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Chemical contributions to taxonomy and phylogeny in the genus artemisia

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The results are still rather meager, but it is to be anticipated that continuing accumulation of chemical information will aid in bringing about an increased understanding of taxonomic and phylogenetic relationships between the plants of this family.

The genera of the tribe Anthemideae from which sesquiterpenes have been isolated are *Artemisia*, *Achillea*, *Chrysanthemum*, *Anthemis*, *Tanacetum* and *Matricaria*. Of these, about 45 species of *Artemisia* have been examined; it is with these that this article will be largely concerned.

Several schemes of subclassification of the genus have been used, the one usually adopted being that, after Besser and DeCandolle, in which four sections are recognized. The floral characters which differentiate them are described by the following key[5]:

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

Ward has remarked that these groupings may not be natural, for members of particular sections often differ markedly in other characters—habit, foliage, inflorescence, and so on—and members of different sections are often distinguished only by the floral characters that delimit the sections[6]. Nevertheless, to provide a form for the discussion to follow, this classification will be used. The implication that the chemical data are being used to support or dispute the relationships reflected in this arrangement is necessarily inherent in this form of presentation. Yet what is being done is no more than to introduce chemical constituents as additional characters, giving them *a posteriori* weighting with the aim of refining, altering or supporting the hypothesis represented by the classification with which the data are compared. Since the goal of taxonomic classification is the construction of an arrangement that reflects the evolutionary relationship between the groups that are being dealt with, it is to be hoped that the ultimate result of the introduction of chemical characters, which may mirror the genetic background of a plant more accurately than do many other phenetic characters, will be to add to the phyletic significance of the intimate biosynthetic mechanisms; it is in the latter that the phyletic relationships will best be discerned.

THE SESQUITERPENE LACTONE CONSTITUENTS

The sesquiterpene lactones of the Compositae include six principal structural classes having the carbon skeletons shown in *Figure 1*[7]. The *Anthemideae* have been found to contain santanolides, guaianolides and germacranolides, all of which are represented in *Artemisia*. Neither the tribe, any one of the individual genera, nor any of the sections as described above is characterized by the presence of only one of these types, as the *Senecioneae*

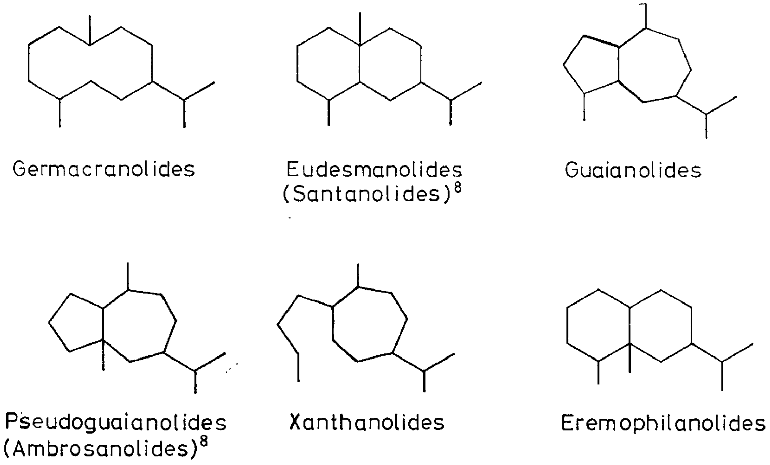


Figure 1. Principal classes of sesquiterpene lactones

are characterized by eremophilanolides and the *Ambrosieae* by ambrosanolides. Certain characteristics of some of the sections and sub-sections of the genus Artemisia are, however, to be discerned.

Section *Dracunculus*

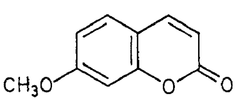
The most conspicuous feature of the chemistry of the section *Dracunculus* is the complete absence of the sesquiterpene lactones that are present in all of the other sections. That this is a characteristic of the section is a conclusion that must be held in reserve until a larger number of representative species are examined; but from the experience of the authors it would seem probable that lactones, if present, would have been encountered by some of those who have studied these plants in the past. An examination of *A. pycnocephala* DC. in this laboratory failed to disclose their presence in this species.

The three species of the section *Dracunculus* that have been examined are characterized by their content of coumarins, often in considerable amount. Although coumarins do not appear to be of taxonomic or phylogenetic significance in the genus, they are common constituents in several of the sections and so are recorded here (*Figure 2*). Much further study of this section is needed before the absence of sesquiterpene lactones can be regarded as an established chemical character.

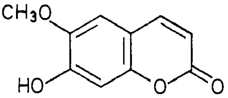
Section *Absinthium*

Five species[13] of the section *Absinthium* have been investigated in detail. Only guaianolides have been found, and it is of interest to observe that, with the exception of deacetylmatricarin from *A. austriaca*, these compounds are proazulenes or proazulenogens (*Figure 3*). The close relationship of artabsin to arborescine, and of sieverin to globicin is apparent from their structures. Artabsin can be derived by loss of water from the glycol corresponding to the epoxide, arborescine.

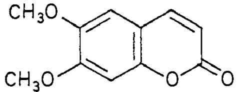
Deacetylmatricarin (VIII), which is not a proazulenogen, is also characteristic of several species in the sections *Abrotanum* and *Seriphidium*. It is



(I)
Herniarin
A. dracunculus L.[9]



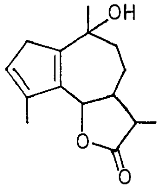
(II)
Scopoletin
A. capillaris Thunb.[10]



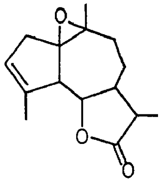
(III)
Esculetin dimethyl ether

A. capillaris Thunb.
A. dracunculus L.
A. scoparia W. and K.[11]

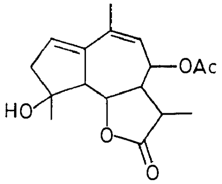
Figure 2. Coumarins of section *Dracunculus*[12]



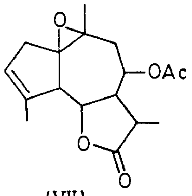
(IV)
Artabsin[14,15]
A. absinthium L.



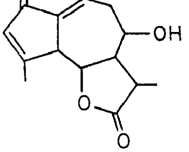
(V)
Arborescine
A. arborescens L.[16]
A. sieversiana Willd. (?)[17]



(VI)
Sieverin
A. sieversiana Willd.[18]
A. macrocephala Jacq.[19]



(VII)
Globicin
A. macrocephala Jacq.[19]
(*Matricaria globifera* L.)[20]



(VIII)
Deacetylmatricarin[21]
A. austriaca Jacq.[13]

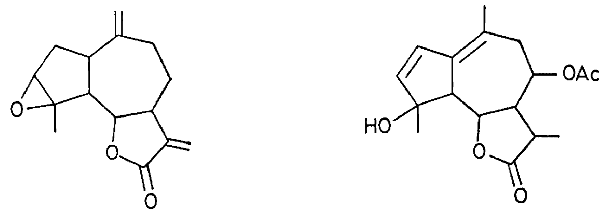
Figure 3. Guaianolides of section *Absinthium*

apparent that VIII represents a more oxidized state than sieverin (VI) or globicin (VII) and thus is a step along the path of increasing structural complexity. The possible phylogenetic significance (if any) of differing oxidation levels in related compounds is still unknown[22], and it must suffice here only to call attention to the uncertain taxonomic position[13] of *A. austriaca* and the presence of VIII in this species.

These observations, scanty though they are, are consistent with the assignment of *A. absinthium*, *A. arborescens*, *A. sieversiana* and perhaps *A. macrocephala* to positions of close affinity. The position of *A. austriaca* cannot be clarified from the evidence available, for it is to be noted that two species of the genus *Matricaria* contain matricarin (XII) (acetate of VIII) and globicin (VII). Thus, neither of these compound types appear to have taxonomic weight.

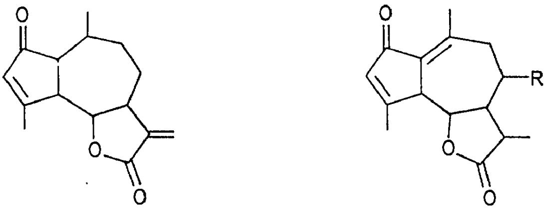
Section *Abrotanum*

Eight species of this section have been studied in some detail[23]. Unlike *Absinthium*, both guaianolides and santanolides have been isolated from species of this section. Among the guaianolides (*Figure 4*) no single structural type is prevalent; compounds are found ranging from matricin (X), reminiscent of the guaianolides of *Absinthium* species, to matricarin (XII), a



(IX)
Estafiatin
A. mexicana Baker.[24]

(X)
Matricin
A. carruthii Wood.[26]
(*Matricaria chamomilla* L.)[25]

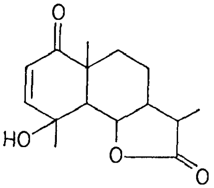


(XI)
Arbiglovin
A. bigelovii Gray.[27]

R=OAc, Matricarin (XII); Artilesin
R=OH, Deacetylmatricarin (VIII)
A. tilesii Ldb.[28]

Figure 4. Guaianolides of section *Abrotanum*[29]

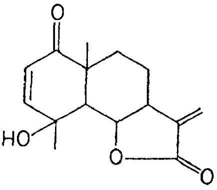
characteristic constituent of some species of the section *Seriphidium*. The santanolides (*Figure 5*) of the section *Abrotanum* include one compound that occurs also in a species of the section *Seriphidium;* one whose 1-epimer is found in a *Chrysanthemum;* and one which possesses the unique A-ring of santonin. Thus, whatever the taxonomic justification for the sectional arrangement of *Artemisia,* there is no apparent relationship between this classification and the new characters provided by chemical analyses.



(XIII)

Vulgarin (Tauremisin)

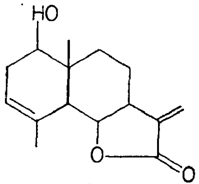
A. vulgaris L.
(=*A. verlotorum* Lamotte)[32]



(XIV)

Arglanine

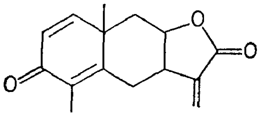
A. douglasiana Bess.[33]
(=*A. vulgaris heterophylla* H. and C.)



(XV)

Douglanine

A. douglasiana Bess.[34,35]



(XVI)

Yomogin

A. princeps Pamp.[36]

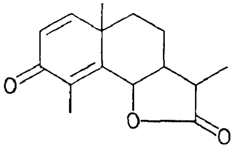
Figure 5. Santanolides of section *Abrotanum*

A. bigelovii is regarded as a member of the section *Abrotanum* by Ward[6] and by Hall and Clements[30], but is placed in a group of *Seriphidium* species classed as the section *Tridentatae* Rydb. by Beetle[31]. Again, the wide structural diversity found in the compounds of the sections *Abrotanum* and *Seriphidium* (and, indeed, in that section of the latter set apart as the *Tridentatae*—see below) provides no common point of reference from which to seek a relationship between section classification and chemical structure.

Section *Seriphidium*

Species placed in this section appear, from their chemical characteristics, to belong to two, perhaps three, large groups. One of these, consisting of Old World species, contains santonins (α- and β-) along with a number of santanolides of more or less closely related structures. A second group, including the large section classified by Beetle[31] as *Tridentatae* and represented by the western sagebrushes, contains no santonin and is characterized principally (but not uniquely) by the presence of guaianolides. *A. balchanorum* Krasch. is unique in that it is the only species of the section that has yielded germacranolides.

The santonins are the most frequently described constituents of the section *Seriphidium;* some eighteen or twenty Old World species (taking into account synonymy) have been found to contain α- or β-santonin, or, in some cases, both (*Figure 6*).



α-Santonin (C-11 CH_3,α) (XVII)
β-Santonin (C-11 CH_3,β) (XVIII)

A. caerulescens L.; *A. ramosa* C. Sm.; *A. cina* Berg;
A. maritima L.*; *A. pauciflora* Stechm.;
A. monogyna Wald.; *A. fragrans* Willds.*;
A. finita Kitam., *A. kurramensis* Qaz.;
A. transiliensis P. Pol., *A. serotina* Bge.,
A. terrae-albae Krasch.; *A. compacta* Fisch.
A. tenuisecta Nov.; *A. juncea* Kar. et Kir.*;
A. sublessingiana (Kell.) Krasch; *A. lercheana* Web.*
A. turanica Krasch.

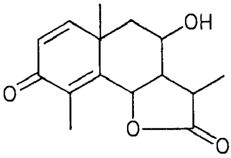
Figure 6. Santonin-containing species of section *Seriphidium*[37, 38]

The species starred(*) in *Figure 6* have yielded additional compounds; in all but one case (*A. juncea*) these are santanolides (*Figure 7*)[39]. It will be noted that, without exception, all of the santanolides of these species contain the saturated lactone (i.e., CH—CH_3 at C-11, 13).

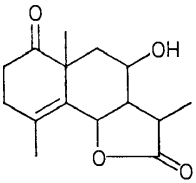
Santanolides are not, however, confined to the santonin-containing species. Compounds of this class that have been isolated from other *Seriphidium* species are shown in *Figure 8*.

Species of the section *Seriphidium* that lack santonin, although not lacking in santanolides (see *Figure 8*), appear to be more typically characterized by the presence of guaianolides (*Figure 9*). *A. tridentata* (both species studied), *A. nova*, and *A. tripartita rupicola* contain guaianolides in large amount, often approaching 1 per cent by weight of the dry plant. The santanolides which accompany the guaianolides in these plants are present in very minute concentrations, requiring elaborate manipulative techniques for their isolation. Observations of this kind again point up the necessity that should be recognized by phytochemists for conducting detailed searches for minor constituents, for it is probable that these will prove to have an importance in chemotaxonomic or chemophylogeny equal to that of the prominent constituents.

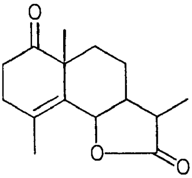
Artemisia balchanorum Krasch. is unique not only in the section *Seriphidium* but in the genus as well, for it contains, along with balchanin (XXIV),



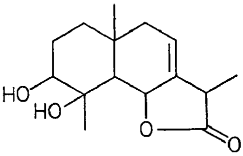
(XIX)
Artemisin
A. maritima L.



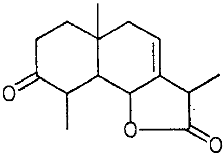
(XX)
ψ-Santonin
A. maritima L



(XXI)
Finitin
A. finita Kitam

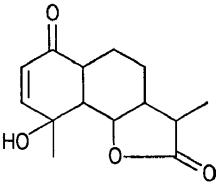


(XXII)
Mibulactone (?)
A. monogyna Wald.

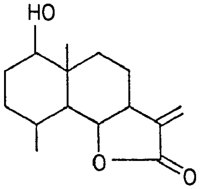


(XXIII)
Monogynin (?)
A. monogyna Wald.

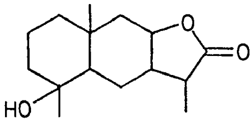
Figure 7. Additional santanolides of santonin-containing species of ***Artemisia***



(XIII)
Vulgarin (Tauremisin)
A. taurica Willd.[33]
A. fragrans Willd.[40]
A. szowitziana (Bess.) Krasch.[40]

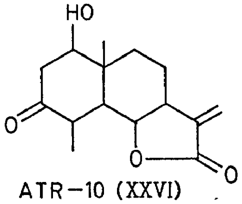


(XXIV)
Balchanin
A. balchanorum Krasch.[41]



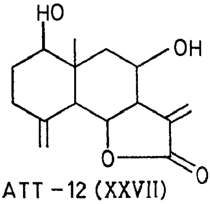
ATR−9 (XXV)

A. tripartita Gray ssp.
rupicola Beetle[42]



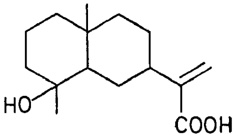
ATR−10 (XXVI)

A. tripartita
ssp. *rupicola*[42]



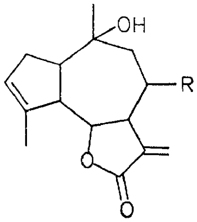
ATT −12 (XXVII)

A. tridentata Nutt.
ssp. *tridentata*[42]



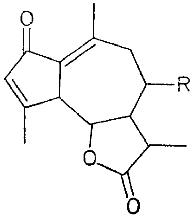
Vachanic acid
(= ilicic acid ?) (XXVII)
A. vachanica Krasch.[43]

Figure 8. Santanolides of section *Seriphidium*[44]



R=OAc, Cumambrin A (XXX)
R=OH, Cumambrin B (XXXI)
R=H, Deoxycumambrin (XXXII)

A. tripartita Gray ssp. *rupicola*[47]	XXX, XXXI, XXXII
A. nova Nels.[47]	XXX, XXXI, XXXII



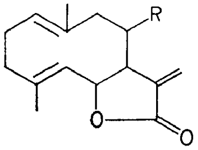
R=OAc, Matricarin (XII)
R=OH, Deacetylmatricarin (VIII)
R=H, Deacetoxymatricarin (XXIX)

A. tridentata Nutt. ssp. *tridentata*[42]	VIII, XII, XXIX
A. tridentata Nutt. ssp. *parishii* (Gray) H. and C.[42]	XXIX
A. cana Pursh. ssp. *cana*[42]	VIII, XII
A. juncea Kar. et Kir.[45]	VIII
A. lercheana Web.[46]	VIII
A. leucodes Schrenk.[21]	VIII, XXIX

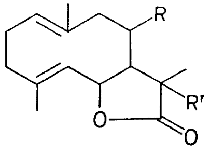
(also in *A. tilesii* (VIII, XII), *A. austriaca* (VIII), and in *Achillea* and *Matricaria* spp.).

Figure 9. Guaianolides of section *Seriphidium*

four closely related germacranolides (*Figure 10*). Costunolide (XXXIII) represents a point in the probable biosynthetic pathway from farnesol to the many lactones of the family that is near the starting point of metabolic elaboration. It is found in several tribes of Compositae, and its taxonomic usefulness is doubtful. The chemotaxonomic-phylogenetic significance of



R = H, costunolide (XXXIII)
R = OH, hydroxycostunolide (XXXIV)



R = OH, R′ = H, balchanolide (XXXV)
R = OAc, R′ = H, balchanolide acetate (XXXVI)
R = R′ = OH, hydroxybalchanolide (XXXVII)
(XXXVI) also in *Achillea millefolium* L.)[50]

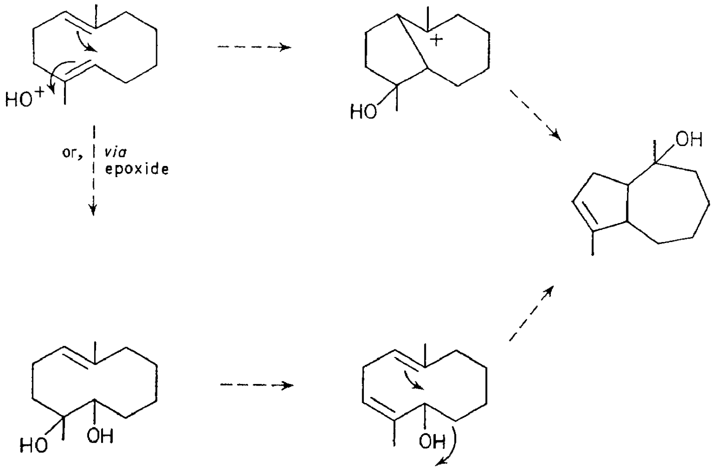
Figure 10. Lactones of *Artemisia balchanorum*[48, 49]

the occurrence of a compound that occupies a position at an early stage of a scheme of biosynthesis is not yet clear; but the complete departure of *A. balchanorum* from the pattern of lactone composition of other members of the section in which it is placed seems to set this species apart. It is clear, however, that even in this section, more members of which have been examined than of any of the other three, too little is known to press speculation further.

RELATED GENERA OF THE TRIBE

The close affinity of the several genera of the *Anthemideae* is borne out by the occurrence in *Achillea*, *Matricaria* and *Chrysanthemum* of either the same [matricarin (XII), matricin (X)] or closely related [santamarine[35], douglanine (XV)] compounds in these genera and in *Artemisia*. The force of observations of this kind is, however, greatly lessened by the discovery that two *Artemisia* species and two *Ambrosia* species also contain identical guaianolides, namely, the cumambrins (XXX, XXXI). Other findings in the author's laboratory reinforce the view that single compounds are unreliable guides to taxonomic affinities—at least, as taxonomic classifications are presently made. For instance, the compound eupatoriopicrin, first isolated from *Eupatorium cannabium* L., (tribe *Eupatorieae*), has recently been found as a prominent (in some cases nearly the only) constituent of *Venegasia carpesoides* DC., *Eriophyllum staechadifolium* Lag. var. *artemisiaefolium* (Less.) McBr. and *Chaenactis carphoclinia* Gray, all members of the tribe *Helenieae*[51].

Eupatoriopicrin, a germacranolide, is close to the biosynthetic origin of the sesquiterpene lactones and, like costunolide, may be of wide and non-specific occurrence in the family for this reason. A similar comment may be made in respect to the cumambrins (XXX–XXXII), found in both *Artemisia* and *Ambrosia* species. Cumambrin can be seen to be derivable by a simple and nonexceptional ring closure of a germacranolide, and is not the result of involved and unique structural elaborations (as are, for example, santonin, the matricarin derivatives, and many of the ambrosanolides). The formation of part of the structure of a cumambrin by an oxidative cyclization of a germacranolide is suggested in the formulation of *Figure 11*.



(XXXVIII) (XXXIX)

Figure 11. Possible biosynthetic route to cumambrin-type compounds from Germacranolide precursors[52]

Conjectures such as these, tentative as they are, emphasize what in the view of many phytochemists[53] is the principle of biochemical systematics, namely, that considerations of chemosystematics should be based primarily upon biosynthetic pathways. The sesquiterpene lactones appear to be a group of compounds ideally adapted to this purpose. They represent a large class of compounds nearly unique to a discrete group of higher plants, and have what may be assumed to be a common biosynthetic origin from which they are elaborated in a limited number of ways. This elaboration of structure is the control of genetic factors which will ultimately determine the phylogenetic description of the family.

SUMMARY

In only two groups of species within the genus *Artemisia* do chemical characters appear at present to have taxonomic utility; but it must be recognized that the evidence upon which any use to which chemical characters might be put is still scanty in the extreme.

No species presently classed in the section *Dracunculus* has so far yielded a compound of the sesquiterpene lactone class, and these plants are notably richer in coumarins than are species of other sections. It is noteworthy that the genus *Oligosporus* Cass., distinguished from *Artemisia* by a morphology that differs markedly from that of the other sections, is what now corresponds to the section *Drancunculus*. If the absence of sesquiterpene lactones in this section is confirmed in the examination of additional species, it may be suggested that the early separation of the section as the distinct genus *Oligosporus* should be reconsidered by taxonomists.

The santonin-containing species of the *Seriphidium* are distributed throughout the Section (per Poljakov) *Seriphidium* of Poljakov's subgenus *Seriphidium*, and include a number of Asian species; yet santonin has not been found in any *Artemisia* indigenous to the New World. Hall and Clements suggest that the North American *Seriphidium* may have developed independently of the Old World species, and that both are derivatives of *Abrotanum*. While not a compelling argument, the presence of the same or structurally similar guaianolides in several *Tridentatae* and in several *Abrotanum* species suggests a close genetic affinity between these groups. The presence of vulgarin (tauremisin) in both *Seriphidium* and *Abrotanum* is consistent with this view.

Continued chemical investigation of the chemistry of *Artemisia* species of as many different kinds as can be obtained will undoubtedly provide information that will at length make it possible for chemistry to contribute to the taxonomy and phylogeny of this large and interesting genus. Moreover, because of the several examples of chemical similarities between *Artemisia* and *Ambrosia*, it may be expected that continued comparative studies of these two genera (or of the tribes to which they belong) will provide further valuable information that will bear upon the phylogenetic relationships between them[54].

Acknowledgement

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References

[1] J. C. Willis (rev. by H. K. Airy Shaw). *A Dictionary of the Flowering Plants and Ferns*, *7th* edition, Cambridge University Press, 1966. In the *6th* edition (1951) the genus is said to consist of 280 species.

[2] Many more santonin-containing species are recorded in the literature, but many of these have recently been reduced by synonymy.

[3] Sesquiterpene lactones of the class under discussion here have been isolated only from two other plant families, the *Magnoliaceae* and the *Umbelliferae*, in neither of which have they yet been found to be of wide and general occurrence.

[4] J. C. Willis (ref. 1) gives 13000 species. C. L. Porter (*Taxonomy of Flowering Plants*, W. H. Freeman and Co., San Francisco, 1959), gives 23000.

[5] P. Poljakov. *Flora U.S.S.R.*, **26**, 425–631 (1961), divides the genus into three subgenera: *Artemisia* (which includes *Abrotanum* and *Absinthium* as sections), *Dracunculus* and *Seriphidium;* and each of these into numerous subsections.

[6] G. H. Ward. *Artemisia* in North America. A Cytotaxonomic Study. Contr. Dudley Herb. **4**, 155–205 (1953).

[7] The classes shown are each represented in nature by from several to many individual lactones. In addition to these, a number of minor variants are known; e.g., the psilostachyins, vernomenin, etc.

[8] Name proposed by V. Herout. *Planta Medica, Suppl.* 97–106 (1966).

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[b] T. A. Geissman, unpublished results.

[10a] K. Imai and N. Sampei. *Ann. Rep. Takamine Lab.* **4**, 54 (1952); *Chem. Abstr.* **49**, 3474 (1955).

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[11a] A. N. Bankovskaya and A. I. Bankovskii. *Chem. Abstr.* **55**, 17776 (1961).

[b] D. B. Parihar and S. Dutt. *Proc. Indian Acad. Sci.* **25A**, 153 (1947).

[c] G. Singh, G. V. Nain and H. P. Aggarwal. *Chem. and Ind.* 1294 (1954).

[12] *A. capillaris* and *A. dracunculus* contain 3-(2-butynyl)-isocoumarin, undoubtedly of linear polyketide origin and related to the acetylenes in which the Compositae abound. See N. A. Sorenson, The Taxonomic Significance of Acetylenic Compounds, In *Recent Advances in Phytochemistry*, T. J. Mabry, Ed., Appleton-Century-Crofts, New York, 1968.

[13] One of these, *A. austriaca* Jacq., is placed in section 4, *Absinthium*, of the subgenus *Artemisia*, by Poljakov (ref. 5) but is found in section *Abrotanum* in DeCandolle's (1838) arrangement.

[14] T. A. Geissman and T. E. Winters. *Tetrahedron Letters* 3145 (1968).
An alternative location of the double bonds (at 1,2/4,5) is proposed by K. Vokac, Z. Samek, V. Herout and F. Sorm. *Tetrahedron Letters* 3855 (1968).
An earlier structure, now discarded, had the double bonds at 1,2/3,4 [M. Suchy, V. Herout and F. Sorm. *Coll. Czech. Chem. Comm.* **29**, 1829 (1964)]

[15] The stereochemistry of some, but not all, of the compounds to be discussed in this review is known; but unless the configuration details are relevant to the theme of the discussion they will ordinarily not be specified.

[16] R. B. Bates, Z. Cekan, V. Prochazka and V. Herout. *Tetrahedron Letters* 1127 (1963).

[17] A compound called sieversinin, reported by M. V. Nazarenko and L. I. Leont'eva. *Khim. Prir. Soedin* **2**, 399 (1966), is said to be a stereoisomer of arborescin. Since it has the same melting point, rotation and n.m.r. spectrum as arborescin, it will be recorded here provisionally as that compound.

[18] M. V. Nazarenko. *Zhur. Priklad. Khim.* **38**, 2372 (1965).

[19] M. V. Nazarenko. *Zhur. Priklad. Khim.* **34**, 1633 (1961), has reported the discovery in the pollen of *A. macrocephala* Jacq. of two compounds, $C_{17}H_{22}O_5$, m.p. 128–131° and 150–151°. These properties agree with those of sieverin and globicin, and the compounds are provisionally regarded to be these guaianolides.

[20] R. B. Bates, V. Prochazka and Z. Cekan. *Tetrahedron Letters* 877 (1963).

[21] K. S. Rybalko. *Zh. Obshch. Khim.* **33**, 2734 (1963).

[22] J. J. Willaman and H. L. Li. *Econ. Bot.* **17**, 180 (1963); **22**, 239 (1968), discuss the question of the phylogenetic implications of structural complexity in the plant alkaloids.

[23] A qualitative survey by A. Viehover and R. G. Copen. *J. Amer. Chem. Soc.* **45**, 1942 (1923), in which numerous *Artemisia* species were tested for the presence of santonin, included a number of members of the section *Abrotanum*, but no observations useful to the present purpose were made.

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[27] W. Herz and P. S. Santhanam. *J. Org. Chem.* **30**, 4340 (1965).

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[29] Coumarins are also found in this section: scopoletin (*A. abrotanum* L., *A. afra* Jacq.); herniarin (*A. princeps* Pamp.); and umbelliferone (*A. sacrorum* Ldb. = *A. gmelinii* W. and St.).

[30] H. M. Hall and F. E. Clements. *The Phylogenetic Method in Taxonomy*, Carnegie Inst. Wash., Publ. No. 325 (1923).

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[32a] T. A. Geissman and G. A. Ellestad. *J. Org. Chem.* **27**, 1855 (1962).

[b] K. S. Rybalko and L. Dolejs. *Coll. Czech. Chem. Comm.* **26**, 2909 (1961).

[33] S. Matsueda and T. A. Geissman. *Tetrahedron Letters* 2013 (1967).

[34] S. Matsueda and T. A. Geissman. *Tetrahedron Letters* 2159 (1967).

[35] Douglanine is 1-αOH. The 1-epimer, santamarine, is found in *Chrysanthemum parthenium* L. [R. deVivar and H. Jimenez. *Tetrahedron* **21**, 1741 (1965)]

[36] T. A. Geissman. *J. Org. Chem.* **31**, 2523 (1966).

[37] The species listed are those found in Poljakov's revision of the genus (ref. 5). It is to be noted that variances exist; for example, *A. compacta* Fisch. = *A. maritima* L. in Index Kewensis.

[38] The presence of santonin in several of the species in this list is noted only by Poljakov[5]; these are *A. terrae-albae*, *A. juncea*, *A. turanica* and *A. tenuisecta*. The original source of these disclosures was not found.

[39] Since many of the investigations of santonin-containing plants were carried out before the advent of modern separation techniques, and because they had as their principal aim the analysis of plants for the drug, it can scarcely be doubted that many of the species recorded as containing santonin only contain other, still unrevealed, constituents.

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[41] M. Suchy. *Coll. Czech. Chem. Comm.* **27**, 2925 (1962).

[42] M. A. Irwin and T. A. Geissman, unpublished work.

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[44] Scopoletin and the new (to nature) compound, 6-hydroxy-7-methoxycoumarin, are found in *A. nova*, *A. tripartita*, ssp. *rupicola* and two species of *A. tridentata*. The latter compound, the structure of which was established in the course of the studies in this laboratory, was reported as a constituent of *A. messerschmidiana* Bess. [= *A. gmelinii* Web. et Stech. (Poljakov, ref. 5)] by Duk Ryong Hahn [Yaknak Hoeji **10**, 20 (1966)] in a paper that has only recently come to our attention [*Chem. Abstr.* **68**, 12202C (1968)].

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[49] M. Suchy, V. Herout and F. Sorm. *Coll. Czech. Chem. Comm.* **28**, 1620 (1963).

[50] J. Hochmannova, V. Herout and F. Sorm. *Coll. Czech. Chem. Comm.* **26**, 1826 (1961).

[51] Unpublished findings in the author's laboratory.

[52] The intermediate (XXXVIII) represents the glycol corresponding to parthenolide, a constituent of *Chrysanthemum* and *Hymenoclea* (tribe *Ambrosieae*) species.

[53] See, for example, H. Erdtman, Chemistry in Chemosystematics. In *Recent Advances in Phytochemistry*, T. J. Mabry, Ed., Appleton-Century-Crofts, 1968.

[54] Since the preparation of this manuscript in 1968, continuing developments in the chemistry of *Artemisia* have lead to enlargement of the subject discussed in this paper. Amplification of these studies will be found in a paper soon to be published in a Commemorative Volume dedicated to Professor T. R. Seshadri.