
A. dracunculoides Pursh	Forestdale, Navajo Co., Arizona, U.S.A.	8-Hydroxyarbiglovin (**124**), Gu, tentative structure, $C_{15}H_{16}O_4$, mp 206–212°	[164]
A. filifolia Torrey	Willcox, Cochise Co., Arizona, U.S.A.	Colartin (**104**), Eu, $C_{15}H_{24}O_3$, mp 107–108°, $[\alpha]_D^{24}$ +19.4° ($CHCl_3$; *c* 0.88)	[163]
		SERIPHIDIUM	
A. amoena Poljak.	Kazakh SSR, U.S.S.R.	Santonin (**11**), Eu	[80]
A. balchanorum Krasch	Moldavian SSR, U.S.S.R.	Costunolide (**59**), Gr, $C_{15}H_{20}O_2$, mp 106–107°, $[\alpha]_D^{20}$ +128° ($CHCl_3$; *c* 10.5) Hydroxycostunolide (**60**), Gr, $C_{15}H_{20}O_3$ Balchanolide (**61**), Gr, $C_{15}H_{22}O_3$, mp 154°, $[\alpha]_D^{20}$ +183° ($CHCl_3$; *c* 1.84) Hydroxybalcanolide (**62**), Gr,	[94–98]

Table 3.—*Continued*

Species	Location	Compounds	References
		$C_{15}H_{20}O_4$, mp 163°, $[\alpha]_D^{20}$ +105° (EtOH; *c* 2.71)	
		Isobalcanolide (**63**), Gr, $C_{15}H_{22}O_3$, mp 133°, $[\alpha]_D^{20}$ +122° ($CHCl_3$; *c* 2.08)	
		Balchanin (santamarine) (**64**), Eu, $C_{15}H_{22}O_3$, mp 142°, $[\alpha]_D^{20}$ +96.6 ($CHCl_3$)	
A. caerulescens L.	Adriatic Sea, Central Europe	α-Santonin (**11**), Eu, $C_{15}H_{18}O_3$, mp 171–172°, $[\alpha]_D^{18}$ −173° (EtOH)	[100, 106, 124]
		β-Santonin (**11**), Eu, $C_{15}H_{18}O_3$, mp 216–218°, $[\alpha]_D^{19}$ −137.2° ($CHCl_3$)	
		Artemin (**69**), Eu, $C_{15}H_{22}O_4$, mp 238–240°, $[\alpha]_D$ +167° (*c* 0.5)	
	Collected in Yugoslavia, grown at Kasukabe, Japan	Santonin (**11**), Eu	[167]
A. cina Berg. ex Poljak.	NA, Eurasia	Santonin (**11**), Eu	[100]
	Chimkent Oblast, Kazakh SSR, U.S.S.R.	Artemisin (**67**), Eu, $C_{15}H_{18}O_4$, mp 202–204°, $[\alpha]_D^{26}$ −80° (*c* 2.5)	[103, 168, 169]
		α-Santonin (**11**), Eu	
A. cina var. *mogoltavica* Poljak.	Leninabad Oblast, Tadzhik SSR, U.S.S.R.	Santonin (**11**), Eu	[80]
A. cina (Berg.) Willkomm	Iran	Santonin (**11**), Eu	[37]
A. compacta Fisch.	Kirgiz SSR, U.S.S.R.	α-Santonin (**11**), Eu	[80]
	Kosh-Agach, Gormo Altay A.O., Russian SFSR, U.S.S.R.	β-Santonin (**11**), Eu	[170]
	NA, U.S.S.R.	β-Santonin (**11**), Eu	[171]
A. finita Kitagawa	Western Shores of Lake Dalai Nor, China	β-Santonin (**11**), Eu	[102, 105]
		Finitin (**68**), Eu, $C_{15}H_{20}O_3$, mp 153–155°, $[\alpha]_D^{12}$ −167.7° ($CHCl_3$; *c* 1.7)	
A. fragrans Willd. (syn. *A. hanseniana* (Bess.) Grossh and *A. chasarica* Rz.)	Divichi, Azerbaijan SSR, U.S.S.R.	α-Santonin (**11**), Eu	[109]
		Tauremisin (**9**), Eu	
	Shemakha, Azerbaijan SSR, U.S.S.R.	Tauremisin (**9**), Eu	[110, 120–122, 124]
		Artemin (**69**), Eu	
		Arsubin (**70**), Eu, $C_{15}H_{22}O_4$, mp 233–234°, $[\alpha]_D^{20}$ +217.2° (EtOH; *c* 1.0)	
		Taurin (**71**), Eu, $C_{15}H_{20}O_3$, mp 118–119°, $[\alpha]_D^{19}$ −120° (EtOH; *c* 5)	
		Stereoisomer of erivanin (**72**), Eu, $C_{15}H_{22}O_4$, mp 193–194°	
	Ankara, Turkey	Santonin (**11**), Eu	[172]
	NA, Eurasia	Santonin (**11**), Eu	[100]
A. fragrans Willd. var. *erivanica* Bess.	Nakhichevan ASSR, Azerbaijan SSR, U.S.S.R.	Erivanin (**72**), Eu, $C_{15}H_{22}O_4$, mp 203–205°, $[\alpha]_D^{20}$ +112° (EtOH; *c* 3.9)	[111, 112, 173]
A. granatensis Boiss	Granada, Spain	Tauremisin (**9**), Eu	[125]
		1-Keto-6β,7α,11β-H-eudesm-4-en-6,12-olide (**73**), Eu, $C_{15}H_{20}O_3$, mp 109–110°, $[\alpha]_D$ −109° (EtOH; *c* 0.2)	
		1-Hydroxy-6β,7α,11β-H-eudesm-4-en-6,12-olide (**74**), Eu, $C_{15}H_{22}O_3$, mp 177–178°, $[\alpha]_D$ +60.9° (*c* 0.23)	
A. halophila Krasch	Syrdar ya Oblast, Uzbek SSR, U.S.S.R.	α-Santonin (**11**), Eu	[107]
		Artemin (**69**), Eu	
A. herba-alba Asso.	Sde Boker (Negev Desert), Israel	Herbolide-A (**56**), Gr, $C_{17}H_{24}O_4$, mp 162–163°, $[\alpha]_D^{25}$ +84° ($CHCl_3$; *c* 0.2)	[92]
		Herbolide-B (**57**), Gr, $C_{17}H_{24}O_5$, mp 209°, $[\alpha]_D^{25}$ +23° (EtOH; *c* 0.37)	
		Herbolide-C (**58**), Gr, $C_{17}H_{24}O_5$, mp 197–198°, $[\alpha]_D^{25}$ −26° (EtOH; *c* 0.1)	
	Ras El-Hikmal, Egypt	α-Santonin (**11**), Eu	[93]
A. hybrida Sag. (syn. *A. maritima* ssp. *salina* Gams var. *hydrida* Sag.)	NA, Central Europe	β-Santonin (**11**), Eu	[174]
A. juncea Kar. et Kir.	Ucharal, Taldy Kurgan Oblast, Kazakh SSR, U.S.S.R.	Santonin (**11**), Eu	[80]
	NA, U.S.S.R.	Deacetylmatricarin (**5**), Gu	[83]

Table 3.—*Continued*

Species	Location	Compounds	References
A. juncea var. *macrosciadia* Poljak.	Alma Ata Oblast, Kazakh, SSR, U.S.S.R.	Santonin (**11**), Eu	[80]
A. kemrudica Krasch§	Chardzhou Oblast, Turkman SSR, U.S.S.R.	Artemin (**69**), Eu	[123]
A. kurramensis Qazilbash	Collected in Pakistan or Afghanistan and grown in Japan and U.S.S.R.	α-Santonin (**11**), Eu β-Santonin (**11**), Eu	[80, 175, 176]
	NA	Lumisantonin (**78**), Eu, $C_{15}H_{18}O_3$, mp 153.5–155°, $[\alpha]_D^{21}$ −150.8° ($CHCl_3$; *c* 2.63)	[132]
A. lercheana Web.	Volgograd Oblast, Russian SFSR, U.S.S.R.	Deacetylmatricarin (**5**), Gu	[90]
	Aktyubinsk Oblast, Kazakh SSR, U.S.S.R.	Santonin (**11**), Eu	[80]
A. leucodes Schrenk.	Alma Ata, Alma Ata Oblast, Kazakh SSR, U.S.S.R.	Deacetylmatricarin (**5**), Gu Deacetoxymatricarin (**55**), Gu, $C_{15}H_{18}O_3$, mp 204–206°, $[\alpha]_D^{25}$ +53.2° ($CHCl_3$; *c* 2.05)	[78, 88, 138]
	Alma Ata Oblast, Kazakh SSR, U.S.S.R.	Santonin (**11**), Eu	[80]
	Samarkand Oblast, Uzbek SSR, U.S.S.R.	Deacetoxymatricarin (**55**), Gu	[89]
A. maritima L. (syn. *A. brevifolia* Wall.)	NA, Eurasia	α-Santonin (**11**), Eu β-Santonin (**11**), Eu Artemisin (**67**), Eu Temisin (**54**), El, $C_{15}H_{20}O_3$, mp 228°, $[\alpha]_D^{20}$ +70° ($CHCl_3$) ψ-Santonin (**65**), Eu, $C_{15}H_{20}O_4$, mp 183–184°, $[\alpha]_D^{20}$ −169° ($CHCl_3$; *c* 2.49) Desoxy-ψ-santonin (**66**), Eu, $C_{15}H_{20}O_3$, mp 101–102°, $[\alpha]_D^{25}$ −207° (EtOH; *c* 0.68)	[87, 100–102, 169, 177–180]
	Iran; Auckmere Haven, England; Edinburgh, Scotland (Royal Botanical Gardens)	Santonin (**11**), Eu	[37, 38]
A. maratima var. *boschniakiana* Bess.	Dnepropetrovsk Oblast, Ukrainian SSR, U.S.S.R.	β-Santonin (**11**), Eu	[90]
A. maritima ssp. *gallica* Willd.	Cabo Corbera, Valencia, Spain	Artemin (**69**), Eu	[124]
A. monogyna Waldst. et Kit.	NA, Eurasia	Mibulactone (**79**), Eu, structure tentative $C_{15}H_{22}O_4$, mp 228–229°, $[\alpha]_D^{10}$ +156.36° Monogyna (**80**), Eu, structure tentative $C_{15}H_{20}O_3$, mp 138°, $[\alpha]_D^{13.5}$ −164° ($CHCl_3$)	[74, 134–136]
	NA, Eurasia	Lumisantonin (**78**), Eu	[133]
	NA, Eurasia	β-Santonin (**11**), Eu	[174]
A. pauciflora Web.	NA, Eurasia	Santonin (**11**), Eu	[100]
A. ramosa Chr. Sm.	Isla de Gran Canaria, Canary Islands	Finitin (**68**), Eu α-Santonin (**11**), Eu	[102, 104, 181]
A. salina Willd. (syn. *A. maritima* L.)	NA, Central Europe	β-Santonin (**11**), Eu	[174]
A. santolina Schrenk.	Southeastern Kara Kum, Chardzhou Oblast, Turkmen SSR, U.S.S.R.	Artesin (**75**), Eu, $C_{15}H_{22}O_3$, mp 172° $[\alpha]_D^{27}$ +49° (EtOH; *c* 2) Arsanin (**76**), Eu, $C_{15}H_{22}O_4$, mp 193–194°, $[\alpha]_D^{20}$ +26° ($CHCl_3$; *c* 3.33) Arsantin (**77**), Eu, $C_{15}H_{22}O_4$, mp 183–185°, $[\alpha]_D^{20}$ +31.5° ($CHCl_3$; *c* 1.78)	[126–131]
A. serotina Bge.	Chayan, Chimkent Oblast and Alma Ata Oblast, Kazakh, SSR, U.S.S.R.	β-Santonin (**11**), Eu	[80, 90]
A. spicata Wulf. (syn. *A. genipi* Webb.)	Piedmont, Italy	Santamarine (**64**), Eu, $C_{15}H_{20}O_3$, mp 134–136°, [α] +96°	[99, 182]
A. spicigera Koch	NA, U.S.S.R.	α-Santonin (**11**), Eu β-Santonin (**11**), Eu	[183]
A. sublessingiana (Kell.) Krasch ex Poljak.§	NA, U.S.S.R.	Arsubin (**70**), Eu	[120–122, 124]

Table 3.—*Continued*

Species	Location	Compounds	References
A. sublessingiana var. *gorjaevii* Poljak.	Taldy Kurgan Oblast. Kazakh SSR, U.S.S.R.	Santonin (**11**), Eu	[80]
A. szowitziana (Bess.) Grossh.	NA, U.S.S.R.	α-Santonin (**11**), Eu	[83]
A. taurica Willd.	Chechen-Ingush, Daghestan, Kalmyk and Stavropol ASSR's, Russian SFSR, U.S.S.R.	Tauremisin (**9**), Eu Artemin (**69**), Eu Taurin (**71**), Eu	[88, 115–117, 119]
	Krym (Crimea) Oblast Ukrainian SSR, U.S.S.R.	Tauremisin (**9**), Eu	[113, 114, 117]
A. tenuisecta Nevski	Tashkent Oblast, Uzbek SSR, U.S.S.R.	α-Santonin (**11**), Eu Artemin (**69**), Eu	[107, 108]
A. tenuisecta var. *glaucina* Poljak.	Kulyab Oblast, Tadzhik SSR, U.S.S.R.	Santonin (**11**), Eu	[80]
A. tenuisecta var. *karataviensis* Poljak.	Kazak SSR, U.S.S.R.	Santonin (**11**), Eu	[80]
A. terrae-albae Krasch ssp. *massagetovii* Krasch	Taldy Kurgan Oblast, Kazakh SSR, U.S.S.R.	Santonin (**11**), Eu	[80]
A. terrae-albae var. *kurdaica* Poljak.	NA, U.S.S.R.	Santonin (**11**), Eu	[80]
A. turanica Krasch var. *diffusa* Krasch ex Poljak.	130 km south Tashkent Tashkent Oblast, Uzbek, SSR, U.S.S.R.	Santonin (**11**), Eu	[80]
A. transiliensis Poljak.	Alma Ata Oblast, Kazakh SSR, U.S.S.R.	Santonin (**11**), Eu	[80]
A. transiliensis var. *boamensis* Poljak.	Issyk Kul Oblast, Kirgiz SSR, U.S.S.R.	Santonin (**11**), Eu	[80]
		TRIDENTATAE	
A. arbuscula Nutt. ssp. *arbuscula*	Grand Teton National Park, Wyoming, U.S.A.	Arbusulin-A (**108**), Eu, $C_{15}H_{22}O_3$, mp 76.5–77.5°, $[\alpha]_D^{24}$ +25.8° ($CHCl_3$; *c* 4.15) Arbusculin-B (**109**), Eu, $C_{15}H_{20}O_2$, mp 86.5–88°, $[\alpha]_D^{24}$ +47.3° ($CHCl_3$; *c* 2.77) Arbusculin-C (**110**), Eu, $C_{15}H_{20}O_3$, mp 150–151°, $[\alpha]_D^{25}$ +113° ($CHCl_3$; *c* 3.06) Arbusculin-D (**113**), Eu, $C_{15}H_{22}O_4$, mp 170–172° Arbusculin-E (**114**), Eu, $C_{15}H_{24}O_4$, mp 160–161°, $[\alpha]_D^{24}$ +3° ($CHCl_3$; *c* 0.75)	[140, 148, 154, 155]
	Badger Pass, Beaverhead Co., Montana, U.S.A.	Tatridin-A (**83**), Gr, $C_{15}H_{20}O_4$, mp 176–177°, $[\alpha]_D^{18}$ −49° (EtOH; *c* 1.1) Tatridin-B (**84**), Gr, $C_{15}H_{20}O_4$, gum Badgerin (**115**), Gr, $C_{15}H_{20}O_5$, mp 207–208°, $[\alpha]_D^{18}$ +8.5° (EtOH; *c* 1.165) Spiciformin (**116**), Gr, $C_{15}H_{20}O_4$, transparent gum, $[\alpha]_D$ +81.70° ($CHCl_3$; *c* 1.63) Deacetyllaurenobiolide (**117**), Gr, $C_{15}H_{20}O_3$, gum, $[\alpha]_D$ +34.50° ($CHCl_3$; *c* 1.603)	[151, 156, 157]
A. bigelovii Gray	Show Low, Navajo Co., Arizona, U.S.A.	Arbiglovin (**120**), Gu, $C_{15}H_{18}O_3$, mp 201–203°, $[\alpha]_D^{26.5}$ +199°	[158, 159]
A. cana Pursh ssp. *cana*	Albany Co., Wyoming, U.S.A.	Deacetylmatricarin (**5**), Gu Matricarin (**26**), Gu Canin (**47**), Gu Ridentin (**81**), Gr, $C_{15}H_{20}O_4$, mp 215–218° dec., $[\alpha]_D^{25}$ −113° (MeOH; *c* 0.46) Artecanin (**91**), Gu, $C_{15}H_{18}O_5$, mp 244–245°, $[\alpha]_D^{23}$ +26.6° (EtOH; *c* 0.82)	[139–142]
	Laurel, Yellowstone Co., Montana, U.S.A.	Deacetylmatricarin (**5**), Gu Canin (**47**), Gu Artecanin (**91**), Gu	[142]

Table 3.—*Continued*

Species	Location	Compounds	References
		Artevasin (**92**), Gr, $C_{15}H_{20}O_4$, mp 208–210°, $[\alpha]_D^{23}$ +177° (MeOH; *c* 0.34)	
A. cana ssp. *viscidula* (Osterhout) Beetle	Laramie, Albany Co., Wyoming, U.S.A.	Arbusculin-B (**109**), Eu	[140, 154]
	Eureka Basin and Beaver Creek, Beaverhead Co., Montana, U.S.A.	Deacetoxymatricarin (**55**), Gu Viscidulin-A (**93**), Gu, $C_{17}H_{22}O_5$, mp 124°, $[\alpha]_D$ +77.0° ($CHCl_3$; *c* 2.14) Viscidulin-B (**94**), Gu, $C_{17}H_{22}O_5$, mp 132–133°, $[\alpha]_D$ +59.3° ($CHCl_3$; *c* 2.3) Viscidulin-C (**95**), Gu, $C_{15}H_{20}O_4$, mp 147°, $[\alpha]_D$ +49.0° ($CHCl_3$; *c* 1.955)	[143]
A. longiloba (Osterhout) Beetle	Long Creek, Beaverhead Co., Montana, U.S.A.	Longilobol (**123**), Eu, $C_{15}H_{26}O_3 \cdot 2H_2O$, mp 176–177°, $[\alpha]_D^{20}$ +95°, (MeOH; *c* 0.77)	[162]
A. nova Nels.	Laramie, Albany Co., Wyoming, U.S.A.	Cumambrin-A (**97**), Gu, $C_{17}H_{22}O_5$, mp 188–190°, $[\alpha]_D$ +103° ($CHCl_3$; *c* 2.79) Cumambrin-B [**98**], Gu, $C_{15}H_{20}O_4$, mp 178–180°, $[\alpha]_D$ + 92.5° ($CHCl_3$; *c* 5.58) 8-Deoxycumambrin-B (**105**), Gu, $C_{15}H_{20}O_3$, mp 117–119° Novanin (**106**), Gr, $C_{17}H_{22}O_4$, oily material	[140, 145, 149]
A. pygmaea Gray	Fredonia, Coconino Co., Arizona, U.S.A.	Pygmol (**121**), Eu, $C_{15}H_{28}O_3$, mp 149–150.5° Cryptomeridiol (**122**), Eu, $C_{15}H_{28}O_2$, mp 134.5–135.5°, $[\alpha]_D^{24}$ −25.8°	[140, 160]
A. rothrockii Gray	Blind Bull Creek, Lincoln Co., Wyoming, U.S.A.	Arbusculin-A (**108**), Eu Arbusculin-C (**110**), Eu Rothin-A (**111**), Eu, $C_{15}H_{20}O_3$, mp 133–134°, $[\alpha]_D^{25}$ +122° ($CHCl_3$; *c* 5.55) Rothin-B (**112**), Eu, $C_{15}H_{20}O_4$, mp 254–256°, $[\alpha]_D^{25}$ +242° (MeOH; *c* 1.45)	[140, 154]
A. tridentata Nutt. *tridentata*	Valyermo and Soledad Canyon, Los Angeles Co., California, U.S.A.	Deacetoxymatricarin (**55**), Gu	[138, 140]
	Rancho Santa Ana Botanical Gardens, Claremont, Los Angeles Co., California, U.S.A.	Ridentin (**81**), Gr Dentatin-B (**82**), Gr, $C_{15}H_{20}O_4$ Tatridin-A (**83**), Gr Tatridin-B (**84**), Gr Tatridin-C (**85**), Gr, $C_{15}H_{18}O_4$, gum Dentatin-A (**86**), Eu, $C_{15}H_{20}O_4$	[138, 140]
	Perma, Sanders Co., Montana, U.S.A.	Deacetylmatricarin (**5**), Gu	[137]
A. tridentata ssp. *tridentata* f. *parishii* (Gray) Beetle	Piru, Ventura Co., California, U.S.A.	Deacetoxymatricarin (**55**), Gu Ridentin (**81**), Gr Parishin-A (**87**), Gu, $C_{15}H_{18}O_4$ Parishin-B (**88**), Gu, $C_{15}H_{18}O_3$, mp 221–223°, $[\alpha]_D$ + 153° Parishin-C (**89**), Gu, $C_{15}H_{18}O_4$, mp 141–143° Isophotosantonic lactone (dihydro-parishin-A) (**90**), Gu, $C_{15}H_{20}O_4$	[139, 140]
	Saugus, Los Angeles Co., California, U.S.A.	Deacetoxymatricarin (**55**), Gu Ridentin (**81**), Gr	[139, 140]
A. tridentata ssp. *vaseyana* (Rydb.) Beetle	Pole Mtn., Albany Co., Wyoming, U.S.A.	Ridentin (**81**), Gr	[140]
	Grass Valley, Missoula Co., Montana, U.S.A.	Arbusculin-A (**108**), Eu Arbusculin-B (**109**), Eu Arbusculin-C (**110**), Eu	[137]
	Sage Creek, Beaverhead Co., Montana, U.S.A.	Artevasin (**92**), Gr Dehydroleucodin (**107**), Gu, $C_{15}H_{16}O_3$, mp 131°, $[\alpha]_D^{22}$ +77° ($CHCl_3$; *c* 2.5)	[150]

Table 3.—*Continued*

Species	Location	Compounds	References
	Happy Jack area, Albany Co., Wyoming, U.S.A.	Artevasin (**92**), Gr	[153]
	Hot Springs, Sanders Co., Montana, U.S.A.	Arbusculin-A (**108**), Eu Arbusculin-B (**109**), Eu Arbusculin-C (**110**), Eu Rothin-A (**111**), Eu Rothin-B (**112**), Eu	[151]
A. tridentata ssp. *vaseyana* f. *spiciformis* (Osterhout) Beetle	Red Rock Lakes, Beaverhead Co., Montana, U.S.A.	Tatridin-A (**83**), Gr Tatridin-B (**84**), Gr Badgerin (**115**), Gr Spiciformin (**116**), Gr Deacetyllaurenobiolide (**117**), Gr	[156, 157]
A. tridentata ssp. *wyomingensis* Beetle and Young	Acton, Yellowstone Co., Montana, U.S.A.	1β-Hydroxysant-3-en-6,12-olide-C(W-A) (**118**), Eu, $C_{15}H_{22}O_3$, mp 132–133°, $[\alpha]_D^{27}$ +78° ($CHCl_3$; *c* 2.07) 1β-Hydroxysant-4(14)-en-6,12-olide-C(W-B) (**119**), Eu, $C_{15}H_{22}O_3$, mp 130–131°, $[\alpha]_D^{31}$ +37° ($CHCl_3$; *c* 2.07)	[137]
A. tripartita Rydb. ssp. *rupicola* Beetle	Pole Mtn., Albany Co., Wyoming, U.S.A.	Artecalin (**32**), Eu Ridentin (**81**), Gr Ridentin-B (**96**), Eu, $C_{15}H_{20}O_4$, mp 188–190° Cumambrin-A (**97**), Gu Cumambrin-B (**98**), Gu Cumambrin-B-oxide (**99**), Gu, $C_{15}H_{20}O_5$, mp 189–190.5° Rupicolin-A (**100**), Gu, $C_{15}H_{18}O_4$, mp 155–156° solidifies and remelts 167–168.5° Rupicolin-B (**101**), Gu, $C_{15}H_{18}O_4$, mp 142–144° Rupin-A (**102**), Gu, $C_{15}H_{18}O_6$, mp dec. 260–300° Rupin-B (**103**), Gu, $C_{17}H_{20}O_7$, mp 235–245° dec. Colartin (**104**), Eu	[52, 139, 140, 145–148]
A. tripartita ssp. *tripartita*	Jackson, Teton Co., Wyoming, U.S.A.	Deacetoxymatricarin (**55**), Gu Ridentin (**81**), Gr	[140]
	Dillon, Beaverhead Co., Montana, U.S.A.	Deacetylmatricarin (**5**), Gu Matricarin (**26**), Gu	[144]
	Ovando, Powell Co., Montana, U.S.A.	Achillin (**25**), Gu Canin (**47**), Gu Artevasin (**92**), Gr Ridentin-B (**96**), Eu	[144]

* Structural class: Gr—germacranolide, Eu—eudesmanolide, Gu—guaianolide, El—elemanolide, C—cadinanolide, MC—modified cadinanolide, P—psilostachyanolide.

† The exact location not available to the present authors.

‡ The presence of santonin in this taxa is only tentative, see text.

§ Author citation not provided in original article, but assigned by us.

*** Just prior to publication, it was discovered that this species belongs in the subgenus *Abrotanum*; this, however, has little effect on the systematic implications.

The most advanced compounds to be discovered are the psilostachyanolides, psilostachyin (**1**) and psilostachyin-C (**2**), which have been reported in *A. vulgaris* from Yugoslavia [24] (Table 3); the only member of the *Vulgares* complex to be investigated outside of the New World. This is interesting because the psilostachyinolides are supposedly biosynthesized from ambrosanolides which have not yet been isolated in the genus.

Artemisia annua also produces interesting sesquiterpene lactones, such as the rare cadinanolide, arteannuin-B (**3**) from plants in Yugoslavia [25], and a modified cadinanolide, qing hau sau (**4**) in mainland China [26]. Deacetylmatricarin (**5**) was found in *A. incana*, endemic to Caucasus, being the only guaianolide presently reported in the Old World *Abrotanum* [27].

Collections of *A. verlotorum* from southeastern Switzerland and southern Germany were identical with the germacranolides, artemorin (**6**), verlotorin (**7**) and anhydroverlotorin (**8**) [28–31], whereas in southeastern Australia (naturalized from Europe) this species contained the eudesmanolide, tauremisin (**9**) [30, 32] which also occurs in *A. judaica* from the Egyptian desert [33–35]. Three other eudesmanolides have been reported; yomogin (**10**) in *A. princeps* from Japan [36],

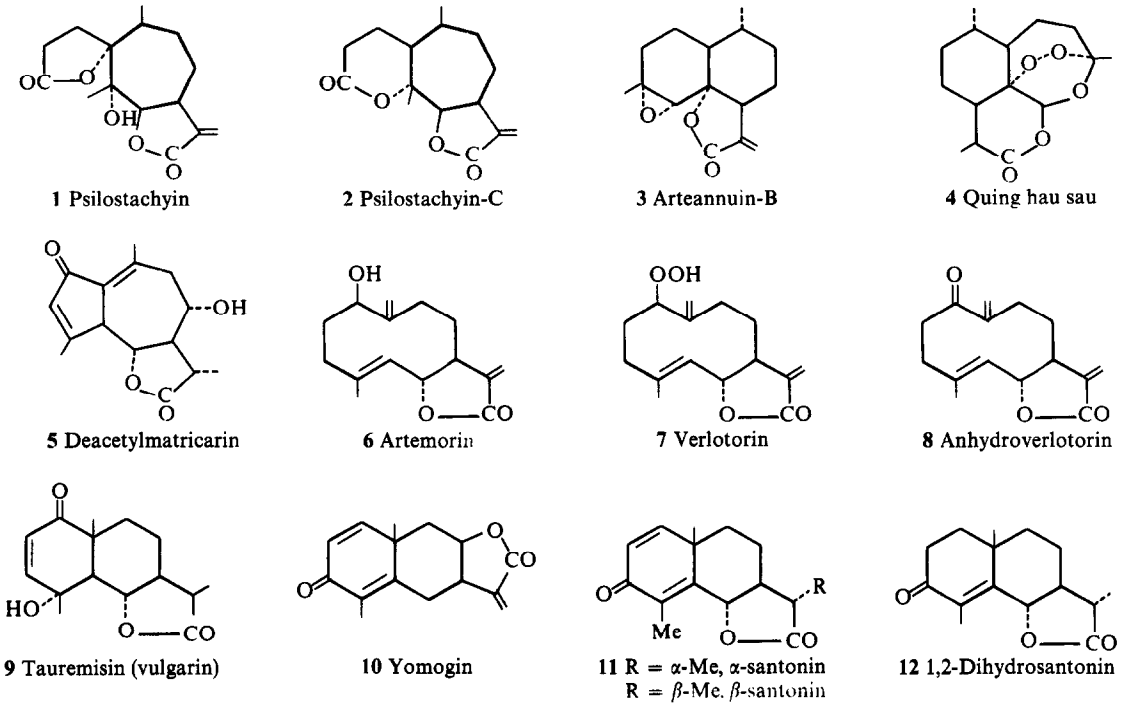


Fig. 2. The sesquiterpene lactones of the Old World *Abrotanum*.

santonin (**11**) in *A. camphorata* from Iran [37] and 1,2-dihydrosantonin (**12**) in *A. stelleriana* [38].

The sesquiterpene lactones of the North American species of *Abrotanum* are not as variable, producing mainly eudesmanolides and guaianolides (Table 3 and Fig. 3), with the exception of two collections of *A. mexicana* (syn. *A. ludoviciana* ssp. *mexicana*), a member of the *Vulgares* complex. Near Mexico City the germacranolide, artemorin (**6**), was isolated from this species, and, from further north, tulipinolide (**13**) was found in the variety *angustifolia* [39]. Several other collections of *A. mexicana* have been gathered in the same vicinities, at different times, resulting in the discovery of two guaianolides, estafiatin (**14**) and chrysartemin-A (**15**) and five eudesmanolides, arglanine (**16**), douglanine (**17**), armexine (**18**), artemexifolin (**19**) and armexifolin (**20**) [39–42]. Nearly every collection of this species was distinct in its lactone content (Table 3).

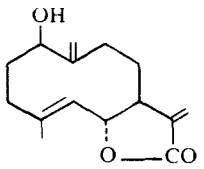
In Arizona, douglanine (**17**), ludovicin-A (**21**), -B (**22**) and -C (**23**) were isolated from *A. ludoviciana* ssp. *mexicana* [43] and a similar compound, ludalbin (**24**), 8-α-acetoxydouglanine, was found in the subspecies *albula* [44]. The guaianolides achillin (**25**) and deacetylmatricarin (**5**) were reported in an unidentified subspecies of *A. ludoviciana* from northern Mexico [45].

Several other species in the *Vulgares* complex have been investigated. Deacetylmatricarin (**5**) and/or matricarin (**26**) were found in *A. tilesii* at two widely separated sites in Alaska [46] and the eudesmanolides arglanine (**16**), douglanine (**17**), and ludovicin-B (**22**) were present in the spring growth of *A. douglasiana* near Los Angeles, California [47, 48], but replaced in the fall growth by the guaianolides, arteglasin-A (**27**) and -B (**28**) [49]. Guaianolides have been reported from separate samples of *A. carruthii*, ludartin (**29**) and its 11,13-dihydro derivative (**30**) in one collection [50] and matricin (**31**) from another in Arizona [51].

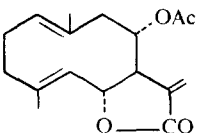
Other New World species, that are not members of the *Vulgares* group have been investigated. Deacetylmatricarin (**5**) and achillin (**25**) were found in *A. klotzchiana* from northern Mexico [45] whereas matricarin (**26**), deacetylmatricarin (**5**), and chrysartemin-A (**15**) were present in plants near Mexico City [41]. Artecalin (**32**) has been reported in *A. californica*, from southern California [52] and artefransin (**33**) was discovered in Arizona samples of *A. franserioides* [53].

In 1923 Viehoever and Capen [54] examined 33 *Artemisia* species from various locations in North America and reported santonin (**11**) to be present in *A. mexicana* (syn. *A. ludoviciana* ssp. *mexicana*), *A. neomexicana* (syn. *A. ludoviciana* ssp. *mexicana*) and *A. wrightii* (syn. *A. carruthii*), all collected in New Mexico. Their methods of analysis were not definitive and their results have not been confirmed by more recent investigations. Santonin (**11**) has not been isolated in any North American *Artemisia*, including recent collections of *A. mexicana*, *A. ludoviciana* ssp. *mexicana* and *A. carruthii* from Arizona and Mexico. Thus, the report of santonin (**11**) [54] in the above taxa should only be tentatively accepted until the results have been confirmed.

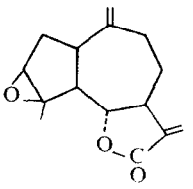
The sesquiterpene lactones in species from the subsection *Vulgares* are biosynthetically and structurally similar, with some compounds (deacetylmatricarin (**5**), arglanine (**16**), douglanine (**17**), ludovicin-B (**22**), achillin (**25**) and matricarin (**26**)) occurring in several species, suggesting close phylogenetic relationships for these taxa. The value of the sesquiterpene lactones in delimiting the *Vulgares* complex is diminished by the occurrence of some of the compounds (deacetylmatricarin (**5**), chrysartemin-A (**15**), achillin (**25**) and matricarin (**26**))



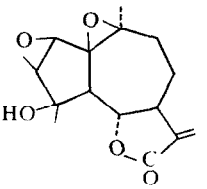
6 Artemorin



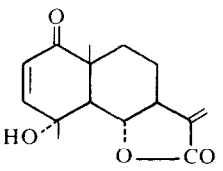
13 Tulipinolide



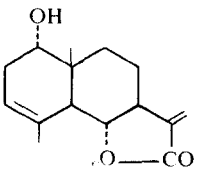
14 Estafiatin



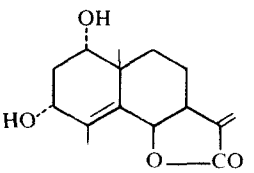
15 Chrysartemin-A



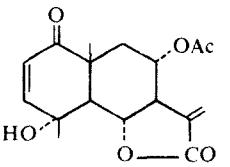
16 Arglanine



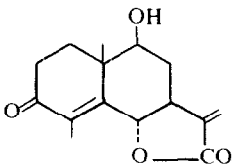
17 Douglanine



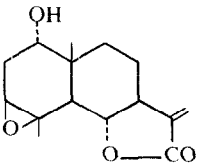
18 Armexine



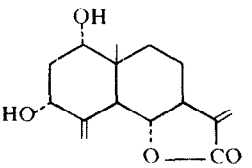
19 Artemexifolin



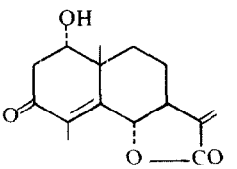
20 Armexifolin



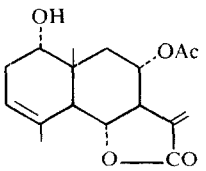
21 Ludovicin-A



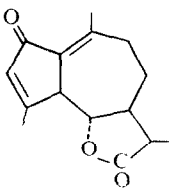
22 Ludovicin-B



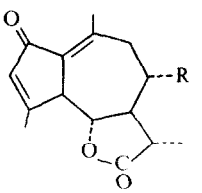
23 Ludovicin-C



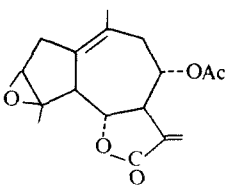
24 Ludalbin



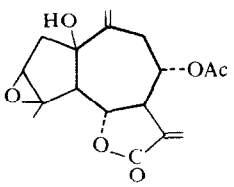
25 Achillin



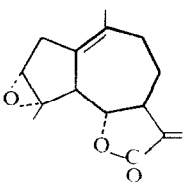
26 R = OAc, Matricarin
5 R = OH, Deacetylmatricarin



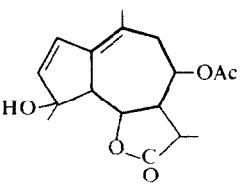
27 Arteglasin-A



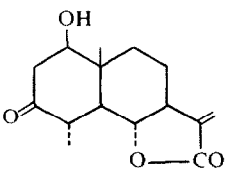
28 Arteglasin-B



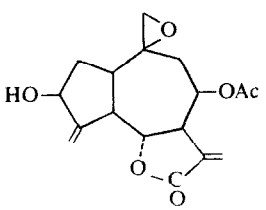
29 Ludartin
30 11,13-Dihydroludartin



31 Matricin



32 Artecalin



33 Artefransin

Fig. 3. The sesquiterpene lactones of the New World *Abrotanum*.

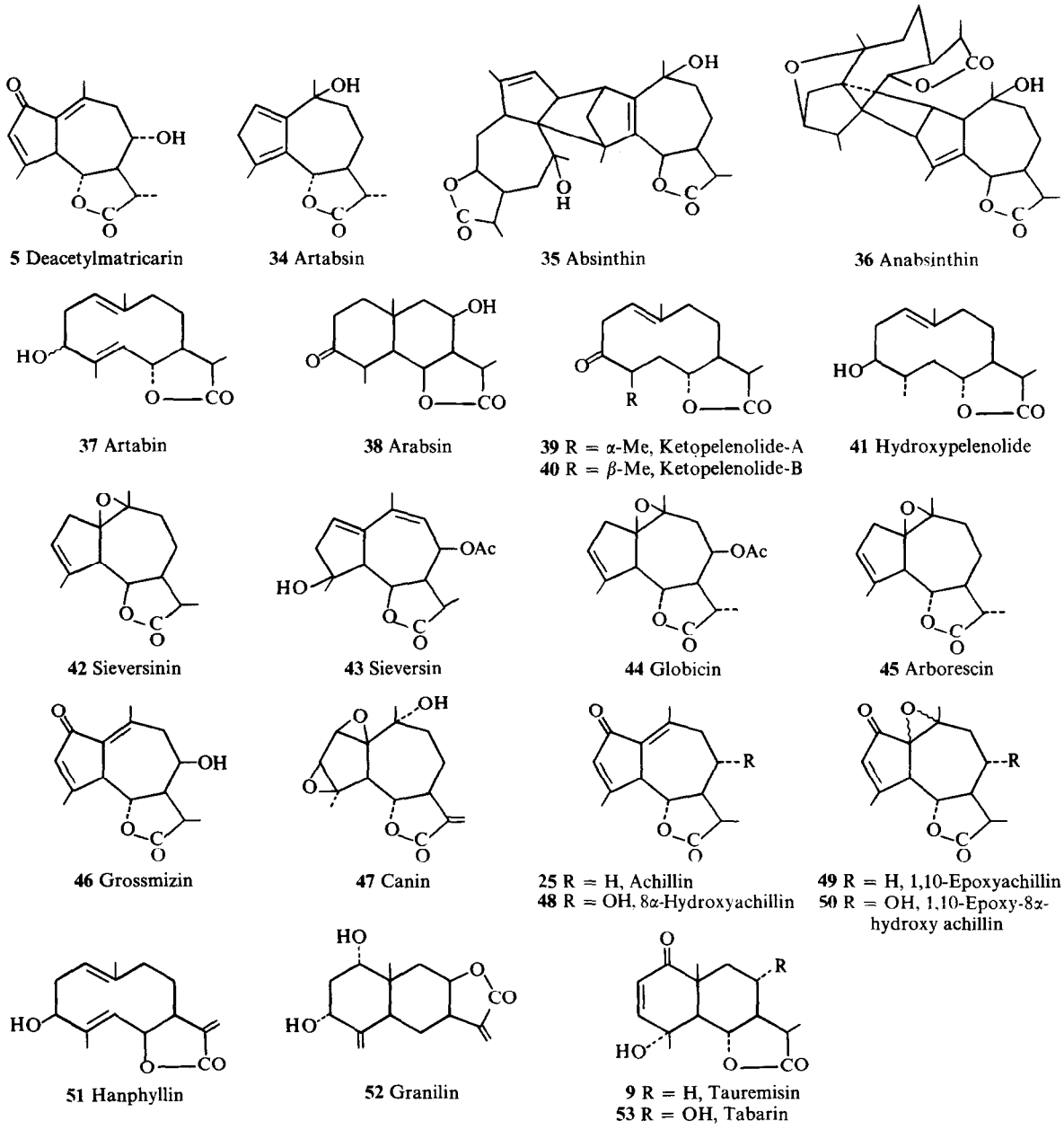


Fig. 4. The sesquiterpene lactones of the subgenus *Absinthium*.

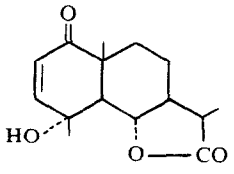
in a species outside the subsection. There is a greater difference in the sesquiterpene lactones produced by the New and Old World species of *Abrotanum* than there is between members and non-members of the *Vulgares*.

ABSINTHIUM

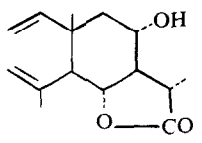
Within the subgenus *Absinthium*, species have been reported to produce germacranolides, eudesmanolides and guaianolides, with a majority of species capable of producing guaianolides (Tables 2 and 3, Fig. 4).

Nearly all investigations have been with plants from Eurasia, except for the isolation of artabsin (**34**) [55–57] from naturalized *A. absinthium* collected in the state of Washington [58]. This compound has been isolated repeatedly from this species in the Old World and with other compounds such as absinthin (**35**) and anabsinthin (**36**) [59–61]. Distinctly different collections of *A. absinthium* have been reported with artabin (**37**) and arabsin (**38**) at one site [62–64] and ketopelenolide-A (**39**) alone [65] or in combination with ketopelenolide-B (**40**) and hydroxypelenolide (**41**) [66–67] at others.

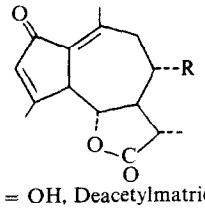
Ketopelenolide-B (**40**) was the only sesquiterpene lactone identified in *A. anethifolia* collected in south central Russia [68] and it was also isolated with sieversinin (**42**) in *A. jacutica* from northeastern Siberia [69]. The latter compound has been extracted from *A. sieversiana* [70] whereas other samples of this species have yielded artabsin (**34**) and absinthin (**35**) in one instance [71] and sieversin (**43**) and globicin (**44**) in another [72–74]. Arborescin (**45**), the stereoisomer of sieversinin (**42**) is present in *A. arborescens* [57, 75–77].



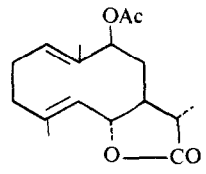
9 Tauremisin (vulgarin)



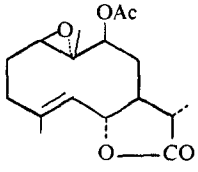
54 Temisin



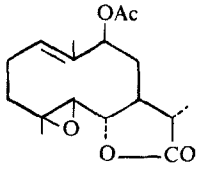
5 R = OH, Deacetylmatricarin
55 R = H, Deacetoxymatricarin



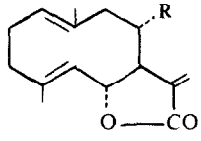
56 Herbolide-A



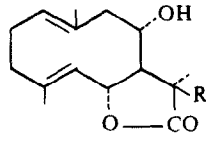
57 Herbolide-B



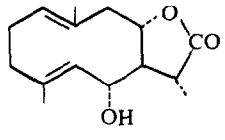
58 Herbolide-C



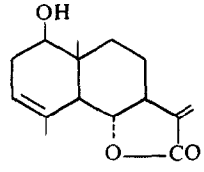
59 R = H, Costunolide
60 R = OH, Hydroxycostunolide



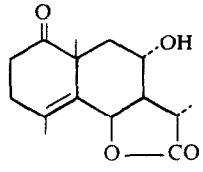
61 R = H, Balchanolide
62 R = OH, Hydroxybalchanolide



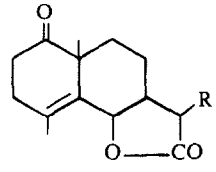
63 Isobalchanolide



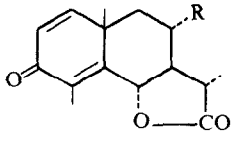
64 Balchanin (santamarine)



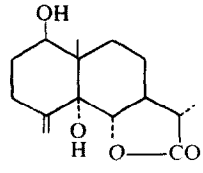
65 ψ-Santonin



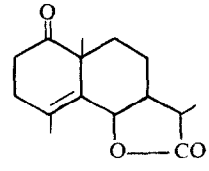
66 R = β-Me Desoxy-ψ-santonin
68 R = α-Me Finitin



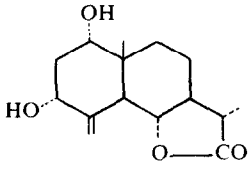
11 R = H, Santonin
67 R = OH, Artemisin



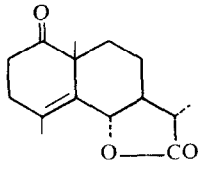
69 Artemin
70 β-C-11,13-Arsubin



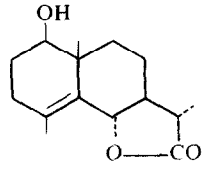
71 Taurin



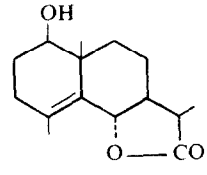
72 Erivanin



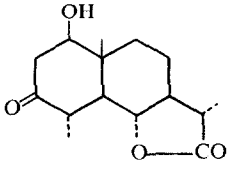
73 1-Keto-6β,7α,11β-H-eudesm-4-en-6,12-olide



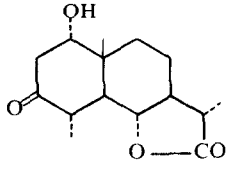
74 1-Hydroxy-6β,7α,11β-H-eudesm-4-en-6,12-olide



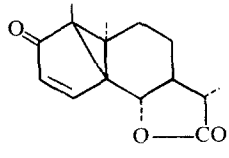
75 Artesin



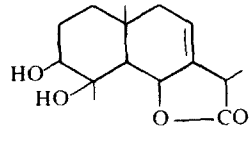
76 Arsanin



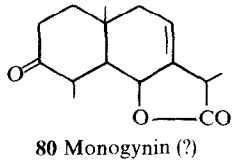
77 Arsantin



78 Lumisantonin

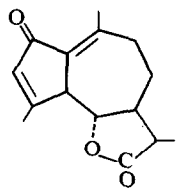


79 Mibulactone (?)

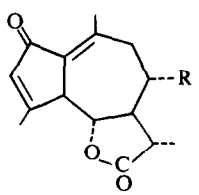


80 Monogynin (?)

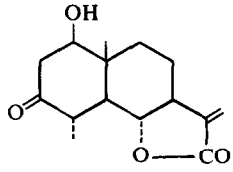
Fig. 5. The sesquiterpene lactones of the Old World *Seriphidium*.



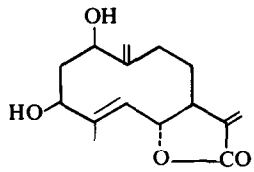
25 Achillin



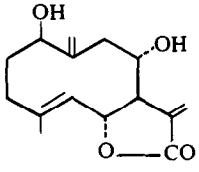
26 R = OAc, Matricarin
5 R = OH, Deacetylmatricarin
55 R = H, Deacetoxymatricarin



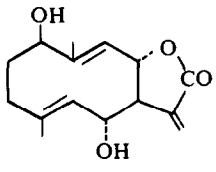
32 Artecalin



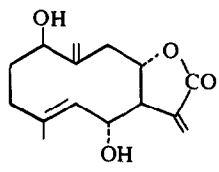
81 Ridentin



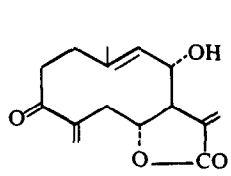
82 Dentatin-B



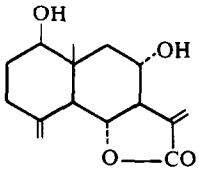
83 Tatridin-A



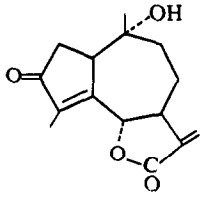
84 Tatridin-B



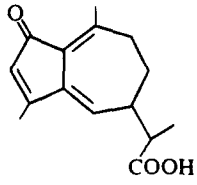
85 Tatridin-C



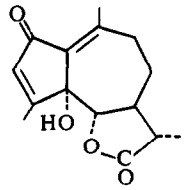
86 Dentatin-A



87 Parishin-A



88 Parishin-B



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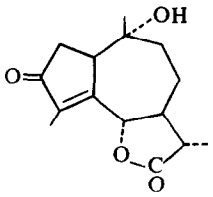
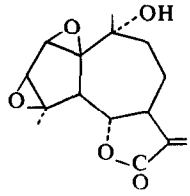
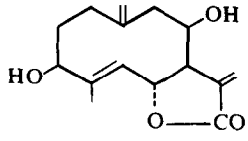


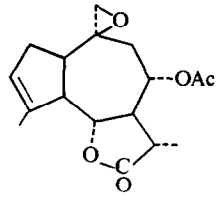
90 Isophotosantonic lactone



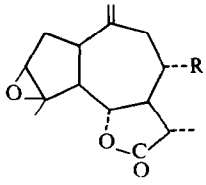
47 Canin
91 α-Epoxys, artecanin



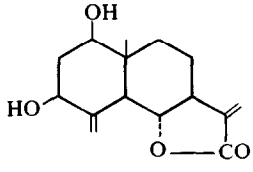
92 Artevasin



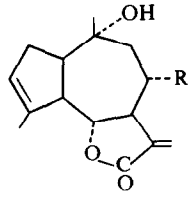
93 Viscidulin-A



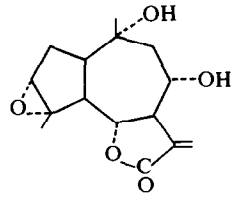
94 R = OAc, Viscidulin-B
95 R = OH, Viscidulin-C



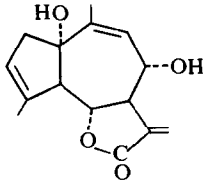
96 Ridentin-B



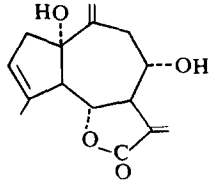
97 R = OAc, Cumambrin-A
98 R = OH, Cumambrin-B
105 R = H, 8-Deoxycumambrin-B



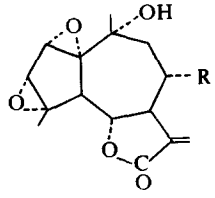
99 Cumambrin-B-oxide



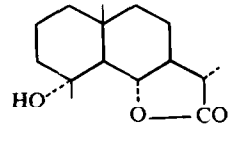
100 Rupicolin-A



101 Rupicolin-B



102 R = OH, Rupin-A
103 R = OAc, Rupin-B



104 Colartin

Fig. 6. *Continued on next page.*

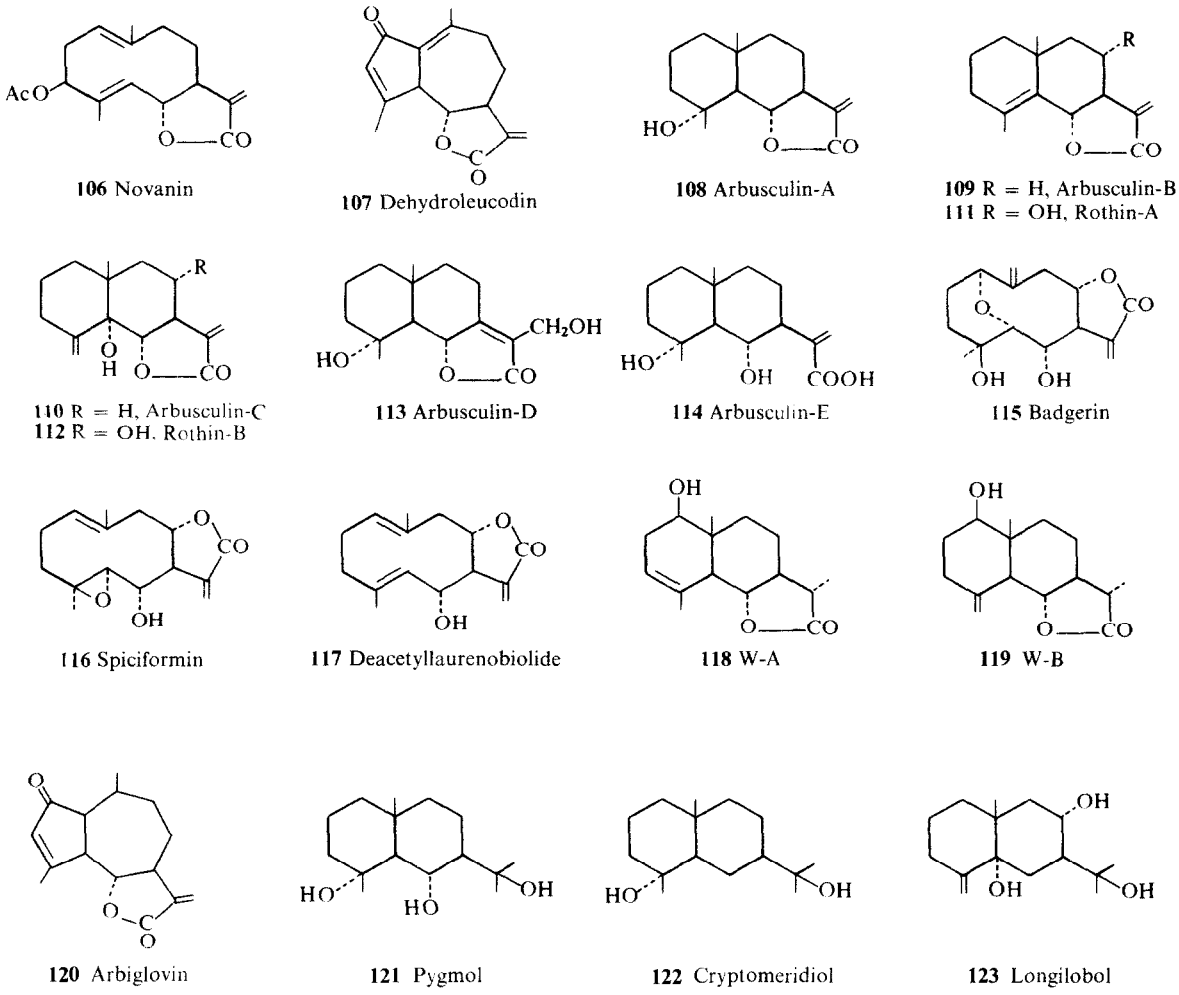


Fig. 6. The sesquiterpene lactones of the New World *Seriphidium* or *Tridentatae*.

Deacetylmatricarin (**5**), common to species of the subgenus *Abrotanum*, and santonin (**11**) have been identified in separate samples of *A. austriaca* [78–80]. A stereoisomer of deactylmatricarin (**5**), grossmizin (**46**), in addition to canin (**47**) was reported in *A. caucasica* collected near the Black Sea [81–83], whereas canin (**47**) alone was present in *A. rutifolia* from a location further east in the Turkestan mountain range [81, 83]. Achillin (**25**) (also an isomer of deacetylmatricarin (**5**)), and the 8α-hydroxy (**48**), the 1,10 epoxy (**49**) and the 1,10 epoxy-8α-hydroxy achillin (**50**) derivatives have been reported in *A. lanata* in Spain [84].

The two remaining species investigated do not produce guaianolides. The germacranolide, hanphyllin (**51**) and the eudesmanolide granilin (**52**) were found in *A. ashurbajevii* from the Kirghiz ASSR, Russia [85], and tauremisin (**9**) and tabarin (**53**) are present in *A. canariensis* endemic to the Canary Islands [86].

The presence or absence of hair on the receptacle is the only morphological characteristic that separates the species of *Abrotanum* and *Absinthium* according to Besser [2]. From the chemical information, it appears that there are no sesquiterpene lactones by which the species can be separated into subgenera. There are several sesquiterpene lactones common to both (deacetylmatricarin (**5**), tauremisin (**9**), achillin (**25**)) and many of the compounds, although not identical, have close biosynthetic relationships, thus supporting the combination of the two subgenera into the single subgenus *Artemisia* [7].

SERIPHIDIUM

Most species within the *Seriphidium* produce eudesmanolides, although a few germacranolides, guaianolides and the single elemanolide, temisin (**54**) from *A. maritima* have been reported [87] (Tables 2 and 3, and Fig. 5). The only guaianolides isolated from this subgenus are deacetylmatricarin (**5**) and/or deacetoxymatricarin (**55**) in *A. leucodes* [78, 88, 89] and deacetylmatricarin (**5**) in *A. juncea* [83] and *A. lercheana* [90]. Filatova [91] considered *A. leucodes* and *A. juncea* to be ancient primitive members of the *Seriphidium* based on karyotypic, anatomical and morphological evidence. It is interesting

that they produce the guaianolide deacetylmatricarin (**5**), that is also found in the more primitive subgenus *Artemisia* from which the *Seriphidium* supposedly arose. Santonin (**11**), a compound characteristic of the *Seriphidium* (discussed below), has also been reported from collections of all three species [80].

Artemisia herba-alba from the Negev Desert in Israel contained the germacranolides, herbolide-A (**56**), -B (**57**) and -C (**58**) [92] whereas Egyptian plants are reported to have santonin (**11**) [93].

The only other species to produce germacranolides is *A. balchanorum* from which costunolide (**59**), hydroxycostunolide (**60**), balchanolide (**61**), hydroxybalchanolide (**62**) and isobalchanolide (**63**) have been isolated [94–97], along with the eudesmanolide, balchanin (santamarine) (**64**) [96–98], which has also been reported in *A. spicata* [99].

The remaining species which have been investigated (approximately 30) contain eudesmanolides, with santonin (**11**) as the most frequently encountered compound, being reported in approximately 26 taxa from across Eurasia. Numerous eudesmanolides have been isolated with santonin (**11**), including ψ-santonin (**65**), desoxy-ψ-santonin (**66**) and artemisin (**67**) from *A. maritima* [100–102], artemisin (**67**) in *A. cina* from the Chimkent region of Russia [103], finitin (**68**) in *A. ramosa* of the Canary Islands [104] and *A. finita* from northern China [105], artemin (**69**) in *A. caerulescens* [106], *A. halophila* [107] and *A. tenuisecta* [108], the latter two species both from the Tashkent region of Russia, and tauremisin (**9**) in *A. fragrans* collected between the Caspian and Black Seas [109]. Another sample of *A. fragrans* from this area contained tauremisin (**9**), artemin (**69**), arsubin (**70**), taurin (**71**) and an isomer of erivanin (**72**) [110]. Erivanin (**72**) has also been reported in this species [111, 112].

Artemisia taurica, in the same environments as *A. fragrans*, also produces tauremisin (**9**), artemin (**69**) and taurin (**71**) [88, 113–119]. The concentration of these compounds show considerable geographic variation and the levels of artemin (**69**) and taurin (**71**) appear to be inversely correlated with the level of tauremisin (**9**) [118]. The greatest concentrations of tauremisin (**9**) were obtained from plants collected in the southwest Crimea and the western shores of the Caspian Sea [117–119].

Some of these compounds are present in other Eurasian species, arsubin (**70**) in *A. sublessingana* [120–122], artemin (**69**) in *A. kemrudica* [123] and *A. maritima* ssp. *gallica* [124], and tauremisin (**9**) along with two other eudesmanolides (1-keto-6β,7α,11β-H-eudesm-4-en-6,12-olide (**73**) and 1-hydroxy-6β,7α,11β-H-eudesm-4-en-6,12-olide (**74**)) in *A. granatensis* from Spain [125]. Similar compounds artesin (**75**), arsanin (**76**) and arsantin (**77**) were obtained from *A. santolina* growing in the northeastern Kara Kum of Russia [126–131] and lumisantonin (**78**) has been discovered in *A. kurramensis* [132] and *A. monogyna* [133]. Mibulactone (**79**) and monogyna (**80**) have been reported in the latter species [74, 134–136].

Most species of *Seriphidium* produce identical or biosynthetically related sesquiterpene lactones, predominantly of the eudesmanolide class with santonin (**11**), artemin (**69**) and tauremisin (**9**) being the most frequently encountered compounds. The sesquiterpene lactone data suggest that the species in the subgenus *Seriphidium* are a distinct and separate group from the subgenus *Artemisia*.

As stated previously, the section *Tridentatae* currently belongs in the subgenus *Seriphidium*. However, for the purpose of this discussion they have been reviewed as separate groups.

TRIDENTATAE

Some species of *Tridentatae* produce only germacranolides, but most can synthesize the more advanced eudesmanolides and guaianolides (Tables 2 and 3, and Fig. 6). The matricarin compounds (**5**, **26**, **55**), reported in the subgenus *Seriphidium* and *Artemisia* (particularly North American *Abrotanum*), are very abundant in the species of *Tridentatae*.

Deacetylmatricarin (**5**) was discovered in samples of *A. tridentata* ssp. *tridentata* from western Montana [137], while deacetoxymatricarin (**55**) was isolated from plants in southern California [138]. Plants of unknown geographic origin from botanical gardens in California were quite different with five germacranolides, ridentin (**81**), dentatin-B (**82**), tatridin-A (**83**), -B (**84**) and -C (**85**) and one eudesmanolide dentatin-A (**86**) [139, 140]. Ridentin (**81**), and deacetoxymatricarin (**55**) were extracted with parishin-A (**87**), -B (**88**), -C (**89**) and isophotosantonic lactone (**90**) from *A. tridentata* ssp. *tridentata* f. *parishii*, also collected in southern California [139, 140].

These compounds have been reported in other species. *Artemisia cana* ssp. *cana* from southcentral Montana and southeastern Wyoming were nearly identical, both having deacetylmatricarin (**5**), canin (**47**), and artecanin (**91**), but differing by the presence of matricarin (**26**) and ridentin (**81**) in the Wyoming sample and artevasin (**92**) in the Montana plants [140–142]. *Artemisia cana* ssp. *viscidula* from western Montana were different, with the presence of deacetoxymatricarin (**55**), viscidulin-A (**93**), -B (**94**) and -C (**95**) [143].

Three collections of *A. tripartita* ssp. *tripartita* have been investigated and are similar to the species described above. Achillin (**25**), canin (**47**), ridentin-B (**96**) and artevasin (**92**) were present in plants from northwestern Montana, matricarin (**26**) and deacetylmatricarin (**5**) were extracted from plants in southwestern Montana [144], and ridentin (**81**) and deacetoxymatricarin (**55**) have been reported from plants near Jackson, Wyoming [140].

Artemisia tripartita ssp. *rupicola* from near Laramie, Wyoming is very interesting because intense investigation of this taxa resulted in the separation and identification of eleven sesquiterpene lactones; seven guaianolides, cumambrin-A (**97**), -B (**98**), cumambrin-B-oxide (**99**), rupicolin-A (**100**), -B (**101**), rupin-A (**102**), -B (**103**); three eudesmanolides, colartin (**104**), artecalin (**32**), ridentin-B (**96**); and one germacranolide, ridentin (**81**) [52, 139, 140, 145–148]. *Artemisia nova* collected from the same geographic area contained cumambrin-A (**97**) and -B (**98**), plus 8-deoxycumambrin-B (**105**) and novanin (**106**) [140, 145, 149].

Artemisia tridentata ssp. *vaseyana* from the high elevation mountain environments in western Montana produces the germacranolide, artevasin (**92**) and the matricarin-like guaianolide, dehydroleucodin (**107**) [150]. On the lower slopes and mountain valleys these plants produce only eudesmanolides, arbusculin-A (**108**), -B (**109**) and -C (**110**), either alone or in combination with their C-8 hydroxylated derivatives, rothin-A (**111**) and

-B (**112**) [137, 151, 152]. Artevasin (**92**) and ridentin (**81**) have been extracted from separate collections of this subspecies in southern Wyoming [140, 153].

Arbusculin-A (**108**) and -C (**110**), rothin-A (**111**) and -B (**112**) are present in *A. rothrockii* from northwestern Wyoming [140, 154], and in the same geographic region, arbusculin-A (**108**), -B (**109**), -C (**110**), -D (**113**) and -E (**114**) were extracted from *A. arbuscula* ssp. *arbuscula* and detected in *A. arbuscula* ssp. *thermopola* [140, 148, 154, 155]. A short distance to the West, arbusculins-A (**108**), -B (**109**) and -C (**110**) have been detected in *A. longiloba* (unpublished results) and *A. cana* ssp. *viscidula* [152], while arbusculin-B (**109**) was extracted from the latter species near Laramie, Wyoming [140, 154].

Artemisia tridentata ssp. *vaseyana* f. *spiciformis* is morphologically very similar to the ssp. *vaseyana*, but chemically distinct, producing five germacranolides, badgerin (**115**), spiciformin (**116**), deacetyllaurenobiolide (**117**), tatridin-A (**83**) and -B (**84**) [156, 157] from sites in southwestern Montana. These same five compounds were reported in *A. arbuscula* ssp. *arbuscula* also from southwestern Montana [156, 157].

A third subspecies in the big sagebrush group, *A. tridentata* ssp. *wyomingensis*, is chemically distinct from the other two subspecies with the eudesmanolides re-referred to as W-A (1β-hydroxysant-3-en-6,12-olide-C, **118**) and W-B (1β-hydroxysant-4(14)-en-6,12-olide-C, **119**) [137].

Artemisia bigelovii has been placed by most taxonomists into the subgenus *Abrotanum* [5, 6, 8]; whereas Beetle [9] placed it into the *Tridentatae*. A single sesquiterpene lactone, arbiglovin (**120**), similar in structure to the matricarins (**5**, **26**, **55**), has been isolated from this species [158, 159]. The matricarins (**5**, **26**, **55**) however, have been isolated from species in both subgenera, thus providing little evidence for the placement of this taxa.

Artemisia pygmaea has also caused some problems. Irwin and Geissman [160] isolated two sesquiterpene alcohols, pygmol (**121**) and cryptomeridiol (**122**) from plants in Arizona, making it appear quite distinct since all the other species contained lactones [161]. More recently the sesquiterpene alcohol, longilobol (**123**), has been reported without associated lactones in *A. longiloba* from southwestern Montana [162], reducing the significance of sesquiterpene alcohols in *A. pygmaea*.

Members of the *Tridentatae* are a closely related group of plants as indicated by their morphology and sesquiterpene lactone chemistry, with many of the compounds such as the arbusculins (**108**–**114**) and matricarins (**5**, **26**, **55**) occurring repeatedly. Except for the presence of deacetyl (**5**) and deacetoxymatricarin (**55**) in three species of *Seriphidium* and three species of *Tridentatae*, there are no other compounds common to both subgenera. One of the obvious differences is the great frequency of santonin (**11**) and related eudesmanolides within the *Seriphidium* and the complete absence of santonin (**11**) and greater frequency of guaianolides in the *Tridentatae*. The *Tridentatae* and the New World *Abrotanum* appear to be more closely related with five sesquiterpene lactones (deacetylmatricarin (**5**), achillin (**25**), matricarin (**26**), artecalin (**32**) and deacetoxymatricarin (**55**)) common to both, and many other compounds structurally and biosynthetically similar. Interestingly, nearly all the germacranolides and eudesmanolides isolated from North American *Abrotanum* and *Tridentatae* species possess a C-11 methylene group whereas in the *Seriphidium*, nearly all the compounds have a C-11 methyl group. Thus the sesquiterpene lactone data indicated that the *Tridentatae* are quite distinct from the *Seriphidium* and closely related to the North American *Abrotanum* supporting McArthur and Plummer's [10] hypothesis that the *Tridentatae* developed in North America, independently of the Old World *Seriphidium*, from ancestors in the subgenus *Artemisia*.

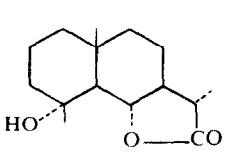
DRACUNCULUS

Sesquiterpene lactones have been discovered in two species of *Dracunculus*, colartin (**104**) in *A. filifolia* [163], and a compound believed to be 8-hydroxyarbiglovin (**124**) in *A. dracunculoides* [164], both species collected in Arizona (Tables 2 and 3, and Fig. 7). Other species have been investigated but no sesquiterpene lactones have been isolated, only coumarins [74]. Although it is now known that sesquiterpene lactones are present in some species, more work is needed to establish their presence or absence as the predominant characteristic in this subgenus.

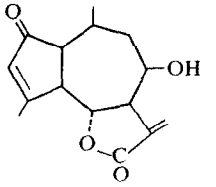
CONCLUSIONS

The sesquiterpene lactone data reviewed here appear to be useful in providing answers for the systematic questions posed in the Introduction. The sesquiterpene lactones suggest that the species in the subsection *Vulgares* are phylogentically a closely related group, but not entirely distinct from other New World *Abrotanum* species outside this subsection. There are greater chemical differences between the New and Old World members of the subgenus *Abrotanum* than there are between members and non-members of the subsection *Vulgares*.

The sesquiterpene lactones also provide insight into the origin of the New and Old World *Seriphidium*. The



104 Cobartin



124 8-Hydroxyarbiglovin

Fig. 7. The sesquiterpene lactones of the subgenus *Dracunculus*.

sesquiterpene lactones of the New World *Seriphidium* or *Tridentatae* are much more similar to those produced by New World species of the subgenus *Abrotanum* than those in the Old World members of the subgenus *Seriphidium*. The sesquiterpene lactones support the hypothesis [10] that the *Tridentatae* developed in North America from ancestors in *Abrotanum* rather than from Old World *Seriphidium*.

Finally the sesquiterpene lactone data indicate that the original subgenera (sections), proposed by Besser [2] for the genus *Artemisia*, be modified. Chemically there seems to be little reason to maintain *Abrotanum* and *Absinthium* as distinct subgenera; they should be combined into the subgenus *Artemisia* as treated by Poljakov [7]. The *Seriphidium* which contains both New and Old World species appears to be polyphyletic and should be revised, with the New World taxa being separated and recognized as the subgenus *Tridentatae*. There is insufficient chemical information to analyse the subgenus *Dracunculus*.

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