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ScienceDirect
Phytochemistry 69 (2008) 607–618
PHYTOCHEMISTRY
www.elsevier.com/locate/phytochem

Review

Sesquiterpene lactones as chemotaxonomic markers in genus *Anthemis*

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Received 18 December 2006; received in revised form 25 July 2007
Available online 11 September 2007

Abstract

Sesquiterpene lactones isolated from the genus *Anthemis* are used as chemotaxonomic markers. The obtained results support with some exceptions the botanical classification in Flora Europaea. Discrepancy between the lactone profile, cluster analysis and classification of *A. melampodina*, *A. macedonica* and *A. austriaca* in the genus *Anthemis* is discussed. The lactone composition of the undescribed as an European species *A. plutonia* correlates well with the guaianolide containing group of sect. *Hiorthia*.

Keywords: Genus *Anthemis*; Asteraceae; Chemotaxonomy; Sesquiterpene lactones

Contents

1. Introduction

Genus *Anthemis* (family Asteraceae, tribe Anthemideae) comprises of 62 species in Europe, which are divided into three subgenera according to the botanical classification (Fernandes, 1976). Subgenus *Anthemis* includes four sections *Hiorthia*, *Anthemis*, *Maruta* and *Chia*. Subgenus *Cota* involves sections *Anthemaria* and *Cota*. The species from subgenus *Ammanthus* are not separated into sections.

Sesquiterpene lactones have received considerable attention because of their ecological functions (Cis et al., 2006;

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0031-9422/$ - see front matter
doi:10.1016/j.phytochem.2007.07.021

Nawrot et al., 1983), biological activity (Zhang et al., 2005; Picman, 1986) and taxonomic significance (Seaman, 1982) as well. They are one of the main classes of secondary metabolites detected in genus *Anthemis*. Four skeletal types of sesquiterpene lactones – guaianolides, germacranolides, eudesmanolides and linear, have been detected in *Anthemis* species. The present paper focuses on sesquiterpene lactones as taxonomic markers in genus *Anthemis*, using the lactone profile of the species studied so far.

2. Sesquiterpene lactones in genus *Anthemis*

The sesquiterpene lactones isolated from representatives of different sections of the genus *Anthemis*, are summarized in Table 1, and their structures are presented in Fig. 1. The studied species are discussed in the order accepted in Flora Europaea (Fernandes, 1976).

2.1. Subgenus Anthemis

2.1.1. Sect. Hiorthia (DC.) R. Fernandes

A. carpatica Willd.: The lactone profile of *A. carpatica* of Serbian origin showed the presence of the highly oxygenated guaianolides **1–9**, **12–18**, **36–43** and the germacranolide **56** (Bulatović et al., 1997; Vajs et al., 2000). The guaianolides **33–35** and the eudesmanolides **81–86** were detected in four Bulgarian plant samples in addition to the compounds **13–16** (Staneva et al., 2002).

A. aetnensis Schouw: Phytochemical study of this Sicilian endemic species resulted in the isolation of lactones of two skeletal types – guaianolides (**19–25**, **30–32**) and germacranolides (**57** and **58**) (Bruno et al., 1997). The reported guaianolides were hydrunthinolides.

A. punctata subsp. *cupaniana* Tod ex Nyman: Ten 4,5-epoxy-1(10),11(13)-germacradien-12,6-olides substituted at C-8 or C-9 (**60–69**) were found in Sicilian endemic taxon (Bruno et al., 1991).

A. cretica L.: Early studies of Bohlmann and Zdero (1975) showed that *A. cretica* produced only germacranolides. *A. cretica* subsp. *montana* yielded three *cis, cis*-germacranolides **70–72**, while *A. cretica* subsp. *tenuiloba* afforded parthenolide **(59)** and 9β-acetoxyparthenolide (the structure was corrected later to 9α-acetoxyparthenolide (**68**) by Bruno et al. (1991). According to the position of the double bond in the five-membered ring three groups of guaianolides – with Δ^2 (**4**, **5**, **7**, **8** and **10**), with Δ^3 (**13**, **14**, **20** – **25**), and with Δ^4 (**38**) were isolated from *A. cretica* subsp. *cretica* collected in Serbia (Vajs et al., 1999).

A. alpestris Hoffmanns. & Link (*Chamaemelum alpestre* Hoffmanns. & Link): This species of Spanish origin yielded hydrunthinolides (**21–24**, **28** and **29**) only (Bruno et al., 2002).

A. hydruntina Groves: The plant growing in Southern Italy afforded three guaianolides – hydrunthinolides A, B and C (**19**, **25** and **27**), differing in the C-8 substituents (Di Benedetto et al., 1991).

A. stribrnyi subsp. *tracica* Velen.: *A. stribrnyi* subsp. *tracica*, an endemic Bulgarian species afforded four germacranolides: **54**, **55**, **59**, and **68** (Staneva et al., 2006). Parthenolide (**59**) was previously described as a constituent of *A. cretica* subsp. *tenuiloba* (Bohlmann and Zdero, 1975) and *A. melampodina* (Zaghloul et al., 1989), while 9α-acetoxyparthenolide **(68)** was found in *A. punctata* subsp. *cupaniana* (Bruno et al., 1991) and in *A. cretica* subsp. *tenuiloba* (Bohlmann and Zdero, 1975).

2.1.2. Sect. Anthemis (Ser. Arvensis Fedorov)

A. arvensis L.: The irregular linear sesquiterpene lactones, antheindurolide A (**105**) and its derivatives **106–110**, as well as antheindurolide-B (**111**) were identified in plants collected in Serbia (Vučković et al., 2006a).

A. auriculata Boiss. (*A. sismondaeana* G.C. Clemanti): Irregular linear lactones were also isolated from *A. auriculata* of Greek and Bulgarian origin. The lactones reported for these two localities possess the same carbon skeleton, but differ in the number of lactone rings. The species occurring in Greece contained monolactones (**92, 101**, and **102**) (Theodori et al., 2006), while the Bulgarian one produced dilactones (**105a–111a**) (Todorova et al., 2007). The latter were found to be C-8 or C-10 stereoisomers of **105–111**, isolated from Serbian *A. arvensis* (Vučković et al., 2006a).

A. macedonica Boiss. & Orph.: This species is distributed in two European countries – Bulgaria and Greece (Fernandes, 1976). Germacranolides and eudesmanolides were isolated from *A. macedonica* (Staneva et al., 2006). Parthenolide (**59**) and its 1β,10α-epoxy- (**73**), 8α-hydroxy- (stizolin) (**60**), 8α-acetyloxy- (**61**), 8α-angeloyloxy- (**62**), and 9α-acetyloxy- (**68**) derivatives were the identified germacranolides. Compounds **59** and **68** are common to *A. macedonica*, *A. stribrnyi* subsp. *tracica* (Staneva et al., 2006), and *A. cretica* subsp. *tenuiloba*, (Bohlmann and Zdero, 1975). The germacranolides **60–62** and **68** were reported as constituents of *A. punctata* subsp. *cupaniana* (Bruno et al., 1991). The eudesmanolide ludalbin (**82**) was found previously in *A. carpatica* (Staneva et al., 2002) while santamarine (**87**) and reynosin (**88**) were detected for the first time in genus *Anthemis*. It is noteworthy that germacranolides were principal constituents of *A. macedonica*.

2.1.3. Sect. Maruta Griseb

A. cotula L.: Several origins of this species have been studied so far. As can be seen below all of them contain irregular linear sesquiterpene lactones. Anthecotuloide (**92**) was the first compound isolated from this species (Bohlmann et al., 1969). The compounds **92**, **93**, **95–97** were found in the species collected in USA (California) (Baruah et al., 1985). Besides them, the lactones **94**, **98**, **105**, and **111** were isolated from a Bulgarian taxon (Staneva et al., 2005). Plant material from former Yugoslavia afforded **92**, **95**, **97–100** (Vučković et al., 2006b).

A. pseudocotula Boiss.: Irregular linear sesquiterpene lactones (**103–105** and **111**) have been reported as compo-

Table 1
Sesquiterpene lactones isolated from genus *Anthemis*

No.	Name	Sources	References
1	Anthemolide A	*A. carpatica*	Vajs et al. (2000), Bulatović et al. (1997)
2	8α-Isobutyryloxyanthemolide A	*A. carpatica*	Vajs et al. (2000)
3	8-Deoxy-9-*O*-acetylanthemolide B	*A. carpatica*	Vajs et al. (2000)
4	Anthemolide B	*A. carpatica* *A. cretica* subsp. *cretica*	Vajs et al. (2000) Vajs et al. (1999)
5	8α-Acetylanthemolide B (8-*O*-acetylanthemolide B)	*A. carpatica* *A. cretica* subsp. *cretica*	Bulatović et al. (1997) Vajs et al. (1999)
6	9-*O*-Acetylanthemolide B	*A. carpatica*	Bulatović et al. (1997)
7	8,9-Di-*O*-acetylanthemolide B	*A. carpatica* *A. cretica* subsp. *cretica*	Bulatović et al. (1997), Vajs et al. (1999)
8	8-*O*-Isobutyryl-9-*O*-acetylanthemolide B	*A. carpatica* *A. cretica* subsp. *cretica*	Vajs et al. (2000), Bulatović et al. (1997) Vajs et al. (1999)
9	8-*O*-Tigloyl-9-*O*-acetylanthemolide B	*A. carpatica*	Vajs et al. (2000)
10	8-*O*-Angeloyl-9-*O*-acetylanthemolide B	*A. cretica* subsp. *cretica*	Vajs et al. (1999)
11	8-Deoxycumambrin B	*A. melampodina*	Zaghloul et al. (1989)
12	Cumambrin B	*A. carpatica*	Vajs et al. (2000)
13	9α-Acetoxycumambrin B	*A. cretica* subsp. *cretica* *A. carpatica* *A. plutonia*	Vajs et al. (1999) Bulatović et al. (1997), Staneva et al. (2002) Bruno et al. (1998)
14	9α-Hydroxycumambrin A	*A. cretica* subsp. *cretica* *A. carpatica* *A. plutonia*	Vajs et al. (1999) Bulatović et al. (1997), Staneva et al. (2002) Bruno et al. (1998)
15	9α-Acetoxycumambrin A	*A. carpatica*	Bulatović et al. (1997), Vajs et al. (2000), Staneva et al. (2002)
16	8-*O*-Isobutyryl-9α-acetoxycumambrin B	*A. carpatica*	Staneva et al. (2002), Vajs et al. (2000)
17[b]	2β-Hydroxyepiligustrin	*A. carpatica*	Vajs et al. (2000)
18	2α-Hydroperoxy-8-*O*-isobutyryl-9α-acetoxycumambrin B	*A. carpatica*	Bulatović et al. (1997), Vajs et al. (2000)
19	Hydruntinolide A	*A. hydruntina* *A. aetnensis*	Di Benedetto et al. (1991) Bruno et al. (1997)
20	(1*S*,2*R*,5*R*,6*R*,7*S*,8*R*,9*R*,10*S*)[a]-10-Hydroxy-2,8,9-triacetoxyguaia-3,11(13)-dien-6,12-olide	*A. cretica* subsp. *cretica* *A. aetnensis*	Vajs et al. (1999) Bruno et al. (1997)
21	(1*S*,2*R*,5*R*,6*R*,7*S*,8*R*,9*R*,10*S*)[a]-2,9-Diacetoxy-8,10-dihydroxyguaia-3,11(13)-dien-6,12-olide	*A. cretica* subsp. *cretica* *A. aetnensis* *A. alpestris*	Vajs et al. (1999) Bruno et al. (1997) Bruno et al. (2002)
22	(1*S*,2*R*,5*R*,6*R*,7*S*,8*R*,9*R*,10*S*)[a]-2-Acetoxy-8,10-dihydroxy-9-(2-methylpropanoyloxy)-guaia-3,11(13)-dien-6,12-olide	*A. cretica* subsp. *cretica* *A. aetnensis* *A. alpestris*	Vajs et al. (1999) Bruno et al. (1997) Bruno et al. (2002)
23	(1*S*,2*R*,5*R*,6*R*,7*S*,8*R*,9*R*,10*S*)[a]-2-Acetoxy-8,10-dihydroxy-9-isovaleryloxyguaia-3,11(13)-dien-6,12-olide	*A. cretica* subsp. *cretica* *A. aetnensis* *A. alpestris*	Vajs et al. (1999) Bruno et al. (1997) Bruno et al. (2002)
24	(1*S*,2*R*,5*R*,6*R*,7*S*,8*R*,9*R*,10*S*)[a]-2-Acetoxy-8,10-dihydroxy-9-(2-methylbutyryloxy)-guaia-3,11(13)-dien-6,12-olide	*A. cretica* subsp. *cretica* *A. aetnensis* *A. alpestris*	Vajs et al. (1999) Bruno et al. (1997) Bruno et al. (2002)
25	Hydruntinolide B	*A. hydruntina* *A. aetnensis* *A. cretica* subsp. *cretica*	Di Benedetto et al. (1991) Bruno et al. (1997) Vajs et al. (1999)
26	(1*R*,5*R*,6*R*,7*S*,8*R*,9*S*,10*S*)[a]-8,9,10-Trihydroxyguaia-3,11(13)-dien-6,12-olide	*A. plutonia*	Bruno et al. (1998)
27	Hydruntinolide C	*A. hydruntina*	Di Benedetto et al. (1991)
28	(1*S*,2*R*,5*R*,6*R*,7*S*,8*R*,9*R*,10*S*)[a]-2,8,9,10-Tetrahydroxyguia-3,11(13)-dien-6,12-olide	*A. alpestris*	Bruno et al. (2002)
29	(1*S*,2*R*,5*R*,6*R*,7*S*,8*R*,9*R*,10*S*)[a]-2,10-Dihydroxy-8-*O*-angeloxy-9-acetoxyguia-3,11(13)-dien-6,12-olide	*A. alpestris*	Bruno et al. (2002)

(*Continued on next page*)

Table 1 (*Continued*)

No.	Name	Sources	References
30	(1*S*,5*R*,6*R*,7*S*,8*R*,9*R*,10*S*)[a]-2,9-Diacetoxy-10-hydroxy-8-(2-methylbutyryloxy)-guaia-3,11(13)-dien-6,12-olide	*A. aetnensis*	Bruno et al. (1997)
31	(1*S*,5*R*,6*R*,7*S*,8*R*,9*R*,10*S*)[a]-2,9-Diacetoxy-10-hydroxy-8-(isovaleryloxy)-guaia-3,11(13)-dien-6,12-olide	*A. aetnensis*	Bruno et al. (1997)
32	(1*S*,5*R*,6*R*,7*S*,8*R*,9*R*,10*S*)[a]-9-Acetoxy-2,8,10-trihydroxyguaia-3,11(13)-dien-6,12-olide	*A. aetnensis*	Bruno et al. (1997)
33	8-*O*-Tigloyl-9α-acetoxycumambrin B	*A. carpatica*	Staneva et al. (2002)
34	10α-Hydroxy-9α-acetoxyguaia-3,11(13)-dien-6,12-olide	*A. carpatica*	Staneva et al. (2002)
35	Cumambrin A	*A. carpatica*	Staneva et al. (2002)
36	Anthemolide C	*A. carpatica*	Vajs et al. (2000), Bulatović et al. (1997)
37	9-*O*-Deacetylanthemolide D	*A. carpatica*	Vajs et al. (2000)
38	Anthemolide D	*A. carpatica* *A. cretica* subsp. *cretica*	Bulatović et al. (1997) Vajs et al. (1999)
39	8α-Isobutyryloxyanthemolide C	*A. carpatica*	Vajs et al. (2000)
40	8α-Propionyloxyanthemolide C	*A. carpatica*	Vajs et al. (2000)
41	8α-Tigloyloxyanthemolide C	*A. carpatica*	Vajs et al. (2000)
42	Anthemolide E	*A. carpatica*	Bulatović et al. (1997)
43	Anthemolide F	*A. carpatica*	Vajs et al. (2000)
44	Estafiatin-8-*O*-angelate	*A. melampodina*	El-Alfy et al. (1989)
45	Estafiatin-8-*O*-isovalerate	*A. melampodina*	El-Alfy et al. (1989)
46	Desacetoxymatricarin	*A. pseudocotula*	Abou El-Ela et al. (1990)
47	Xerantholide	*A. austriaca*	Holub et al. (1982), Staneva et al. (2004)
48	1α-Hydroxyxerantholide	*A. austriaca*	Staneva et al. (2004)
49	6α-Hydroxyxerantholide	*A. austriaca*	Staneva et al. (2004)
50	10α-Hydroxy-11β,13-dihydroxerantholide	*A. austriaca*	Staneva et al. (2004)
51	Xeranthemolide	*A. austriaca*	Staneva et al. (2004)
52	8α-Xydroxyxeranthemolide	*A. austriaca*	Staneva et al. (2004)
53	Spiciformin	*A. altissima*	Konstantinopoulou et al. (2003)
54	Isospiciformin	*A. stribrnyi* subsp. *tracica*	Staneva et al. (2006)
55	Acetylisospiciformin	*A. stribrnyi* subsp. *tracica*	Staneva et al. (2006)
56	(*E*)-1α,10β-Epoxy-3β-acetoxy-6α-hydroxy-germacra-4,11(13)-dien-12,8α-olide	*A. carpatica*	Vajs et al. (2000)
57	(1*R*,3*S*,6*S*,7*R*,8*R*)[a]-1-Hydroxy-3-acetoxy-8-hydroxygermacra-4*Z*,10(14),11(13)-trien-6,12-olide	*A. aetnensis*	Bruno et al. (1997)
58	(1*R*,3*S*,6*S*,7*R*,8*R*)[a]-1-Hydroperoxy-3-acetoxy-8-hydroxygermacra-4*Z*,10(14),11(13)-trien-6,12-olide	*A. aetnensis*	Bruno et al. (1997)
59	Parthenolide	*A. macedonica*; *A. stribrnyi* subsp. *tracica* *A. melampodina* *A.cretica* subsp. *tenuiloba*	Staneva et al. (2006) Zaghloul et al. (1989), Sarg et al. (1990) Bohlmann and Zdero, 1975)
60	Stizolin	*A. macedonica* *A. punctata* subsp. *cupaniana*	Staneva et al. (2006), Bruno et al. (1991)
61	Dehydrolanuginolide	*A. macedonica* *A. punctata* subsp. *cupaniana*	Staneva et al. (2006) Bruno et al. (1991)
62	(4*S*,5*R*,6*S*,7*R*,8*S*)-8-Angeloxy-4,5-epoxygermacra-1(10),11(13)-dien-6,12-olide	*A. macedonica* *A. punctata* subsp. *cupaniana*	Staneva et al. (2006) Bruno et al. (1991)
63	(4*S*,5*R*,6*S*,7*R*,8*S*)-8-Tigloxy-4,5-epoxygermacra-1(10),11(13)-dien-6,12-olide	*A. punctata* subsp. *cupaniana*	Bruno et al. (1991)
64	(4*S*,5*R*,6*S*,7*R*,8*S*)-8-Isobutyryloxy-4,5-epoxygermacra-1(10),11(13)-dien-6,12-olide	*A. punctata* subsp. *cupaniana*	Bruno et al. (1991)
65	(4*S*,5*R*,6*S*,7*R*,8*S*)-8-(2-Methylbutanoyloxy)-4,5-epoxygermacra-1(10),11(13)-dien-6,12-olide	*A. punctata* subsp. *cupaniana*	Bruno et al. (1991)
66	(4*S*,5*R*,6*S*,7*R*,8*S*)-8-Isovaleryloxy-4,5-epoxygermacra-1(10),11(13)-dien-6,12-olide	*A. punctata* subsp. *cupaniana*	Bruno et al. (1991)

Table 1 (*Continued*)

No.	Name	Sources	References
67	9α-Hydroxyparthenolide	*A. punctata* subsp. *cupaniana*	Bruno et al. (1991)
68	9α-Acetoxyparthenolide	*A. punctata* subsp. cupaniana	Bruno et al. (1991)
		A. cretica subsp. *tenuiloba*	Bohlmann and Zdero (1975)
		A. macedonica	Staneva et al. (2006)
		A. stribrnyi subsp. tracica	
69	(4*S*,5*R*,6*S*,7*S*,9*R*,11*R*)-9-Acetoxy-4,5-epoxygermacra-1(10)-en-6,12-olide	*A. punctata* subsp. *cupaniana*	Bruno et al. (1991)
70	Costunolide, *cis,cis*-3α-acetoxy-8β-hydroxy	*A. cretica* subsp. *montana*	Bohlmann and Zdero (1975)
71	Costunolide, *cis,cis*-3α-acetoxy-8β-acetoxy	*A. cretica* subsp. *montana*	Bohlmann and Zdero (1975)
72	Costunolide, *cis,cis*-11,13-dihydro-3α-acetoxy-8β-hydroxy	*A. cretica* subsp. *montana*	Bohlmann and Zdero (1975)
73	Michelenolide	*A. macedonica*	Staneva et al. (2006)
74	1,10-Epoxyparthenolide	*A. melampodina*	El-Alfy et al. (1989)
75	1-*epi*-Tatridin B	*A. altissima*	Konstantinopoulou et al. (2003)
		A. wiedemanniana	Çelik et al. (2005)
76	Tatridin A	*A. altissima*	Konstantinopoulou et al. (2003)
		A. wiedemanniana	Çelik et al. (2005)
77	1α,10β-Epoxy-6α-hydroxy-1,10*H*-inunolide	*A. altissima*	Konstantinopoulou et al. (2003),
78	3β-Hydroxycostunolide	*A. melampodina*	Sarg et al. (1990)
79	Costunolide	*A. melampodina*	Sarg et al. (1990)
80	3β-Acetoxycostunolide	*A. melampodina*	El-Alfy et al. (1989)
81	Douglanin	*A. melampodina*	El-Alfy et al. (1989)
		A. carpatica	Staneva et al. (2002)
82	Ludalbin	*A. carpatica*	Staneva et al. (2002)
		A. macedonica	Staneva et al. (2006)
83	8α-Angeloyloxydouglanin	*A. carpatica*	Staneva et al. (2002)
84	8α-Tigloyloxydouglanin	*A. carpatica*	Staneva et al. (2002)
85	8α-Isobutyryloxydouglanin	*A. carpatica*	Staneva et al. (2002)
86	8α-Hydroxydouglanin	*A. carpatica*	Staneva et al. (2002)
87	Santamarine	*A. macedonica*	Staneva et al. (2006)
88	Reynosin	*A. macedonica*	Staneva et al. (2006)
89	Sivasinolide	*A. altissima*	Konstantinopoulou et al. (2003)
90	Altissin	*A. altissima*	Konstantinopoulou et al. (2003)
91	Desacetyl-β-cyclopyrethrosin	*A. altissima*	Konstantinopoulou et al. (2003)
		A. wiedemanniana	Çelik et al. (2005)
92	Anthecotuloide	*A. cotula*	Bohlmann et al. (1969), Baruah et al. (1985), Staneva et al. (2005); Vučković et al. (2006a)
		A. auriculata	Theodori et al. (2006)
93	6,7 *Z*-Dehydro-5,6-dihydroanthecotuloide	*A. cotula*	Baruah et al. (1985), Staneva et al. (2005)
94	6,7 *E*-Dehydro-5,6-dihydroanthecotuloide	*A. cotula*	Staneva et al. (2005)
95	8-*O*-Dihydroanthecotuloide	*A. cotula*	Baruah et al. (1985), Staneva et al. (2005), Vučković et al. (2006a)
96	5-Oxo-6,7*Z*-dehydro-5,6-dihydroanthecotuloide	*A. cotula*	Baruah et al. (1985), Staneva et al. (2005)
97	5-Oxo-6,13-dehydro-5,6-dihydroanthecotuloide	*A. cotula*	Baruah et al. (1985), Staneva et al. (2005), Vučković et al. (2006a)
98	5-Hydroperoxy-6,13-dehydro-5,6-dihydroanthecotuloide	*A. cotula*	Staneva et al. (2005); Vučković et al. (2006a)
99	Anthecotuloide-5,6-oxide	*A. cotula*	Vučković et al. (2006a)
100	6-Hydroxy-4,5-dehydro-5,6-dihydroanthecotuloide	*A. cotula*	Vučković et al. (2006a)
101	4-Hydroxyanthecotuloide	*A. auriculata*	Theodori et al. (2006)
102	4-*O*-Acetylanthecotuloide	*A. auriculata*	Theodori et al. (2006)
103	Anthepseudolide	*A. pseudocotula*	Abou El-Ela et al. (1990)
104	Anthepseudolide-6-*O*-acetate	*A. pseudocotula*	Abou El-Ela et al. (1990)

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Table 1 (*Continued*)

No.	Name	Sources	References
105	Antheindurolide A	*A. pseudocotula*, *A. indurata*	Abou El-Ela et al. (1990)
		A. cotula	Staneva et al. (2005)
		A. arvensis	Vučković et al. (2006a)
105a	*epi*-Antheindurolide A	*A. auriculata*	Todorova et al. (2007)
106	(5*R*,6*R*+5*S*,6*S*) Antheindurolide A-5,6-oxide	*A. arvensis*	Vučković et al. (2006a)
106a	*epi*-Antheindurolide A-5,6-oxide	*A. auriculata*	Todorova et al. (2007)
107	(6*R*+6*S*) (4*E*) 6-Hydroperoxy-5,6-dihydro-4,5-dehydro-antheindurolide A	*A. arvensis*	Vučković et al. (2006a)
107a	*epi*-(4*E*) 6-Hydroperoxy-5,6-dihydro-4,5-dehydro-antheindurolide A	*A. auriculata*	Todorova et al. (2007)
108	(6*R* or 6*S*) 6-Hydroxy-5,6-dihydro-4,5-dehydro-antheindurolide A	*A. arvensis*	Vučković et al. (2006a)
108a	*epi*-6-Hydroxy-5,6-dihydro-4,5-dehydro-antheindurolide A	*A. auriculata*	Todorova et al. (2007)
109	(5*R* + 5*S*)-5-Hydroperoxy-5,6-dihydro-6,13-dehydro-antheindurolide A	*A. arvensis*	Vučković et al. (2006a)
109a	*epi*-5-Hydroperoxy-5,6-dihydro-6,13-dehydro-antheindurolide A	*A. auriculata*	Todorova et al. (2007)
110	(5*R* + 5*S*) 5-Hydroxy-5,6-dihydro-6,13-dehydro-antheindurolide A	*A. arvensis*	Vučković et al. (2006a)
110a	*epi*-(5*R* + 5*S*) 5-Hydroxy-5,6-dihydro-6,13-dehydro-antheindurolide A	*A. auriculata*	Todorova et al. (2007)
111[c]	Antheindurolide B	*A. pseudocotula*; *A. indurata*	Abou El-Ela et al. (1990)
		A. cotula	Staneva et al. (2005)
		A. arvensis	Vučković et al. (2006a)
111a	*epi*-Antheindurolide B	*A. auriculata*	Todorova et al. (2007)

[a] Relative stereochemistry.
[b] $\Delta^{10,14}$.
[c] Corrected by Vučković et al. (2006a).

nents of this species of Egyptian origin. Desacetoxymatricarin (**46**) was the only lactone with different type of carbon skeleton found in *A. pseudocotula* (Abou El-Ela et al., 1990).

2.2. Subgenus Cota (Gay and Guss)

2.2.1. Sect. Anthemaria Dumort

It was established that of *A. tinctoria* L. (*Cota tinctoria* (L.) Gay), *A. sancti-johannis* Turrill (*A. gaudium-solis* var. *sancti-johannis* (Turrill) Hayek) and *A. macrantha* Heuffel (*A. triumfetti* var. *rigescens* sensu Hayek) do not contain sesquiterpene lactones (Staneva et al., unpublished).

2.2.2. Sect. Cota (Ser. Altissimae Fedorov)

A. altissima L. (*Cota altissima* L.): The lactone composition of Greek plant revealed the presence of germacranolides (**53**, **75**–**77**) and eudesmanolides (**89**–**91**), all of them bearing a 12,8-closed lactone ring (Konstantinopoulou et al., 2003).

A. austriaca Jacq. (*A. cotiformis* Velen.): Xerantholide (**47**) has been found as a constituent of *A. austriaca* of two origins – Turkish and Polish (Holub et al., 1982). In addition, five derivatives of **47** (**48**–**52**) were identified in a Bulgarian taxon (Staneva et al., 2004).

2.3. Subgenus Ammanthus

The literature survey showed that species from subgenus *Ammanthus* were not studied.

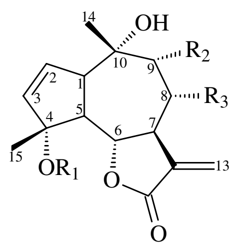
2.4. Anthemis species undescribed in Flora Europaea

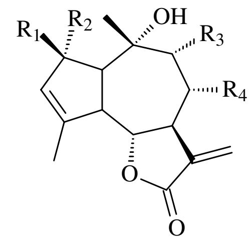
A. plutonia Meikle: The guaianolides **13**, **14**, and **26** have been found in a Cypriot endemic plant (Bruno et al., 1998). These compounds are very similar to the guaianolides isolated from *A. hydruntina* (Di Benedetto et al., 1991) and *A. aetnensis* (Bruno et al., 1997) but do not contain the C-1 substituents. Compounds **13** and **14** were found in *A. carpatica* (Bulatović et al., 1997) and *A. cretica* subsp. *cretica* (Vajs et al., 1999).

A. melampodina Del.: This species is classified in sect. *Anthemis* according to Flora Orientalis (Boissier, 1875). Three skeletal types of lactones – germacranolides (**59, 74**, **78**–**80**), guaianolides (**11**, **44** and **45**), and the eudesmanolide douglanin (**81**) were described for the Egyptian taxa (Zaghloul et al., 1989; El-Alfy et al., 1989; Sarg et al., 1990).

A. indurata Del.: Two linear dilactones, antheindurolide-A (**105**) and -B (**111**) were identified in the originating from Egypt species. The same compounds were reported for *A. pseudocotula* (Abou El-Ela et al., 1990), *A. arvensis* (Vučković et al., 2006a), *A. cotula* (Staneva et al., 2005), and *A. auriculata* (Todorova et al., 2007). *A. indurata* is placed in sect. *Anthemis* in Flora Orientalis (Boissier, 1875).

A. wiedemanniana Fisch. & C.A. Mey.: The species has been classified in sect. *Cota* by Davis (Çelik et al., 2005). The plant material from Turkey was reported to contain lactones (**75**, **76**, and **91)** previously found in *A. altissima* (Çelik et al., 2005).



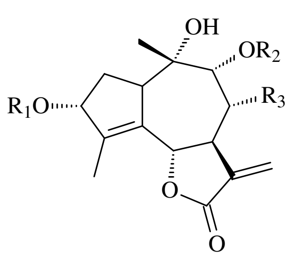


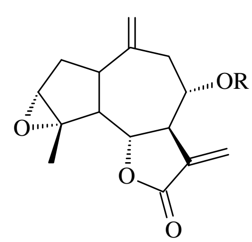
	R1	R2	R3
1	H	OAc	H
2	H	OAc	OiBu
3	OH	OAc	H
4	OH	OH	OH
5	OH	OH	OAc
6	OH	OAc	OH
7	OH	OAc	OAc
8	OH	OAc	OiBu
9	OH	OAc	OTig
10	OH	OAc	OAng

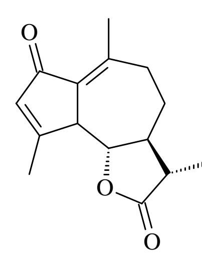
	R1	R2	R3	R4
11	H	H	H	H
12	H	H	H	OH
13	H	H	OAc	OH
14	H	H	OH	OAc
15	H	H	OAc	OAc
16	H	H	OAc	OiBu
17#	OH	H	H	OH
18	H	OOH	OAc	OiBu
19	OAc	H	OAc	H
20	OAc	H	OAc	OAc
21	OAc	H	OAc	OH
22	OAc	H	OiBu	OH
23	OAc	H	OiVal	OH

10,14

	R1	R2	R3	R4
24	OAc	H	O2MeBu	OH
25	OAc	H	OAc	OiBu
26	H	H	OH	OH
27	OAc	H	OAc	OAng
28	OH	H	OH	OH
29	OH	H	OAc	OAng
30	OAc	H	OAc	O2MeBu
31	OAc	H	OAc	OiVal
32	OH	H	OAc	OH
33	H	H	OAc	OTig
34	H	H	OAc	H
35	H	H	H	OAc





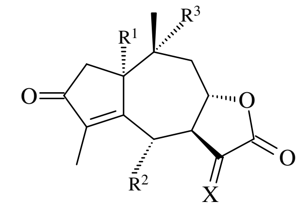


	R1	R2	R3
36	H	Ac	H
37	H	H	OAc
38	H	Ac	OAc
39	H	Ac	OiBu
40	H	Ac	OProp
41	H	Ac	OTig
42	OH	Ac	OAc
43	OH	Ac	OiBu

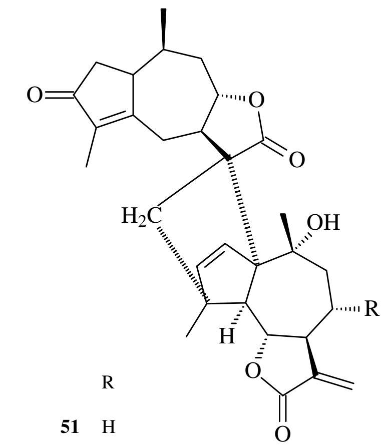
	R
44	Ang
45	iVal

46

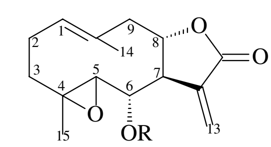
Fig. 1. Sesquiterpene lactones isolated from *Anthemis* species.



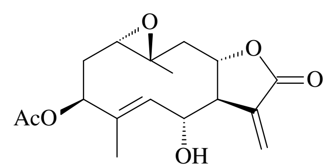
	R_1	R_2	R_3	X
47	H	H	H	CH_2
48	OH	H	H	CH_2
49	H	OH	H	CH_2
50	H	H	OH	CH_3, H



	R
51	H
52	OH



	R
53	H, 4β, 5α
54	H, 4α, 5β
55	OAc, 4α, 5β



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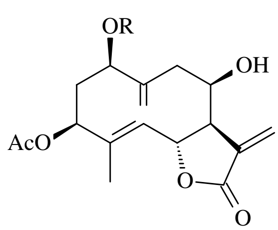
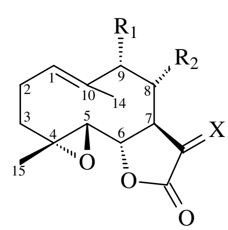
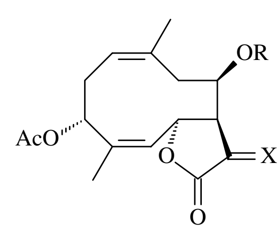


	R
57	H
58	OH

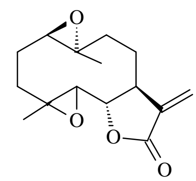


	R_1	R_2	X
59	H	H	CH_2
60	H	OH	CH_2
61	H	OAc	CH_2
62	H	OAng	CH_2
63	H	OTig	CH_2
64	H	OiBu	CH_2
65	H	O2MeBu	CH_2
66	H	OiVal	CH_2
67	OH	H	CH_2
68	OAc	H	CH_2
69	OAc	H	βCH_3, H



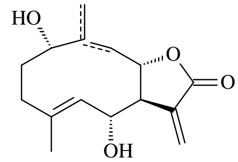
	R	X
70	H	CH_2
71	Ac	CH_2
72	H	β CH_3, H

Fig. 1 (*Continued*)



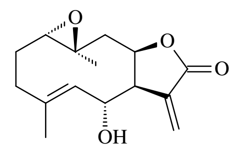
73 4α,5β

74 4β,5α



75 $\Delta^{10,14}$

76 $\Delta^{9,10}$



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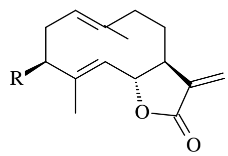
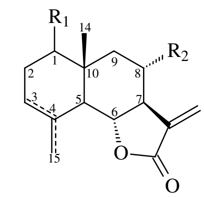
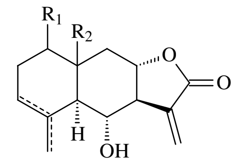


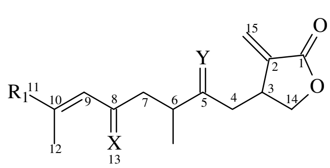
	R
78	OH
79	H
80	OAc



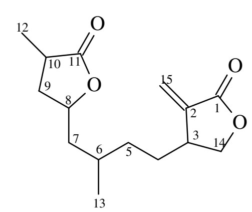
		R_1	R_2
81	$\Delta^{3,4}$	α OH	H, H
82	$\Delta^{3,4}$	α OH	OAc
83	$\Delta^{3,4}$	α OH	OAng
84	$\Delta^{3,4}$	α OH	OTig
85	$\Delta^{3,4}$	α OH	OiBu
86	$\Delta^{3,4}$	α OH	OH
87	$\Delta^{3,4}$	β OH	H
88	$\Delta^{4,15}$	β OH	H



		R_1	R_2
89	$\Delta^{3,4}$	β OH	βCH_3
90	$\Delta^{3,4}$	α OH	αCH_3
91	$\Delta^{4,15}$	β OH	βCH_3



	X	Y	R_1	double bonds and substituents
92	O	H, H	CH_3	Δ^5E
93	O	H, H	CH_3	Δ^6Z
94	O	H, H	CH_3	Δ^6E
95	OH,H	H, H	CH_3	Δ^5E
96	O	O	CH_3	Δ^6Z
97	O	O	CH_3	$\Delta^{6(13)}$
98	O	OOH, H	CH_3	$\Delta^{6(13)}$
99	O	H, H	CH_3	5,6-epoxy
100	O	H, H	CH_3	Δ^4, 6 OH
101	O	H, H	CH_3	Δ^5, 4β OH
102	O	H, H	CH_3	Δ^5, 4β OAc
103	H, H	H, H	CHO	Δ^5, 4 OH
104	H, H	H, H	CHO	Δ^5, 4 OAc



	double bonds and substituents
105	$\Delta^{5,6}$
105a	$\Delta^{5,6}$, 8 or 10 *epi*
106	5,6-epoxy
106a	5,6-epoxy, 8 or 10 *epi*
107	$\Delta^{4,5}$,6 OOH
107a	$\Delta^{4,5}$,6 OOH, 8 or 10 *epi*
108	$\Delta^{4,5}$, 6 OH
108a	$\Delta^{4,5}$, 6 OH, 8 or 10 *epi*
109	$\Delta^{6,13}$, 5 OOH
109a	$\Delta^{6,13}$, 5 OOH, 8 or 10 *epi*
110	$\Delta^{6,13}$, 5 OH
110a	$\Delta^{6,13}$, 5 OH, 8 or 10 *epi*
111	$\Delta^{6,13}$, 5 O
111a	$\Delta^{6,13}$, 5 O, 8 or 10 *epi*

Fig. 1 (*Continued*)

Genus *Anthemis*

1. Subgenus *Anthemis*

1.1. Sect. *Hiorthia*:
1. *A. carpatica* Willd.
2. *A. aetnensis* Schouw
3. *A. punctata* subsp. *cupaniana* Tod. ex Nym
4. *A. cretica* L.
5. *A. alpestris* Hoffmanns. & Link
6. *A. hydruntina* Groves
7. *A. stribrnyi* subsp. *tracica* Velen.
8. *A. plutonia* Meikle*

1.2. Sect. *Anthemis*:
1. *A. arvensis* L.
2. *A. auriculata* Boiss.
3. *A. macedonica* Boiss. & Orph.
4. *A. indurata* Del.*
5. *A. melampodina* Del.*

1.3. Sect. *Maruta*:
1. *A. cotula* L.
2. *A. pseudocotula* Boiss.

1.4. Sect. *Chia* no data

2. Subgenus *Cota*

2.1. Sect. *Anthemaria*:
1. *A. tinctoria* L.
2. *A. sancti-johannis* Turrill
3. *A. macrantha* Heufel

2.2. Sect. *Cota*
1. *A. altissima* L.
2. *A. austriaca* Jacq.
3. *A. wiedemanniana* Fisch. & C.A.Mey*

3. Subgenus *Ammanthus* no data

*Classification according to Flora Orientalis

Scheme 1. Botanical classification of the *Anthemis* species studied.

3. Conclusion

The botanical classification of *Anthemis* species (Fernandes, 1976) studied up to now is presented in Scheme 1. Most of them belong to sect. *Hiorthia*. The presence of hydruntinolides in most of the studied species lead to the suggestion that these components are characteristic for sect. *Hiorthia* (Bruno et al., 2002). However, the isolation of guaianolides, as well as lactones of other skeletal types requires a reconsideration of this suggestion. Thus, according to the skeletal type of the lactones two groups of species could be distinguished. The first one comprises of species containing guaianolides (*A. alpestris, A. hydruntina* and *A. aetnensis*) and the second one consists of species producing germacranolides (*A. stribrnyi* subsp. *tracica* and *A. punctata* subsp. *cupaniana*). The presemce of guaianolide and germacranolide "subsections" can also be seen in the dendogram (Fig. 2). Although, *A. carpatica* and *A. cretica* are more closely related to the guaianolide "subsection" they could not be unambiguously referred in any of them. These two species were combined by the cluster analysis and were placed close to the guaianolide producing plants of sect. *Hiorthia*. Obviously, further studies are required for elucidation the chemotaxonomy in sect. *Hiorthia*.

The similarity of the lactones isolated from the species belonging to sect. *Anthemis* (*A. arvensis, A. auriculata* and *A. indurata*) and sect. *Maruta* (*A. cotula* and *A. pseudocotula*) shows their close relationship. As no linear irregular lactones have been found in any other section, they could be regarded as a chemotaxonomic marker of sections *Anthemis* and *Maruta*. In view of the observations discussed above and the fact that the germacranolides dominate in *A. mace-*

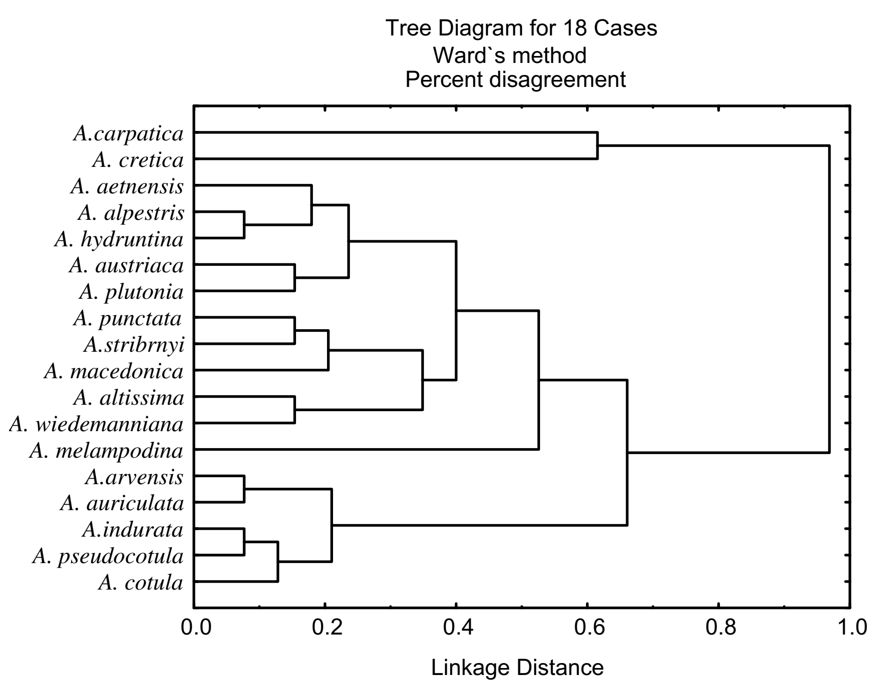


Fig. 2. Dendogram. Tree clustering was made by Statistic 6.0 for 18 cases using percent disagreement for distance measuring and Ward's methods as linkage rule.

donica, suggested more affinities to sect. *Hiorthia* (Kuzmanov, 1984). A close relationship was demonstrated by the cluster analysis between *A. macedonica* and the germacranolides containing species from sect. *Hiorthia* (*A. stribrnyi* subsp. *tracica* and *A. punctata* subsp. *cupaniana*). It is noteworthy that *A. melampodina* differed in its lactone composition from all the species studied so far. The described compounds do not support its classification in sect. *Anthemis* (Boissier, 1875). This species is isolated in the dendogram of the cluster analysis (Fig. 2).

The species from subgenus *Cota* are divided into two sections, *Anthemaria* and *Cota* according to the taxonomical scheme. The significant difference in their lactone contents (presence/absence) supports this classification. Thus, the species from sect. *Anthemaria* have been found to be free of this class of secondary metabolites, while these from sect. *Cota* – *A. altissima*, *A. wiedemanniana*, and *A. austriaca* was reported to contain germacranolides, eudesmanolides, and guaianolides. Regardless of the skeletal type of the isolated lactones, all of them possess a 12,8-closed lactone ring, which could be pointed as a characteristic feature of sect. *Cota*. The cluster analysis showed a very high similarity between *A. altissima* and *A. wiedemanniana*. Although in the dendogram *A. austriaca* is situated closer to the "guanolide" containing species of sect. *Hiorthia* than to *A. altissima* and *A. wiedemanniana*, the 12,8-closed lactone ring of the isolated lactones defined its place in sect. *Cota*. Further phytochemical studies will answer the question if the above mentioned characteristics are specific for sect. *Anthemaria*, and sect. *Cota*.

The last species, which have to be discussed, is the Cypriot endemic *A. plutonia*. The lactone profile, as well as the cluster analysis (Fig. 2) showed high degree of similarity between *A. plutonia* and the guaianolide-containing species of sect. *Hiorthia*.

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