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Review

Sesquiterpenoids in subtribe Centaureinae (Cass.) Dumort (tribe Cardueae, Asteraceae): Distribution, ^{13}C NMR spectral data and biological properties

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In memory of Professor Werner Herz, Department of Chemistry, The Florida State University, Tallahassee, FL, USA, who dedicated his life to the chemistry of sesquiterpenoids.

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Effects on plants

ABSTRACT

Asteraceae Bercht. & J. Presl is one of the biggest and most economically important plant families. The taxonomy and phylogeny of Asteraceae is rather complex and according to the latest and most reliable taxonomic classification of Panero & Funk, based on the analysis of nine chloroplast regions, the family is divided into 12 subfamilies and 35 tribes. One of the largest tribes of Asteraceae is Cardueae Cass. with four subtribes (Carlininae, Echinopinae, Carduinae and Centaureinae) and more than 2500 species. Susanna & Garcia-Jacas have organized the genera of Centaureinae (about 800 species) into seven informal groups, which recent molecular studies have confirmed: 1. Basal genera; 2. Volutaria group; 3. Rhaponticum group; 4. Serratula group; 5. Carthamus group; 6. Crocodylium group; 7. Centaurea group.

This review summarizes reports on sesquiterpenoids from the Centaureinae subtribe of the Asteraceae family, as well as the ^{13}C NMR spectral data described in the literature.

It further reviews studies concerning the biological activities of these metabolites.

For this work, literature data on sesquiterpenes from the Centaureinae subtribe were retrieved with the help of the SciFinder database and other similar data banks. All entries from 1958 until the end of 2011 were considered. This review is addressed to scientists working in the metabolomics field such as chemists, botanists, etc., the spectroscopic data reported make this work a good tool for structural elucidation, the biological section gives useful information to those who wish to study the structure activity relationships.

Contents

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1. Introduction

Asteraceae Bercht. & J. Presl is one of the biggest (more than 23,000 currently accepted species spread across 1620 genera) and most economically important plant families. In fact, many economically important weeds, for example hawkweeds (*Hieracium* sp.), thistles (*Cirsium* sp., *Carduus* sp. and other representatives from tribe Cardueae), yellow star thistle (*Centaurea solstitialis* L.) and dandelion (*Taraxacum officinale*) belong to the Asteraceae. Sunflowers (*Helianthus annuus*) are grown for the oil in their seeds and safflowers (*Carthamus tinctorius*) have been used for a long time as a textile dye. Artichoke (*Cynara cardunculus*) is an example of a crop plant belonging to this family, and many species are used as flavor herbs (marigold, various daisies, fleabane, chrysanthemums, dahlias, zinnias) or medicines (grindelia, echinacea, yarrow and many others). Furthermore, pyrethrum daisies (*Tanacetum coccineum*) provide a popular and relatively bio-friendly insecticide (Smissen, 2003).

According to the last and most reliable taxonomic classification of Panero and Funk (2002, 2008), based on analysis of nine chloroplast regions, the family is divided into 12 subfamilies and 35 tribes. One of the largest tribes of the Asteraceae is Cardueae Cass. with four subtribes (Carlininae, Echinopinae, Carduinae and Centaureinae) and more than 2500 species. Subtribe Centaureinae (about 800 species) is the most derived group and is characterized by achenes with a lateral–adaxial insertion areole, a double pappus, and, with a few exceptions, unarmed leaves (Wagenitz and Hellwig, 1996). Susanna and Garcia-Jacas (2007) have organized the genera of Centaureinae into several informal groups, which recent molecular studies have confirmed as natural: 1. Basal genera;

Table 1
List of the studied Centaureinae taxa, divided into seven groups, proposed by Susanna and Garcia-Jacas.

Group 1 Basal genera	Group 2 Volutaria group	Group 3 Rhaponticum group	Group 4 Serratula group	Group 5 Carthamus group	Group 6 Crocodylium group	Group 7 Centaurea group
Aetheopappus (Cass.) Wagenitz & Hellwig	*Amberboa* Vall. (= *Volutarella* Cass.)	*Acroptilon* Cass.	*Serratula* L. s.str.	*Carthamus* L.	*Crocodylium* Vaill	*Acrolophus* Cass.
Amblyopogon (DC.) Wagenitz & Hellwig	*Cyanopsis* Cass.	*Callicephalus* C.A. Mey		*Phonus* Hill.		*Aegialophila* Boiss. & Heldr.
Cheirolophus Cass.	*Goniocaulon* Cass.	*Centaurothamnus* Wagenitz & Dittrich		*Carduncellus* Adans.		*Calcitrapa* Adans.
Crupina (Pers.) DC.	*Karvandarina* Rech. f			*Femeniasia* Susanna		*Centaurea* L. s.str.
Czerniakowskya (Czerep.) Wagenitz & Hellwig	*Mantisalca* Cass.	*Leuzea* DC.				*Chartolepis* Cass.
Heterolophus (Cass.) Wagenitz & Hellwig	*Plagiobasis* Schrenk	*Ochrocephala* Dittrich				*Cnicus* L.
Hyalinella (Tzvelev) Wagenitz & Hellwig	*Russowia* C.Winkl.	*Oligochaeta* (DC) K. Koch				*Colymbada* Hill
Odontolophoidei (Tzvelev) Wagenitz & Hellwig	*Tricholepis* DC.	*Rhaponticum* Vall.				*Corethropsis* DC.
Odontolophus (Cass.) Wag. et Hell.	*Valutaria* Cass.	*Stemmacantha* Cass.				*Cyanus* Mill.
Plectocephalus D.Don						*Grossheimia* Sosn. & Takht.
Psephellus Cass.						*Hymenocentron* (Cass.) DC.
Rhaponthicoides Vaill.						*Jacea* Mill.
Sosnowskya (Takht.) Wagenitz & Hellwig						*Lepteranthus* (DC.) DC.
Stizolophus Cass.						*Melanoloma* Cass.
Uralepis (DC.) Wagenitz & Hellwig						*Mesocentron* (Cass.) DC.
Xanthopsis (DC.) Wagenitz & Hellwig						*Microlophus* (Cass.) DC.
Zoegea L.						*Paraphysis* (DC.) Wagenitz
						Pectinastrum (Cass.) DC.
						Phalolepis (Cass.) DC.
						Plumosipappus (Czerep.) Wagenitz
						Pseudophaeopappus Wagenitz
						Pseudoseridia Wagenitz
						Protocyanus Dobrocz.
						Pteracantha Wagenitz
						Ptosimopappus Boiss
						Seridia Juss.
						Seridioides DC.
						Solstitiaria (Hill) Dobrocz.
						Stephanochilus Coss. & Durieu ex Benth. & Hook f.
						Tetramorphaea (DC.) Boiss.
						Triplocentron (Cass.) Spach
						Wagenitzia Dostàl

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2. Volutaria group; 3. Rhaponticum group; 4. Serratula group; 5. Carthamus group; 6. Crocodylium group; 7. Centaurea group.

Basal genera – unarmed, annual to perennial herbs or shrubs with solitary or corymbose capitula and double pappus; basal chromosome numbers are usually $x = 15$.

Volutaria group – annual to perennial herbs with heterogamous capitula and large and showy sterile radiant florets, with staminodes. Achenes have basal hilum and pappus of scales.

Rhaponticum group – unarmed perennial herbs with homogamous capitula and involucral bracts with very large, scarious appendages, usually silvery-white; pappus is deciduous in a ring.

Serratula group – unarmed perennial herbs or shrubslets with homogamous capitula and rudimentary appendages of bracts; achenes have basal hilum and double, easily deciduous pappus.

Carthamus group – annual or perennial herbs or shrublets, usually spiny with homogamous capitula and compressed, very hard achenes, which have lateral hilum and double pappus.

Crocodylium group – annual or perennial herbs with fleshy, glandular leaves and heterogamous capitula. All florets are with many stalked glands and densely sericeous achenes.

Centaurea group – annual to perennial herbs or shrubs, usually unarmed with heterogamous capitula and scarious involucral bracts with a variable apical appendage, spiny or unarmed. Sterile florets are radiant and showy; achenes – oblong, compressed with lateral–adaxial insertion areole; pappus is double with pinnulate or plumose outer bristles; basal chromosome numbers are $x = 7$, 8, 9, 10, 11, 12.

This review summarizes reports on sesquiterpenoids from the Centaureinae subtribe of the Asteraceae family, as well as the ^{13}C NMR spectral data described in the literature.

According to the taxonomic scheme of Susanna and Garcia-Jacas (2007), the genera of subtribe Centaureinae are classified in seven groups. In Table 1 are listed the Centaureinae taxa, studied so far by reason of their horology, karyology, genome size, DNA sequences, secondary metabolites, etc., as each taxon is arranged in the appropriate group, following the classification mentioned above. Some of the taxa in the Table have generic rank, while other are subgenera, sections or synonyms. Our aim was to include in the table all investigated Centaureinae taxa, but not to define their taxonomic rank. The Table contains a total of 72 taxonomic units.

The larger group is Centaurea (group 7) that comprises 32 taxa. So far only 19 of the 72 representatives of the subtribe Centaureinae have been investigated for the occurrence of sesquiterpenes.

As we can see from the data here reported, not only most species but also the majority of the genera of the Centaureinae have not yet been investigated for their sesquiterpene profile. The authors hope that the compilation of data provided in the present review will be helpful for people who plan to conduct further research on the Centaureinae, as they might provide first indications on which compounds to expect in members of this subtribe not yet investigated.

2. Sesquiterpenes

An extensive bibliographic search identified a total of 287 different sesquiterpenes from 218 species belonging to these 19 genera, among which the most intensively studied genera is *Centaurea* (166 taxa). The analysis of the sesquiterpene structures of the subtribe Centaureinae allows us to point out some interesting chemotaxonomic structural features. Except for *Centaurea calcitrapa*, *C. solstitialis* and *Serratula latifolia*, from which also compound **287** and two bisabolanes (**285**–**286**) were isolated, in all the other taxa of Centaureinae only germacranes, elemanes, eudesmanes and guaianes occur (Fig. 1). With the exception of three eudesmanes (**121**, **122**, **124**) and four guaianes (**280**–**283**) isolated from *S. latifolia* and a few other eudesmanes occurring mainly in the genera *Cheirolophus* and *Phonus*, all the sesquiterpenes have an α-oxygenated function at C-6 that, normally, is involved in the formation of the C-6/C-12 γ-lactone or, in some cases, is present as a free hydroxyl group. In contrast to other genera of the Asteraceae family, belonging to different subtribes, the oxygenated function at C-8 is almost always α-orientated and, if present, the ester side chains are often linked at this carbon, although it is possible to find the ester moiety in other positions. The 42 side chains present in the sesquiterpenoids from Centaurineae subtribe are depicted in Fig. 2 and Table 2 reports their ^{13}C NMR spectroscopic data.

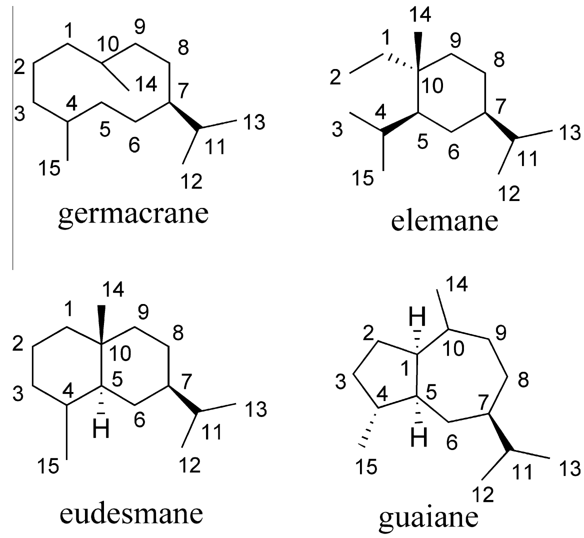

Fig. 1. Sesquiterpene skeletons.

All the sesquiterpenes are listed with their semi-systematic and trivial names and the genera and species, ordered alphabetically, in which the compounds have been found. By far the most common compound in the Centaureinae is cnicin (**19**) present in 83 taxa followed by the guaianolides cynaropicrin (**162**, 68 taxa), janerin (**208**, 38 taxa) and chlorohyssopifolin A (**224**, 29 taxa).

2.1. Germacranes

The germacranes (68 compounds) detected in the subtribe Centaureinae are listed in Table 3. Except for the heliangolides **59**–**68**, present in *Centaurea paui*, *Centaurea tweediei* and *Centaurea sulphurea*, and for a few C10(C14) enes all of them have a *trans*-C-1(C-10)/*trans*-C-4 configuration. They are almost all C-6/C-12 olides with the typical exocyclic C-11/C-13 double bond or with a C-11/C-13 dihydro moiety: only compounds **51** and **52** do not have the lactone and the artemisiifolin derivatives **53**–**57** show a C-8/C-12 olide ring. The presence of a primary alcohol or acetoxy at C-15 and of the α-oxygenated function at C-8 are common features for almost all these germacranolides: in fact only few compounds have a C-15 methyl, mainly co-occurring with a C-4/C-5 epoxy ring, and just nine (**1**–**3**, **5**, **28**, **38**, **48**, **51**, **52**) are devoid of the oxygenated function at C-8.

Table 4 reports a complete list of all ^{13}C NMR spectroscopic data quoted in the literature.

2.2. Elemanes

All the elemanes (29 compounds, Table 5) have an α-orientated hydroxyl or ester at C-8 (except **87** which is devoid of functionality) and an oxygenated function at C-15, mainly a primary alcohol, but in three cases (compounds **70**, **83**, and **85**) an aldehyde. In five cases (compounds **93**–**97**) the C-6/C-

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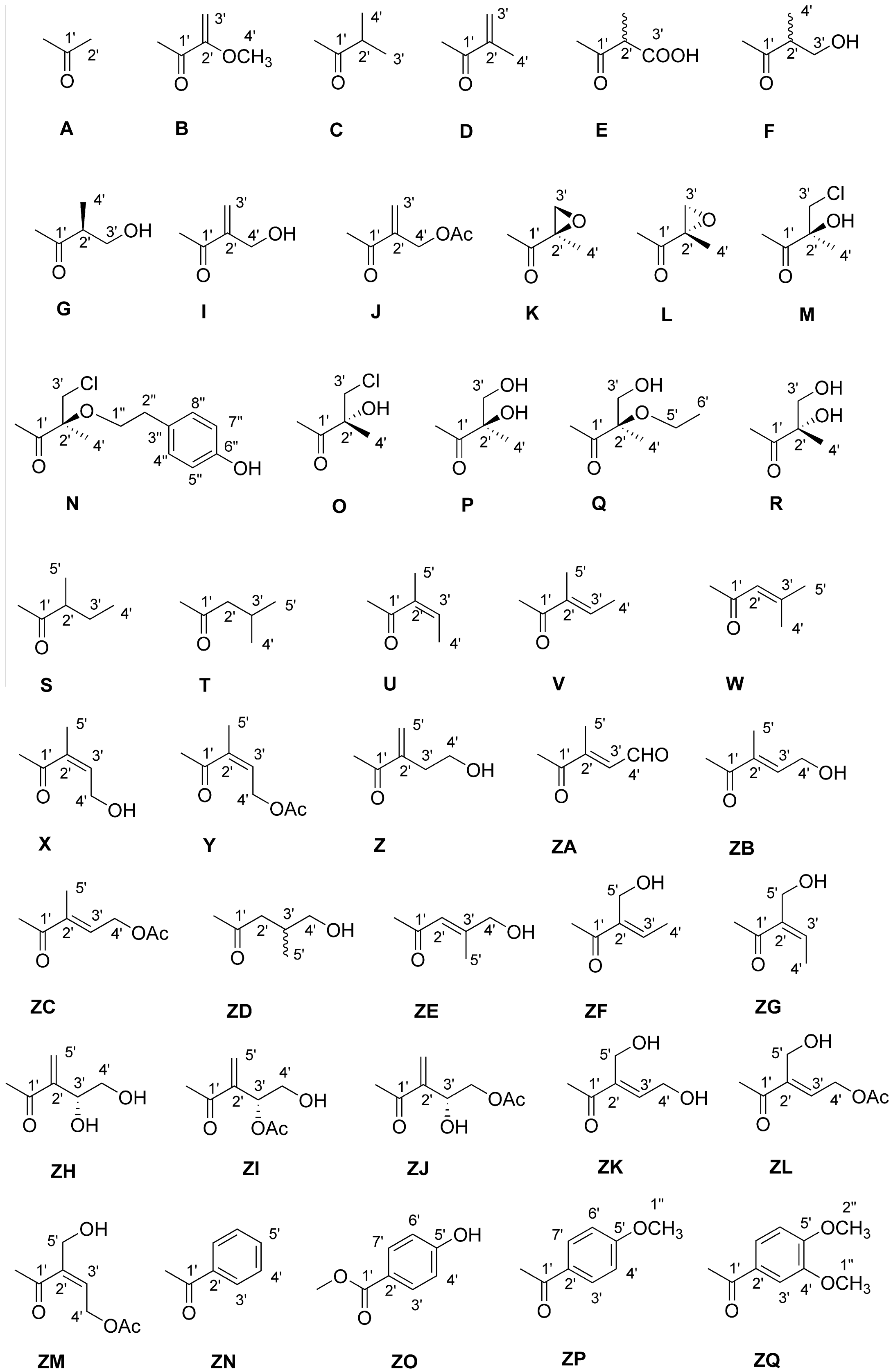

Fig. 2. Natural ester chains (acyl groups).

12 γ-lactone is open showing a free α-hydroxyl at C-6 and a carbomethoxy function at C-12. Only compound **92** has a C-8/C-12 γ-lactone. Table 6 reports a complete list of all ^{13}C NMR spectroscopic data quoted in the literature.

Table 2
^{13}C NMR spectral data ($CDCl_3$) of the side chains (S.C.) in sesquiterpenoids in the Subtribe Centaureinae.

S.C.	1′	2′	3′(7′)	4′(6′)	5′	1″	2″	3″	4″,8″	5″,7″	6″	Ref.
A	170.5	20.8										Cardona et al. (1997)
B												not reported in the literature
C	176.0	34.1	19.3	18.5								Bruno et al. (2011)
D	166.1	136.2	124.6	18.4								Bruno et al. (2011)
E[a]	169.7	45.9	180.2	15.2								Khan et al. (2004a)
F	174.8	41.9	64.4	13.5								Bruno et al. (2011)
F[a]	174.5	42.2	63.9	14.9								Khan et al. (2004a)
G	175.1	42.4	64.4	13.5								Marco et al. (1992)
I	165.2	139.0	127.6	62.3								Bruno et al. (2011)
I[a]	165.7	141.0	125.1	61.8								Khan et al. (2005a)
J	164.3	135.0	121.5	62.2		170.3	20.6					Buděšínský and Šaman (1995)
J[a]	167.0	nr	nr	nr		175.0	21.0					Bruno et al. (2011)
K	169.9	53.8	52.8	17.3								Hamburger et al. (1993)
L	170.1	53.7	52.9	17.2								Hamburger et al. (1993)
M	173.1	74.7	51.2	23.4								Hamburger et al. (1993)
N[b]	173.9	79.3	51.8	24.0		71.5	36.4	131.0	116.2	130.9	156.2	Dai et al. (2001)
O	173.1	75.1	50.9	23.9								Hamburger et al. (1993)
P	175.0	75.8	68.5	21.6								Bruno et al. (2005a)
Q												not reported in the literature
R	174.8	76.0	68.1	21.6								Fernandez et al. (1989)
S	175.4	41.3	26.6	11.5	16.5							Buděšínský and Šaman (1995)
T	171.4	43.3	25.3	22.2	22.2							Buděšínský and Šaman (1995)
U	166.4	126.9	140.0	15.8	20.3							Buděšínský and Šaman (1995)
V	166.7	128.4	138.6	14.6	12.8							Bruno et al. (2011)
W	164.9	115.1	159.3	20.4	27.5							Buděšínský and Šaman (1995)
Y	165.5	127.8	140.2	63.0	19.3	171.1	20.9					Buděšínský and Šaman (1995)
Z	166.9	136.6	35.0	61.1	128.0							Buděšínský and Šaman (1995)
ZA[a]	166.6	130.2	132.7	193.1	13.2							Youssef (1998)
ZB	166.1	135.0	141.3	59.8	12.8							Bruno et al. (2011)
ZB[c]	166.8	126.9	143.7	59.2	12.5							Youssef and Frahm (1994a)
ZC[a]	168.2	128.9	143.5	59.7	12.6	176.4	22.1					Youssef and Frahm (1994a)
ZD	172.1	38.4	32.7	67.1	16.7							Bruno et al. (2011)
ZE	165.2	112.4	159.9	66.8	15.7							Bruno et al. (2011)
ZF	166.4	131.7	140.7	14.1	56.7							Bruno et al. (2011)
ZF[a]	167.4	132.1	141.9	14.3	55.7							Youssef (1998)
ZG	165.6	131.4	142.5	15.7	63.8							Buděšínský and Šaman (1995)
ZH[a]	166.6	142.3	71.9	66.7	127.0							Csapi et al. (2010)
ZH[d]	165.2	141.9	70.2	65.4	125.3							Barrero et al. (1997a)
ZH[b]	166.6	142.4	71.8	66.7	127.2							Santos et al. (1995)
ZJ	164.6	138.3	69.7	67.1	127.6	171.4	20.8					Karioti et al. (2002)
ZK	165.9	131.5	145.1	58.8	56.8							Buděšínský and Šaman (1995)
ZL	165.1	130.6	138.6	63.3	62.5	171.1	20.5					Saroglou et al. (2005)
ZM	n.r.	n.r.	141.5	63.2	62.5	n.r.	20.8					Cardona et al. (1991)
ZN	165.9	130.2	129.7	128.7	133.3							Buděšínský and Šaman (1995)
ZO[b]	167.1	122.1	132.7	115.7	162.6							Stevens et al. (1991)
ZP	164.7	122.3	132.4	114.0	163.7	55.6						Buděšínský and Šaman (1995)
ZQ	166.8	123.9	114.0 (124.1)	146.1 (111.7)	150.0	56.0	51.8					Khan et al. (2008)

n.r. = not reported.
[a] In MeOD.
[b] In acetone-d_6.
[c] In CD_2Cl_2/DMSO-d_6 7:1.
[d] In DMSO-d_6.

2.3. Eudesmanes

The eudesmane (44 compounds, Table 7) all have a *trans* fused decalin moiety. Many of them carry a free β-oriented hydroxyl group at C-1 and an aldehyde at C-4 that can be α or β oriented. The stereochemistry of C-4 can easily be determined by ^{1}H NMR spectra. In fact, in the case of 15β-CHO (compounds **103**,**107**, **109**,**111**,**113**,**117**,**119**,**138**) the signal of the aldehydic proton can be found in the range 9.94–9.91 δ (*brs*), whereas if the aldehydic group is α-orientated (compounds **101**,**102**,**104**,**105**,**108**,**110**, **112**,**115**,**118**,**137**), the proton signal is up-field shifted (9.68–9.33 δ, *d*, *J* = 4.2–3.9 Hz). Also some eudesmanes show the presence of a carboxy or carbomethoxy group at C-12, rather than the γ-lactone. Table 8 reports a complete list of all ^{13}C NMR spectroscopic data quoted in the literature.

2.4. Guaianes

Guaianes comprise the most numerous class, containing 143 compounds (Table 9). They have all a 1,5-*cis* junction and, with the exception of compounds **280**–**283**, isolated from *S. latifolia*, they are all *trans*-6,12 lactones. The presence of a C-8 oxygenated function (α-alcohol or ester, never ketone) is also a common feature. There are, however, a few exceptions: **216** and **283** carry an oxygenated function in C-1, while a few compounds carry this function on C-9 (**151**, **153**, **155**, **156**, **271**). Also the occurrence of a C-10/C-14 double bond is a common functionality, and only **152**, **154**, **262**, **272**, **273**, and **280**–**282** have a different structural moiety. Guaianes listed in Table 9 were grouped on the basis of the C-4/C-15 functionality: double bound (**142**–**205**), epoxyde (**206**–**216**), chlorohydrine (**217**–**235**), diol (**236**–**261**), methyl

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Table 3
Germacranes isolated from taxa of the Subtribe Centaureinae.

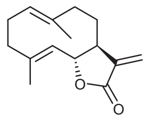
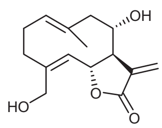
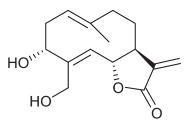
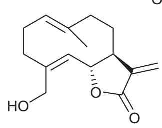
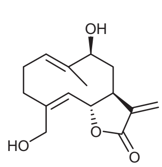
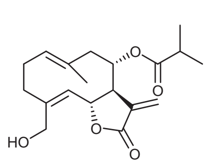
No	Structure	Name	Taxa	Ref.
1		costunolide	*Centaurea acaulis*	Bentamane et al. (2005)
			Centaurea kurdica	Appendino and Özen (1993)
2		8-Desoxy-salonitenolide; 15-hydroxycostunolide	*Centaurea kurdica*	Appendino and Özen (1993)
3		3α,15-Dihydroxy-costunolide	*Centaurea lusitanica*	Nowak et al. (1989a), Nowak (1992)
4		Salonitenolide	*Aegialophila pumila*	El-Marsy et al. (1984)
			Centaurea achaia	Skaltsa et al. (2000a)
			Centaurea affinis	Janaćković et al. (2004)
			Centaurea alba	Fernandez et al. (1995)
			Centaurea alba ssp. *caliacrae*	Geppert et al. (1983)
			Centaurea alba ssp. *deusta*	Geppert et al. (1983)
			Centaurea aspera	Barrero et al. (1995)
			Centaurea aspera ssp. *scorpiurifolia*	Barrero et al. (1995)
			Centaurea aspera ssp. *stenophylla*	Barrero et al. (1995), Marco et al. (2005)
			Centaurea bombycina	Barrero et al. (2000)
			Centaurea calcitrapa	Geppert et al. (1983), Jakupovic et al. (1986)
			Centaurea crithmifolia	Geppert et al. (1983), Gousiadou and Skaltsa (2003)
			Centaurea crocodylium	Horoszkiewicz-Hassan and Nowak (2001)
			Centaurea derventana	Tešević et al. (1998a)
			Centaurea eriophora	Geppert et al. (1983)
			Centaurea friderici	Geppert et al. (1983)
			Centaurea grisebachii	Djeddi et al. (2008a)
			Centaurea iberica	Sham'yanov et al. (1998)
			Centaurea malacitana	Barrero et al. (1988), Barrero et al., 1995
			Centaurea maroccana	Barrero et al. (2000)
			Centaurea melitensis	Barrero et al. (1989)
			Centaurea orphanidea	Gousiadou and Skaltsa (2003)
			Centaurea paniculata	Geppert et al. (1983)
			Centaurea paui	Cardona et al. (1997), Gousiadou and Skaltsa (2003)
			Centaurea pontica	Geppert et al. (1983)
			Centaurea pseudomaculosa	Turdybekov et al. (1989), Adekenov (1995)
			Centaurea salonitana	Suchy et al. (1967), Rybalko et al. (1975), Gonzalez et al. (1977a), Daniewski et al. (1992), Nowak et al. (1996)
			Centaurea stoebe	Huneck et al. (1986a)
			Centaurea weldeniana	Geppert et al. (1983)
			Cheriolophus intybaceus	Marco et al. (1994)
			Cnicus benedictus	Vanhaelen-Fastre and Vanhaelen (1974), Vanhaelen-Fastre and Vanhaelen (1976), Vanhaelen and Vanhaelen-Fastre (1975), Tsankova et al. (1994)
5		Stenophyllolide	*Centaurea aspera*	Marco et al. (2005)
			Centaurea aspera ssp. *scorpiurifolia*	Barrero et al. (1995)
			Centaurea aspera ssp. *stenophylla*	Sanchez Paradera et al. (1968), Gonzalez et al. (1977a), Picher et al. (1984a), Amigo et al. (1984), Barrero et al. (1995), Marco et al. (2005)
			Centaurea aspera ssp. *subinermis*	Cardona et al. (1991)
			Centaurea lusitanica	Nowak et al. (1996)
			Centaurea malacitana	Barrero et al. (1988), Barrero et al. (1995), Barrero et al. (1997a)
6		15-Hydroxy-8α-isobutyryloxy-costunolide; 4′-desoxyarctiopicrin	*Cheiroluphus intybaceus*	Marco et al. (1994)
			Cheiroluphus mauritanicus	Marco et al. (1994)

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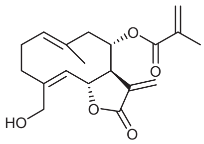
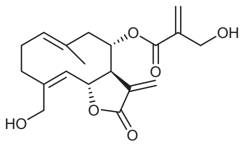
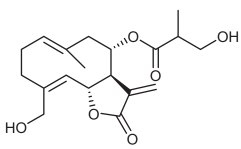
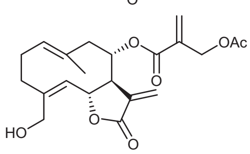
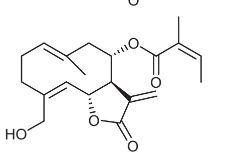
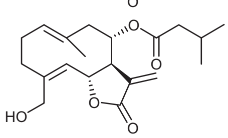
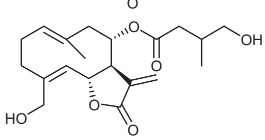
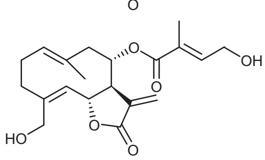
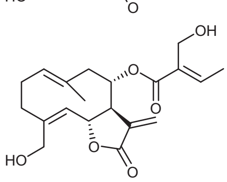
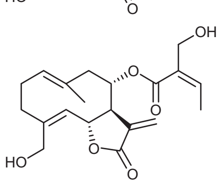
Table 3 (*continued*)

No	Structure	Name	Taxa	Ref.
7		8α-(2′-methyl-2′-propenoyl)-salonitenolide; 15-hydroxy-8α-(α-methylacryloyl)-costunolide	*Centaurea achaia* *Cheiroluphus intybaceus* *Cheirolophus* × *hortigenus*	Skaltsa et al. (2000a) Marco et al. (1994) Marco et al. (1994)
8		Onopordopicrin	*Centaurea achaia* *Centaurea aspera* *Centaurea aspera* ssp. *stenophylla* *Centaurea eryngioides* *Centaurea incana* *Centaurea melitensis* *Centaurea moesiaca* *Centaurea nicaensis* *Centaurea scoparia* *Centaurea sonchifolia* *Centaurea tagananensis* *Centaurea tweediei* *Cheirolophus x hortigenus* *Cheiroluphus intybaceus*	Skaltsa et al. (2000a) Marco et al. (2005) Marco et al. (2005) Sarg et al. (1989) Barrero et al. (2000) Barrero et al. (1989) Trendafilova et al. (2007) Bruno et al. (1996) Youssef (1998) Lonergan et al. (1992) Gonzalez et al. (1984), Nowak et al. (1986a) Fortuna et al. (2001), Cabral et al. (2008), Bach et al. (2011) Marco et al. (1994) Marco et al. (1994)
9		salonitenolide-8-(4′-hydroxyisobutyrate); arctiopicrin	*Centaurea eryngioides* *Centaurea gigantea* *Centaurea melitensis*	Sarg et al. (1989) Shoeb et al. (2007a) Barrero et al. (1989)
10		amarin	*Centaurea amara* *Centaurea malacitana* *Centaurea nicaensis*	Gonzalez et al. (1980a) Barrero et al. (1988) Bruno et al. (1996)
11		8α-Angeloyl-salonitenolide	*Centaurea aspera* ssp. *stenophylla*	Marco et al. (2005)
12		Arbutifolin	*Centaurea arbutifolia*	Gonzalez et al. (1981)
13		8α-(4′-hydroxy-3′-methylbutanoyl)-salonitenolide	*Centaurea achaia* *Centaurea gigantea*	Skaltsa et al. (2000a) Shoeb et al. (2007a)
14		8α-(4′-hydroxy-2′-methyl-2′-butenoyl)-salonitenolide	*Centaurea achaia*	Skaltsa et al. (2000a)
15		8α-(5′-hydroxytigloyl)-salonitenolide	*Centaurea achaia* *Centaurea glomerata* *Cheiroluphus intybaceus*	Skaltsa et al. (2000a) El-Marsy et al. (1985) Marco et al. (1994)
16		8α-(5′-hydroxyangeloyl)-salonitenolide	*Centaurea aspera* ssp. *stenophylla* *Centaurea moesiaca* *Centaurea phrygia* *Cnicus benedictus*	Marco et al. (2005) Trendafilova et al. (2007) Tsankova and Ognyanov (1985) Tsankova et al. (1994)

(*continued on next page*)

Table 3 (*continued*)

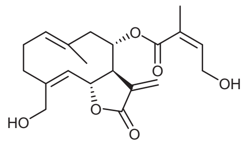
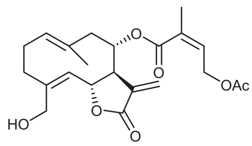
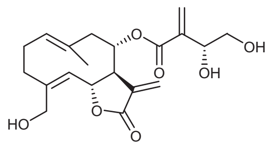
No	Structure	Name	Taxa	Ref.
17		8α-(4′-hydroxyangeloyl)-salonitenolide	*Centaurea glomerata*	El-Marsy et al. (1985)
18		8α-(4′-acetoxyangeloyl)-salonitenolide	*Centaurea aspera* ssp. *stenophylla*	Marco et al. (2005)
			Centaurea malacitana	Barrero et al. (1997a)
19		Cnicin	*Aegialophila pumila*	El-Marsy et al. (1984)
			Amberboa lippii	Mezache et al. (2010)
			Centaurea aegialophila	Bruno et al. (2001)
			Centaurea affinis	Janać ković et al. (2004), Tešević et al. (2007)
			Centaurea africana	Gonzalez et al. (1977a), Nowak et al. (1986a)
			Centaurea aggregata	Nowak et al. (1984), Gousiadou and Skaltsa (2003)
			Centaurea alba	Gonzalez et al. (1977a), Fernandez et al. (1995)
			Centaurea alexandrina	Ismail et al. (1986)
			Centaurea aplopea	Nowak et al. (1984), Gousiadou and Skaltsa (2003)
			Centaurea aplopea ssp. *lunensis*	Nowak et al. (1984), Gousiadou and Skaltsa (2003)
			Centaurea araneosa	Farrag et al. (1993)
			Centaurea arenaria	Nowak et al. (1984), Gousiadou and Skaltsa (2003), Tešević et al. (2007), Csapi et al. (2010)
			Centaurea arenaria ssp. *majorowii*	Nowak et al. (1984), Gousiadou and Skaltsa (2003)
			Centaurea arenaria ssp. *odesana*	Nowak et al. (1984), Gousiadou and Skaltsa (2003)
			Centaurea aspera	Geppert et al. (1983), Barrero et al. (1995)
			Centaurea aspera ssp. *scorpiurifolia*	Barrero et al. (1995)
			Centaurea aspera ssp. *stenophylla*	Barrero et al. (1995), Marco et al. (2005)
			Centaurea attica	Skaltsa et al. (1999), Gousiadou and Skaltsa (2003)
			Centaurea attica ssp. *drakiensis*	Nowak et al. (1984), Gousiadou and Skaltsa (2003)
			Centaurea attica ssp. *ossaea*	Nowak et al. (1984), Gousiadou and Skaltsa (2003)
			Centaurea bombycina	Barrero et al. (2000)
			Centaurea bruguierana	Rustaiyan et al. (1982), Harraz et al. (1994)
			Centaurea calcitrapa	Drozdz (1967), Rybalko et al. (1975), Gonzalez et al. (1977a), Gonzalez et al., 1978a, Karawya et al. (1975), Geppert et al. (1983), Jakupovic et al. (1986), Marco et al. (1992)
			Centaurea calolepis	Baykan Erel et al. (2011)
			Centaurea calvescens	Nowak et al. (1984), Gousiadou and Skaltsa (2003)
			Centaurea castellana	Gonzalez et al. (1977a)
			Centaurea cineraria	Nowak et al. (1984), Gousiadou and Skaltsa (2003)
			Centaurea cinerar. ssp. *busambarensis*	Bruno et al. (1998)
			Centaurea cineraria ssp. *umbrosa*	Bruno and Herz (1988);Gousiadou and Skaltsa (2003)
			Centaurea cineraria var. *circae*	Nowak et al. (1984), Gousiadou and Skaltsa (2003)
			Centaurea crocodylium	Horoszkiewicz-Hassan and Nowak (2001)
			Centaurea cuneifolia	Salan and Öksük (1999), Gousiadou and Skaltsa (2003), Tešević et al. (2007)
			Centaurea cuneifolia ssp. *pallida*	Nowak et al. (1984), Gousiadou and Skaltsa (2003)
			Centaurea derventana	Tešević et al. (1998a)
			Centaurea deusta	Karioti et al. (2002)
			Centaurea diffusa	Drozdz (1966), Rybalko et al. (1975), Gonzalez et al. (1977a), Milkova et al. (1993), Fortuna et al. (2002), Gousiadou and Skaltsa (2003), Cabral et al. (2008), Bach et al. (2011)

Table 3 (*continued*)

No	Structure	Name	Taxa	Ref.
			C. diffusa var. *brevispina* = *C. bovina*	Nowak et al. (1984), Gousiadou and Skaltsa (2003)
			Centaurea eriophora	Geppert et al. (1983)
			Centaurea eryngioides	Sarg et al. (1989)
			Centaurea exarata	Nowak et al. (1984), Nowak et al. (1986a), Gousiadou and Skaltsa (2003)
			Centaurea glaberima (*Tricholepis*)	Tešević et al. (2007)
			Centaurea granatensis	Barrero et al. (2000)
			Centaurea grisebachi	Nowak et al. (1984), Gousiadou and Skaltsa (2003), Djeddi et al. (2008a)
			Centaurea grisebachi ssp. *confusa*	Nowak et al. (1984), Gousiadou and Skaltsa (2003)
			Centaurea iberica	Drozdz (1967), Rybalko et al. (1975), Gonzalez et al. (1977a), Sham'yanov et al. (1998)
			Centaurea kartschiana	Nowak et al. (1984), Gousiadou and Skaltsa (2003)
			Centaurea leucophaea	Nowak et al. (1984), Gousiadou and Skaltsa (2003)
			Centaurea lusitanica	Geppert et al. (1983), Nowak (1992), Nowak et al. (1996)
			Centaurea maculosa	Rybalko et al. (1975), Gonzalez et al. (1977a), Kelsey and Locken (1987), Landau et al. (1994), Gousiadou and Skaltsa (2003), Meepagala et al. (2006)
			Centaurea malacitana	Barrero et al. (1988), Barrero et al. (1995, 1997a)
			Centaurea mantoudii	Nowak et al. (1984), Gousiadou and Skaltsa (2003)
			Centaurea mariolensis	Maymò et al. (1999)
			Centaurea maroccana	Barrero et al. (2000), Bentamene et al. (2007)
			Centaurea micranthos	Drozdz (1968), Gonzalez et al. (1977a)
			Centaurea moesiaca	Trendafilova et al. (2007)
			Centaurea monticola	Barrero et al. (2000)
			Centaurea napifolia	Bruno et al. (1995)
			Centaurea nicaensis	Bruno et al. (1996)
			Centaurea orphanidea	Nowak et al. (1984), Gousiadou and Skaltsa (2003)
			Centaurea ovina	Drozdz (1967), Rybalko et al. (1975), Gonzalez et al. (1977a)
			Centaurea pallescens	Ali et al. (1987)
			Centaurea pallidior	Nowak et al. (1984), Gousiadou and Skaltsa (2003)
			Centaurea paniculata ssp. *castellana*	Bruno et al. (2002)
			Centaurea paui	Cardona et al. (1997), Gousiadou and Skaltsa (2003)
			Centaurea pelia	Nowak et al. (1984), Gousiadou and Skaltsa (2003)
			Centaurea pseudomaculosa	Adekenov et al. (1979, 1986a), Adekenov (1995)
			Centaurea raphanina ssp. *mixta*	Panagouleas et al. (2003)
			Centaurea rhenana ssp. *savranica*	Nowak et al. (1984), Gousiadou and Skaltsa (2003)
			Centaurea rocheliana	Geppert et al. (1983)
			Centaurea rothmalerana	Santos et al. (1995)
			Centaurea sphaerocephala	Bruno et al. (1994)
			Centaurea spinosa	Nowak et al. (1984), Gousiadou and Skaltsa (2003), Saroglou et al. (2005)
			Centaurea splendens	Tešević et al. (2007)
			Centaurea squarrosa	Tarasov et al. (1973), Gonzalez et al. (1977a), Isamukhamedova et al. (1977)
			Centaurea stoebe	Suchy and Herout (1962), Rybalko et al. (1975), Gonzalez et al. (1977a), Huneck et al. (1986a), Tešević et al. (2007)
			Centaurea sulphurea	Geppert et al. (1983), Gonzalez et al. (1984), Barrero et al. (2000), Lakhal et al. (2010)
			Centaurea thessala ssp. *drakiensis*	Skaltsa et al. (1999), Georgiadou et al. (2000), Gousiadou and Skaltsa (2003)
			Centaurea transiens	Nowak et al. (1984), Gousiadou and Skaltsa (2003)
			Centaurea tymphaea	Nowak et al. (1984), Gousiadou and Skaltsa (2003)

(*continued on next page*)

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Table 3 (*continued*)

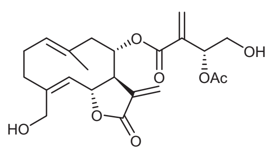
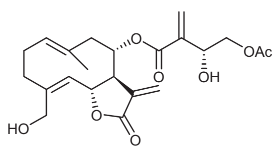
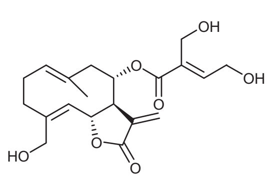
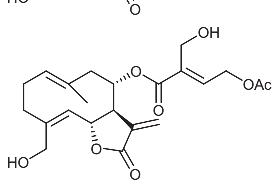
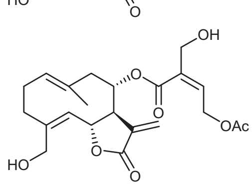
No	Structure	Name	Taxa	Ref.
			Centaurea tymphaea ssp. *brevispina*	Nowak et al. (1984), Gousiadou and Skaltsa (2003)
			Centaurea vallesiaca	Geppert et al. (1983), Landau et al. (1994), Gousiadou and Skaltsa (2003)
			Centaurea zuccariniana	Nowak et al. (1984), Koukoulitsa et al. (2002), Gousiadou and Skaltsa (2003)
			Cnicus benedictus	Korte and Beckmann (1958), Suchy et al. (1959a), Suchy et al. (1959b), Suchy et al. (1960), Vanhaelen-Fastre (1968), Vanhaelen-Fastre (1972), Samek et al. (1969), Rybalko et al. (1975), Vanhaelen-Fastre and Vanhaelen (1976), Tsankova et al. (1994), Kataria (1995)
20		Cnicin 3′-*O*-acetyl	*Centaurea deusta*	Karioti et al. (2002)
			Centaurea moesiaca	Trendafilova et al., 2007
21		Cnicin 4′-*O*-acetyl	*Centaurea alba*	Fernandez et al. (1995)
			Centaurea aspera	Barrero et al. (1995)
			Centaurea aspera ssp. *scorpiurifolia*	Barrero et al. (1995)
			Centaurea aspera ssp. *stenophylla*	Barrero et al. (1995), Marco et al. (2005)
			Centaurea attica	Skaltsa et al. (1999), Gousiadou and Skaltsa (2003)
			Centaurea calcitrapa	Jakupovic et al. (1986), Marco et al. (1992)
			Centaurea cineraria ssp. *umbrosa*	Bruno and Herz (1988), Gousiadou and Skaltsa (2003)
			Centaurea derventana	Tešević et al. (1998a)
			Centaurea deusta	Karioti et al. (2002)
			Centaurea diffusa	Fortuna et al. (2002)
			Centaurea malacitana	Barrero et al. (1988, 1995, 1997a)
			Centaurea mariolensis	Maymò et al. (1999)
			Centaurea maroccana	Barrero et al. (2000)
			Centaurea moesiaca	Trendafilova et al. (2007)
			Centaurea monticola	Barrero et al. (2000)
			Centaurea napifolia	Bruno et al. (1995)
			Centaurea orphanidea	Gousiadou and Skaltsa (2003)
			Centaurea paniculata ssp. *castellana*	Bruno et al. (2002)
			Centaurea paui	Cardona et al. (1997), Gousiadou and Skaltsa (2003)
			Centaurea sphaerocephala	Bruno et al. (1994)
			Centaurea spinosa	Saroglou et al. (2005)
			Centaurea thessala ssp. *drakiensis*	Skaltsa et al. (1999), Georgiadou et al. (2000), Gousiadou and Skaltsa (2003)
			Centaurea zuccariniana	Koukoulitsa et al. (2002)
			Cnicus benedictus	Tsankova et al. (1994)
22		8α-(4′,5′-dihydroxytigloyloxy)-salonitenolide	*Centaurea achaia*	Skaltsa et al. (2000a)
23		8α-*O*-(4′-acetoxy-2′-hydroxymethylbuten-2′-oyloxy)-salonitenolide	*Centaurea spinosa*	Saroglou et al. (2005)
24		Salonitenolide-8-*O*-(4′-acetoxy-5′-hydroxy-angelate)	*Centaurea alba*	Fernandez et al. (1995)
			Centaurea aspera	Marco et al. (2005)
			Centaurea aspera ssp. *stenophylla*	Marco et al. (2005)
			Centaurea bombycina	Barrero et al. (2000)
			Centaurea deusta	Karioti et al. (2002)
			Centaurea derventana	Tešević et al. (1998a)
			Centaurea grisebachi	Djeddi et al. (2008a)
			Centaurea moesiaca	Trendafilova et al. (2007)
			Centaurea paui	Cardona et al. (1997), Gousiadou and Skaltsa (2003)
			Centaurea stoebe	Huneck et al. (1986a)
			Centaurea thessala ssp. *drakiensis*	Skaltsa et al. (1999)

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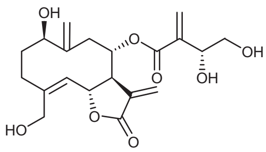
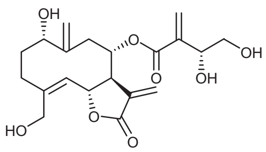
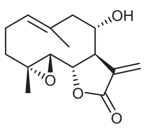
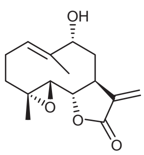
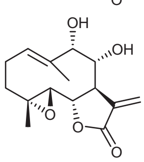
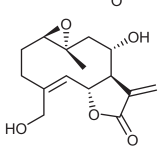
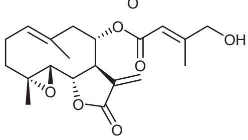
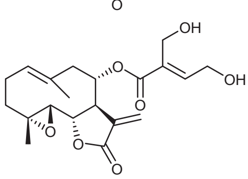
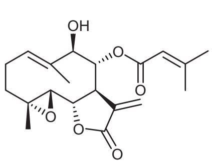
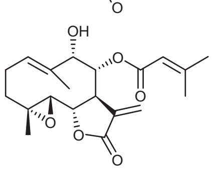
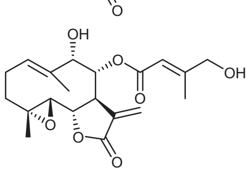
Table 3 (*continued*)

No	Structure	Name	Taxa	Ref.
25		1β,15-dihydroxy-8α-(3,4-dihydroxy-2- methylenebutanoyloxy)-4*E*,10(14),11(13)-germacratriene-12,6α- olide	*Centaurea moesiaca*	Trendafilova et al. (2007)
26		1α,15-dihydroxy-8α-(3,4-dihydroxy-2- methylenebutanoyloxy)-4*E*,10(14),11(13)-germacratriene-12,6α- olide	*Centaurea moesiaca*	Trendafilova et al. (2007)
27		stizolin	*Stizolophus balsamita*	Mukhametzhanov et al. (1969a, 1971), Rybalko et al. (1975), Gonzalez et al. (1977a),Nowak (1992), Suleimenov et al. (2005a)
28		9α-hydroxypartenolide	*Zoegea baldshuanica*	Buděšinský et al. (1984), Nowak (1992), Nowak et al. (1996)
29		8α,9α-dihydroxypartenolide	*Stizolophus balsamita*	Mukhametzhanov et al. (1969a), Nowak et al. (1996), Nowak (1992)
30		8,15-dihydroxy-1(10)-epoxy-germacr-4-ene	*Centaurea sphaerocephala*	Bruno et al. (1994)
31		1(10)-en-4α,5β-epoxy-8α-(4′-hydroxysenecioate)-germacrane	*Centaurea coronopifolia*	Öksüz and Ayyildiz (1986)
32		stizolicin	*Centaurea coronopifolia*	Mukhametzhanov et al. (1969b, 1970), Rybalko et al. (1975), Öksüz and Ayyildiz (1986)
			Centaurea solstitialis	Mukhametzhanov et al. (1969c), Rybalko et al. (1975), Gonzalez et al. (1977a), Naidenova et al. (1988)
			Stizolophus balsamita	Rybalko et al. (1975), Cassady et al. (1984), Nowak (1992)
33		balsamin	*Stizolophus balsamita*	Rybalko et al. (1976), Nowak (1992)
34		9-*epi*-balsamin	*Centaurea coronopifolia*	Öksüz and Ayyildiz (1986)
			Stizolophus balsamita	Suleimenov et al. (2005a)
35		8α-(4′-hydroxy-sencioyloxy)-9α-hydroxy-parthenolide; 9-*epi*-4′-hydroxybalsamin	*Centaurea coronopifolia*	Öksüz and Ayyildiz (1986)
			Stizolophus balsamita	Nowak et al. (1989b, 1996), Nowak (1992), Suleimenov et al. (2005a)

(*continued on next page*)

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Table 3 (*continued*)

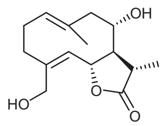
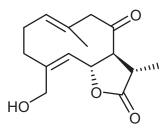
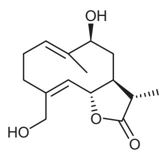
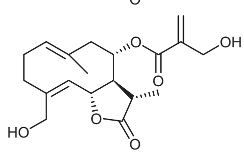
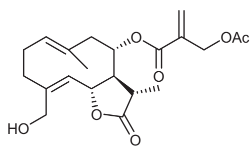
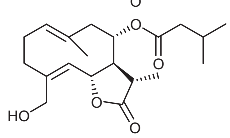
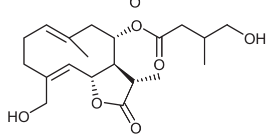
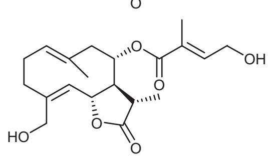
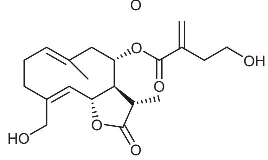
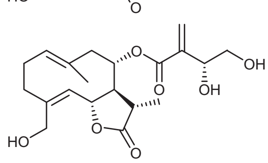
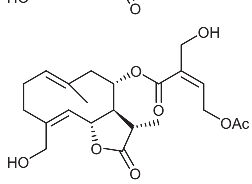
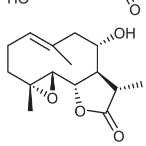
No	Structure	Name	Taxa	Ref.
36		11β,13-dihydrosalonitenolide	*Centaurea achaia* *Centaurea alba* *Centaurea aspera* *Centaurea calcitrapa* *Centaurea maroccana* *Centaurea nicaensis* *Centaurea paui* *Centaurea pullata*	Skaltsa et al. (2000a) Fernandez et al. (1995) Marco et al. (2005) Marco et al. (1992) Barrero et al. (2000) Medjroubi et al. (2003a) Cardona et al. (1997), Gousiadou and Skaltsa (2003) Djeddi et al. (2008b)
37		8-oxo-15-hydroxygermacra-1(10),*E*,4*Z*-dien-11βH-12,6α-olide	*Centaurea aspera*	Marco et al. (2005)
38		11βH,13-dihydrostenophyllolide	*Centaurea aspera* *Centaurea aspera* ssp. *stenophylla* *Centaurea aspera* ssp. *subinermis*	Marco et al. (2005) Marco et al. (2005), Picher et al. (1984b) Cardona et al. (1991)
39		11βH,13-dihydroonopordopicrin	*Centaurea glomerata*	El-Marsy et al. (1985)
40		dihydroamirin	*Centaurea amara* *Centaurea nicaensis*	Gonzalez et al. (1980a) Bruno et al. (1996)
41		11,13-dihydroarbutifolin	*Centaurea arbutifolia*	Gonzalez et al. (1981)
42		8α-(4′-hydroxy-3′-methylbutanoyl)-11β,13- dihydrosalonitenolide	*Centaurea achaia*	Skaltsa et al. (2000a)
43		8α-(4′-hydroxy-2′-methyl-2′-butenoyl)-11β,13-dihydrosalonitenolide	*Centaurea glomerata*	El-Marsy et al. (1985)
44		11β,13-dihydro-19-desoxycnicin	*Centaurea pullata*	Benayache et al. (1992), Djeddi et al. (2007)
45		11β,13-dihydrocnicin	*Centaurea nicaensis* *Centaurea pullata*	Bruno et al. (1996), Medjroubi et al. (2003a) Benayache et al. (1992), Djeddi et al. (2007)
46		8α-*O*-(4′-acetoxy-5′-hydroxyangeloyl)-11β,13-dihydrosalonitenolide	*Centaurea pullata*	Djeddi et al. (2007)
47		11,13-dihydrostizolin	*Stizolophus balsamita*	Suleimenov et al. (2005a)

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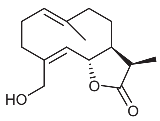
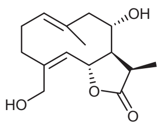
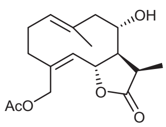
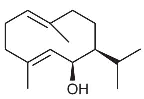
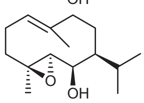
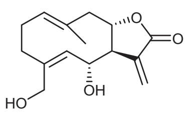
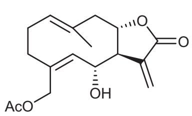
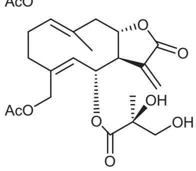
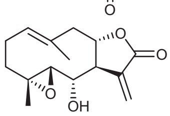
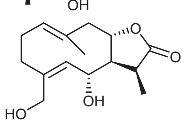
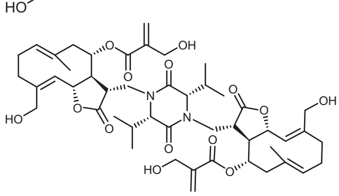
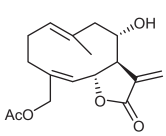
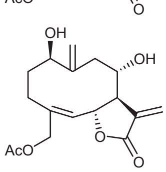
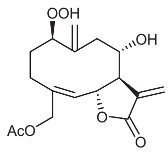
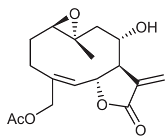
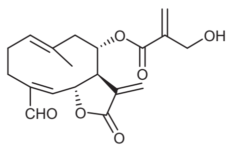
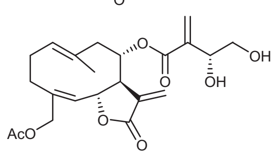
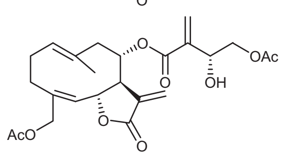
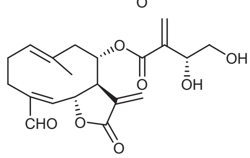
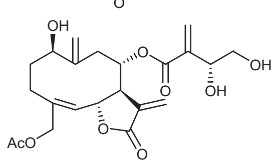
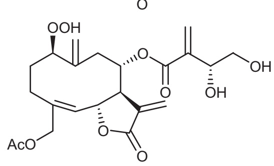
Table 3 (*continued*)

No	Structure	Name	Taxa	Ref.
48		11α,13-dihydro-8-desoxysalonitenolide	*Centaurea kurdica*	Appendino and Ö zen (1993)
49		11α,13-dihydrosalonitenolide	*Centaurea calcitrapa*	Marco et al. (1992)
50		Cebellin M	*Centaurea bella*	Nowak (1992, 1993a,b), Nowak et al. (1996)
51		germacra-1(10),4-dien-6β-ol	*Phonus arborescens*	Barrero et al. (1997b)
52		shiromool	*Phonus arborescens*	Barrero et al. (1997b)
53		artemisiifolin	*Centaurea castellana*	Gonzalez et al. (1984), Gousiadou and Skaltsa (2003)
			Centaurea polyacantha	Nowak et al. (1996)
			Centaurea seridis	Gonzalez et al. (1973a, 1977a)
			Centaurea sonchifolia	Gonzalez et al. (1984)
			Centaurea sphaerocephala	Nowak et al. (1996)
			Cnicus benedictus	Vanhaelen-Fastre and Vanhaelen (1976)
54		15-Acetylartemisiifolin	*Centaurea polyacantha*	Nowak et al. (1996)
			Centaurea seridis	Gonzalez et al. (1973a, 1977a)
			Centaurea sonchifolia	Gonzalez et al. (1984)
			Centaurea sphaerocephala	Nowak et al. (1996)
55		Scabiolide	*Centaurea scabiosa*	Suchy et al. (1962a,b, 1965a, 1968), Rybalko et al. (1975), Gonzalez et al., 1977a
			Centaurea solstitialis	Mukhametzhanov et al. (1969c)
56		isospiciformin	*Stizolophus balsamita*	Nowak et al. (1989b, 1996), Nowak (1992)
57		Salonitolide	*Centaurea salonitana*	Suchy et al. (1965b), Rybalko et al. (1975), Gonzalez et al. (1977a), Daniewski et al. (1992)
			Centaurea seridis	Gonzalez et al. (1973a, 1977a)
58		Onopordopicrin-valine dimeric adduct	*Centaurea aspera* ssp. *stenophylla*	Marco et al. (1991), Marco et al., 2005
59		15-acetoxy-8α-hydroxy-7αH,6βH-germacra-4*E*, 1(10),11(13)-trien-12,6-olide	*Centaurea paui*	Cardona et al. (1997)
60		15-acetoxy-1β,8α-dihydroxy-7αH,6βH- germacra-4*E*,10(14),11(13)-trien-12,6-olide	*Centaurea paui*	Cardona et al. (1997), Gousiadou and Skaltsa (2003)

(*continued on next page*)

Table 3 (*continued*)

No	Structure	Name	Taxa	Ref.
61		15-acetoxy-1β-hydroperoxy-8α-hydroxy-7αH,6βH-germacra-4*E*,10(14),11(13)-trien-12,6-olide	*Centaurea paui*	Cardona et al. (1997), Gousiadou and Skaltsa (2003)
62		15-acetoxy-1β,10α-epoxy-8α-hydroxy- 7αH,6βH-germacra-4*E*,11(13)-dien-12,6-olide	*Centaurea paui*	Cardona et al. (1997), Gousiadou and Skaltsa (2003)
63		8-(4′-hydroxy-methacroyloxy)-15-oxohelianga-1(10)-4,11(13)-trien-6,12-olide	*Centaurea tweediei*	Fortuna et al. (2001)
64		15-acetoxy-8α-*O*-(3,4-dihydroxy-2-methylene-butanoyloxy)- 7αH,6βH-germacra-4*E*,1(10),11(13)-trien-12,6-olide	*Centaurea paui*	Cardona et al. (1994)
			Centaurea sulphurea	Lakhal et al. (2010)
65		15-acetoxy-8α-*O*-(3,hydroxy-4acetoxy-2-methylene-butanoyloxy)- 7αH,6βH-germacra-4*E*,1(10),11(13)-trien-12,6-olide	*Centaurea paui*	Cardona et al. (1994)
66		Sulphurein	*Centaurea sulphurea*	Lakhal et al. (2010)
67		15-acetoxy-8α-*O*-(3,4-dihydroxy-2-methylene-butanoyloxy)- 1β-hydroxy-7αH,6βH-germacra-4*E*,10(14), 11(13)-trien-12,6-olide	*Centaurea paui*	Cardona et al. (1997), Gousiadou and Skaltsa (2003)
68		15-acetoxy-8α-*O*-(3,4-dihydroxy-2-methylene-butanoyloxy)- 1β-hydroperoxy-7αH,6βH-germacra-4*E*,10(14), 11(13)-trien-12,6-olide	*Centaurea paui*	Cardona et al. (1997), Gousiadou and Skaltsa (2003)

(**262**–**283**) and C15-nor (**284**). Table 10 reports a complete list of all ^{13}C NMR spectroscopic data quoted in the literature. In contrast to the other classes of sesquiterpenes, the guaianes of Centaurineae have a large variety of side chain esters linked at C-8 and many of them have a stereogenic center at C-2′. A useful tool has been identify in order to determinate the absolute stereochemistry of the C-2′ carbon of the side chain. In fact as reported in Table 11 the ^{1}H NMR values of the epimeric side chains are practically identical whereas the diagnostic signal is H13b. In the case of a C-2′ *R* stereochemistry it resonates in the range ($CDCl_3$) δ 5.56–5.64, instead for a C-2′ *S* stereochemistry the range is δ 5.71–6.07 (Table 11).

2.5. Others

Four sesquiterpenes with different skeletons are listed in Table 12 and the ^{13}C NMR spectroscopic data of carabrone (**287**) is inserted in Table 10.

3. Chemotaxonomic remarks

The analysis of sesquiterpene skeletons (Table 13) occurring in the 210 taxa belonging to the subtribe Centaureinae, reveals the presence of two main classes: 75 taxa contain exclusively guaiane-type sesquiterpenes whereas 68 taxa contain exclusively germacrane-type sesquiterpenes. Only 12 skeleton combinations among the 15 possible occur in this subtribe. No taxa contains at the same time all the four skeletons neither guaines, eudesmanes and elemanes, nor elemanes alone. Only five species do not contain either guianes or germacranes (*Centaurea cadmea*, *Centaurea granata*, *Centaurea hierapolitana*, *Centaurea phyllocephala*, *Centaurea pamphilica*).

Furthermore,*Centaurea conifera*, *Centaurea incana*, *Centaurea salonitana*, *Centaurea scabiosa* and *C. solstitialis* have been shown to have germacranes, guaianes or eudesmane depending on the collection place.

It is noteworthy that only one species (*Centaurea chilensis*) contains both guaines and elemanes but they were found in two separate investigations.

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Table 4
^{13}C NMR data of germacranes.

C	**1**$^{a}_{1}$	**2**$^{a}_{2}$	**4**$^{a}_{3}$	**5**$^{n.r.}_{4}$	**6**$^{a}_{5}$	**7**$^{a}_{5}$	**8**$^{a}_{6}$	**8**$^{b}_{3}$	**8**$^{c}_{7}$	**9**$^{c}_{7}$	**9**$^{d}_{8}$	**10**$^{n.r.}_{4}$	**11**$^{a}_{3}$	**13**$^{a}_{2}$	**13**$^{d}_{8}$	**14**$^{a}_{9}$	**15**$^{a}_{5}$	**16**$^{a}_{3}$	**18**$^{a}_{3}$
1	127.1	126.5	128.7	127.4*	129.5	129.6	129.7	129.8	129.9	130.1	129.5	130.4	129.5	129.5	129.8	129.6	129.7	129.8	129.8
2	26.3	28.6	26.3	25.3	26.4	26.4	26.0	26.3	26.4	26.8	25.7	26.8	26.3	26.3	26.4	26.3	26.4	26.3	26.3
3	39.5	35.4	35.0	34.5†	34.7	34.7	34.5	34.7	34.5	34.9	34.0	34.9	34.7	34.7	33.8[l]	29.7	34.8	34.7	34.6
4	140.1	143.3	143.6	143.3	143.8	143.8	144.5	144.2	144.7	145.0	144.9	145.1	143.8	143.8	144.9	143.7	143.7	143.9	143.9
5	127.3	128.8	128.5	126.0*	128.8	128.7	127.9	128.4	128.6	128.6	128.5	129.0	128.8	128.7	128.3	128.6	128.6	128.6	128.6
6	81.9	80.1	76.5	77.8	77.2	77.1	77.3	76.6	76.9	77.1	77.3	77.4	76.7	76.6	76.9	76.4	76.5	76.6	76.7
7	50.4	50.5	54.7	46.6	52.9	53.1	52.8	53.0	53.0	52.9	52.4	53.5	53.0	52.7	52.0	53.0	53.1	53.0	52.9
8	28.2	27.7	70.9	35.7†	72.3	72.9	72.8	73.1	73.2	73.1	72.8	74.0	72.2	72.5	72.7	72.9	73.0	72.8	73.0
9	41.0	40.8	52.5	79.5	48.9	48.8	48.8	48.7	48.7	49.2	48.4	49.1	49.0	49.0	48.7	48.7	48.8	48.9	48.8
10	136.9	137.7*	134.0	140.0	132.6	132.7	132.1[g]	132.4	132.6	133.3	132.3	133.0	132.7	132.6	132.7	133.2	132.6	132.4	132.4
11	141.5	139.5*	136.3	n.r.	135.4	135.5	135.2[g]	135.4	136.9	137.0	135.9	137.4	135.6	135.3	136.9	135.5*	135.5	135.5	135.6
12	170.5	170.2	171.1	169.5	169.7	169.8	170.5[h]	169.9	169.8	170.3	171.0	170.1	169.8	169.7	170.2	169.7	169.7	169.8	169.7
13	119.6	120.0	127.0	119.0	125.4	125.3	125.6	125.5	124.3	128.8	124.8	123.9	125.1	125.8	124.7	125.2	125.3	125.3	125.0
14	16.1	15.9	16.9	10.4	16.7	16.8	16.6	16.8	16.5	16.8	15.7	16.9	16.9	16.7	17.1	16.7	16.8	16.8	16.8
15	17.3	61.2	60.9	58.7	61.5	61.6	60.5	61.3	60.4	60.6	59.6	60.9	61.5	61.4	59.7	61.5	61.6	61.5	61.5
1′					176.0	166.1	165.0[h]	165.1	165.2	174.8	174.7	165.5	166.8	172.1	174.1	166.1	166.2	166.1	165.7
2′					34.1	136.2	139.6[g]	139.4	141.5	43.4	42.7	141.6	127.3	38.4	38.3	135.0*	132.1	131.6	128.2
3′					19.3	126.4	125.7	126.3	123.7	64.3	63.6	127.2	139.5	32.7	33.4	141.3	141.5	141.7	140.1
4′					18.5	18.4	60.9	62.1	60.8	14.0	12.8	67.9	15.9	61.7	65.9	59.8	14.4	15.9	62.8
5′													20.5	16.7	17.0	12.8	56.9	64.9	19.7
1″												170.9							170.8
2″												20.7							20.9

C	**19**$^{b}_{3}$	**19**$^{c}_{10}$	**19**$^{e}_{11}$	**21**$^{a}_{3}$	**22**$^{e}_{12}$	**24**$^{a}_{3}$	**25**$^{b}_{13}$	**26**$^{b}_{13}$	**27**$^{a}_{14}$	**28**$^{a}_{14}$	**35**$^{a}_{15}$	**36**$^{a}_{16}$	**36**$^{b}_{17}$	**36**$^{a,n}_{17}$	**37**$^{a}_{3}$	**38**$^{a}_{18}$	**39**$^{a}_{2}$	**44**$^{a}_{19}$	**45**$^{a}_{19}$
1	129.8	130.8	130.9	129.9	131.1	129.8	77.2	76.2	128.0	121.9	126.6[g]	128.2	128.6	129.4	132.3	127.2*	129.4*	129.3	129.2
2	26.1	26.8	26.9	26.3	27.4	26.1	34.2	33.9	24.7	23.5	23.5[h]	25.9	26.1	26.1	24.8	25.4	26.1	25.7	25.5
3	34.6	35.5	35.2	34.7	35.4	34.6	28.0	28.3	35.7	36.3	35.9[h]	34.7	34.9	35.0	33.4	34.6†	34.7	34.3	34.1
4	144.6	145.6	145.5	144.1	145.7	144.3	147.6[g]	147.4[g]	61.5	61.3	60.7	142.6	142.7	138.0	145.1	141.8	142.8	143.3[g]	143.1[g]
5	128.0	129.6	129.7	128.4	130.1	128.2	121.8	121.7	66.4	66.6	66.8[i]	129.3	129.5	131.6	128.3	127.7*	129.0*	128.3	128.0
6	77.1	78.7	78.7	76.4	78.9	76.9	75.2	75.9	78.3	82.4	80.6[i]	76.6	76.4	76.1	75.3	78.5#	76.1	76.3	76.3
7	53.0	54.1	54.1	53.0	54.2	52.7	50.9	50.3	52.2	37.6	34.0[i]	59.9	60.1	58.2	64.4	51.0	58.3	58.0[h]	57.8[h]
8	73.1	74.6	74.5	73.3	74.8	73.3	73.3	73.8	71.3	37.6	75.5[i]	71.4	72.0	72.9	203.6	35.9†	73.8	73.3	73.1
9	48.6	47.0	49.0	48.6	48.9	48.7	29.5	30.1	52.0	71.4	75.5[i]	52.2	52.9	49.1	57.4	78.8#	49.0	48.8	48.6
10	132.1	133.1	133.2	132.3	133.0	132.1	136.8	136.6	130.0	137.5	133.7	133.9	133.9	132.9	126.5	139.1	132.6	132.4[g]	132.1[g]
11	135.3	137.3	137.4	135.4	137.6	135.4	137.1	137.0	134.0	139.8	133.5[j]	40.6	40.8	40.3	40.5	41.2	40.2	39.9[h]	39.8[h]
12	170.5	172.0	172.1	169.8	172.5[g]	170.2	170.2[h]	170.8[h]	169.8	169.4	169.6	180.3	179.9	177.7	177.1	177.6	178.0	178.9	178.9[i]
13	125.5	125.2	125.3	125.3	125.9	125.3	121.8	121.6	128.5	121.1	125.5	17.3	17.6	17.0	13.6	12.5	17.0	16.6	16.0
14	16.7	17.0	17.0	16.8	17.4	16.8	118.1	117.9	18.1	16.4	13.9[k]	16.8	17.1	16.8	16.0	10.0	16.6	16.3	16.4
15	60.7	60.9	60.7	61.5	61.1	60.8	61.0	61.1	17.4	17.3	17.1[k]	60.4	61.1	61.6	60.1	59.7	61.5†	60.3	59.8[j]
1′	165.1	166.6	166.6	164.6	167.5[g]	164.8	164.4[h]	164.2[h]			166.1			170.7			165.3	166.6	164.8[i]
2′	139.7	142.4	142.3	138.8	133.7	131.7	139.7[g]	140.1[g]			111.8[g]			21.2			139.3	137.0[g]	139.7[g]
3′	70.8	71.8	71.9	69.5	147.2	140.3	70.5	72.4			160.5[j]			169.8			126.3	34.9	70.3
4′	65.8	66.7	66.7	67.3	59.7	62.8	65.4	66.0			66.6			21.0			62.4†	60.6	65.3[j]
5′	127.1	127.2	127.0	127.8	57.0	62.3	126.9	127.1			15.5[k]							127.4	126.2
1″				171.3		171.1													
2″				20.8		20.8													

C	**46**$^{a}_{20}$	**48**$^{a}_{21}$	**49**$^{a,n}_{17}$	**51**$^{a,o}_{22}$	**53**$^{a}_{23}$	**53**$^{c}_{23}$	**58**$^{f,m}_{24}$	**59**$^{a}_{25}$	**60**$^{a}_{26}$	**62**$^{a}_{26}$	**64**$^{a}_{25}$	**65**$^{a}_{25}$	**66**$^{a}_{27}$	**67**$^{a}_{26}$	**68**$^{a}_{26}$
1	129.3	125.6	129.3	121.3	128.9	131.3	129.8*	127.6	72.0	61.5	128.5	128.7	127.8	72.3	85.7
2	26.0	25.2	26.5	25.2	24.9	26.1	26.5	24.5	31.0	26.3	24.6	24.7	24.1	31.1	26.2
3	34.5	40.9	35.3	35.7	36.1	32.1	35.0	25.8	24.5	24.7	27.0	27.1	22.3	24.5	24.4
4	142.9	141.8	137.1	133.0	140.4	141.6	144.6	134.8	134.7	134.0	134.2	134.3	142.0	134.2	134.4
5	128.7	129.3	130.8	131.4	128.9	129.7	129.2*	125.7	125.7	125.3	125.4	125.3	146.7	125.3	125.6
6	75.9	79.2	75.0	68.6	69.2	71.4	77.4	76.7	75.0	75.2	76.5	76.4	75.6	74.7	74.5

(continued on next page)

Table 4 (*continued*)

C	$\mathbf{46}^{a}_{20}$	$\mathbf{48}^{a}_{21}$	$\mathbf{49}^{a,n}_{17}$	$\mathbf{51}^{a,o}_{22}$	$\mathbf{53}^{a}_{23}$	$\mathbf{53}^{c}_{23}$	$\mathbf{58}^{f,m}_{24}$	$\mathbf{59}^{a}_{25}$	$\mathbf{60}^{a}_{26}$	$\mathbf{62}^{a}_{26}$	$\mathbf{64}^{a}_{25}$	$\mathbf{65}^{a}_{25}$	$\mathbf{66}^{a}_{27}$	$\mathbf{67}^{a}_{26}$	$\mathbf{68}^{a}_{26}$
7	57.9	49.5	53.4	49.3	50.7	52.3	52.9	52.5	52.3	52.6	50.5	50.5	49.1	50.2	50.0
8	73.6	26.6	70.7	24.3	81.1	81.3	74.1	67.3	72.5	67.4	70.1	69.5	69.1	74.2	74.4
9	49.0	35.3	47.5	39.0	41.0	42.7	49.4†	49.0	43.0	49.0	46.1	46.3	45.5	40.2	41.1
10	132.6	137.2	133.4	135.7	129.6	128.6	133.1	132.1	144.3	56.3	131.1	131.1	131.6	143.5	139.0
11	39.8	40.9	39.6	31.7	135.1	138.1	47.0	136.3	137.5	137.2	136.7	136.7	132.8	138.1	138.2
12	177.8	179.7	178.1	21.5	171.4	170.7	178.3	169.9	n.r.	170.4	169.5	169.1	169.2	168.9	169.0
13	16.9	10.8	10.6	21.2	127.4	126.3	49.6†	127.7	127.7	128.4	127.5	127.4	129.9	127.2	127.2
14	16.5	15.9	16.6	17.0	21.1	21.5	16.9	16.9	115.4	16.7	16.7	16.8	15.0	116.3	120.4
15	61.3	60.7	61.7	16.4	61.5	61.1	60.8#	67.0	66.2	66.6	66.8	66.9	194.0	66.1	66.2
1′	164.5		170.7				165.9				164.8	164.4	164.8	164.7	164.8
2′	131.5		21.2				142.5				139.4	138.5	139.3	139.1	138.3
3′	140.4		169.8				124.1				70.9	70.2	70.1	71.3	71.2
4′	62.7		20.9				61.2#				65.7	67.4	65.0	65.7	65.7
5′	62.4										126.6	127.1	126.1	127.0	127.0
1″	170.6						177.6	170.5	n.r.	169.1	170.5	170.5		170.5	170.7
2″	20.7						69.5	20.9	20.9	20.8	20.8	20.8		20.8	20.9
1‴							32.1					171.3			
2‴							20.1					20.9			
3‴							19.0								

n.r. = not reported. [a] In $CDCl_3$. [b] In $CDCl_3$/MeOD. [c] In acetone-d_6. [d] In DMSO-d_6. [e] In CD_3OD. [f] In pyridine-d_5. [g,h,i,j,k] Inverted with respect to the original paper. [l] Amended with respect to the original paper. [m] Spectrum not assigned in the original paper. [n] As acetate. [o] P/β,α/N conformer. [*,†,#] These values may be interchanged.

[1]Hibasami et al. (2003); [2]Lazari et al. (1998); [3]Marco et al. (2005); [4]Barrero et al. (1988); [5]Marco et al. (1994); [6]Lonergan et al. (1992); [7]Barrero et al. (1989); [8]Shoeb et al. (2007a); [9]Garcia et al. (1996); [10]Santos et al. (1995); [11]Csapi et al. (2010); [12]Skaltsa et al. (2000a); [13]Trendafilova et al. (2007); [14]Bruno et al. (1991a); [15]Suleimenov et al. (2005a); [16]Medjroubi et al. (2003a); [17]Marco et al. (1992); [18]Cardona et al. (1991); [19]Benayache et al. (1992); [20]Djeddi et al. (2007); [21]Appendino and Özen (1993); [22]Barrero et al. (1999); [23]Jimeno et al. (2004); [24]Marco et al. (1991); [25]Cardona et al. (1994); [26]Cardona et al. (1997); [27]Lakhal et al. (2010).

Starting from botanical considerations the distribution of sesquiterpenes within the groups of Centaureinae provides useful information.

Almost all of the six genera (39 taxa) belonging to the first group of Centaureinae, named "Basal genera" (*Psephellus*, *Rhaponticoides*, *Cheirolophus*, *Plectocephalus*, *Stizolophus* and *Zoegea*) contain guaianes with the exception of *Stizolophus* and *Zoegea* which show the presence of germacranes only.

The representatives of *Psephellus* usually contain only guaianes. All the analyses (incl. molecular approaches) confirm that *Rhaponticoides* (=*Centaurea* sect. *Centaurea*) and related taxa are a very isolated group of species. This group is always placed in a basal position, far removed from the bulk of the genus (Garcia-Jacas et al., 2006). A recent survey of Centaureinae and Plectocephalus (Susanna et al., 2011), based on nuclear internal transcribed spacers (ITS) analyses, identified *Stizolophus* and *Zoegea* as sisters to the rest of this group.

Four of the five species included in the second group of Centaureinae, *Volutaria*, contain only guaianes, the fifth species,*Amberboa lippii*, in addition has the germacrane **19**.

All the taxa of the third group, *Rhaponticum*, except *Leuzea conifera* and *Raponticum uniflorum*, possess guaianes. This group of about 40 species ranged among the early branching taxa of Asteraceae, Centaureinae, according to the recent phylogenetic reconstructions based on molecular data (Hidalgo et al., 2006).

The fourth group (*Serratula*) contains only guaianes and eudesmanes. The only studied species of the fifth group (*Carthamus*) *Carthamus arborescens*, contains germacranes and eudesmanes, but not guaianes, while the studied species of the sixth group, *Crocodylium*, – germacranes and elemanes. The ITS phylogeny suggests that *Aegialophila* and *Crocodylium* form a strongly supported clade, more connected to the *Carthamus* complex than to the *Acrocentron* group (Garcia-Jacas et al., 2006).

With regard to the seventh group, *Centaurea*, we analyzed data about the sesquiterpenoids of 153 taxa belonging to 19 sections: *Acrocentron*, *Calcitrapa*, *Acrolophus*, *Phalolepis*, *Jacea*, *Seridia*, *Microlophus*, *Tetramorphaea*, *Lepteranthus*, *Cheirolepis*, *Cyanus*, *Cynaroides*, *Cheirolepis*, *Ptosimopappus*, *Melanoloma*, *Pseudophaeopappus*, *Solstitiaria*, *Chartolepis*, *Grossheimia*.

Our research on sesquiterpenoids of the 63 taxa of sections *Acrolophus* and *Phalolepis* shows that all representatives, except *Centaurea exarata* and *C. incana*, do not contain guaianes. The results of molecular investigations pointed out that these sections are consistently associated in well-supported clades (BS = 100%, PP = 1 · 0), named *Acrolophus–Phalolepis* (Garcia-Jacas et al., 2000). These sections are morphologically similar, and the separation of *Acrolophus* and *Phalolepis* is clearly artificial. *C. exarata*, in contrast to the other representatives of the group contains guaianes. Its affiliation into the *Acrolophus* sect. is not also supported by the recent molecular studies placing it in the section *Jacea* (clade *Jacea–Lepteranthus*), although this inclusion is not supported by morphological studies. However, the chromosome number of *C. exarata* ($x = 11$) coincides with the basic number found in the *Jacea* sect., a fact that justifies its inclusion in this section.

Our results do not seem to support the recognition of *Jacea* and *Lepteranthus* as separate sections and these data are in accordance with the molecular survey (Garcia-Jacas et al., 2006).

The section *Seridia*, comprising taxa found exclusively in the western Mediterranean area, never contain guaianes. On the other hand the section *Solstitiaria* has mainly guaianes and the sections *Micrlophus* and *Chartolepis* contain guaianes exclusively.

The representatives of the sect. *Cyanus* usually do not contain sesquiterpenoids. In this study, information about two species of this section and their sesquiterpenoid profile, characterized by the presence of guaianes only, is included.

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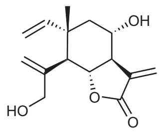
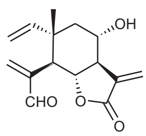
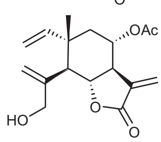
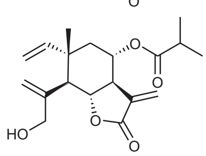
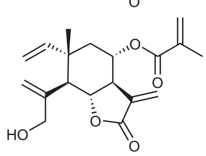
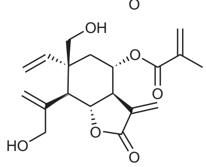
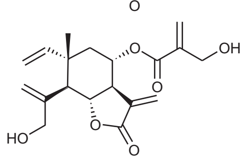
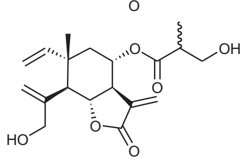
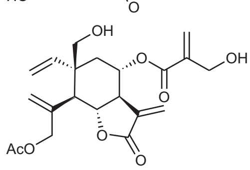
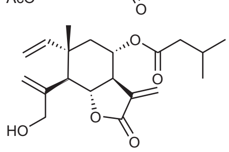
Table 5
Elemanes isolated from taxa of the Subtribe Centaureinae.

No	Structure	Name	Taxa	Ref.
69		Dehydromelitensin	*Centaurea aegialophila*	Bruno et al. (2001)
			Centaurea amara	Gonzalez et al. (1980a)
			Centaurea aspera ssp. *stenophylla*	Picher et al. (1984a)
			Centaurea aspera ssp. *subinermis*	Cardona et al. (1991)
			Centaurea castellana	Gonzalez et al. (1984);Gousiadou and Skaltsa (2003)
			C. cineraria ssp. *busambarensis*	Bruno et al. (1998)
			Centaurea cuneifolia	Salan and Öksük (1999), Gousiadou and Skaltsa (2003)
			Centaurea grisebachii	Djeddi et al. (2008a)
			Centaurea malacitana	Barrero et al. (1995, 1988)
			Centaurea napifolia	Bruno et al. (1995)
			Centaurea paui	Cardona et al. (1997), Gousiadou and Skaltsa (2003)
			Centaurea pullata	Gonzalez et al. (1974a, 1977a)
			Centaurea salonitana	Salan and Öksük (2003)
			Centaurea sphaerocephala	Bruno et al. (1994)
70		8α-hydroxy-15-oxo-5,7αH,6βH-elema-1,3,11(13)- trien-12,6-olide	*Centaurea paui*	Cardona et al. (1997), Gousiadou and Skaltsa (2003)
71		dehydromelitensin 8α-acetate	*Centaurea bruguierana*	Harraz et al. (1994)
72		dehydromelitensin 8-(2′-methylpropanoate)	*Centaurea chilensis*	Negrete et al. (1993)
73		dehydromelitensin 8-(2′-methyl-2′-propenoate)	*Centaurea chilensis*	Negrete et al. (1993)
74		hierapolitanin A	*Centaurea hierapolitana*	Karamenderes et al. (2007a)
75		8α-(4′-hydroxy-methacryloyl)-dehydromelitensin	*Centaurea achaia*	Skaltsa et al. (2000a), Koukoulitsa et al. (2002)
			Centaurea eryngioides	Sarg et al. (1989)
			Centaurea tagananensis	Gonzalez et al. (1984), Nowak et al. (1986a)
			Cheirolophus intybaceus	Marco et al. (1994)
76		11,13-dehydromelitensin β-hydroxyisobutyrate	*Centaurea melitensis*	Gonzalez et al. (1975, 1977a)
77		hierapolitanin B	*Centaurea hierapolitana*	Karamenderes et al. (2007a)
78		Isoarbutifolin	*Centaurea arbutifolia*	Gonzalez et al. (1981)

(*continued on next page*)

Table 5 (*continued*)

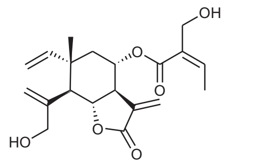
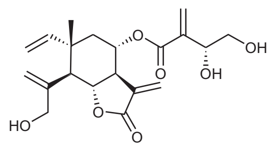
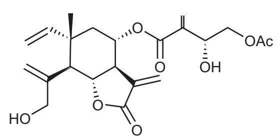
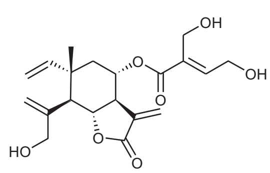
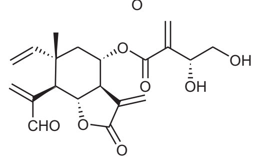
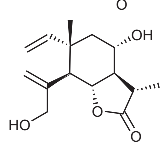
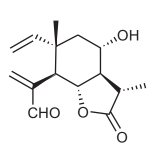
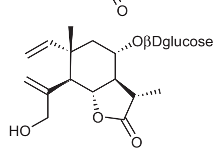
No	Structure	Name	Taxa	Ref.
79		8α (5′-hydroxyangeloyl)-11,13-dehydromelitensin	*Centaurea phrygia*	El-Marsy et al. (1985)
80		8α-(3′,4′-dihydroxy-2′-methylene-butanoyloxy)- dehydromelitensin; isocnicin	*Centaurea aegialophila*	Bruno et al. (2001)
			Centaurea attica	Skaltsa et al. (1999), Gousiadou and Skaltsa (2003)
			Centaurea calcitrapa	Marco et al. (1992), Aboul-Ela (1994)
			Centaurea cinerar. ssp. busambarensis	Bruno et al. (1998)
			Centaurea cineraria ssp. *umbrosa*	Bruno and Herz (1988), Gousiadou and Skaltsa (2003)
			Centaurea cuneifolia	Salan and Öksük (1999), Gousiadou and Skaltsa (2003)
			Centaurea deusta	Karioti et al. (2002)
			Centaurea grisebachi	Djeddi et al. (2008a)
			Centaurea moesiaca	Trendafilova et al. (2007)
			Centaurea napifolia	Bruno et al. (1995)
			Centaurea orphanidea	Gousiadou and Skaltsa (2003)
			Centaurea paniculata ssp. *castellana*	Bruno et al. (2002)
			Centaurea phyllocephala	Lazari et al. (2008)
			Centaurea spinosa	Saroglou et al. (2005)
			Centaurea thessala subsp. *drakiensis*	Skaltsa et al. (2000b), Georgiadou et al. (2000), Gousiadou and Skaltsa (2003)
			Centaurea zuccariniana	Koukoulitsa et al. (2002)
			Cnicus benedictus	Tsankova et al. (1994)
81		8α-(3′-hydroxy-4′-acetoxy-2′-methylene-butanoyloxy)-dehydromelitensin	*Centaurea deusta*	Karioti et al. (2002)
			Centaurea diffusa	Fortuna et al. (2002)
			Centaurea napifolia	Bruno et al. (1995)
			Centaurea phyllocephala	Lazari et al. (2008)
			Centaurea sphaerocephala	Bruno et al. (1994)
			Centaurea thessala ssp. *drakiensis*	Skaltsa et al. (2000b), Georgiadou et al. (2000), Gousiadou and Skaltsa (2003)
82		8α-(4′,5′-dihydroxy-tigloyloxy)-11,13-dehydromelitensin	*Centaurea achaia*	Skaltsa et al. (2000a)
83		8α-(3′,4′-dihydroxy-2′-methylene-butanoyloxy)-15-oxo-5, 7αH,6βH-elema-1,3,11(13)-trien-12,6-olide	*Centaurea diffusa*	Fortuna et al. (2002)
			Centaurea paui	Cardona et al. (1994)
			Centaurea spinosa	Saroglou et al. (2005)
84		Melitensin	*Centaurea amara*	Gonzalez et al. (1980a)
			Centaurea aspera ssp. *stenophylla*	Tortajada et al. (1988), Picher et al. (1984a)
			Centaurea aspera ssp. *subinermis*	Cardona et al. (1991)
			Centaurea calcitrapa	Marco et al. (1992)
			Centaurea melitensis	Gonzalez et al. (1971, 1975, 1977a, 1978a), Rybalko et al. (1975)
			Centaurea napifolia	Bruno et al. (1995)
			Centaurea nicaensis	Medjroubi et al. (2003a)
			Centaurea pullata	Djeddi et al. (2008b)
			Centaurea tagananensis	Gonzalez et al. (1984), Nowak et al. (1986a)
85		8α-hydroxy-15-oxo-5,7αH,6,11βH-elema-1,3-dien- 12,6-olide	*Centaurea paui*	Cardona et al. (1997), Gousiadou and Skaltsa (2003)
86		melitensin-8α-*O*-β-D-glucopyranoside	*Centaurea salonitana*	Salan and Öksük (2003)

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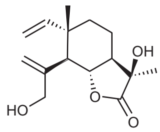
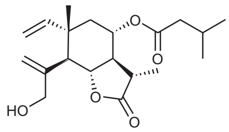
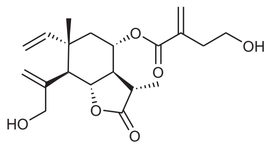
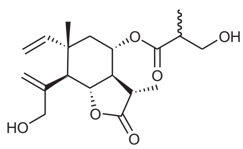
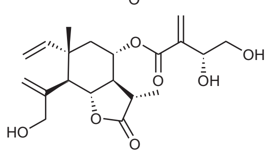
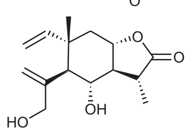
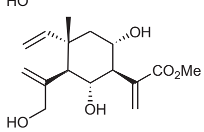
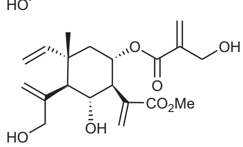
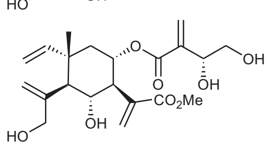
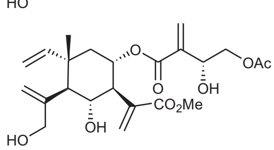
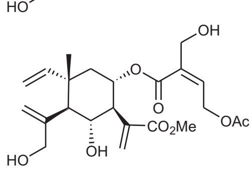
Table 5 (*continued*)

No	Structure	Name	Taxa	Ref.
87		8-deoxy-11β-hydroxy-melitensin	*Centaurea castellana*	Gonzalez et al. (1984), Gousiadou and Skaltsa (2003)
88		11,13-dihydroisoarbutifolin	*Centaurea arbutifolia*	Gonzalez et al. (1981)
89		8α-*O*-(4′-hydroxy-2′-methylenebutanoyloxy)-melitensin	*Centaurea pullata*	Djeddi et al. (2008b)
90		Melitensin β-hydroxyisobutyrate	*Centaurea melitensis*	Gonzalez et al. (1975, 1977a)
91		5α,6β,7α,8β,11β(H)-15-hydroxy-8-(1′,2′-dihydroxyethyl)-acryloelema-1,3-dien-6,12-olide	*Centaurea nicaensis*	Bruno et al. (1996), Medjroubi et al. (2003a)
92		Isomelitensin	*Centaurea aspera* ssp. *subinermis*	Cardona et al. (1991)
93		Methyl 8α,6α,15-trihydroxyelema-1,3,11(13)-trien-12-oate	*Centaurea aspera* ssp. *subinermis*	Cardona et al. (1992)
94		Elemacarmanin	*Centaurea achaia* *Centaurea aspera* *Cheirolophus intybaceus*	Skaltsa et al. (2000a), Koukoulitsa et al. (2002) Marco et al. (2005) Marco et al. (1994)
95		Methyl 8α-(3′,4′-dihydroxy-2′-methylene-butanoyloxy)-6α,15-dihydroxyelema-1,3,11(13)-trien-12-oate	*Centaurea attica* *Centaurea deusta* *Centaurea paui* *Centaurea spinosa*	Skaltsa et al. (1999), Gousiadou and Skaltsa (2003) Karioti et al. (2002) Cardona et al. (1997), Gousiadou and Skaltsa (2003) Saroglou et al. (2005)
96		Methyl 8α-(3′-hydroxy-4′-acetoxy-2′-methylene-butanoyloxy)-6α, 15-dihydroxyelema-1,3,11(13)-trien-12-oate	*Centaurea deusta*	Karioti et al. (2002)
97		Methyl 8α-*O*-(4′-acetoxy-5′-hydroxyangelate)-6α,15-dihydroxyelema-1,3,11(13)-trien-12-oate	*Centaurea aspera* ssp. *stenophylla*	Marco et al. (2005)

Our study presents data of the sesquiterpenoids from 16 taxa of the sect. *Acrocentron*. This group is defined mainly on the basis of pollen type, but also by achene characters, involucral bracts morphology and molecular data (ITS spacers of the nuclear ribosomal DNA). The representatives contain all main types of sesquiterpenoids – germacanes, elemanes, eudesmanes, guaianes.

In order to find further correlations among taxa, based only on the sesquiterpene composition, a statistical approach was used (see Supporting information). The cluster analysis of the taxa belonging to subtribe Centaurinae according to the presence/absence of single sesquiterpenes, carried out by Primer 6 programme (Clarke and Gorley, 2006), allow us to draw some considerations.

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Table 6
^{13}C NMR data of elemanes.

C	**69**$^{a}_{1}$	**70**$^{a}_{2}$	**72**$^{a}_{3}$	**73**$^{a}_{3}$	**74**$^{b}_{4}$	**75**$^{a}_{5}$	**76**$^{a}_{6}$	**77**$^{b}_{4}$	**80**$^{a}_{7}$	**83**$^{a}_{8}$	**84**$^{a}_{9}$	**85**$^{a}_{2}$	**89**$^{a}_{10}$	**91**$^{a}_{9}$	**92**$^{a}_{11}$	**93**$^{a}_{12}$	**94**$^{a}_{13}$	**95**$^{a}_{2}$	**97**$^{a}_{14}$
1	146.1	145.5	147.9	147.9	143.8	145.6	145.6	143.8	145.6	144.9	146.3	145.7	145.6	145.8	146.5	146.9	146.3	146.2	146.2
2	112.7	112.6	113.0	113.0	113.1	113.1	112.6	114.5	113.1	113.1	112.5	112.5	112.8	113.0	112.4	111.7	111.9	112.1	112.1
3	114.9	137.7	113.3	113.3	112.5	115.1	113.7	116.0	115.1	137.9	114.5	137.4	114.6	114.8	116.8	114.7	114.9	114.9	115.0
4	143.9	144.8	145.6	145.6	145.1	143.6	143.5*	138.2	143.6	144.5	144.4	145.3	144.0	144.1	145.3	146.6^{c}	146.2	146.2	146.3
5	50.6	46.2	51.8	51.7	51.9	50.6	50.2	51.8	50.6	46.1	50.4	46.6	50.1	50.3	57.6*	55.5	55.3	55.3	55.3
6	78.8	77.4	80.0	80.0	78.7	78.6	78.8	78.5	78.7	77.4	78.7	77.3	78.2	78.4	76.4	70.7	71.0	70.9	71.0
7	55.0	55.0	53.1	53.0	52.3	52.3	51.9	51.2	52.4	52.2	58.4	58.5	55.9	56.0	57.4*	58.1	54.6	54.7	54.8
8	67.5	67.6	70.4	71.0	70.5	69.6	68.8	70.3	69.7	69.6	68.8	69.0	70.4	70.7	71.3	67.8	70.9	71.1	71.4
9	49.8	49.4	46.2	46.1	42.2	45.0	44.7	41.8	45.0	44.6	49.4	49.3	44.8	44.9	42.8	47.1	43.5	43.5	43.6
10	41.9	42.0	43.0	42.9	46.3	41.9	41.6	46.4	41.9	42.0	41.7	41.8	41.1	41.6	n.r.	40.1	40.2	40.2	40.3
11	137.4	137.2	139.1	139.1	138.6	136.6	136.3*	139.7	136.7^{c}	136.4	41.5	41.4	40.8	41.0	41.6	138.4^{c}	138.0	138.0	138.0
12	169.7	n.r.	171.4	171.4	169.2	169.2	170.0	169.8	169.1	169.2	178.6	179.0	178.1	177.8	179.1	167.7	167.2	167.1	167.2
13	120.5	120.6	119.6	119.6	117.8	120.2	120.5	119.5	120.1	120.3	14.3	14.3	13.8	14.1	14.3	128.6	128.3	128.4	128.7
14	18.9	18.2	19.3	19.3	66.5	18.7	18.2	65.5	18.4	17.9	18.9	18.3	18.5	18.7	19.8	18.7	18.3	18.3	18.3
15	67.3	193.6	66.7	66.7	65.5	67.3	66.1	66.5	67.3	193.6	67.3	193.5	67.1	67.2	67.5	67.7	67.7	67.8	67.8
1′			173.7	167.7	166.2	165.3	174.8	165.5	165.2	165.1			166.0	165.3			165.4	165.2	164.9
2′			35.2	137.4	136.7	139.1	42.1	141.5	139.0^{c}	139.0			136.6	139.0			139.4	139.1	131.4
3′			19.1	127.0	125.4	126.7	63.9	124.8	71.2	71.0			35.0	71.1			125.8	71.6	140.8
4′			19.0	18.4	17.7	62.3	13.0	60.3	64.8	65.8			61.3	65.7			62.2	65.7	63.9
5′									127.5	127.5			127.8	127.4				126.8	62.9
1″								170.6											170.8
2″								21.3											20.9
OCH_3																52.1	52.0	52.0	52.1

n.r.=not reported. [a]In $CDCl_3$. [b]In DMSO-d_6. [e]Inverted with respect to the original paper.
[1]Cardona et al. (1989); [2]Cardona et al. (1997); [3]Negrete et al. (1993); [4]Karamenderes et al. (2007a); [5]Marco et al. (1994); [6]El-Moghazy et al. (2002); [7]Bruno and Herz (1988); [8]Cardona et al. (1994); [9]Medjroubi et al. (2003a); [10]Djeddi et al. (2008b);[11]Cardona et al. (1991); [12]Cardona et al. (1992); [13]Tortajada et al. (1988); [14]Marco et al. (2005).
* These values may be interchanged.

Two taxa show the lowest grade of resemblance with respect to all the others: *C. solstitialis* and *C. scoparia* both of seventh group.

The *Psephellus* are divided in two taxonomic groups containing the same compounds: the first one representing the sect. *Psephellus* (*Psephellus carthalinicus*, *Psephellus colchicus*, *Psephellus daghestanicus*, *Psephellus dealbatus*, *Psephellus karabaghensis*, *Psephellus nogmovii*, *Psephellus somcheticus* and *Psephellus zangezuri*) to which also *Psephellus taochius* can be added; the second group joining the sects. *Leucophyllae* and *Hypoleucae* (*Psephellus leucophyllus*, *Psephellus declinatus* and *Psephellus hypoleucus*) (Fig. 3).

Although *Centaurea phaedopappoides* belongs to the *Psephellus* group, it is instead correlated by a superimposable occurrence of the same three compounds with the following taxa: *Stemmamarca rhapontica*, *Centaurea thracica*, *Centaurothamnus maximus*, *Leuzea rhaponticoides* and *Leuzea rhapontica* ssp.*helenipholia*. This group is also close to other four taxa: *Stemmamarca carthamoides*, *Centaurea isaurica*, *Centaurea janeri* and *Centaurea marshalliana*, the latter belonging to *Psephellus* group too.

A close resemblance was found among *Centaurea ragusina*, *Centaurea sventenii*, *Centaurea canariensis*, *Centaurea deflexa* and *Amberboa tubiliflora* in which almost the same sesquiterpenes occur (Fig. 3).

Most species of the *Acrolophus* section is strictly correlated by cluster analysis and represent the largest group (38 taxa) (Fig. 4), although this correlation is based on the occurrence of only one sesquiterpene, cnicin (**19**), widely diffused in this section. In spite of this, three taxa, not belonging to the *Acrolophus* section (*Centaurea granatensis*, *Centaurea raphanina* ssp. *mixta* of the *Colymbada* section and *Centaurea rocheliana* of the *Jacea* section), are grouped in this cluster. Other groups are close and they are characterized by the presence of **19** and/or salonitenolide (**4**) along with few other sesquiterpenes. In these clusters, besides taxa of the *Acrolophus* section (*Centaurea mariolensis*, *Centaurea monticola*, *C. exarata*), taxa of the *Calcitrapa* sect. (*Centaurea iberica*, *Centaurea pontica*), *Colymbada* sect. (*Centaurea crocodylium* and *Centaurea aegialophila*), *Seridia* sect. (*Centaurea eriophora*), *Jacea* sect. (*Centaurea weldeniana*), *Phalolepis* sect. (*Centaurea alba* ssp. *caliacrae* and *C. alba* ssp. *deusta*), *Tetramorphaea* sect. (*Centaurea brugueriana*) and *Rhaponticoides* sect. (*Centaurea africana*) are represented. All of them have been classified in the seventh group with the exception of *C. africana* belonging to the first group.

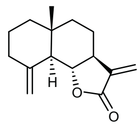
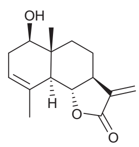
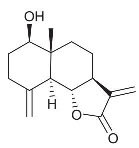
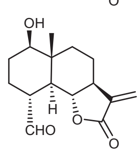
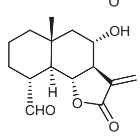
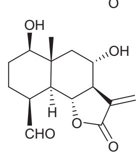
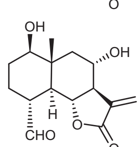
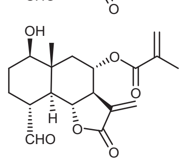
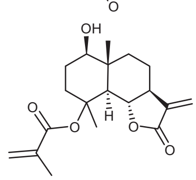
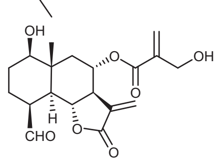
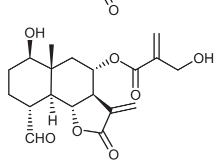
Five taxa of the *Acrolophus* sect. (*Centaurea cuneifolia, Centaurea cineraria* ssp. *busambarensis, C. cineraria* ssp. *umbrosa, Centaurea paniculata* ssp. *castellana, Centaurea zuccariniana*) along with *C. aegialophila* (*Colymbada* sect.) seem to represent a separate cluster from the other *Acrolophus* taxa, containing cnicin (**19**) with other compounds (**69**, **80**, **104**). Other minor groups, correlated by the same sesquiterpene composition, can be observed in the full dendrogram reported in Supporting information.

On the basis of these observations it seem possible to consider cnicin (**19**) and salonitenolide (**4**), having the same sesquiterpene skeleton, as markers of *Acrolophus* section as other authors have already stated (Gousiadou and Skaltsa, 2003).

Starting from this last consideration, we grouped compounds according to the same sesquiterpene skeleton having the same oxidation state and neglecting any ester side chain occurring (Supporting information). The cluster analysis of this new set of data discloses new information (Figs. 5 and 6). The groups obtained by this model were clearly wider and only ones with maximum similarity are considered. A first cluster of *Centaurea grisebachi*, *Centaurea orphanidea*, *Centaurea thessala* ssp. *drakiensis* and *C. zuccariniana*, all belonging to the *Acrolophus* section, was obtained. Two other taxa resulted close to it: *Centaurea malacitana* and *C. phyllocephala* both included in the seventh group as *Acrolophus*.

The greatest cluster, formed by 56 taxa, includes almost all the species belonging to the *Acrolophus* section along with some other ones of seventh group with the exception of *Centaurea derventana* and *Centaurea glaberima* for which the exact placing in the sections is not ascertained. Another interesting cluster involves species of the *Acrolophus* section and precisely *C. grisebachi*, *C. orphanidea*, *C. thessala* ssp. *drakiensis* and *C. zuccariniana*. These taxa show a peculiarity with respect to the other *Acrolophus* taxa because they contain not only germacranes but also elemanes and eudesmanes. Eight taxa of the seventh group are joined in a cluster: four of *Acrolophus* (*C. cineraria* ssp. *busambarensis*, *C. cineraria* ssp. *umbrosa*, *C. cuneifolia* and *C. paniculata* ssp. *castellana*); two of *Colymbada*

Table 7
Eudesmanes isolated from taxa of the Subtribe Centaureinae.

No	Structure	Name	Taxa	Ref.
98		β-cyclocostunolide	*Centaurea acaulis*	Bentamane et al. (2005)
99		Santamarin	*Centaurea acaulis* *Centaurea ornata* *Centaurea uniflora* ssp. *nervosa*	Bentamane et al. (2005) Navarro et al. (1990) Appendino et al. (1986)
100		Reynosin	*Centaurea kurdica* *Centaurea uniflora* ssp. *nervosa*	Appendino and Özen (1993) Appendino et al. (1986)
101		Sonchucarpolide	*Cheirolophus sempervirens*	Marco et al. (1994)
102		Stoebenolide	*Centaurea paui* *Centaurea stoebe*	Cardona et al. (1997), Gousiadou and Skaltsa (2003) Huneck et al. (1986a)
103		8α-hydroxy-4-*epi*-sonchucarpolide	*Centaurea grisebachi* *Centaurea orphanidea* *C. thessala* ssp. *drakiensis*	Djeddi et al. (2008a) Gousiadou and Skaltsa (2003) Skaltsa et al. (2000b),Georgiadou et al. (2000), Koukoulitsa et al. (2002), Gousiadou and Skaltsa (2003)
104		8α-hydroxy-sonchucarpolide	*Centaurea zuccariniana*	Koukoulitsa et al. (2002)
105		1-hydroxy-8-methacryloxy-15-oxoeudesm-11(13)-en-6,12-olide	*Centaurea tweediei*	Fortuna et al. (2001)
106		vahlenin	*Centaurea hyssopifolia* *Centaurea linifolia*	Gonzalez et al. (1974b, 1977a), Nowak et al. (1986a) Gonzalez et al. (1973b, 1978b), Nowak et al. (1986a)
107		8α-(4′-hydroxy-methacryloyloxy)-4-*epi*-sonchucarpolide	*Centaurea achaia*	Skaltsa et al. (2000a)
108		8α-(4′-hydroxy-methacryloyloxy)-sonchucarpolide	*Centaurea achaia* *Cheirolophus x hortigenus*	Skaltsa et al. (2000a) Marco et al. (1994)

(*continued on next page*)

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Table 7 (*continued*)

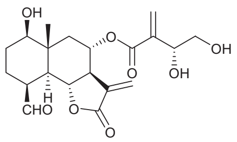
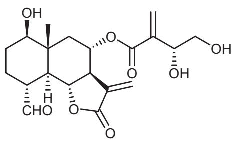
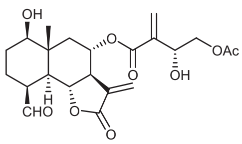
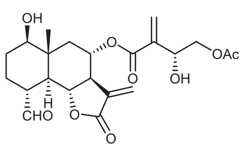
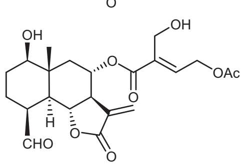
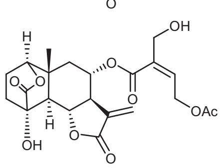
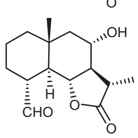
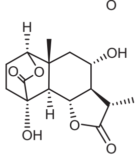
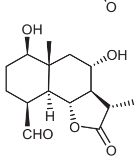
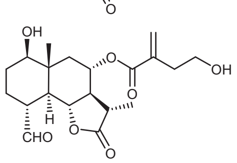
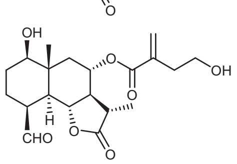
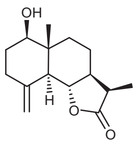
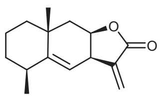
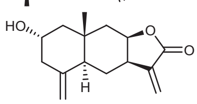
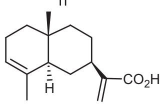
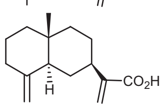
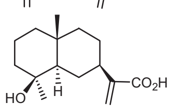
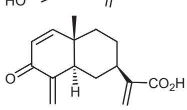
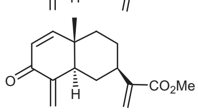
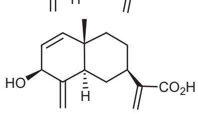
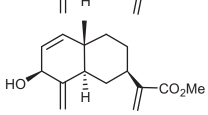
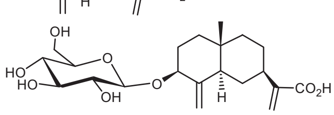
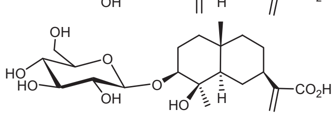
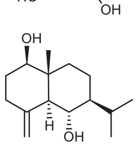
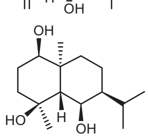
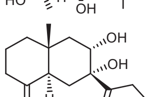
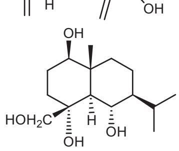
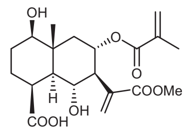
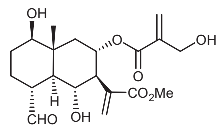
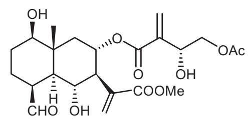
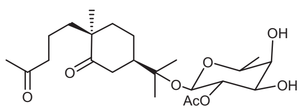
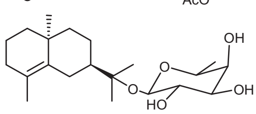
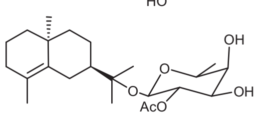
No	Structure	Name	Taxa	Ref.
109		Malacitanolide	*Centaurea attica*	Skaltsa et al. (2000b), Gousiadou and Skaltsa (2003)
			Centaurea grisebachi	Djeddi et al. (2008a)
			Centaurea malacitana	Barrero et al. (1997a)
			Centaurea moesiaca	Trendafilova et al. (2007)
			Centaurea orphanidea	Gousiadou and Skaltsa (2003)
			Centaurea phyllocephala	Lazari et al. (2008)
			Centaurea spinosa	Saroglou et al. (2005)
			Cent. thessala ssp. *drakiensis*	Georgiadou et al. (2000), Gousiadou and Skaltsa (2003)
110		4-*epi*-malacitanolide	*Centaurea grisebachi*	Djeddi et al. (2008a)
			Centaurea spinosa	Saroglou et al. (2005)
111		8α-(3′-hydroxy-4′-acetoxy-2′-methylene-butanoyloxy)-4- *epi*-sonchucarpolide; 4′-acetyl-malacitanolide	*Centaurea attica*	Skaltsa et al. (2000b)
			Centaurea deusta	Koukoulitsa et al. (2002), Karioti et al. (2002)
			Centaurea grisebachi	Djeddi et al. (2008a)
			Centaurea moesiaca	Trendafilova et al. (2007)
			Centaurea orphanidea	Gousiadou and Skaltsa (2003)
			Centaurea spinosa	Saroglou et al. (2005)
112		8α-(3′-hydroxy-4′-acetoxy-2′-methylene-butanoyloxy)-sonchucarpolide; 4′-acetyl-4-*epi*-malacitanolide	*Centaurea deusta*	Koukoulitsa et al., 2002, Karioti et al. (2002)
			Centaurea grisebachi	Djeddi et al. (2008a)
113		8α-*O*-(4′-acetoxy-2′-hydroxy-methylbuten-2′-oyloxy)-4-*epi*-sonchucarpolide	*Centaurea spinosa*	Saroglou et al. (2005)
114		4α-hydroxy-8α-*O*-(4′-acetoxy-5′-hydroxyangelate)-11(13)-eudesmen-12,6α-15,1β-diolide	*Centaurea aspera* ssp. *subinermis*	Cardona et al. (1991)
115		8α-hydroxy-11β,13-dihydro-onopordaldehyde	*Centaurea granata*	Medjroubi et al. (1998)
			Centaurea pullata	Djeddi et al. (2008b)
116		4α,8α-dihydroxy-11βH-eudesma-12,6α-15, 1β-diolide	*Centaurea aspera* ssp. *subinermis*	Cardona et al. (1991)
117		8α-hydroxy-11β,13-4-*epi*-sonchucarpolide	*Centaurea pullata*	Djeddi et al. (2008b)
118		8α-*O*-(4′-hydroxy-2′-methylene-butanoyloxy)-11β,13-dihydrosonchucarpolide	*Centaurea pullata*	Djeddi et al. (2007)
119		8α-*O*-(4′-hydroxy-2′-methylene-butanoyloxy)-11β,13- dihydro-4-*epi* -sonchucarpolide	*Centaurea pullata*	Djeddi et al. (2007)

Table 7 (*continued*)

No	Structure	Name	Taxa	Ref.
120		11-*epi*-dihydroreynosin	*Centaurea ornata*	Navarro et al. (1990)
121		Alantolactone	*Serratula latifolia*	Rustaiyan and Feramarzi (1988)
122		Ivalin	*Centaurea cadmea* *Serratula latifolia*	Karamenderes et al. (2007b) Rustaiyan and Feramarzi (1988)
123		Isocostic acid; 12-carboxy-3,11(13)-eudesmadiene	*Cheirolophus mauritanicus*	Marco et al. (1994)
124		Costic acid	*Cheirolophus mauritanicus* *Serratula latifolia*	Marco et al. (1994) Rustaiyan and Feramarzi (1988)
125		4-*epi*-illicic acid	*Cherirolophus mauritanicus*	Marco et al. (1994)
126		3-oxo-1,2-dehydrocostic acid	*Cheirolophus x hortigenus* *Cherirolophus sempervirens*	Marco et al. (1994) Marco et al. (1994)
127		3-oxo-1,2-dehydrocostic acid methyl ester	*Centaurea arguta*	Gadeschi et al. (1989)
128		3-hydroxy-1,2-dehydrocostic acid	*Centaurea canariensis* ssp. *subexpinnata* *Cheirolophus sempervirens*	Bohlmann and Gupta (1981) Marco et al. (1994)
129		3-hydroxy-1,2-dehydrocostic acid methyl ester	*Centaurea arguta*	Gadeschi et al. (1989)
130		Hierapolitanin C	*Centaurea hierapolitana*	Karamenderes et al. (2007a)
131		Hierapolitanin D	*Centaurea hierapolitana*	Karamenderes et al. (2007a)
132		1β,6α-dihydroxy-4(15)-eudesmene	*Centaurea conifera* (*Leuzea conifera*)	Fernandez et al. (1995)
133		Pterodontriol D	*Centaurea pamphylica*	Shoeb et al. (2007b)
134		Rhaponticol	*Rhaponticum uniflorum*	Cheng et al. (1995), Wei et al. (1997), Zhang et al. (2010)
135		1β,4α,6α,15-tetrahydroxy-eudesmane	*Centaurea aspera* ssp. *subinermis*	Cardona et al. (1992)

(*continued on next page*)

Table 7 (*continued*)

No	Structure	Name	Taxa	Ref.
136		Methyl 1,6-dihydroxy-8-methacryloxyeudesm-11(13)-en-15-oic acid-12-oate	*Centaurea tweediei*	Fortuna et al. (2001)
137		4-*epi*-carmanin	*Centaurea achaia*	Skaltsa et al. (2000a)
138		atticin	*Centaurea attica*	Skaltsa et al. (2000b)
139		4,5-dioxo-10-*epi*-4,5-seco-γ-eudesmol-2′-*O*-acetyl-*β*-D-fucopyranoside	*Phonus arborescens*	Barrero et al. (1997b)
140		10-*epi*-γ-eudesmol-*β*-D-fucopyranoside	*Phonus arborescens*	Barrero et al. (1997b)
141		10-*epi*-γ-eudesmol-2′-*O*-acetyl-*β*-D-fucopyranoside	*Phonus arborescens*	Barrero et al. (1997b)

(*C. aegialophila* and *Centaurea eryngioides*); one of *Jacea* (*Centaurea phrygia*) and one of *Tetramorphea* (*C. brugueriana*). The separation of *Psephellus* in two groups is still effective in this model but other species are involved. This time, the taxa belonging to the *Psephellus* group (*Psephellus* sect.) are joined with *Chartolepis biebersteinii*, *Centaurea hermannii* and also with *C. phaedopappoides*, *S. rhapontica*, *C. thracica*, *C. maximus*, *L. rhaponticoides*, *L. rhapontica* ssp.*helenipholia* that, in the previous single compound analysis, resulted rather separated from the *Psephellus* group. The others *Psephellus* taxa (sects. *Leucophyllae* and *Hypoleucae*) are grouped with *Cheirolophus junoniaus*, *Cheirolophus teydis*, *Cheirolophus uliginosus*, *Cheirolophus sventenii*, *Centaurea americana*, *C. canariensis*, all belonging to first group as *Psephellus*, with *Centaurea collina*, *Centaurea ptosimopappoides*, *Centaurea kotschy*, *C. ragusina*, *Centaurea debeauxii* ssp. *thuillieri* (all of seventh group) and with *Amberboa divaricata*, *Centaurea pabotii* and *Tricholepis glaberrima*.

Finally, using this model, *Centaurea aspera* ssp. *subinermis*, *C. paui* and *Acroptilon repens* are the taxa showing the lowest resemblance in this subtribe.

4. Biological activity

4.1. Antimicrobial

Antimicrobial activity of cynoropicrin (**162**) was screened using 22 strains including Gram+ and Gram− bacteria and the yeasts *Candida albicans* and *Candida tropicalis*. The MIC varied from 100 to 2500 μg/mL, against the strains of bacteria and yeasts evaluated (Schinor et al., 2004). Antibacterial activity against *Staphylococcus aureus*, *Escherichia coli* and *Pseudomonas aeruginosa* was also demonstrated (Modonova et al., 1986). Cnicin (**19**) and cynaropicrin (**162**) have been identified as potent, irreversible inhibitors of the bacterial enzyme MurA of *E. coli* and *P. aeruginosa* showing an activity comparable to fosfomycin expecially for the latter bacterial strain (IC_{50} = 10.5 μM). They covalently bind the thiol group of Cys115 and their unsaturated ester side chain has pivotal importance for the inhibition of MurA. These results provided evidence that MurA is a target protein of sesquiterpene lactones (SLs), which is probably highly relevant for their known antibacterial effect (Bachelier et al., 2006).

Further studies established the structure of the antibacterial target enzyme MurA in complex with its substrate UNAG (UDP-N-acytilglucosamine) and its potent inhibitor cnicin (**19**) by X-ray. The structure reveals that MurA has catalyzed the formation of a covalent adduct between cnicin and UNAG. This adduct, formed by an unusual "anti-Michael" 1,3-addition of UNAG to an α,β-unsaturated carbonyl side chain of cnicin, inhibits MurA (Steinbach et al., 2008).

Cnicin (**19**) has bactericidal activity against *Bordetella bronchiseptica*, *P. aeruginosa*, *S. aureus*, *Brucella abortus* (Karawya et al., 1975; Vanhaelen-Fastre, 1972) and, starting from salonitenolide (**4**), several esters have been prepared. Cnicin (**19**), salonitenolide (**4**), the elemane **80** and several synthetic compounds were tested for their antibacterial activity against *Bacillus cereus*, *Bacillus subtilis*, *P. aeruginosa*, *S. aureus*, *Streptococcus faecalis*, *E. coli*, *Proteus mirabilis* and *Salmonella typhi*. The 8,15-diesters showed a good activity (MIC = 6.25–12.5 μg/mL), comparable with that of cnicin (**19**) (MIC = 3.12–12.5 μg/mL). The 15-monoester compounds were not very active indicating that esterification at the C-8 position is an important structural feature for antibacterial properties (Bruno et al., 2003).

Compounds **19**, **21**, **23**,**80**, **83**, **95**, **109**, **110**, **111** and **113** isolated from *Centaurea spinosa*, were tested *in vitro* against three Gram+ and three Gram− bacteria. They were all inactive against tested Gram− bacteria whereas compounds **83**, **110** and **113** showed an activity against *Micrococcus flavus* from four to six times higher than streptomycin (MIC = 0.6, 0.6 and 0.4 μg/mL, respectively) and compounds **19**, **21**, **23**, **80** and **83** showed a moderate activity against *B. cereus* (Saroglou et al., 2005). Also compound **32** exhibited moderate antibacterial activity only toward Gram+ bacteria (Suleimenov et al., 2005b). Compounds **36**, **44**, **45**, **46**, **84**, **89**, **115**, **117**, **118** and **119**, isolated from *Centaurea pullata*, were tested

Table 8
^{13}C NMR data of eudesmanes.

C	**98**$^{a}_{1}$	**99**$^{a}_{1}$	**100**$^{a}_{1}$	**101**$^{e}_{2}$	**103**$^{a}_{3}$	**104**$^{a}_{4}$	**107**$^{a}_{5}$	**108**$^{b}_{6}$	**109**$^{c}_{7}$	**110**$^{a}_{8}$	**111**$^{a}_{3}$	**112**$^{a}_{9}$	**113**$^{a}_{8}$	**114**$^{a}_{10}$	**115**$^{b}_{11}$	**116**$^{a}_{10}$	**117**$^{a}_{5}$	**118**$^{a}_{12}$	**119**$^{a}_{12}$	
1	41.9	75.2	78.3	79.6	76.4	77.1	78.0	76.4	75.9	76.9	78.0	76.3	77.8	76.0*	26.1	76.3*	78.2	76.9	77.7	
2	21.7	32.8	31.4	29.2	25.6	24.3	27.2	24.3	26.7	24.6	27.1	27.6	27.8	30.2†	19.3	30.3†	27.3	28.1	27.6	
3	39.8	121.3	33.6	24.9	20.6	28.3	22.4	27.6	21.8	23.1	22.7	22.6	23.1	38.5†	40.4	38.6†	22.4	24.1	23.6	
4	144.4	133.4	142.5	48.7	43.8	47.7	44.9	47.6	44.7	47.8	44.9	47.5^{h}	46.0	n.r.	48.9	n.r.	45.1	47.6	45.0	
5	55.1	52.2	53.1	48.9	46.7	48.2	48.9	48.0	47.2	48.1	48.8	48.2	48.4	57.3$^{\#}$	48.4	57.7$^{\#}$	48.6	47.7	48.4	
6	80.1	81.5	79.6	83.2	74.4	78.8	76.1	78.9	76.0	78.8	76.1	78.6	76.1	74.2*	79.2	74.0*	76.0	78.1	75.7	
7	50.1	51.0	49.7	50.0	55.0	55.5	53.8	52.6	52.3	55.3	53.7	52.7	54.0	51.5$^{\#}$	59.2	57.3$^{\#}$	59.8	56.3	56.9	
8	22.9	21.2	21.5	23.2	65.8	67.4	69.9	69.5	69.5	69.5	69.7	69.8	70.5	69.1*	68.3	68.3*	68.9	70.3	70.1	
9	36.0	34.3	35.8	37.3	47.3	47.2	43.9	42.5	43.4	43.5	43.8	43.6^{h}	44.2	42.7†	51.5	46.9†	48.3	42.3	43.5	
10	38.7	40.9	43.0	41.9	41.2	40.7	41.5	40.7	41.0	41.9	41.5	40.8	41.9	n.r.	35.1	n.r.	41.2	40.5	40.8	
11	139.7	139.1	139.4	140.0	136.5	136.8	136.3	136.0	137.5	136.6	136.4	136.0	136.6	135.4	41.2	40.5	41.7	40.3	40.1	
12	170.7	171.0	170.5	170.9	172.5	170.8	169.2	169.0	169.3	170.2	171.5	169.2	169.6	n.r.	178.0	n.r.	178.5	176.3	177.4	
13	116.5	116.6	116.6	116.8	119.2	120.8	120.5	120.3	118.7	120.2	120.8	120.4	121.2	120.0	14.3	14.3	14.3	13.8	13.8	
14	18.1	11.0	11.6	21.2	11.8	13.0	13.9	12.6	13.4	12.8	13.9	14.1	15.6	13.2	19.3	13.5	14.2	12.7	13.9	
15	109.2	23.2	110.6	203.3	200.1	202.6	201.8	203.3	203.7	202.2	201.9	201.8	211.0	n.r.	203.2	n.r.	202.1	202.0	201.7	
1′							165.2	165.3	165.2	166.5	164.7	164.6	165.1	n.r.				166.1	165.9	
2′							139.0	139.4	141.9	^{g}	138.3	138.3	130.6	n.r.				136.6	137.0	
3′							126.7	126.0	70.2	71.5	69.7	69.7	138.6	141.5				35.1	35.1	
4′							62.3	61.0	65.4	65.9	67.1	67.1	63.3	63.2				61.3	61.4	
5′									125.3	127.6	128.1	127.6	62.5	62.5				128.3	127.3	
1″											171.5^{g}	171.4	171.1	n.r.						
2″											n.r.	20.8	20.5	20.8						
C	**120**$^{n.r.}_{13}$	**121**$^{a}_{2}$	**122**$^{e}_{14}$	**123**$^{a}_{15}$	**124**$^{a}_{1}$	**125**$^{a}_{6}$	**126**$^{a}_{16}$	**128**$^{a}_{16}$	**130**$^{f}_{17}$	**131**$^{f}_{17}$	**132**$^{a}_{18}$	**133**$^{e}_{19}$	**133**$^{f}_{20}$	**134**$^{a}_{21}$	**135**$^{a}_{22}$	**137**$^{a}_{23}$	**138**$^{a}_{3}$	**139**$^{d}_{24}$	**140**$^{a}_{24}$	**141**$^{d}_{24}$
1	78.5	41.0	41.2	27.3	41.8	43.8*	161.2	141.6	35.9	34.0	49.0	79.3	76.6	36.0	80.5	77.1	78.0	18.6	38.8	39.6
2	31.5	22.2	66.3	22.8	23.4	18.0	126.9	127.1	27.5	27.5	31.9	29.4	29.5	22.9	28.0*	27.8	26.7	36.8	19.1	19.7
3	36.2	36.8	47.5	121.0	41.1	41.4*	189.3	70.7	81.6	82.1	35.1	36.7	32.0	37.0	29.6*	24.0	22.3	43.6	32.2	32.7
4	143.0	41.1	147.3	134.6	145.3	72.2	145.5	150.2	151.0	72.2	146.2	72.7	69.0	146.9	n.r.	48.5	45.0	208.0	134.7	134.9
5	53.2	133.0	45.7	46.7	49.9	51.8	47.9	47.5	44.3	48.7	55.9	47.9	47.9	43.3	57.6†	50.8	48.8	214.8	124.9	125.1
6	78.3	122.3	27.6	40.0	27.4	27.5†	26.8	28.7	29.8	26.1	67.0	73.1	73.1	41.2	75.6	70.9	76.2	39.8	38.3	38.8
7	48.3	46.3	40.6	40.1	39.4	40.1	38.5	39.2	39.8	40.6	49.3	51.2	51.2	77.1	51.8†	55.9	53.9	50.4	44.4	45.0
8	20.4	77.0	76.8	37.7	30.0	26.4†	28.8	29.2	27.1	23.0	18.2	23.4	24.7	70.2	22.3*	70.5	70.3	21.9	21.9	22.8
9	33.7	42.2	51.9	29.3	36.8	41.2*	36.8	37.7	40.7	44.3	36.3	41.4	34.0	43.4	39.7*	41.3	44.0	39.2	24.8	25.4
10	42.8	34.3	34.1	32.2	35.9	33.7	37.5	37.8	35.5	33.7	41.7	41.5	34.0	37.0	39.1	38.8	n.r.	48.3	34.2	34.5
11	38.8	142.1	142.8	145.1	150.5	145.2	145.2	145.2	147.0	147.1	26.0	25.9	28.8	153.4	29.6	137.2	n.r	78.6	81.2	80.6
12	179.9	170.6	170.0	172.0	172.2	172.2	171.9	172.2	169.9	170.0	16.2	24.5	24.8	64.6	18.5$^{\#}$	166.9	n.r.	23.1	26.8	27.2
13	9.7	119.9	119.5	125.0	124.6	124.9	125.6	125.2	121.5	121.2	21.1	25.1	29.1	114.7	20.7$^{\#}$	129.3	128.7	22.0	26.2	25.7
14	11.7	17.2	19.1	15.5	16.3	18.7	17.8	19.2	15.3	18.0	11.6	14.7	14.1	16.6	12.8$^{\#}$	12.0	11.9	25.4	19.7	19.8
15	110.5	17.6	108.2	21.0	105.4	30.1	118.2	104.6	108.5	20.1	107.8	22.6	22.7	105.5	80.4	202.7	203.6	29.8	23.3	23.2
1′									101.4	101.5						165.2	n.r.	96.0	97.2	95.8
2′									74.0	73.7						139.1	n.r.	73.4	71.7	73.5
3′									77.2	76.9						125.9	69.6	72.6	72.1	72.6
4′									70.3	70.4						62.3	67.4	73.0	74.1	73.2
5′									76.4	76.8							127.6	70.8	70.3	70.6
6′									61.4	61.5								16.9	16.6	16.9
1″																	n.r.	170.2		170.1
2″																	20.6	21.2		21.2
OCH_3																52.1	52.1			

n.r. = not reported.
[a] In $CDCl_3$. [b] In $CDCl_3$/MeOD. [c] In DMSO-d_6. [d] In acetone–d_6. [e] In pyridine-d_5. [f] In CD_3OD. [g] Amended with respect to the original paper. [h] Amended by authors [*Z. Naturforsch. C.* , (2004), **59c**, 612]. *,†,# These values may be interchanged. [1] Yang et al., 1997; [2] Buděšinský and Šaman (1995); [3] Skaltsa et al., 2000b; [4] Koukoulitsa et al. (2002); [5] Lazari et al., 1998; [6] Marco et al. (1994); [7] Barrero et al., 1997a; [8] Saroglou et al. (2005); [9] Karioti et al., 2002; [10] Cardona et al. (1991); [11] Medjroubi et al., 1998; [12] Djeddi et al., 2007; [13] Navarro et al., 1990; [14] Karamenderes et al., 2007b; [15] Fontana et al. (2007); [16] Al-Sheddi et al., 2002; [17] Karamenderes et al., 2007a; [18] Su et al., 1995; [19] Zhao, 1997; [20] Shoeb et al., 2007b; [21] Wei et al., 1997; [22] Cardona et al., 1992; [23] Skaltsa et al., 2000a; [24] Barrero et al., 1997b.

Table 9
Guaianes isolated from taxa of the Subtribe Centaureinae.

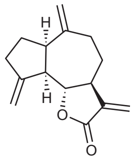
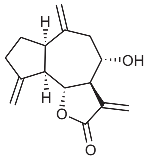
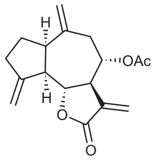
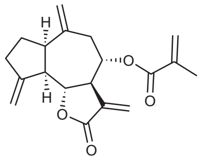
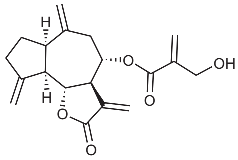
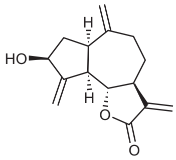
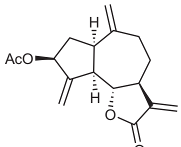
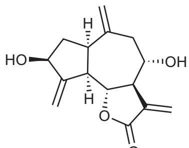
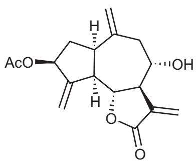
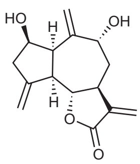
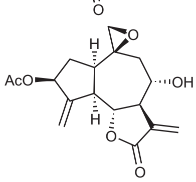
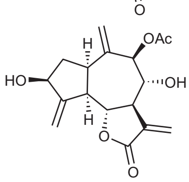
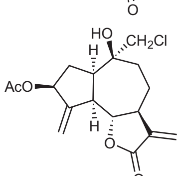
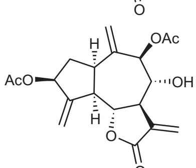
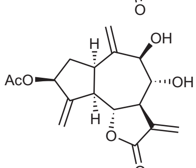
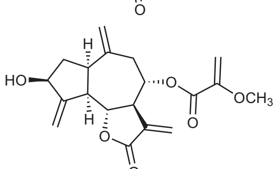
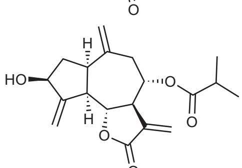
No	Structure	Name	Taxa	Ref.
142		Dehydrocostus lactone	*Centaurea chilensis*	Negrete et al. (1984)
143		8α-hydroxy-dehydrocostus lactone	*Centaurea canariensis* ssp. *subexpin.*	Bohlmann and Gupta (1981), Nowak et al. (1986a)
			Centaurea chilensis	Negrete et al. (1984)
			Cheirolophus x hortigenus	Marco et al. (1994)
			Cheirolophus sempervirens	Marco et al. (1994)
144		8α-acetoxy-dehydrocostus lactone	*Centaurea chilensis*	Negrete et al. (1988a)
			Centaurea floccosa	Negrete et al. (1988a)
145		8α-methacryloyloxy-dehydrocostus lactone	*Centaurea canariensis* ssp. *subexpin.*	Bohlmann and Gupta (1981), Nowak et al. (1986a)
146		Subexpinnatin; 3-desoxycynaropicrin	*Centaurea canariensis* ssp. *subexpin.*	Bohlmann and Gupta (1981), Gonzalez et al. (1982), Gonzalez Collado et al. (1986a)
147		zaluzanin C	*Centaurea ptosimopappa*	Çelik et al. (2006)
			Cheirolophus x hortigenus	Marco et al. (1994)
			Cheirolophus sempervirens	Marco et al. (1994)
148		Zaluzanin D	*Centaurea acaulis*	Bentamane et al. (2005)
			Centaurea ptosimopappa	Çelik et al. (2006)
149		Desacylcynaropicrin; 8-hydroxyzaluzanin C; 8-desacylsauprin; deacylaguerin A	*Acroptilon repens*	Zha and Hou (2008)
			Amberboa muricata	Gonzalez et al. (1973b, 1977a), Khan et al. (2010)
			Amberboa tubiliflora	Omar et al. (1983), Ahmed et al. (1990), Khan et al. (2010)
			Centaurea aegyptiaca	Sarg et al. (1987)
			Centaurea behen	Rustaiyan et al. (1981a),Ohno et al. (1973),Nowak et al. (1986a)
			Centaurea canariensis	Gonzalez et al. (1977a, 1978c,a, 1980b)
			Centaurea canariensis ssp. *subexpin.*	Gonzalez et al. (1977a, 1978c,a, 1980b)
			Centaurea chilensis	Negrete et al. (1988a)
			Centaurea clementei	Gonzalez et al. (1977a), Massanet et al. (1983), Nowak et al. (1986a), Gonzalez Collado et al. (1986a)
			Centaurea collina	Fernandez et al. (1989)
			Centaurea deflexa	Chicca et al. (2011)
			Centaurea floccosa	Negrete et al. (1988a)
			Centaurea kotschyi	Öksüz and Putun (1983)
			Centaurea linifolia	Gonzalez et al. (1977a), Nowak et al. (1986a)
			Centaurea ornata	Bastos et al. (1994)
			Centaurea ptosimopappa	Çelik et al. (2006)
			Centaurea ragusina	Mahmoud et al. (1986)
			Centaurea scoparia	Youssef and Frahm (1994b), Helal et al. (1997)

Table 9 (*continued*)

No	Structure	Name	Taxa	Ref.
			Centaurea solstitialis	Gonzalez et al. (1983), Jakupovic et al. (1986)
			Centaurea sventenii	Gonzalez et al. (1977a)
			Centaurea tagananensis	Gonzalez et al. (1984), Nowak et al. (1986a)
			Cheirolophus x *hortigenus*	Marco et al. (1994)
			Cheirolophus junoniaus	Gonzalez et al. (1993)
			Cheirolophus mauritanicus	Marco et al. (1994)
			Cheirolophus uliginosus	Marco et al. (1994)
			Grossheimia macrocephala	Barbetti et al. (1985), Piacentini et al. (1986), Piacentini et al., 1987
150		Kandavanolide	*Centaurea acaulis*	Bentamane et al. (2005)
			Centaurea kandavanensis	Rustaiyan and Ardebili (1984)
			Centaurea nicolai	Vajs et al. (1999)
			Centaurea salonitana	Daniewski et al. (1993), Nowak et al. (1996)
151		2α,9β-dihydroxy-dehydrocostus lactone	*Acroptilon repens*	Zhao et al. (2006)
152		salograviolide B	*Centaurea nicolai*	Vajs et al. (1999)
			Centaurea salonitana	Daniewski et al. (1993), Nowak et al. (1996)
153		3-deacetyl-9-*O*-acetyl-salograviolide A	*Centaurea nicolai*	Vajs et al. (1999)
154		14-chloro-10-β-hydroxy-10(14)-dihydrozaluzanin D	*Centaurea acaulis*	Bentamane et al. (2005)
155		9-acetylsalograviolide A	*Centaurea nicolai*	Vajs et al. (1999)
156		Salograviolide A; 9β-hydroxykandavanolide	*Centaurea ainetensis*	Ghantous et al. (2008), El-Najjar et al. (2008), Al-Saghir et al. (2009)
			Centaurea kandavanensis	Rustaiyan and Ardebili (1984)
			Centaurea nicolai	Vajs et al. (1999)
			Centaurea salonitana	Daniewski et al. (1992), Rychlewska et al. (1992), Nowak et al. (1996)
157		4′-nor-2′-methoxy-cynaropicrin	*Grossheimia macrocephala*	Barbetti et al. (1985)
158		Aguerin A	*Centaurea arbutifolia*	Gonzalez et al. (1981)
			Centaurea canariensis	Gonzalez et al. (1977a, 1978c)
			Centaurea pabotii	Marco et al. (1992)
			Centaurea salonitana	Daniewski et al. (1993)
			Cheirolophus junoniaus	Gonzalez et al. (1993)
			Cheirolophus mauritanicus	Marco et al. (1994)
			Cheirolophus metlesicsii	Gonzalez et al. (1993)
			Cheriolophus sempervirens	Marco et al. (1994)
			Cheirolophus teydis	Gonzalez et al. (1993)

(*continued on next page*)

Table 9 (*continued*)

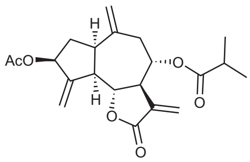
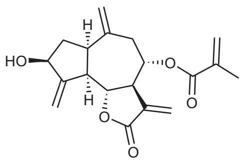
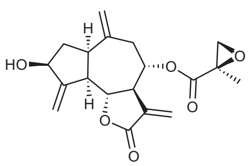
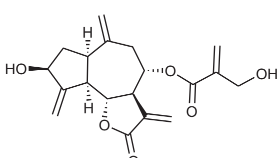
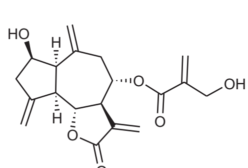
No	Structure	Name	Taxa	Ref.
159		Acetylaguerin A	*Cheirolophus metlesicsii*	Gonzalez et al. (1993)
160		Aguerin B; [a]aguerin β	*Acroptilon repens*	Stevens (1982), Nowak et al. (1986a)
			Amberboa tubuliflora	Ahmed et al. (1990)[a], Khan et al. (2010)
			Centaurea arguta	Gadeschi et al. (1989)
			Centaurea behen	Rustaiyan et al. (1981a), Öksüz et al. (1982), Nowak et al. (1986a)
			Centaurea canariensis	Gonzalez et al. (1977a, 1978c)
			Centaurea canariensis ssp. subexpin.	Gonzalez et al. (1977a, 1978c, 1982), Gonzalez Collado et al. (1986a)
			Centaurea deflexa	Chicca et al. (2011)
			Centaurea linifolia	Gonzalez et al. (1977a, 1978c,b), Nowak et al. (1986a)
			Centaurea musimomum	Medjroubi et al. (2005)
			Centaurea ragusina	Mahmoud et al. (1986)
			Centaurea solstitialis ssp. *schouwii*	Bruno et al. (1991b)
			Centaurea sventenii	Gonzalez et al. (1977a, 1978c)
			Chartolepis glastifolia	Öksük and Topçu (1994)
			Cheirolophus x hortigenus	Marco et al. (1994)
			Cheirolophus teydis	Gonzalez et al. (1993)
			Cheirolophus uliginosus	Marco et al. (1994)
			Grossheimia macrocephala	Barbetti et al. (1985)
			Rhaponticum pulchrum	Cis et al. (2006), Zhang et al. (2010)
			Rhaponticum uniflorum	Huneck and Knapp (1986)
161		15-deoxyrepin; salograviolide C	*Centaurea bella*	Nowak (1993a,b);Nowak et al. (1996)
			Centaurea salonitana	Daniewski et al. (1993)[a]; Nowak et al. (1996)
			Centaurea solstitialis	Jakupovic et al. (1986)
			Psephellus carthalinicus	Nowak et al. (1986b,a, 1996);Nowak (1992)
		[a]The stereochemistry of the side chain was not indicated in the original paper. Here it is given on the basis of the NMR values.	*Psephellus colchicus*	Nowak et al. (1986b, 1996), Nowak (1992)
			Psephellus daghestanicus	Nowak et al. (1986b, 1996), Nowak (1992)
			Psephellus dealbatus	Nowak et al. (1986b,a, 1996), Nowak (1992)
			Psephellus declinatus	Nowak et al. (1986b,a, 1996), Nowak (1992)
			Psephellus hypoleucus	Nowak et al. (1986b, 1996), Nowak (1992)
			Psephellus karabaghensis	Nowak et al. (1986b, 1996), Nowak (1992)
			Psephellus leucophyllus	Nowak et al. (1986b,a, 1996), Nowak (1990, 1992)
			Psephellus nogmovii	Nowak (1992), Nowak et al. (1996)
			Psephellus somcheticus	Nowak et al. (1986b, 1996), Nowak (1992)
			Psephellus taochius	Nowak et al. (1986b)
			Psephellus zangezuri	Nowak et al. (1986b,a, 1996), Nowak (1992)
			Rhaponticum uniflorum	Huneck and Knapp (1986)
162		cynaropicrin; sauprin	*Acroptilon repens*	Stevens (1982), Jakupovic et al. (1986), Nowak et al. (1986a), Zhao et al. (2006), Zha and Hou (2008)
			Amberboa divaricata	Forgacs et al. (1981), Rojatkar et al. (1997)
			Amberboa muricata	Gonzalez et al. (1973b, 1977a), Nowak et al. (1986a), Khan et al. (2010)
			Amberboa ramosa	Harrison and Kulshreshtha (1984), Khan et al. (2010)
			Amberboa tubuliflora	Omar et al. (1983), Ahmed et al. (1990), Khan et al. (2010)
			Centaurea adjarica	Nowak (1992), Nowak et al. (1996)
			Centaurea aegyptiaca	El Dahmy et al. (1985)
			Centaurea africana	Gonzalez et al. (1977a), Nowak et al. (1986a)
			Centaurea americana	Ohno et al. (1973), Nowak et al. (1986a)
			Centaurea arguta	Gadeschi et al. (1989)
			Centaurea behen	Rustaiyan et al. (1981a), Öksüz et al. (1982), Nowak et al. (1986a)
			Centaurea bella	Nowak (1992, 1993a,b), Daniewski and Nowak (1993)
			Centaurea clementei	Gonzalez et al. (1977a), Massanet et al. (1983), Nowak et al. (1986a), Gonzalez Collado et al. (1986a)
			Centaurea canariensis	Gonzalez et al. (1977a, 1978c,a, 1980b)
			Centaurea canariensis ssp. *subexpin.*	Gonzalez et al. (1977a), Gonzalez Collado et al. (1985, 1986a), Nowak et al. (1986a)
			Centaurea debeauxii ssp. *thuillieri*	Geppert et al. (1983), Nowak et al. (1986a)
			Centaurea deflexa	Chicca et al. (2011)

Table 9 (*continued*)

No	Structure	Name	Taxa	Ref.
			Centaurea exarata	Nowak et al. (1986a), Gousiadou and Skaltsa (2003)
			Centaurea helenoides	Yayli et al. (2006)
			Centaurea hermannii	Öksük et al. (1994)
			Centaurea hololeuca	Rosselli et al. (2006a)
			Centaurea hyssopifolia	Nowak et al. (1986a)
			Centaurea kotschyi	Öksüz and Putun (1983)
			Centaurea linifolia	Gonzalez et al. (1977a), Nowak et al. (1986a)
			Centaurea musimomum	Medjroubi et al. (2005)
			Centaurea ornata	Bastos et al. (1994)
			Centaurea phaeopappoides	Nowak et al. (1986a, 1989a, 1996), Nowak (1992)
			Centaurea ptosimopappa	Çelik et al. (2006)
			Centaurea ptosimopappoides	Öksük and Serin (1997)
			Centaurea ragusina	Mahmoud et al. (1986)
			Centaurea scabiosa	Kaminskii et al. (2010a), Kaminskii et al. (2010b), Kaminskii et al., 2010c, Kaminskii et al. (2011)
			Centaurea scoparia	Dawidar et al. (1989), Youssef and Frahm (1994b)
			Centaurea solstitialis sspschouwii	Bruno et al. (1991b)
			Centaurea solstitialis	Gonzalez et al. (1983), Merrill and Stevens (1985), Jakupovic et al. (1986), Wang et al. (1991), Hamburger et al. (1991), Cheng et al. (1992), Hay et al. (1994), Tešević et al. (1998b)
			Centaurea sventenii	Gonzalez et al. (1977a)
			Centaurea tagananensis	Gonzalez et al. (1984), Nowak et al. (1986a)
			Centaurea thracica	Nowak et al. (1986a, 1989a, 1996),Nowak (1992)
			Centaurothamnus maximus	Muhammad et al. (2003)
			Chartolepis bieberstenii	Nowak et al. (1986c, 1996),Nowak (1992)
			Chartolepis glastifolia	Nowak et al. (1986a,c, 1996), Nowak (1992)
			Chartolepis intermedia	Nowak et al. (1986a,c, 1996), Nowak (1992)
			Chartolepis pterocaula	Nowak et al. (1986c, 1996), Nowak (1992)
			Cheirolophus x *hortigenus*	Marco et al. (1994)
			Cheirolophus junoniaus	Gonzalez et al. (1993)
			Cheirolophus mauritanicus	Marco et al. (1994)
			Cheirolophus sempervirens	Marco et al. (1994)
			Cheirolophus teydis	Gonzalez et al. (1993)
			Cheirolophus uliginosus	Marco et al. (1994)
			Grossheimia macrocephala	Daniewski et al. (1982), Barbetti et al. (1985), Nowak et al. (1986a), Piacentini et al. (1986), Piacentini et al., 1987
			Leuzea rhapontica ssp. *helenifolia*	Nowak et al. (1988), Nowak (1992)
			Leuzea rhaponticoides	Nowak et al. (1988, 1996), Nowak (1992)
			Psephellus carthalinicus	Nowak et al. (1986b,a, 1996), Nowak (1992)
			Psephellus colchicus	Nowak (1992), Nowak et al. (1996)
			Psephellus daghestanicus	Nowak (1992), Nowak et al. (1996)
			Psephellus dealbatus	Nowak et al. (1986b,a, 1996), Nowak (1992)
			Psephellus declinatus	Nowak et al. (1986b,a, 1996), Nowak (1992)
			Psephellus hypoleucus	Nowak et al. (1986b, 1996), Nowak (1992)
			Psephellus karabaghensis	Nowak (1992), Nowak et al. (1996)
			Psephellus leucophyllus	Nowak et al. (1986b,a, 1996), Nowak (1992)
			Psephellus nogmovii	Nowak (1992), Nowak et al. (1996)
			Psephellus somcheticus	Nowak (1992), Nowak et al. (1996)
			Psephellus zangezuri	Nowak et al. (1986b,a, 1996), Nowak (1992)
			Rhaponticum pulchrum	Cis et al. (2006), Zhang et al. (2010)
			Rhaponticum serratuloides	Nowak et al. (1986a), Berdin et al. (1999)
			Rhaponticum uniflorum	Huneck and Knapp (1986)
			Stemmamarca carthamoides	Nowak et al. (1986a, 1988, 1996), Nowak (1990, 1992), Sorova et al. (2008), Kokoska and Janovska (2009)
			Stemmamarca rhapontica	Nowak et al. (1986a, 1996)
			Tricholepis glaberrima	Singhal et al. (1982), Nowak et al. (1986a), Bhattacharyya et al. (1996)
163		acroptin	*Acroptilon repens*	Serkerov and Aleskerova (1982)

(*continued on next page*)

Please cite this article in press as: Bruno, M., et al. Sesquiterpenoids in subtribe Centaureinae (Cass.) Dumort (tribe Cardueae, Asteraceae): Distribution, ^{13}C NMR spectral data and biological properties. Phytochemistry (2013), http://dx.doi.org/10.1016/j.phytochem.2013.07.002

Table 9 (*continued*)

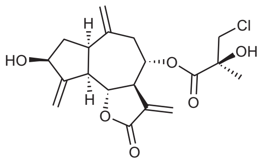
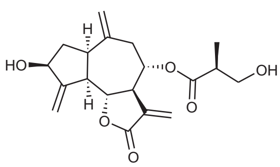
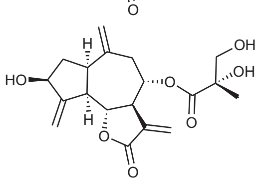
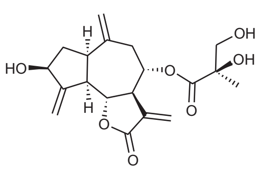
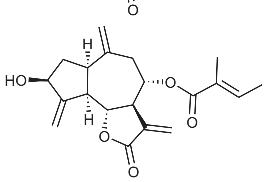
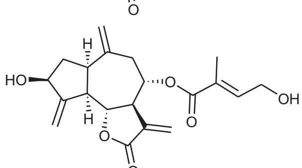
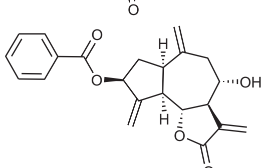
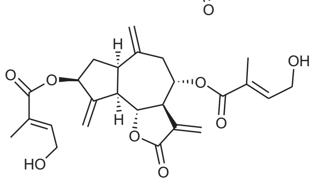
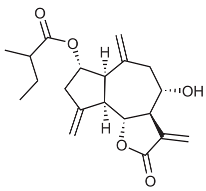
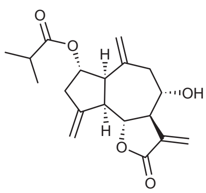
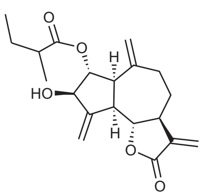
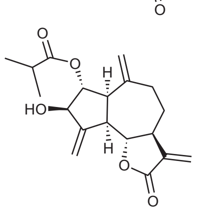
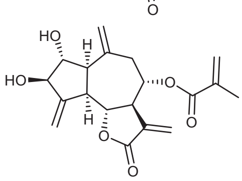
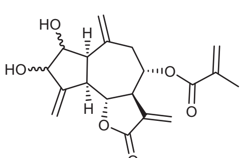
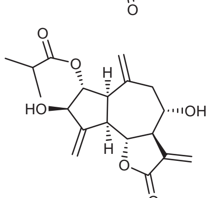
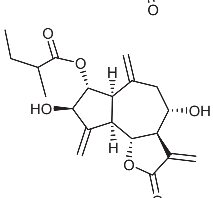
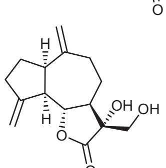
No	Structure	Name	Taxa	Ref.
164		Linichlorin B	*Centaurea kotschyi* *Centaurea linifolia* *Centaurea musimomum* *Centaurea salonitana* *Centaurea solstitialis* *Psephellus carthalinicus* *Psephellus colchicus* *Psephellus daghestanicus* *Psephellus dealbatus* *Psephellus declinatus* *Psephellus hypoleucus* *Psephellus karabaghensis* *Psephellus leucophyllus* *Psephellus nogmovii* *Psephellus somcheticus* *Psephellus taochius* *Psephellus zangezuri*	Öksüz and Putun (1983), Gürkan et al. (1998) Gonzalez et al. (1977a, 1978b), Nowak et al. (1986a) Medjroubi et al. (2005) Nowak et al. (1996) Jakupovic et al. (1986), Tešević et al. (1998b) Nowak et al. (1986b,a, 1996), Nowak (1992) Nowak et al. (1986b, 1996), Nowak (1992) Nowak et al. (1986b, 1996), Nowak (1992) Nowak et al. (1986b,a, 1996), Nowak (1992) Nowak et al. (1986b,a, 1996), Nowak (1992) Nowak et al. (1986b, 1996), Nowak (1992) Nowak et al. (1986b, 1996),Nowak (1992) Nowak et al. (1986b,a, 1996), Nowak (1990, 1992) Nowak (1992), Nowak et al. (1996) Nowak et al. (1986b, 1996), Nowak (1992) Nowak et al. (1986b) Nowak et al. (1986b,a, 1996), Nowak (1992)
165		Deacylcynaropicrin 8-O-[(S)-3′-hydroxy-2′-methylpropionate]	*Centaurea paboti* *Cheirolophus mauritanicus*	Marco et al., 1992 Marco et al. (1994)
166		(2′*S*)-17,18-dihydroxy-aguerin A; 3α-dihydro-4(15)-dehydrogrosshemin-α,β-dihydroxyisobutyrate [a]The side chain reported in the original paper has been amended	*Centaurea collina* *Centaurea ornata*	Fernandez et al. (1987)[a], 1989[a] Navarro et al., 1990
167		(2′*R*)-17,18-dihydroxy-aguerin A	*Centaurea kotschyi*	Öksüz and Putun (1983)
168		(1*S*,3*S*,5*R*,6*R*,7*R*,8*S*)-8-tigloyloxy-3-hydroxyguai-4(15),10(14),11(13)-triene-6,12-olide	*Centaurea scoparia*	Helal et al. (1997)
169		Cebellin F	*Centaurea adjarica* *Centaurea bella* *Centaurea scoparia* *Chartolepis glastifolia*	Nowak et al. (1986d, 1989a, 1996, 1992) Nowak et al. (1986d, 1996), Nowak (1990, 1992, 1993a,b) Helal et al. (1997) Nowak et al. (1986c, 1996)
170		8α-hydroxy-3β-(benzoyloxy)-1αH,5αH,6βH,7αH-guai-4(15),10(14),11(13)-trien-6,12-olide	*Centaurea scoparia*	Youssef (1998)
171		3β,8α-*O*-di-(4′-hydroxytygloyl)-1αH, 5αH,6βH,7αH-guai-4(15),10(14),11(13)-triene-6, 12-olide	*Centaurea scoparia*	Helal et al. (1997)

Table 9 (*continued*)

No	Structure	Name	Taxa	Ref.
172		Cebellin K	*Centaurea bella*	Nowak (1992, 1993a,b), Nowak et al. (1996)
173		Cebellin N	*Centaurea bella*	Daniewski and Nowak (1993), Nowak (1993a,b), Nowak et al. (1996)
174		Cebellin L	*Centaurea bella*	Nowak (1992, 1993a,b), Nowak et al. (1996)
175		Cebellin O	*Centaurea bella*	Daniewski and Nowak (1993), Nowak (1993a,b), Nowak et al. (1996)
176		Repdiolide	*Acroptilon repens* *Centaurea adjarica* *Centaurea bella* *Rhaponticum pulchrum* *Rhaponticum serratuloides* *Stemmacantha carthamoides*	Stevens (1982), Nowak et al. (1986a) Nowak et al. (1989a, 1996), Nowak (1992) Nowak et al. (1986d, 1996), Nowak (1990, 1992, 1993a,b) Cis et al. (2006), Zhang et al. (2010) Berdin et al. (2001) Nowak et al. (1988, 1996), Nowak (1992), Kokoska and Janovska (2009)
177		2,3-dihydroxy-8-methacryloyloxy-dehydrocostuslactone	*Acroptilon repens*	Rustaiyan et al. (1981b), Rustaiyan and Nazarians (1984)
178		Cebellin B	*Centaurea bella*	Nowak et al. (1986d, 1996), Nowak (1990, 1992, 1993a,b)
179		Cebellin A	*Centaurea bella*	Nowak et al. (1986d, 1996), Nowak (1990, 1992, 1993a,b)
180		3-Desoxysolstitialin A	*Centaurea imperialis*	Rustaiyan et al. (1984)

(*continued on next page*)

Table 9 (*continued*)

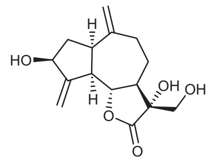
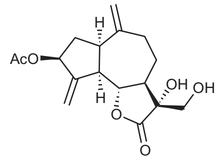
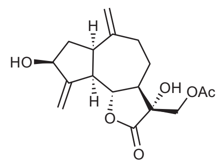
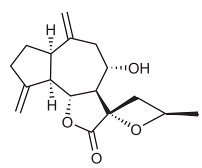
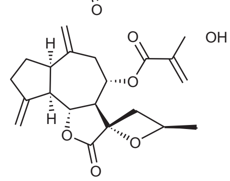
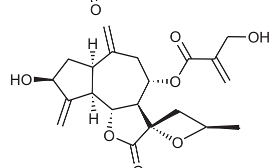
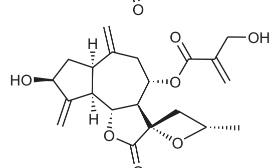
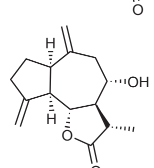
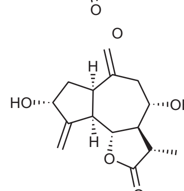
No	Structure	Name	Taxa	Ref.
181		Solstitialin A	*Centaurea depressa* *Centaurea imperialis* *Centaurea solstitialis*	Akkol et al. (2009) Rustaiyan et al. (1984) Thiessen et al. (1969), Thiessen and Hope (1970), Rybalko et al. (1975), Gonzalez et al. (1977a, 1983), Sakakibara et al. (1977), Merrill and Stevens (1985), Naidenova et al. (1988), Wang et al. (1991), Hamburger et al. (1991), Cheng et al. (1992), Tešević et al. (1998b), Yesilada et al. (2004), Gürbüz and Yesilada (2007), Akkol et al. (2009)
182		3-Acetylsolstitialin A	*Centaurea solstitialis*	Wang et al. (1991), Hamburger et al. (1991), Cheng et al. (1992)
183		13-Acetylsolstitialin A	*Centaurea behen* *Centaurea depressa* *Centaurea imperialis* *Centaurea solstitialis*	Gürkan et al. (1998) Akkol et al. (2009) Rustaiyan et al. (1984) Zarghami and Heinz (1969), Gonzalez et al. (1977a, 1983), Wang et al. (1991), Hamburger et al. (1991), Cheng et al. (1992), Hay et al. (1994), Tešević et al. (1998b), Yesilada et al. (2004), Gürbuz et al. (2006), Gürbüz and Yesilada (2007), Akkol et al. (2009),Ozcelik et al. (2009)
184		Subexpinnatin C	*Centaurea canariensis* ssp. *subexpin.*	Gonzalez Collado et al. (1985, 1986a)
185		Subexpinnatin B	*Centaurea canariensis* ssp. *subexpin.*	Gonzalez Collado et al. (1985, 1986a)
186		Clementein B	*Centaurea clementei*	Gonzalez Collado et al. (1986b,a)
187		Clementein	*Centaurea clementei*	Massanet et al. (1983), Gonzalez Collado et al. (1986b,a)
188		8α-hydroxy-11β-13H-dehydrocostus lactone	*Amberboa ramosa* *Centaurea canariensis* ssp. *subexpin.*	Khan (2004) Bohlmann and Gupta (1981), Nowak et al. (1986a)
189		3-*epi*-11,13-dihydro-deacylcynaropicrin	*Amberboa ramosa* *Centaurea canariensis* ssp. *subexpin.*	Khan (2004), Khan et al. (2010) Gonzalez Collado et al. (1985, 1986a)

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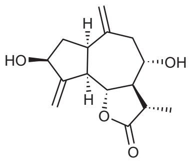
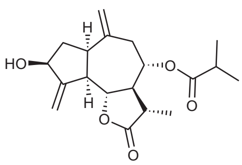
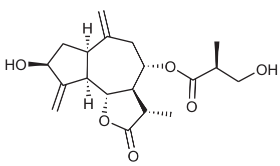
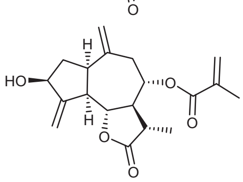
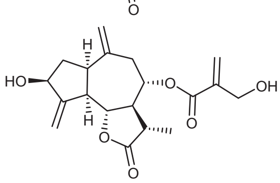
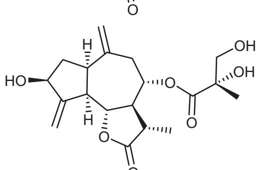
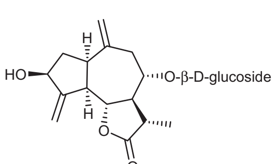
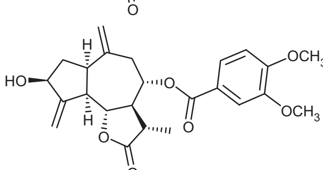
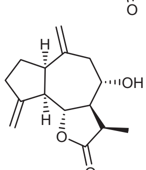
Table 9 (*continued*)

No	Structure	Name	Taxa	Ref.
190		11β,13-dihydro-deacylcynaropicrin; 11βH-11,13-dihydro-deacylaguerin A	*Amberboa ramosa* *Centaurea canariensis* ssp. *subexpin.* *Centaurea collina* *Centaurea paboti* *Centaurea ptosimopappa* *Centaurea ptosimopappoides* *Centaurea salonitana* *Centaurea solstitialis* *Cheirolophus junoniaus* *Cheirolophus mauritanicus* *Cheirolophus metlesicsii* *Cheirolophus teydis* *Cheirolophus uliginosus* *Tricholepis glaberrima*	Khan et al. (2005a), Ibrahim et al. (2010) Gonzalez Collado et al. (1985, 1986a) Fernandez et al. (1989) Marco et al., 1992 Çelik et al. (2006) Öksük and Serin (1997) Salan and Öksük (2003) Tešević et al. (1998b) Gonzalez et al. (1993) Marco et al. (1994) Gonzalez et al. (1993) Gonzalez et al. (1993) Marco et al. (1994) Singhal et al., 1982
191		11βH-11,13-dihydro-aguerin A	*Cheirolophus mauritanicus* *Cheirolophus metlesicsii*	Marco et al. (1994) Gonzalez et al. (1993)
192		deacylcynaropicrin 8-*O*-[(*S*)-3-hydroxy-2-methylpropionate]	*Cheirolophus mauritanicus*	Marco et al. (1994)
193		11β,13-dihydroaguerin B	*Cheirolophus uliginosus*	Marco et al. (1994)
194		11β,13-dihydrocynaropicrin	*Cheirolophus uliginosus*	Marco et al. (1994)
195		Deacylcynaropicrin 8-*O*-(2S,3-dihydroxy-2-methylpropionate)	*Centaurea collina*	Fernandez et al., 1987[a], 1989[a]
196		11βH-11,13-dihydrodesacylcynaropicrin-8-β-D-glucoside; 3β-hydroxy-11β,13-dihydro-8α-*O*-β-D-glucozaluzanin C	*Centaurea chilensis*	Negrete et al. (1988b)
197		3β-hydroxy-8α-(3′,4′-dimethoxybenzoyloxy)-11β, 13-dihydro-1αH,5αH,6βH,7αH-guai-4(15), 10(14)-dien-6,12-olide	*Centaurea scoparia*	Youssef (1998)
198		8α-hydroxy-11α-13H-dehydrocostus lactone	*Amberboa ramosa*	Khan et al. (2005a, 2010)

(*continued on next page*)

Table 9 (*continued*)

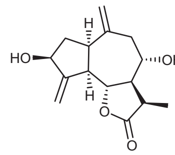
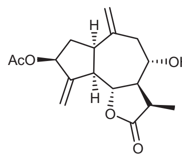
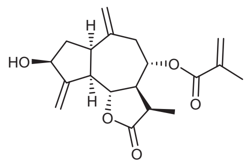
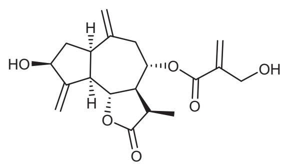
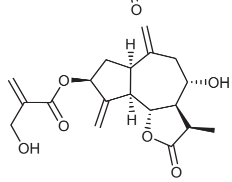
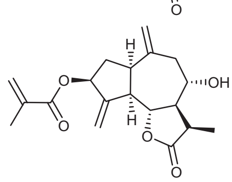
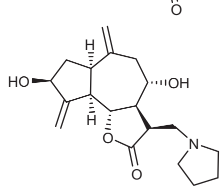
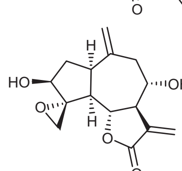
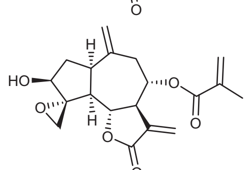
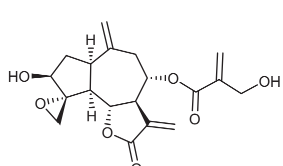
No	Structure	Name	Taxa	Ref.
199		8α-hydroxy-11α,13-dihydrozaluzanin C; 11αH-11,13-dihydro-deacylaguerin A; 11α,13-dihydro-deacylcynaropicrin	*Centaurea aegyptiaca*	El Dahmy et al. (1985)
			Centaurea ptosimopappa	Çelik et al. (2006)
			Centaurea scoparia	Helal et al. (1997), Kakuda et al. (1998)
			Cheirolophus metlesicsii	Gonzalez et al. (1993)
200		sinaicin	*Centaurea salonitana*	Salan and Öksük (2003)
			Centaurea sinaica	Al-Easa et al. (1990)
201		11α,13-dihydro-8α-methacryloyloxy-zaluzanin C	*Leuzea longifolia*	Santos et al. (1988)
202		11α,13-dihydro-8α-(2′-hydroxymethyl)-acryloyloxy-zaluzanin C	*Leuzea longifolia*	Santos et al. (1988)
203		11α,13-dihydro-3β-methacryloyloxy-zaluzanin C	*Leuzea longifolia*	Santos et al. (1988)
204		11α,13-dihydro-3β-methacryloyloxy-zaluzanin C	*Leuzea longifolia*	Santos et al. (1988)
205		8α-hydroxy-11α,13-dihydro-13-*N*-pyrrolidin-zaluzanin C;	*Acroptilon repens*	Zha and Hou (2008)
206		8-desacylrepin	*Centaurea aegyptiaca*	Sarg et al. (1987)
			Centaurea scoparia	Helal et al. (1997)
			Centaurea solstitialis	Jakupovic et al. (1986)
207		8-deacyloxy-8α-(methylacryloxy)-subteolide; 19-desoxyjanerin; 17,18-desoxyrepin	*Centaurea adjarica*	Nowak et al. (1996)
			Centaurea bella	Daniewski and Nowak (1993), Nowak (1993a,b), Nowak et al. (1996)
			Centaurea incana	Massiot et al. (1986)
			Centaurea musimomum	Medjroubi et al. (2005)
			Centaurea solstitialis	Jakupovic et al. (1986)
			Chartolepis glastifolia	Öksük and Topçu (1994)
			Rhaponticum pulchrum	Cis et al. (2006), Zhang et al. (2010)
208		Janerin	*Acroptilon repens*	Stevens (1982), Rustaiyan and Nazarians (1984), Nowak et al. (1986a), Jakupovic et al. (1986)
			Centaurea adjarica	Nowak et al. (1986d, 1989a, 1996), Nowak (1992)
			Centaurea aegyptiaca	Sarg et al. (1987)
			Centaurea babylonica	Bruno et al. (2005a)

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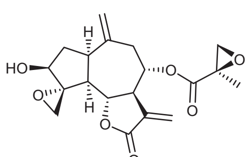
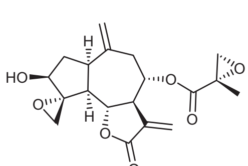
Table 9 (*continued*)

No	Structure	Name	Taxa	Ref.
			Centaurea bella	Geppert et al. (1983), Nowak et al. (1986d, 1996), Nowak (1990, 1992, 1993a,b)
			Centaurea conifera (=*Leuzea conifera*)	Bruno et al. (1998)
			Centaurea hermannii	Öksük et al. (1994)
			Centaurea hololeuca	Rosselli et al. (2006)°
			Centaurea incana	Massiot et al. (1986)
			Centaurea isaurica	Flamini et al., 2004
			Centaurea janeri	Gonzalez et al. (1977a,b)
			Centaurea marshalliana	Nowak et al. (1989a, 1996), Nowak (1992)
			Centaurea musimomum	Medjroubi et al. (2005)
			Centaurea phaeopappoides	Nowak et al. (1986a, 1989a, 1996), Nowak (1992)
			Centaurea ptosimopappa	Çelik et al. (2006)
			Centaurea scoparia	Youssef and Frahm (1994b)
			Centaurea sinaica	Sarg et al. (1988)
			Centaurea solstitialis	Merrill and Stevens (1985)
			Centaurea thracica	Nowak et al. (1989a, 1996), Nowak (1992)
			Centaurea uniflora ssp. *nervosa*	Appendino et al. (1986)
			Centaurothamnus maximus	Muhammad et al. (2003)
			Chartolepis biebersteinii	Nowak et al. (1986c, 1996), Nowak (1992)
			Chartolepis glastifolia	Nowak et al. (1986a,c, 1996), Nowak (1992)
			Chartolepis pterocaula	Nowak et al. (1986c, 1996), Nowak (1992)
			Leuza rhapontica ssp. *helenifolia*	Nowak et al. (1988, 1992)
			Leuzea rhaponticoides	Nowak et al. (1988, 1996), Nowak (1992)
			Psephellus carthalinicus	Nowak et al. (1986b,a, 1996), Nowak (1992)
			Psephellus colchicus	Nowak et al., 1986b, 1996, Nowak (1992)
			Psephellus daghestanicus	Nowak et al. (1986c, 1996), Nowak (1992)
			Psephellus dealbatus	Nowak et al. (1986b,a, 1996), Nowak (1992)
			Psephellus karabaghensis	Nowak et al. (1986b, 1996), Nowak (1992)
			Psephellus nogmovii	Nowak (1992), Nowak et al. (1996)
			Psephellus somcheticus	Nowak et al. (1986b, 1996), Nowak (1992)
			Psephellus taochius	Nowak et al. (1986b)
			Psephellus zangezuri	Nowak et al. (1986b,a, 1996), Nowak (1992)
			Rhaponticum pulchrum	Cis et al. (2006), Zhang et al. (2010)
			Stemmamarca carthamoides	Nowak et al. (1988, 1996), Nowak (1992), Kokoska and Janovska (2009)
			Stemmamarca rhapontica	Nowak et al. (1996)
209		Repin	*Acroptilon repens*	Evstratova et al., 1966;Rybalko et al. (1975), Gonzalez et al. (1977a), Rustaiyan et al. (1981b), Stevens (1982), Mallabaev et al. (1982), Rustaiyan and Nazarians (1984), Nowak et al. (1986a), Stevens et al. (1990), Robles et al. (1997)
			Centaurea adjarica	Nowak et al. (1989a, 1996), Nowak (1992)
			Centaurea aegyptiaca	Sarg et al. (1987)
			Centaurea babylonica	Bruno et al. (2005a)
			Centaurea bella	Geppert et al. (1983), Nowak et al. (1986d, 1996), Nowak (1990, 1992, 1993a,b)
			Centaurea conifera (=*Leuzea conifera*)	Bruno et al. (1998)
			Centaurea hololeuca	Rosselli et al. (2006a)
			Centaurea hyrcanica	Evstratova et al. (1969, 1972), Rybalko et al. (1975), Gonzalez et al. (1977a)
			Centaurea musimomum	Medjroubi et al. (2005)
			Centaurea scabiosa	Kaminskii et al., 2010b, Krasnov et al. (2011)
			Centaurea solstitialis	Merrill and Stevens (1985), Jakupovic et al. (1986), Hamburger et al. (1993)
			Chartolepis biebersteinii	Nowak et al. (1986c, 1996), Nowak (1992)
			Chartolepis glastifolia	Nowak et al. (1986a,c, 1996), Nowak (1992)
			Chartolepis pterocaula	Nowak et al. (1986c, 1996), Nowak (1992)
			Psephellus carthalinicus	Nowak et al. (1986b,a, 1996), Nowak (1992)
			Psephellus colchicus	Nowak et al. (1986b, 1996), Nowak (1992)
			Psephellus daghestanicus	Nowak et al. (1986b, 1996), Nowak (1992)
			Psephellus dealbatus	Nowak et al. (1986b,a, 1996), Nowak (1992)
			Psephellus karabaghensis	Nowak et al. (1986b, 1996), Nowak (1992)
			Psephellus nogmovii	Nowak (1992), Nowak et al. (1996)
			Psephellus somcheticus	Nowak et al. (1986b, 1996), Nowak (1992)
			Psephellus taochius	Nowak et al. (1986b)
			Psephellus zangezuri	Nowak et al. (1986b,a, 1996), Nowak (1992)
210		subluteolide	*Centaurea conifera* (=*Leuzea conifera*)	Bruno et al. (1998)
			Centaurea incana	Massiot et al. (1986)
			Centaurea solstitialis	Merrill and Stevens (1985), Hamburger et al., 1993

(*continued on next page*)

Table 9 (*continued*)

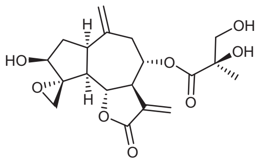
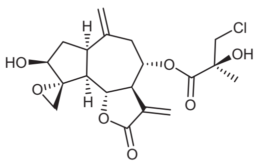
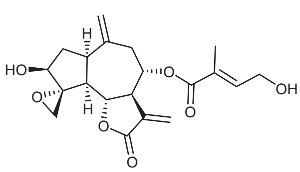
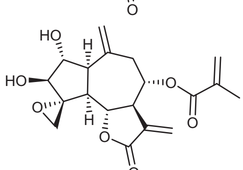
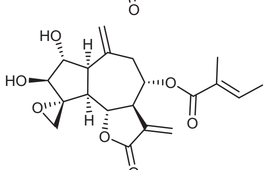
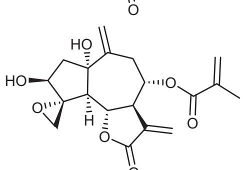
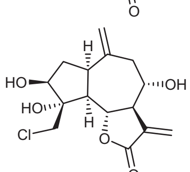
No	Structure	Name	Taxa	Ref.
211		Babylin A	*Centaurea babylonica*	Bruno et al. (2005a)
212		Chlorohyssopifolin C; acroptilin	*Acroptilon repens*	Evstratova et al., 1967, 1971, 1973, Gonzalez et al. (1977a), Rustaiyan et al. (1981b), Mallabaev et al., 1982, Rustaiyan and Nazarians (1984)
			Centaurea adjarica	Nowak et al. (1986d, 1989a, 1996), Nowak (1992)
			Centaurea babylonica	Bruno et al. (2005a)
			Centaurea bella	Geppert et al. (1983), Nowak et al. (1986d, 1996), Nowak (1990, 1992, 1993a,b)
			Centaurea hyrcanica	Evstratova et al., 1972, Rybalko et al. (1975), Gonzalez et al. (1977a)
			Centaurea hyssopifolia	Gonzalez et al., 1974b, 1977a, Nowak et al. (1986a)
			Centaurea incana	Massiot et al. (1986)
			Centaurea linifolia	Gonzalez et al. (1977a, 1978b), Nowak et al. (1986a)
			Centaurea marshalliana	Nowak et al. (1989a, 1996), Nowak (1992)
			Centaurea solstitialis	Merrill and Stevens (1985), Jakupovic et al. (1986)
			Chartolepis biebersteinii	Nowak et al. (1986c, 1996), Nowak (1992)
			Chartolepis glastifolia	Nowak et al. (1986a,c, 1996), Nowak (1992)
			Chartolepis pterocaula	Nowak et al. (1986c, 1996), Nowak (1992)
			Psephellus carthalinicus	Nowak et al. (1986b,a, 1996), Nowak (1992)
			Psephellus colchicus	Nowak et al. (1986b, 1996), Nowak (1992)
			Psephellus daghestanicus	Nowak et al. (1986b, 1996), Nowak (1992)
			Psephellus dealbatus	Nowak et al. (1986b,a, 1996), Nowak (1992)
			Psephellus karabaghensis	Nowak et al. (1986b, 1996), Nowak (1992)
			Psephellus nogmovii	Nowak (1992), Nowak et al. (1996)
			Psephellus somcheticus	Nowak et al. (1986b, 1996), Nowak (1992)
			Psephellus taochius	Nowak et al. (1986b)
			Psephellus zangezuri	Nowak et al. (1986b,a, 1996), Nowak (1992)
			Rhaponticum serratuloides	Berdin et al. (1999)
213		cebellin P	*Centaurea adjarica*	Nowak (1992)
			Centaurea bella	Nowak et al. (1986d, 1993a,b), Nowak et al. (1996)
			Centaurea scoparia	Helal et al. (1997)
			Centaurea uniflora ssp. *nervosa*	Appendino et al. (1986)
214		epoxyrepdiolide	*Acroptilon repens*	Stevens (1982), Nowak et al. (1986a)
			Centaurea aegyptiaca	Sarg et al. (1987)
215		8α-tigloyloxy-2α,3β-dihydroxy-4α- epoxydehydrocostulactone	*Centaurea uniflora* ssp. *nervosa*	Appendino et al. (1986)
216		Cebellin I	*Centaurea adjarica*	Nowak et al., 1986d, 1989a, 1996, Nowak (1992)
			Centaurea bella	Nowak et al. (1986d, 1996), Nowak (1990, 1992, 1993a,b)
217		Chlorohyssopifolin B	*Amberboa ramosa*	Khan (2004, 2010)
			Centaurea aegyptiaca	El Dahmy et al. (1985)
			Centaurea hyssopifolia	Gonzalez et al. (1972a, 1977a), Rybalko et al. (1975), Nowak et al. (1986a)
			Centaurea linifolia	Gonzalez et al. (1977a, 1978b), Nowak et al. (1986a)
			Centaurea scoparia	Youssef and Frahm, 1994a, Helal et al. (1997)

Table 9 (*continued*)

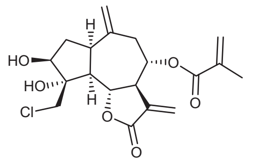
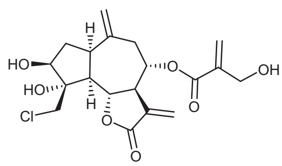
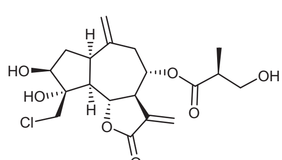
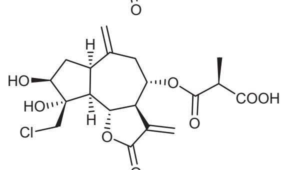
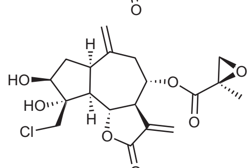
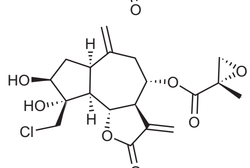
No	Structure	Name	Taxa	Ref.
218		19-deoxychlorojanerin; linochlorin A; elgin	*Acroptilon repens*	Mallabaev et al., 1982, Jakupovic et al. (1986)
			Centaurea adjarica	Nowak et al. (1996)
			Centaurea aegyptiaca	El Dahmy et al. (1985)
			Centaurea bella	Daniewski and Nowak (1993), Nowak (1993a,b), Nowak et al. (1996)
			Centaurea hermannii	Öksük et al. (1994)
			Centaurea linifolia	Gonzalez et al. (1977a, 1978b), Nowak et al. (1986a)
			Centaurea musimomum	Medjroubi et al. (2005)
			Centaurea scoparia	Dawidar et al., 1989
			Centaurea solstitialis	Tešević et al. (1998b)
			Chartolepis glastifolia	Öksük and Topçu (1994)
219		Chlorojanerin; cebellin C	*Acroptilon repens*	Jakupovic et al. (1986)
			Amberboa ramosa	Khan (2004), Khan et al. (2005a, 2010)
			Centaurea adjarica	Nowak et al. (1989a, 1996), Nowak (1992)
			Centaurea aegyptiaca	El Dahmy et al. (1985)
			Centaurea bella	Nowak et al. (1986d, 1996), Nowak (1990, 1992, 1993a,b)
			Centaurea conifera (=*Leuzea conifera*)	Fernandez et al. (1995)
			Centaurea hermannii	Öksük et al. (1994)
			Centaurea janeri	Gonzalez et al. (1977a,b)
			Centaurea marshalliana	Nowak et al. (1989a, 1996), Nowak (1992)
			Centaurea musimomum	Medjroubi et al. (2005)
			Centaurea phaeopappoides	Nowak et al. (1989a, 1996), Nowak (1992)
			Centaurea ptosimopappa	Çelik et al. (2006)
			Centaurea scoparia	Dawidar et al., 1989, Youssef and Frahm (1994a), Mattern et al., 1996
			Centaurea sinaica	Sarg et al. (1988)
			Centaurea solstitialis	Yesilada et al. (2004), Gürbuz et al. (2006), Gürbüz and Yesilada (2007), Ozcelik et al. (2009)
			Centaurea thracica	Nowak et al. (1989a, 1996), Nowak (1992)
			Centaurothamnus maximus	Muhammad et al. (2003)
			Chartolepis biebersteinii	Nowak et al. (1986c, 1996), Nowak (1992)
			Chartolepis glastifolia	Nowak et al. (1986a,c, 1996), Nowak (1992)
			Chartolepis pterocaula	Nowak et al. (1986c, 1996), Nowak (1992)
			Leuza rhapontica ssp. *helenifolia*	Nowak et al., 1988, Nowak (1992)
			Leuzea rhaponticoides	Nowak et al. (1988, 1996), Nowak (1992)
			Rhaponticum pulchrum	Cis et al. (2006), Zhang et al. (2010)
			Stemmamarca carthamoides	Nowak et al. (1988, 1996), Nowak (1992), Kokoska and Janovska (2009)
			Stemmamarca rhapontica	Nowak et al. (1996)
220		4β-(chloromethyl)-3β,4α-dihydroxy,8α- [(S)-3-hydroxy-2-methyl-propionyloxy]-1αH,5αH, 6βH,7αH-guaia-10(14),11(13)-dien-6,12-olide	*Amberboa ramosa*	Khan et al., 2004a, 2010
221		4β-(chloromethyl)-3β,4α-dihydroxy,8α- [(S)-2-carboxypropionoxy]-1αH,5αH,6βH, 7αH-guaia-10(14),11(13)- dien-6,12-olide	*Amberboa ramosa*	Khan et al., 2004a, 2010
222		17,18-epoxy-19-deoxy-chlorojanerin; solstiziolide	*Centaurea adjarica*	Nowak (1992), Nowak et al. (1996)
			Centaurea aegyptiaca	El Dahmy et al. (1985)
			Centaurea bella	Nowak (1992, 1993a,b), Nowak et al. (1996)
			Centaurea solstitialis	Merrill and Stevens (1985), Jakupovic et al. (1986)
223		*epi*-solstiziolide	*Centaurea incana*	Massiot et al. (1986)
			Centaurea solstitialis	Merrill and Stevens (1985)
			Chartolepis glastifolia	Öksük and Topçu (1994)

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Table 9 (*continued*)

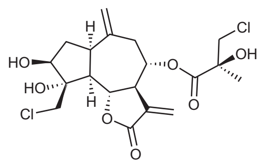
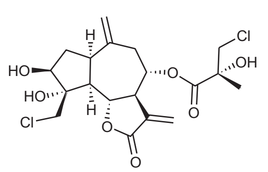
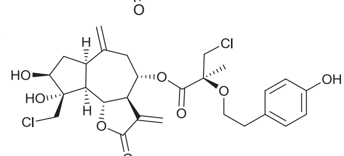
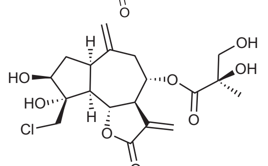
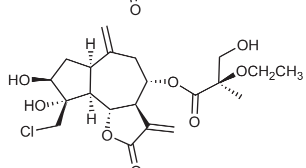
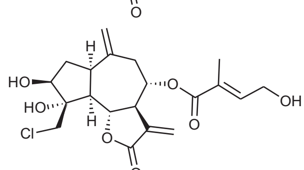
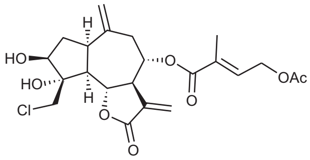
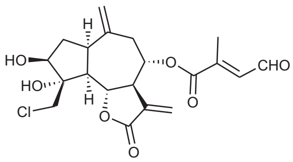
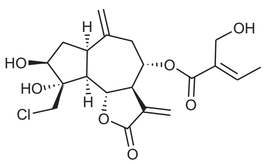
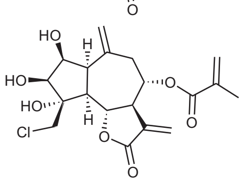
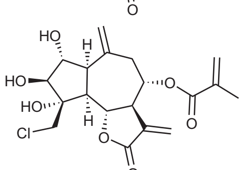
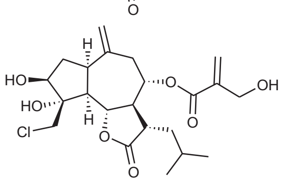
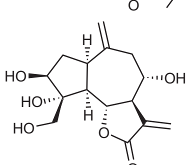
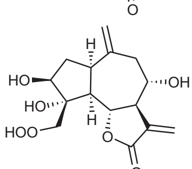
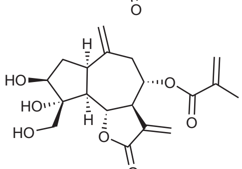
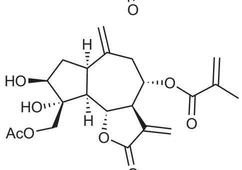
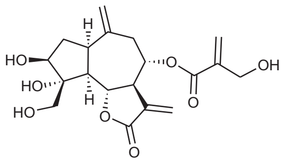
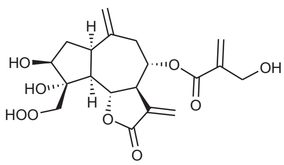
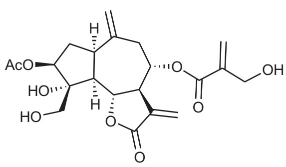
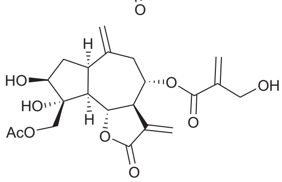
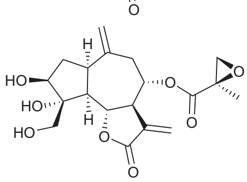
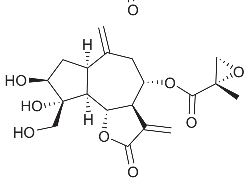
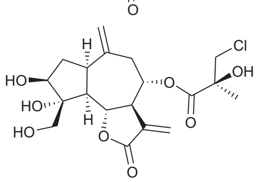
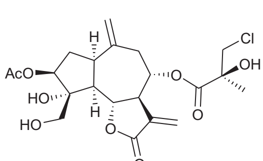
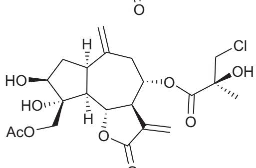
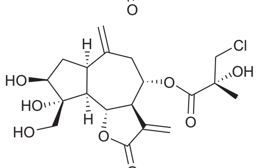
No	Structure	Name	Taxa	Ref.
224		chlorohyssopifolin A; centaurepensin; hyrcanin	*Acroptilon repens*	Harley-Mason et al. (1972), Gonzalez et al. (1977a), Cassady et al. (1979), Rustaiyan et al. (1981b), Mallabaev et al. (1982), Rustaiyan and Nazarians (1984)
			Centaurea adjarica	Nowak et al. (1989a, 1996), Nowak (1992)
			Centaurea aegyptiaca	El Dahmy et al. (1985)
			Centaurea bella	Nowak et al. (1986d, 1996), Nowak (1990, 1992, 1993a,b)
			Centaurea conifera (=*Leuzea conifera*)	Fernandez et al., 1995
			Centaurea hyrcanica	Evstratova et al., 1972, Rybalko et al. (1975)
			Centaurea hyssopifolia	Gonzalez et al. (1972a, 1977a), Rybalko et al. (1975), Nowak et al. (1986a)
			Centaurea imperialis	Rustaiyan et al. (1984)
			Centaurea linifolia	Gonzalez et al. (1977a, 1978b), Nowak et al. (1986a)
			Centurea musimomum	Medjroubi et al. (2005)
			Centaurea nigra	Gonzalez et al. (1974a, **?**), Gousiadou and Skaltsa (2003)
			Centaurea scoparia	Helal et al. (1997)
			Centaurea sinaica	Sarg et al. (1988), Al-Easa et al. (1990)
			Centaurea solstitialis	Sakakibara et al. (1977), Cassady et al. (1979), Jakupovic et al. (1986), Tešević et al. (1998b), Gürbuz et al. (2006), Ozcelik et al. (2009)
			Chartolepis biebersteinii	Nowak et al. (1986c, 1996),Nowak (1992)
			Chartolepis glastifolia	Nowak et al. (1986a,c, 1996), Nowak (1992), Öksük and Topçu (1994)
			Chartolepis pterocaula	Nowak et al. (1986c), Nowak (1992), Nowak et al. (1996)
			Psephellus carthalinicus	Nowak et al. (1986b,a, 1996), Nowak (1992)
			Psephellus colchicus	Nowak et al. (1986b, 1996), Nowak (1992)
			Psephellus daghestanicus	Nowak et al. (1986b, 1996), Nowak (1992)
			Psephellus dealbatus	Nowak et al. (1986b,a, 1996), Nowak (1992)
			Psephellus karabaghensis	Nowak et al. (1986b, 1996), Nowak (1992)
			Psephellus nogmovii	Nowak (1992), Nowak et al. (1996)
			Psephellus somcheticus	Nowak et al. (1986b, 1996), Nowak (1992)
			Psephellus taochius	Nowak et al. (1986b)
			Psephellus zangezuri	Nowak et al. (1986b,a, 1996), Nowak (1992)
			Rhaponticum serratuloides	Berdin et al. (1999)
			Rhaponticum uniflorum	Jiang et al. (1996)
			Serratula strangulata	Dai et al. (2001)
225		chlorohyssopifolin A 17-*epi*; 17-*epi* -centaurepensin	*Centaurea conifera* (=*Leuzea conifera*)	Fernandez et al. (1995)
			Centaurea musimomum	Medjroubi et al. (2005)
			Centaurea solstitialis	Tešević et al. (1998b)
			Chartolepis glastifolia	Öksük and Topçu (1994)
226		17-*O*-(p-hydroxy-phenylethanol)-centaurepensin	*Serratula strangulata*	Dai et al. (2001)
227		chlorohyssopifolin E	*Centaurea aegyptiaca*	Sarg et al. (1987)
			Centaurea hyssopifolia	Gonzalez et al. (1974b, 1977a)
			Centaurea linifolia	Gonzalez et al. (1977a, 1978b), Nowak et al. (1986a)
228		Chlorohyssopifolin D	*Centaurea hyssopifolia*	Gonzalez et al. (1974b, 1977a)
			Centaurea linifolia	Gonzalez et al. (1977a, 1978b), Nowak et al. (1986a)
229		deacetylcentaurepensin-8-*O*-(4′-hydroxy)-tiglate; cebellin D	*Centaurea adjarica*	Nowak et al. (1989a, 1996), Nowak (1992)
			Centaurea bella	Nowak et al. (1986d, 1996), Nowak (1990, 1992, 1993a,b)
			Centaurea imperialis	Rustaiyan et al. (1984)
			Centaurea marshalliana	Nowak et al. (1989a, 1996), Nowak (1992)
			Centaurea scoparia	Youssef and Frahm (1994a), Helal et al. (1997)

Table 9 (*continued*)

No	Structure	Name	Taxa	Ref.
			Centaurea solstitialis *Chartolepis glastifolia* *Chartolepis pterocaula*	Nowak (1992), Nowak et al. (1996); Tešević et al. (1998b) Nowak et al. (1986c, 1996), Nowak (1992) Nowak (1992), Nowak et al. (1996)
230		chloroscoparin	*Centaurea scoparia*	Youssef and Frahm (1994a)
231		4β-(chloromethyl)-3β,4α-dihydroxy-8α- (3′-formyl-2′-methyl-propenoyloxy)-1αH,5αH,6βH, 7αH-guai-10(14),11(13)-dien-6,12-olide	*Centaurea scoparia*	Youssef (1998)
232		4β-(chloromethyl)-3β,4α-dihydroxy-8α- (sarracenoyloxy)-1αH,5αH,6βH,7αH-guai-10(14),11(13)-dien-6,12-olide	*Centaurea scoparia*	Youssef (1998)
233		repensolide; cebellin E	*Acroptilon repens* *Centaurea adjarica* *Centaurea bella* *Rhaponticum pulchrum* *Stemmamarca carthamoides*	Jakupovic et al. (1986) Nowak et al. (1989a, 1996), Nowak (1992) Nowak et al. (1986d, 1996), Nowak (1990, 1992, 1993a,b) Cis et al. (2006), Zhang et al. (2010) Nowak et al. (1988, 1996), Nowak (1992), Kokoska and Janovska (2009)
234		chlororepdiolide	*Acroptilon repens*	Stevens and Wong (1986)
235		diain	*Centaurea scoparia*	Youssef and Frahm (1994b)
236		15-deschloro-15-hydroxy-chlorohysssopifolin B	*Amberboa ramosa*	Khan et al. (2005a, 2010)
237		hermanoid 2; 15-deschloro-15-hydroperoxy-chlorohysssopifolin B	*Centaurea hermannii*	Öksük et al. (1994)
238		pterocaulin; repdiolide triol	*Centaurea incana* *Chartolepis biebersteinii* *Chartolepis glastifolia* *Chartolepis pterocaula*	Massiot et al. (1986) Nowak et al. (1986c, 1996), Nowak (1992) Öksük and Topçu (1994) Nowak et al. (1986c, 1996), Nowak (1990, 1992)
239		Rhaserolide	*Rhaponticum serratuloides*	Berdin et al. (1999), Zhang et al. (2010)

(*continued on next page*)

Table 9 (*continued*)

No	Structure	Name	Taxa	Ref.
240		15-deschloro-15-hydroxychlorojanerin	*Amberboa ramosa*	Khan et al. (2005a, 2010)
			Centaurea conifera (=*Leuzea conifera*)	Bruno et al. (1998)
			Centaurea hololeuca	Rosselli et al. (2006a)
			Centaurea scoparia	Dawidar et al., 1989
			Rhaponticum pulchrum	Cis et al. (2006), Zhang et al. (2010)
241		Hermanoid 1 15-deschloro-15-hydroperoxy-chlorojanerin	*Centaurea hermannii*	Öksük et al. (1994)
			Chartolepis glastifolia	Öksük and Topçu (1994)
242		15-deschloro-3β-acetyl-15-hydroxy-chlorojanerin	*Centaurea hermannii*	Öksük et al. (1994)
243		cebellin G; 15-deschloro-15-acetoxy-chlorojanerin	*Centaurea adjarica*	Nowak et al. (1986d)
			Centaurea bella	Nowak et al. (1986d, 1996), Nowak (1990, 1992, 1993a,b)
			Centaurea hermannii	Öksük et al. (1994)
			Centaurea hololeuca	Rosselli et al. (2006a)
			Centaurea scoparia	Dawidar et al., 1989
			Rhaponticum pulchrum	Cis et al. (2006), Zhang et al. (2010)
244		babylin B	*Centaurea babylonica*	Bruno et al. (2005a)
			Centaurea conifera (=*Leuzea conifera*) or **245**	Bruno et al. (1998)
			Centaurea hololeuca	Rosselli et al. (2006a)
245		15-deschloro-15-hydroxy-episolstiolide	*Chartolepis glastifolia*	Öksük and Topçu (1994)
246		cebellin J; desacyllinochlorin C; 15-deacetylrhaposerin	*Centaurea adjarica*	Nowak et al. (1996)
			Centaurea babylonica	Bruno et al. (2005a)
			Centaurea bella	Nowak et al. (1986d, 1996), Nowak (1990, 1992, 1993a,b)
			Centaurea hololeuca	Rosselli et al. (2006a)
			Centaurea linifolia	Gonzalez et al. (1977a), Nowak et al. (1986a)
			Chartolepis glastifolia	Öksük and Topçu (1994)
			Rhaponticum serratuloides	Berdin et al. (2001), Zhang et al. (2010)
247		linochlorin C	*Centaurea linifolia*	Gonzalez et al. (1977a, 1978b), Nowak et al. (1986a)
248		rhaposerin	*Rhaponticum serratuloides*	Berdin et al. (1999), Zhang et al. (2010)
249		Epicebellin J	*Chartolepis glastifolia*	Ö ksü k and Topç u (1994)

Please cite this article in press as: Bruno, M., et al. Sesquiterpenoids in subtribe Centaureinae (Cass.) Dumort (tribe Cardueae, Asteraceae): Distribution, ^{13}C NMR spectral data and biological properties. Phytochemistry (2013), http://dx.doi.org/10.1016/j.phytochem.2013.07.002

Table 9 (*continued*)

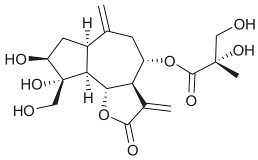
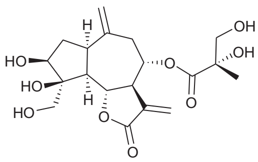
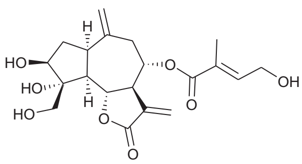
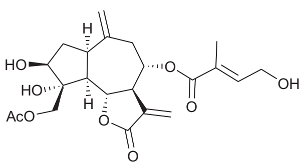
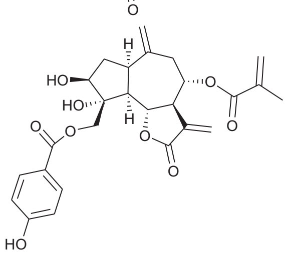
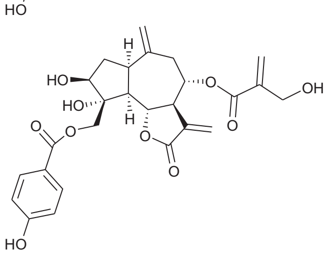
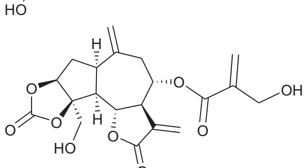
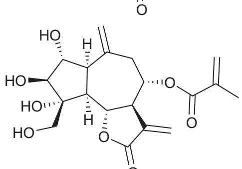
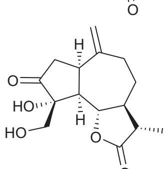
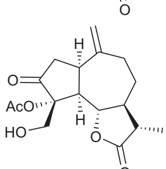
No	Structure	Name	Taxa	Ref.
250		Sinicin A	*Centaurea pseudosinaica*	Amer et al. (2001)
251		Sinicin B	*Centaurea pseudosinaica*	Amer et al. (2001)
252		13-deschloro-15-hydroxy-8-desacylcentaurepensin-8-*O*-(4′-hydroxy)- tiglate	*Centaurea imperialis*	Rustaiyan et al. (1984)
253		Cebellin H	*Centaurea bella*	Nowak et al. (1986d, 1996), Nowak (1990, 1992, 1993a,b)
254		19-desoxypicrolide A	*Chartolepis glastifolia*	Öksük and Topçu (1994)
255		Picrolide A	*Acroptilon repens*	Stevens et al. (1991)
256		Hololeucin	*Centaurea hololeuca*	Rosselli et al. (2006b)
257		Rhaserin	*Rhaponticum serratuloides*	Berdin et al. (2001), Zhang et al. (2010)
258		3-oxo-4α-hydroxy-15-hydroxy-1αH,5αH, 6βH,7αH,11βH-guai-10(14)-ene-6,12-olide	*Centaurea musimomum*	Medjroubi et al. (1997)
259		3-oxo-4α-acetoxy-15-hydroxy-1αH,5αH, 6βH,7αH,11βH-guai-10(14)-ene-6,12-olide	*Centaurea musimomum*	Medjroubi et al. (1997)

Table 9 (*continued*)

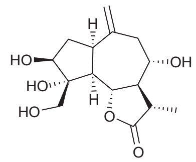
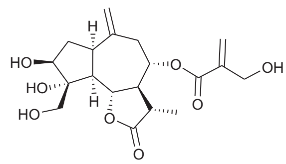
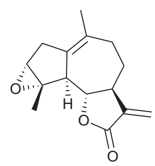
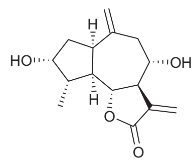
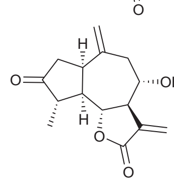
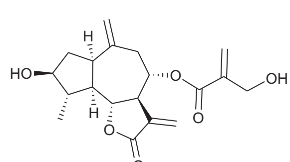
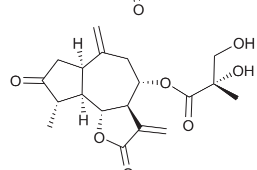
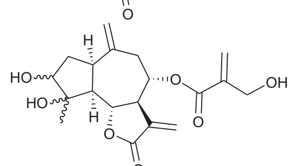
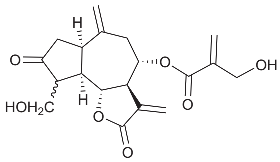
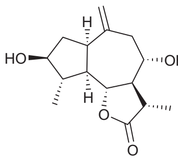
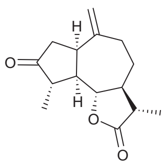
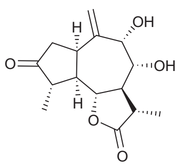
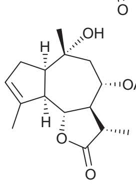
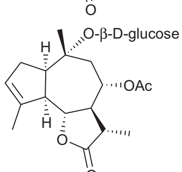
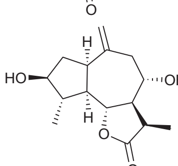
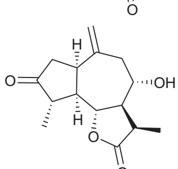
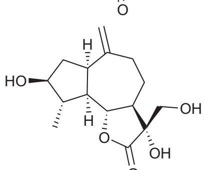
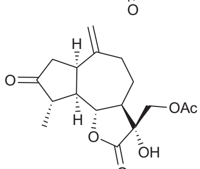
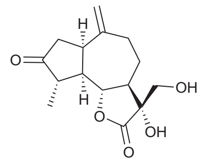
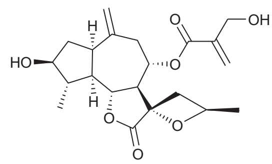
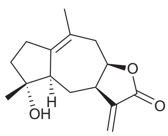
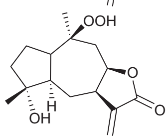
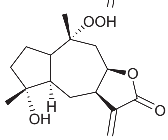
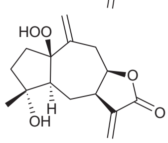
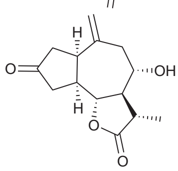
No	Structure	Name	Taxa	Ref.
260		Saussureolide	*Amberboa ramosa*	Khan et al. (2005b, 2010)
261		ramosine; 15-dechloro-15-hydroxychlorojanerin	*Amberboa ramosa*	Khan et al. (2004b, 2010)
262		ludartin	*Amberboa ramosa*	Khan et al. (2004c)
263		Grosheiminol	*Grossheimia macrocephala*	Daniewski et al. (1982), Barbetti et al. (1985)
264		Grosshemin; grosheimin	*Amberboa lippii*	Gonzalez et al. (1967), Gonzalez et al., 1970, Gonzalez et al., 1977a, Gonzalez et al., 1978a, Breton et al. (1968), Bermejo et al. (1969), Rybalko et al. (1975), Khan et al. (2010)
			Centaurea behen	Rustaiyan et al. (1981a), Öksüz et al. (1982), Nowak et al. (1986a), Gürkan et al. (1998)
			Centaurea helenioides	Yayli et al. (2006)
			Centaurea ornata	Gonzalez et al. (1977a)
			Centaurea ruthenica	Adekenov et al. (1986b), Adekenov (1995)
			Centaurea scabiosa	Krasnov et al. (2006), Kaminskii et al. (2010b,c)
			Chartolepis glastifolia	Nowak et al. (1986a)
			Chartolepis intermedia	Mukhametzhanov et al. (1969d), Rybalko et al. (1975), Nowak et al. (1986a,c, 1996), Adekenov et al. (1986b, 1991), Nowak (1992), Adekenov (1995)
			Chartolepis pterocaula	Nowak et al. (1986c, 1996), Nowak (1990, 1992)
			Grossheimia macrocephala	Rybalko et al. (1964), Rybalko et al., 1975, Rybalko and Sheichenko (1965), Sheichenko and Rybalko (1970, 1972), Bialecki et al. (1973), Gonzalez et al. (1977a, 1978a), Daniewski et al. (1982), Barbetti et al. (1985), Nowak et al. (1986a), Monea (1986), Piacentini et al. (1986, 1987), Adekenov (1995)
			Grossheimia ossica	Bialecki et al. (1973), Popova et al. (1974)
265		Muricatin	*Amberboa muricata*	Gonzalez et al. (1973b, 1977a), Nowak et al. (1986a), Khan et al. (2010)
266		grosheimin-2′*S*,3′-dihydroxy-isobutyrate	*Centaurea ornata*	Navarro et al. (1990)[a], Bastos et al. (1994)
		[a]Stereochemistry of the side chain not assigned in the original paper.		
267		Acrorepiolide	*Acroptilon repens*	Rustaiyan et al. (1981b), Rustaiyan and Nazarians (1984)

Table 9 (*continued*)

No	Structure	Name	Taxa	Ref.
268		15-hydroxy-8-(4′-hydroxymethacroyloxy)-10(14),11(13)-guaiadien-6,12-olide	*Centaurea tweediei*	Fortuna et al. (2001)
269		Isolipidiol	*Amberboa lippii*	Gonzalez et al. (1970, 1977a), Rybalko et al. (1975), Khan et al. (2010)
			Amberboa muricata	Gonzalez et al. (1973b, 1977a), Nowak et al. (1986a), Khan et al. (2010)
			Centaurea clementei	Gonzalez Collado et al. (1986a)
			Grossheimia macrocephala	Daniewski et al. (1982), Nowak et al. (1986a)
270		tetrahydro-dehydrozaluzanin C; dihydroestafiatone	*Centaurea webbiana*	Gonzalez et al. (1972b, 1977a, 1978a)
271		8α,9α-dihydroxy-4β,15,11β,13-tetrahydro-dehydrozaluzanin C	*Amberboa tubuliflora*	Ahmed et al. (1990), Khan et al. (2010)
272		Amberbin A; dihydrocumambrin A	*Amberboa ramosa*	Ibrahim et al. (2010)
273		Amberbin B	*Amberboa ramosa*	Ibrahim et al. (2010)
274		Lipidiol	*Amberboa lippii*	Gonzalez et al. (1970, 1977a, 1978a), Rybalko et al. (1975), Khan et al. (2010)
275		Amberboin	*Amberboa lippii*	Gonzalez et al. (1967), Gonzalez et al., 1970, Gonzalez et al., 1977a, Gonzalez et al., 1978a, Bermejo et al. (1969), Rybalko et al. (1975), Khan et al. (2010)
			Centaurea sinaica	Al-Easa et al. (1990)
276		cynaratriol	*Centaurea musimomum*	Lopes-Rodriguez et al. (2009)
277		4β,15-dihydro-3-dehydro-13-acetylsolstitialin A	*Centaurea behen*	Öksüz et al. (1982, 1993)
			Centaurea musimomum	Nowak, 1990, Medjroubi et al. (2005)
			Centaurea solstitialis ssp. *shouwii*	Bruno et al. (1991b), Ö ksü z et al. (1993)

(*continued on next page*)

Table 9 (*continued*)

No	Structure	Name	Taxa	Ref.
278		4β,15-dihydro-3-dehydrosolstitialin A	*Centaurea behen* *Centaurea musimomum* *Centaurea ptosimopappa*	Rustaiyan et al. (1981a) Gonzalez-Platas et al. (1999), Medjroubi et al. (2003b) Çelik et al. (2006)
279		Clementein C	*Centaurea clementei*	Gonzalez Collado et al. (1986b,a)
280		Pseudoivalin	*Serratula latifolia*	Rustaiyan and Feramarzi (1988)
281		4α-hydroxy-10β-hydroperoxyguaia-1,11(13)-dien-12, 8β-olide	*Serratula latifolia*	Rustaiyan and Feramarzi (1988)
282		4α-hydroxy-10α-hydroperoxyguaia-1,11(13)-dien-12, 8β-olide	*Serratula latifolia*	Rustaiyan and Feramarzi (1988)
283		4α-hydroxy-1β-hydroperoxyguaia-10(14),11(13)-dien-12, 8β-olide	*Serratula latifolia*	Rustaiyan and Feramarzi (1988)
284		(3a,3a*R*,4*S*,6a*R*,9a*S*,9b*R*)-4-hydroxy-3-methyl-6-methyleneoctahydroazuleno[4,5-b]furan-2,8(3H,9bH)-dione	*Centaurea deflexa*	Chicca et al. (2011)

against six bacteria and eight fungal species. All compounds showed greater antibacterial and antifungal activities than the positive control used, streptomicyn and miconazole, respectively (Djeddi et al., 2007, 2008b). On the other hand compounds **34** and **35**, epoxygermacranes isolated from *Stizolophus balsamita*, exhibited only moderate antimicrobial activity against three bacterial strains and antifungal activity toward *Candida candicans* (Suleimenov et al., 2005a), and 8-hydroxyzaluzanin C (**149**) against *S. aureus*, and *E. coli* (Ndom et al., 2006). Antimicrobial properties against *S. aureus* and *Micrococcus luteus* were determined, by disc diffusion method, for compounds **142** and **143**, structurally similar to **149** (Negrete et al., 1984).

Santamarin (**99**), alantolactone (**121**), pseudoivalin (**280**), 9α-hydroxypartenolide (**28**) and grosshemin (**264**) were shown to have antibiotic activity against five bacteria, the best compound being 9α-hydroxypartenolide (**28**) (Picman, 1983a). This germacrane at concentrations of 50 and 100 μg/disc, inhibited the growth of several microorganism showing the most relevant antibacterial activity against *E. coli* (El Hassany et al., 2004).

In radio-respirometric bioassays against *Mycobacterium tuberculosis* and *Mycobacterium avium*, dehydrocostus lactone (**142**) exhibited MIC of 2 and 16 μg/mL, respectively (Cantrell et al., 1998), whereas costunolide (**1**), santamarine (**99**), reynosin (**100**) (Fischer et al., 1998) and alantolactone (**121**) (Cantrell et al., 1999) are moderately active against *M. tuberculosis* with MIC around 32–64 μg/mL.

Costunolide (**1**) and dehydrocostus lactone (**142**), were the compounds responsible for the antimycobacterial activity against *M. tuberculosis* H37Rv with MICs of 6.3 and 12.5 mg/L, respectively. Antimycobacterial activity against drug-resistant (rifampicin-resistant) *M. tuberculosis* clinic isolates appeared to be better for the mixture than for pure compounds because of a synergistic effect (Luna-Herrera et al., 2007). Costunolide (**1**), isolated from *Chrysanthemum boreale*, also showed antibacterial activity against *Vibrio parahaemolyticus*, *B. subtilis*, *B. cereus* and *S. aureus* (Jang et al., 1998a).

The antibacterial activity of costunolide (**1**) against six plant pathogenic bacteria, *Pseudomonas solanacearum*, *Sarcina lutea*, *Agrobacterium tumefaciens*, *Erwinia amylovolora*, *Erwinia cartovora* and *Corynebacterium fascians*, was also evaluated using the agar dilution method. Costunolide was as effective as streptomycin against *C. fascians* with a MIC value of 10 mg/L (Abdelgaleil and Ahmed, 2005).

Anti-*Helicobacter pylori* effect of costunolide (**1**) was also investigated using one commercial strain (*H. pylori* ATCC 43504) and three clinical strains (*H. pylori* 4, 43, 82548). Costunolide exhibited

Table 10
^{13}C NMR data of guaianes.

C	$142^{a,p}_{1}$	142^{a}_{2}	143^{a}_{3}	147^{a}_{3}	148^{a}_{4}	149^{a}_{5}	149^{b}_{6}	150^{a}_{7}	152^{a}_{8}	153^{a}_{9}	154^{a}_{10}	155^{a}_{9}	156^{a}_{9}	158^{a}_{7}	160^{a}_{7}	161^{a}_{8}	162^{a}_{5}	164^{a}_{11}	165^{a}_{12}	$166^{n.r.}_{13}$
1	47.3	47.6	49.3	44.0	44.6	45.2	46.0	45.6	45.1	48.8*	44.8	48.8*	48.7*	45.4	45.3	45.3	45.3	45.6[j]	45.3	45.3
2	30.7	30.3	30.3	38.9	36.5	39.2	40.0	36.5	34.4	38.1	33.8	36.0	36.1	39.0	39.1	39.1[j]	39.1	39.1	39.0	38.3
3	32.4	32.6	32.0	73.3	74.7	73.7	73.1	74.7	71.8	73.6	75.6	74.5	74.6	73.7	73.8	73.8	73.7	73.7	73.5	73.2
4	151.0	151.2	150.0	152.9	148.0	152.4	154.3	147.3	146.7[j]	152.0	149.9	147.4	146.9	152.3	152.4	152.2[k]	152.2	152.0	152.1	151.8
5	51.7	52.0	53.1	49.8	50.3	51.3	51.9	51.7	52.0	48.3*	50.0	47.8*	47.0*	51.4	51.4	51.4	51.4	51.7[j]	51.4	51.5
6	85.0	85.2	78.6	83.9	83.3	79.0	80.9	78.1	76.6	78.8	85.0	78.8	79.4	78.7	78.6	78.3[l]	78.6	78.1	78.6	78.1
7	44.8	45.1	51.0	45.4	45.3	51.0	51.7	51.1	50.5	40.9	46.0	41.1	40.9	47.7	47.7	47.7	47.6	47.3	47.2	46.9
8	30.4	30.9	72.2	30.4	30.6	71.9	74.1	72.0	74.3	75.2	24.0	75.2	77.6	73.9	74.1	75.2[l]	74.3	75.9	73.9	75.2
9	36.0	36.3	42.7	34.0	34.5	41.3	42.9	41.4	36.3	81.0	37.8	81.0	79.7	37.0	37.2	36.9[j]	37.0	35.8	36.5	35.6
10	148.9	149.2	143.7	147.9	147.7	142.7	144.7	142.3	58.4	143.8	74.9	143.7	147.7	141.9	141.9	141.3[k]	141.8	141.4	141.9	141.6
11	139.4	139.7	138.1	139.6	139.5	138.1	140.6	138.0	138.3[j]	136.3	139.2	135.9	136.1	137.7	137.5	137.4[k]	137.4	137.5	137.3	136.8
12	169.9	170.2[j]	169.9	170.0	170.0	169.9	172.0	169.5	170.7	170.0	169.3	170.6	171.1	169.6	169.2	169.8	169.2	168.8	169.6	169.5
13	119.7	120.2[j]	123.3	120.1	120.4	123.2	122.9	123.2	123.2	125.1	120.0	125.5	125.3	122.2	122.6	122.3	122.7	122.1	123.0	123.6
14	112.3	112.6[k]	116.1	114.3	114.4	117.1	117.0	117.5	55.7	113.6	53.1	113.8	112.5	117.9	118.1	118.8	118.2	118.7	118.1	118.1
15	109.2	109.6[k]	111.1	111.0	113.6	113.2	112.1	115.8	116.6	111.9	114.5	113.1	112.4	113.2	113.5	113.7	113.5	114.1	113.6	113.8
1′					170.8			170.7	169.3	169.6	169.3	170.6	170.4	176.4	166.4	168.8	165.4	171.7	171.1	174.8
2′					21.3			21.3	21.2	21.1	21.2	21.1	20.9	34.2	136.1	53.8	139.4	74.7	42.4	76.0
3′														18.9	126.6	52.8	126.6	51.1	64.4	68.1
4′														18.6	18.3	17.4	62.1	23.4	13.5	21.6
1″												169.9								
2″												21.0								

C	168^{a}_{14}	169^{a}_{14}	171^{a}_{14}	$176^{a,p}_{16}$	176^{i}_{16}	180^{a}_{17}	181^{e}_{18}	181^{i}_{16}	182^{e}_{18}	183^{a}_{18}	184^{e}_{19}	186^{e}_{20}	188^{a}_{21}	189^{d}_{21}	190^{a}_{5}	191^{a}_{7}	192^{a}_{3}	193^{a}_{3}	194^{a}_{3}	$195^{n.r.}_{13}$
1	45.3	45.1	45.5	51.4	46.8	47.3	42.8	43.5	44.1	42.9	44.5*	44.9	47.2	43.6	44.2	44.3	44.3	44.0	44.1	44.5
2	39.1	38.9	36.3	77.3	78.9	30.1	38.0	39.4	36.6	38.3	30.5	39.1	30.1[j]	41.3	39.0	38.9	38.8	38.6	38.6	38.7
3	73.7	73.6	75.0	78.9	79.8	32.3	72.7	73.2	75.4	73.3	30.2	73.3	32.3[j]	75.0	73.6	73.6	73.6	73.4	73.5	73.3
4	152.3	152.1	152.2	147.2	151.3	149.6	152.3	155.4	149.1	154.6	151.6	153.5	151.1	155.7	153.0	152.8	152.7	152.6	152.5	152.4
5	51.3	51.2	51.4	46.5	52.9	52.1	52.2	53.4	52.4	52.5	53.3	51.7	52.5	50.4	50.7	50.7	50.7	50.3	50.4	51.0
6	78.4[n]	78.6	77.4[n]	78.8	78.5	85.0	82.1	83.2	82.8	82.0	79.7	79.0	80.2	80.3	79.1	79.0	78.9	78.9	78.8	78.7
7	47.8	47.5	47.7	47.9	48.4	47.5	49.9	50.7	51.1	49.6	55.5	51.0	55.4	55.7	56.0	53.2	53.1	53.2	53.3	52.2
8	73.8	74.1	74.1	73.8	74.5	25.2	26.2	27.7	26.7	26.9	68.0	70.3	75.1	73.7	74.9	75.7	76.1	76.0	76.2	77.7
9	37.2	36.9	37.5	35.8	36.8	36.0	35.6	37.6	36.3	35.9	32.3	30.0	47.0	48.4	44.8	40.5	40.3	40.3	40.3	39.0
10	141.9	141.7	141.6	139.4	141.5	132.0	148.7	150.5	148.6	148.6	145.1	143.0	144.5	145.8	143.2	142.3	142.1	142.1	142.0	141.8
11	137.4	137.3	137.2	137.2	138.9	77.2	n.r.	78.6	n.r.	75.5	76.5	75.5	41.6	39.8	42.0	41.3	41.4	41.2	41.2	41.3
12	169.2	169.2	169.1	169.1	169.2	180.0	179.0	180.5	179.7	176.5	178.9	178.1	179.1	178.5	178.6	177.8	177.8	177.8	177.7	178.4
13	122.6	122.7	122.9	n.r.	121.3	64.6	62.9	64.9	63.5	64.1	44.1*	43.1	16.1	15.4	15.9	15.6	15.5	15.4	15.4	15.2
14	118.0	118.1	118.4	n.r.	119.2	112.4[j]	113.1	112.9	113.6	113.6	115.0	117.1	114.3[k]	113.4[j]	116.2	117.2	117.4	117.1	117.3	117.5
15	113.5	113.4	116.0	n.r.	111.9	109.8[j]	110.4	108.7	113.6	111.3	110.4	112.5	109.7[k]	110.9[j]	112.0	112.4	112.5	112.1	112.4	112.8
1′	166.9	166.2	167.2	166.5	166.5							165.5				176.2	174.9	166.3	165.2	175.0
2′	128.3	127.7	128.4	135.9	136.7							140.9				34.2	42.1	135.9	139.1	75.9
3′	136.6	141.9	141.3	n.r.	124.6							125.0				19.1	64.4	126.4	126.4	68.0
4′	14.6	59.7	59.9	n.r.	18.3							61.1				18.7	13.5	18.2	62.1	21.8
5′	12.0	12.7	12.8																	
1″			166.4								66.4	64.3								
2″			128.0								24.7	24.1								
3″			140.6																	
4″			59.8																	
5″			12.8																	

C	$196^{a,o}_{22}$	198^{a}_{23}	199^{a}_{24}	201^{a}_{25}	202^{a}_{25}	203^{e}_{25}	204^{a}_{25}	205^{d}_{26}	206^{a}_{14}	207^{a}_{7}	208^{a}_{7}	208^{i}_{27}	209^{a}_{28}	210^{a}_{28}	211^{a}_{29}	212^{i}_{27}	213^{a}_{14}	214^{i}_{16}	215^{g}_{30}	217^{b}_{31}
1	44.6	48.4	43.6	43.7	43.8	44.4	44.3	44.0	45.2	45.7[j]	45.7[j]	45.8	45.6	45.4	46.2	46.1	45.6	47.2	49.2*	48.9
2	36.6	29.7	38.6	38.6	38.6	46.6	46.7	38.9	37.3	37.7	37.7	38.8	37.5	37.4	38.0[j]	38.9	37.5	78.3	73.1	40.0
3	74.9	33.6	73.7	73.7	73.8	75.6	75.9	73.0	75.0	76.1	76.1	75.2	75.0	75.7	76.5	75.3	76.1	79.5	77.2†	77.1
4	148.2	150.3	152.7	152.6	152.5	150.1	150.3	154.3	68.4	68.3	68.2	69.1	68.3	68.2	68.2	69.1	68.2	66.6	65.4	85.8

Table 10 (*continued*)

C	$196^{a,o}_{22}$	198^{a}_{23}	199^{a}_{24}	201^{a}_{25}	202^{a}_{25}	203^{e}_{25}	204^{a}_{25}	205^{d}_{26}	206^{a}_{14}	207^{a}_{7}	208^{a}_{7}	208^{i}_{27}	209^{a}_{28}	210^{a}_{28}	211^{a}_{29}	212^{i}_{27}	213^{a}_{14}	214^{i}_{16}	215^{g}_{30}	217^{b}_{31}
5	51.1	52.9	49.9	49.8	49.9	50.2	50.6	49.7	52.4	53.1	53.1	52.8	53.0	52.7	53.7	53.2	52.9	53.1	47.1*	59.8
6	79.2	79.4	78.9	79.0	78.8	79.1	79.5	79.3	77.4	77.0	76.8	77.5	76.7	76.6	76.6	77.3	76.9	78.0	77.4†	79.0
7	54.1	50.7	53.4	50.7	50.7	53.6	53.5	57.6	51.1	47.9[j]	47.9[j]	47.8	47.9	47.6	47.5	47.6	48.0	49.4	51.7	50.6
8	85.3	70.0	69.9	72.0	72.2	70.8	70.4	73.3	71.5	74.0	74.2	74.3	76.0	75.1	75.8	75.2	74.0	74.4	78.9†	72.5
9	42.8	36.2	45.0	40.4	40.3	36.5	36.5	42.7	40.8	36.5	36.5	36.8	36.1	36.5	35.3[j]	36.1	36.5	37.0	36.7	40.0
10	142.8	144.4	143.1	142.2	142.3	142.2	145.4	145.0	142.2	141.6	141.4	142.2	140.9	141.3	140.9	142.8	141.3	141.0	135.2	145.2
11	41.9	42.6	38.1	38.1	38.1	39.1	39.1	46.5	137.8	137.2	137.0	138.6	137.0	136.4	137.3	138.5	137.0	138.4	136.9	140.3
12	178.3	178.2	179.1	178.3	177.3	179.2	179.2	175.8	170.3	169.2	169.0	169.0	168.9	169.2	168.7	169.0	169.1	169.0	168.4	171.6
13	16.3	16.1	11.2	11.3	11.3	11.2	11.2	56.5	123.1	122.6	122.7	121.4	122.3	123.5	122.2	121.3	122.7	121.4	121.9	122.6
14	117.1	116.0	115.9	117.0	117.3	115.0	115.0	110.3	117.3	118.4	118.6	117.7	118.8	118.6	119.3	118.0	118.6	119.4	119.4	116.9
15	114.5	110.7	112.6	112.7	113.1	113.6	113.5	114.9	48.4	48.5	48.5	48.5	48.5	48.4	48.5	48.9	48.5	47.8	47.3	50.1
1′	101.5			166.4	166.8	165.8	167.2	53.7		166.5	165.3	165.7	169.9	170.1	175.0	173.3	166.5	165.5	166.5	
2′	72.1			136.2	144.3	145.4	137.6	23.6		136.0	139.3	143.1	53.8	53.7	75.8	75.3	127.9	136.6	128.1	
3′	73.3			126.1	126.3	123.2	126.2	23.6		126.7	126.7	127.7	52.8	52.9	68.5	52.1	141.7	126.5	138.2	
4′	68.6			18.2	62.3	61.3	18.4	53.7		18.2	62.2	60.9	17.3	17.2	21.6	24.2	59.8	18.3	11.9	
5′	72.1																12.7		14.4	
6′	62.1																			

C	218^{a}_{7}	219^{a}_{7}	219^{b}_{23}	219^{i}_{32}	220^{b}_{33}	221^{b}_{33}	222^{a}_{38}	223^{a}_{28}	224^{a}_{28}	224^{i}_{27}	225^{a}_{28}	226^{d}_{34}	229^{h}_{31}	230^{b}_{31}	231^{b}_{35}	232^{b}_{35}	234^{i}_{36}	235^{b}_{6}	236^{b}_{23}
1	47.1	47.1	48.9	46.6	50.0	50.0	46.4	46.2	46.4	48.6	46.6	48.6	47.6	49.0	47.8	48.3	58.4	48.6	48.3
2	37.8	37.8	39.6	40.3	40.1	40.0	37.7	37.6	37.9	40.3	38.0	40.0	39.1	40.0	39.7	40.2	83.3	39.9	37.8
3	77.3	77.2	77.0	76.5	77.0	77.1	77.2	76.0	76.0	76.3	76.1	76.6	76.1	77.0	76.2	77.0	84.1	77.0	77.9
4	84.5	84.5	85.5	85.4	85.9	85.9	84.5	84.4	84.6	85.3	84.7	85.2	84.4	85.8	84.6	85.2	83.9	85.9	85.8
5	57.6	57.5	59.1	59.6	59.4	59.5	57.5	57.4	57.5	59.4	57.5	59.2	58.5	59.8	58.3	59.2	60.1	60.0	55.5
6	76.4	76.3	78.7	77.6	78.4	78.5	77.2	77.2	77.2	77.5	77.4	77.3	77.1	78.5	77.2	77.3	77.6	78.5	79.4
7	46.6	46.5	47.9	48.7	47.7	47.5	47.1	46.9	47.3	46.5	47.1	46.9	46.4	47.6	46.5	46.9	47.2	49.9	51.6
8	73.9	74.1	75.6	74.5	75.4	75.5	75.0	75.0	75.9	75.4	76.0	76.1	74.1	75.6	74.3	75.0	74.4	76.8	70.7
9	35.2	35.2	36.1	35.4	35.9	35.9	34.8	35.1	34.6	35.1	34.7	35.2	35.1	35.9	35.0	35.6	36.7	36.7	36.8
10	142.3	142.2	144.4	144.8	144.9	144.9	141.6	142.1	141.8	144.6	142.0	144.6	143.9	145.1	143.8	145.0	142.8	145.2	144.7
11	137.0	136.8	139.2	139.0	139.9	139.9	136.8	136.2	136.9	138.9	136.4	139.0	138.0	139.5	138.2	139.3	138.8	44.7	139.5
12	168.8	168.7	171.0	169.2	170.9	170.9	168.5	168.7	168.3	169.0	168.3	169.4	169.0	170.8	169.7	170.8	169.0	180.1	173.2
13	122.7	122.8	122.3	121.1	122.4	122.5	122.5	123.7	122.4	121.1	123.3	121.5	121.6	122.1	122.3	122.1	120.9	40.1	122.7
14	117.9	117.9	117.4	116.9	117.7	117.7	118.3	118.0	118.5	117.1	118.3	117.5	116.8	117.5	116.5	117.2	118.0	116.7	116.3
15	49.9	49.8	50.2	51.3	50.2	50.2	49.9	49.8	50.0	51.2	50.0	50.4	50.1	50.1	50.0	50.1	50.9	49.9	64.5
1′	166.5	166.4	166.5	165.9	174.5	169.7	169.9	170.1	173.1	173.5	173.0	173.9	166.8	168.2	166.6	167.4	166.5	166.4	
2′	136.0	139.3	141.5	142.4	42.2	45.9	53.8	53.7	74.7	75.2	75.1	79.3	126.9	128.9	130.2	132.1	136.7	142.1	
3′	126.6	126.8	126.2	124.9	63.9	180.2	52.8	52.9	51.2	52.2	50.9	51.8	143.7	143.5	132.7	141.9	126.3	125.3	
4′	18.2	62.3	61.6	61.1	14.9	15.2	17.4	17.3	23.4	24.3	23.9	24.0	59.2	59.7	193.1	14.3	18.3	61.5	
5′													12.5	12.6	13.2	55.7			
1″												71.5		176.4				26.6	
2″												36.4		22.1				23.7	
3″												131.0						21.9	
4″												116.2							
5″												130.9							
6″												156.2							
7″												130.9							
8″												116.2							

C	238^{a}_{7}	239^{i}_{27}	240^{b}_{23}	241^{a}_{37}	$243^{a/d}_{37}$	244^{a}_{29}	246^{a}_{38}	246^{i}_{39}	248_{27}	249^{a}_{38}	254^{a}_{38}	255^{d}_{32}	255^{i}_{32}	256^{d}_{40}	257^{i}_{39}	258^{a}_{41}	259^{a}_{41}	$260^{a,q}_{11}$	261^{b}_{42}	262^{a}_{43}
1	43.6	47.5	48.1	43.6	43.5	43.9	44.1	47.1	47.6	44.2	47.9	47.6	46.6	47.1	52.5	39.6	39.7	41.5	48.3	133.9*
2	38.6	40.0	38.0	38.5	37.2	38.0[j]	38.1*	39.8	40.4	38.1*	38.4	39.5	40.1	37.9	78.4	43.9	43.9	32.8	37.5	33.6
3	77.4	77.1	77.2	75.9	76.2	77.0	77.9†	77.1	77.0	77.9†	77.1	77.0	77.1	85.1	84.5	219.7	219.0	78.2	77.9	63.8
4	83.5	84.2	85.5	83.5	83.9	83.5	84.5	85.8	84.3	84.5	83.9	84.7	84.7	95.7	81.0	77.2	75.6	81.4	85.8	67.1
5	54.9	58.3	56.5	58.1	56.7	55.3	56.1	57.7	58.3	56.1	57.9	58.3	58.6	52.7	54.8	51.4	51.4	55.0	55.5	52.5
6	77.3	77.5	79.0	78.3	74.0	78.0	77.5†	77.9	77.5	77.5†	77.6	77.5	77.7	77.3	77.7	87.2	86.9	76.9	79.4	80.7

7	47.7	46.7	50.6	46.5	46.1	47.5	47.6	47.0	46.8	47.7	46.0	46.9	47.7	47.5	47.8	49.3	49.6	53.7	57.6	54.5
8	74.1	74.6	75.7	74.3	76.4	75.2	76.2	75.6	75.4	76.5	74.1	74.7	74.5	75.5	74.5	26.9	27.2	75.4	75.7	25.8
9	36.4	35.8	36.4	37.6	35.3	36.9[j]	37.8[*]	36.2	35.5	37.8[*]	35.8	35.8	35.7	44.5	39.6	38.6	38.5	42.0	36.8	34.0
10	141.8	144.6	144.5	142.1	142.0	141.3	141.8	144.6	144.5	141.8	143.7	144.8	144.8	144.7	141.4	149.0	148.8	140.5	144.7	134.9[*]
11	136.7	139.1	139.1	134.8	139.2	136.6	136.8	138.9	138.9	137.1	139.1	139.2	139.1	138.5	138.2	47.1	47.2	40.5	43.1	139.4
12	169.7	169.2	172.7	168.0	172.0	168.9	169.7	169.4	169.1	169.9	169.2	169.3	169.3	169.9	169.3	178.9	176.2	176.8	180.5	169.5
13	123.2	120.7	122.4	122.4	121.4	123.2	123.5	121.1	121.0	124.2	124.5	121.2	120.9	124.4	121.0	13.9	14.1	15.7	16.1	117.8
14	117.2	116.6	116.2	117.5	116.5	117.7	118.4	116.7	117.0	118.5	115.6	117.0	116.9	118.0	116.8	112.5	112.9	117.2	116.1	22.7
15	63.5	67.5	64.4	63.1	65.7	63.8	63.8	63.9	67.5	63.8	66.9	67.3	67.6	65.4	63.6	63.1	64.1	64.1	64.3	19.0
1′	166.3	166.5	165.7	162.2[?]	165.0	169.8	173.5	173.5	173.4	173.5	165.6	165.8	165.9	166.1	166.0		170.4		165.3	
2′	136.0	136.8	141.0	136.3	135.6	53.9	75.1	75.4	75.4	75.4	142.2	141.9	142.4	142.6	136.3		20.7		141.9	
3′	126.5	126.3	125.1	126.6	124.8	52.8	51.7	52.2	52.2	51.8	126.1	124.7	124.7	125.6	124.0				125.9	
4′	18.2	18.3	61.8	62.4	60.7	14.4	23.4	23.3	24.3	23.8	27.1	61.0	61.0	61.9	17.9				62.4	
1″		171.1			165.0				171.1		167.5	167.1	167.2	153.4						
2″		20.9			20.2				20.9		123.7	122.4	122.1							
3″											132.1	132.7	132.6							
4″											115.1	115.7	115.9							
5″											162.3	162.6	163.4							
6″											115.1	115.7	115.9							
7″											132.1	132.7	132.6							

C	**263**[i] [11]	**264**[a] [44]	**265**[e] [20]	**266**[a] [45]	**269**[b] [46]	**270**[a] [47]	**271**[a] [48]	**272**[a] [50]	**272**[b] [50]	**273**[b] [50]	**276**[a,q] [51]	**277**[a] [52]	**278**[a] [52]	**279**[e] [20]	**284**[a] [53]	**287**[a] [54]
1	43.3	40.1	43.4	40.7	43.6	39.7	38.4	53.5	55.5	53.0	42.6[†]	39.5	39.6	42.9	40.3	22.9
2	38.5	43.2	40.7	42.3	35.5	44.0	43.1	33.6	34.0	34.0	36.8[*]	43.7	43.9	41.3	44.1	23.3
3	87.4	219.1	78.1	218.2	79.1	219.2	219.3	125.6	127.1	126.8	84.4	219.1	219.7	78.2	219.0	43.6
4	44.9	46.9	46.7	46.7	48.2	47.2	30.5	143.4	143.8	144.0	43.6[†]	47.1	47.1	47.1	44.1	208.5
5	51.4	51.0	51.7	51.5	52.3	50.9	50.9	54.5	52.7	55.0	50.8[†]	51.2	51.4	54.6	52.2	34.3
6	81.6	82.3	81.9	80.6	83.9	88.5	77.4	80.5	82.1	82.3	79.9	86.8	87.2	81.4	82.9	30.7
7	49.9	49.1	50.4	46.5	60.0	48.6	44.4	51.2	54.4	52.3	48.6[†]	49.5	49.4	51.2	55.6	37.8
8	67.8	73.1	75.2	75.9	77.1	32.9	72.3	74.3	75.5	75.4	27.5	27.1	26.9	71.9	70.5	75.6
9	41.6	47.9	n.r.	40.7	48.9	39.0	83.2	41.7	44.2	42.8	35.3[*]	38.3	38.6	38.5	49.2	37.3
10	143.5	143.1	142.2	141.5	146.3	149.1	147.5	73.3	73.4	81.1	148.7	148.7	148.9	142.8	143.5	17.2
11	136.3	136.3	137.8	135.6	43.5	41.7	47.5	41.9	46.6	42.1	79.7	75.5	77.2	75.9	47.9	139.0
12	169.3	169.9	170.5	168.9[j]	181.9	178.2	179.5	178.1[j]	180.8[j]	181.0[j]	171.7	176.2	178.8	178.2	175.9	170.4
13	121.2	125.8	123.0	125.2	16.8	13.3	11.1	15.3	15.8	15.7	62.7	64.0	63.1	43.2	15.2	122.5
14	116.8	115.6	116.9	117.3	115.1	112.5	114.9	31.5	29.5	26.1	113.1	112.7	112.5	115.9	116.3	18.2
15	18.3	14.9	18.4	15.1	18.8	14.0	14.3	17.5	17.4[k]	17.7	18.0	14.0	13.9	18.6		30.0
1′			165.5	174.7[j]						98.4		169.2		165.5		
2′			140.2	75.5						78.2		20.5		140.9		
3′			126.0	67.9						71.8				125.0		
4′			61.1	21.9						75.5				61.1		
5′										77.7						
6′										62.9						
1″								170.1[j]	172.1[j]	172.1[j]				64.4		
2″								21.3	21.2[k]	21.3				24.2		

[a] In $CDCl_3$. [b] In MeOD. [c] In DMSO-d_6. [d] In acetone-d_6. [e] In $CDCl_3$/MeOD. [f] In $CDCl_3$/pyridine-d_5. [g] In $CDCl_3$/DMSO-d_6 9:1. [h] In CD_2Cl_2/DMSO-d_6 7:1. [i] In pyridine-d_5. [j,k,l,m] Inverted with respect to the original paper. [n] Amended with respect to the original paper. [o] As penta-acetate. [p] Not assigned in the original paper. [q] As tri-acetate. [*,†,#] These values may be interchanged.

[1]Negrete et al. (1984); [2]Hsu HF et al. (2009); [3]Marco et al. (1994); [4]Hibasami et al. (2003); [5]Choi et al. (2005); [6]Youssef and Frahm (1994b); [7]Marco et al. (1993); [8]Daniewski et al. (1993); [9]Vajs et al. (1999); [10]Bentamane et al. (2005); [11]Buděšinský and Šaman (1995); [12]Marco et al. (1992); [13]Fernandez et al. (1989); [14]Helal et al. (1997); [15]Stevens (1982); [16]Stevens and Merrill (1985); [17]Meragelman et al. (1998); [18]Wang et al. (1991); [19]Collado et al. (1987); [20]Gonzalez Collado et al. (1986b); [21]Li and Jia (1989); [22]Negrete et al. (1988b); [23]Khan et al. (2005a); [24]Li et al. (2008); [25]Santos et al. (1988); [26]Zha and Hou (2008); [27]Berdin et al. (1999); [28]Hamburger et al. (1993); [29]Bruno et al. (2005a); [30]Appendino et al. (1986); [31]Youssef and Frahm (1994a); [32]Stevens et al. (1991); [33]Khan et al. (2004a); [34]Dai et al. (2001); [35]Youssef (1998); [36]Stevens and Wong (1986); [37]Öksük et al. (1994); [38]Öksük and Topçu (1994); [39]Berdin et al. (2001); [40]Rosselli et al. (2006b); [41]Medjroubi et al. (1997); [42]Khan et al. (2004b); [43]Sosa et al. (1989); [44]Yayli et al. (2006); [45]Navarro et al. (1990); [46]Jang et al. (2000); [47]Krishna Kumari et al. (2003); [48]Ahmed et al. (1990); [49]Lee et al. (2003); [50]Ibrahim et al. (2010); [51]Bernhard et al. (1979); [52]Medjroubi et al. (2003b); [53]Chicca et al. (2011); [54]Fontana et al. (2007).

Table 11
H^1 NMR diagnostic signals of guaionolides with epimeric side chains.

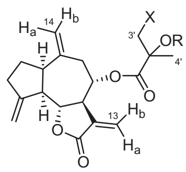
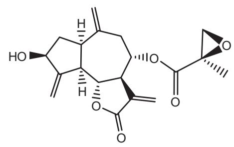
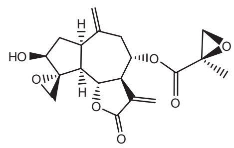
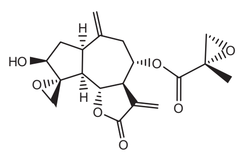
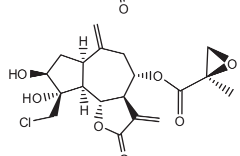
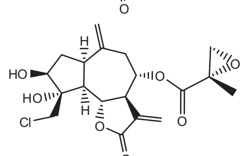
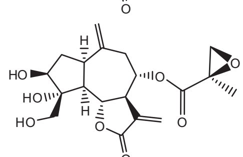
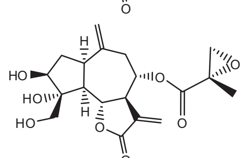
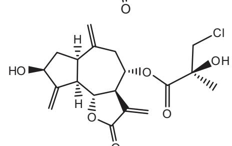
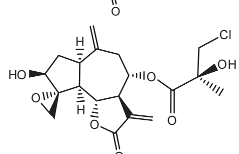
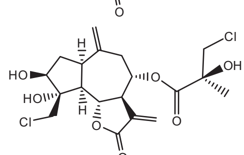
			H13b	H14b	H3′a	H3′b	H4′	solv.	Ref.
161	15-Desoxyrepin		5.58	4.97	3.17	2.82	1.62	$CDCl_3$	Daniewski et al. (1993)
209	Repin		5.57	4.98	3.17	2.83	1.62	$CDCl_3$	Bruno et al. (2005a)
			5.59	4.96	3.01	2.85	1.57	acetone-d_6	Bruno et al. (2005a)
			5.56	4.96	3.15	2.81	1.60	$CDCl_3$	Hamburger et al. (1993)
210	Subteolide		5.71	4.92	3.16	2.82	1.60	$CDCl_3$	Hamburger et al. (1993)
222	Solstiziolide		5.57	4.84	3.17	2.81	1.61	$CDCl_3$	Hamburger et al. (1993)
223	Episolstiziolide		5.74	4.79	3.17	2.82	1.60	$CDCl_3$	Hamburger et al. (1993)
244	Babylin B		5.64	4.98	3.17	2.83	1.62	$CDCl_3$	Bruno et al. (2005a)
245	15-Deschloro-15-hydroxy-episolstiolide		5.86	4.97	3.19	2.82	1.62	$CDCl_3$	Öksük and Topçu (1994)
164	Linochlorin B		5.60	5.10	3.90	3.65	1.50	$CDCl_3$	Gonzalez et al. (1978b)
212	Acroptilin		5.57		3.88	3.65	1.56	$CDCl_3$	Bruno et al. (2005a)
			5.71		3.91	3.73	1.54	$CDCD_3$	Bruno et al. (2005a)
			5.85		4.18	4.06	1.55	Pyridine-d_5	Bruno et al. (2005a)
			5.66		3.96	3.77	1.55	acetone-d_6	Bruno et al. (2005a)
224	Centaurepensin		5.57	5.00	3.87	3.63	1.55	$CDCl_3$	Hamburger et al. (1993)
			5.75	5.07	4.10	4.00	1.70	pyridine-d_5	Berdin et al. (1999)

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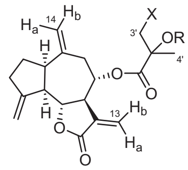
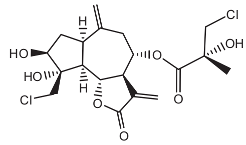
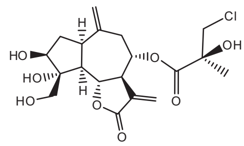
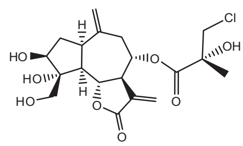
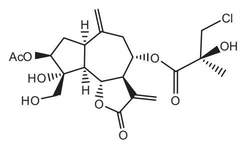
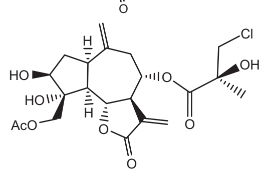
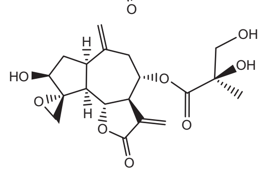
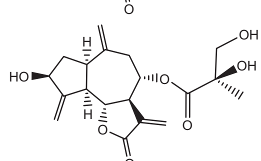
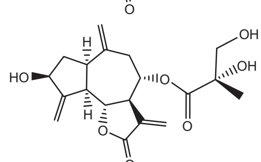
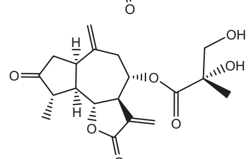
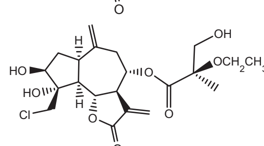
Table 11 (*continued*)

			H13b	H14b	H3′a	H3′b	H4′	solv.	Ref.
225	17-*epi*-centaurepensin		5.83	4.81	3.87	3.63	1.55	$CDCl_3$	Hamburger et al. (1993)
246	Cebellin J		5.64	5.04	3.87	3.65	1.56	$CDCl_3$	Bruno et al. (2005a)
249	Epicebellin J		5.87	4.91	3.87	3.64	1.55	n.r.	Öksük and Topçu (1994)
247	Linochlorin C		5.60	5.02	3.90	3.65	1.55	$CDCl_3$	Gonzalez et al. (1978b)
248	Rhaposerine		5.74	5.04	4.07	3.97	1.67	pyridine-d_5	Berdin et al. (1999)
211	Babylin A		5.60	5.12	3.88	3.64	1.42	$CDCl_3$	Bruno et al. (2005a)
167	17,18-dihydroxy-aguerin A		5.60	5.09	3.87	3.64	1.40	$CDCl_3$	Öksüz and Putun (1983)
166	(2′*S*)-17,18-dihydroxy-aguerin A		5.90 5.91		3.86 3.78	3.61 3.57	1.34 1.34	$CDCl_3$ n.r.	Navarro et al. (1990) Fernandez et al. (1987)
266	Grosheimin-2′,3′-dihydroxy-isobutyrate		6.07		3.82	3.61	1.34	$CDCl_3$	Navarro et al. (1990)
228	Chlorohyssopifolin D		5.73	4.90	3.76	3.44	1.40	Acetone-d_6	Gonzalez et al. (1974b)

(*continued on next page*)

Table 11 (*continued*)

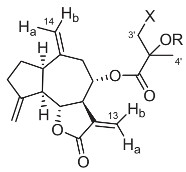
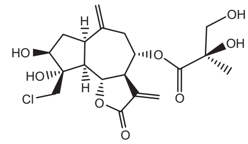
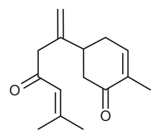
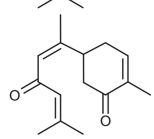
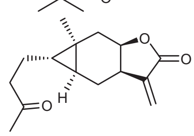
			H13b	H14b	H3′a	H3′b	H4′	solv.	Ref.
									
227	Chlorohyssopifolin E		5.70	5.01	3.86	3.56	1.39	Acetone-d_6	Gonzalez et al. (1974b)

Table 12
Other sesquiterpenes isolated from taxa of the Subtribe Centaureinae.

No	Structure	Name	Taxa	Ref.
285		4,9-Dioxo-bisabol-2,7(14),10-triene	*Centaurea calcitrapa*	Jakupovic et al. (1986)
286		4,9-Dioxo-bisabol-2,7*E*,10-triene	*Centaurea calcitrapa*	Jakupovic et al. (1986)
287		Carabrone	*Serratula latifolia*	Rustaiyan and Feramarzi (1988)

potent anti-*H. pylori* activity, and the MIC was around 100–200 μg/mL. However, costunolide had no inhibitory effect of *H. pylori* urease activity at the concentation used for the growth inhibition assay. The most used drugs for the treatment of *H. pylori* infection, i.e. proton pump inhibitors (omeprazole, lansoprazole), affect the inhibtion of *H. pylori* urease activity or the inhibition of *H. pylori* survival by urease-independent mechanisms. Costunolide, apparently exploits the latter type mechanism (Park et al., 1997).

Antimicrobial tests on costunolide (**1**), isolated from *Cosmos caudatus*, indicated a complete inhibitory activity against *S. aureus* and *Saccharomyces cerevisiae*, partial inhibitory activity against *B. subtilis*, slight inhibitory activity against *C. albicans* and negative inhibitory activity against *E. coli* and *P. aeruginosa* at concentrations of 100 μg/mL and 1 mg/mL, respectively (Ragasa et al., 1997).

Antimicrobial properties of 13-acetyl solstitialin A (**183**), chlorojanerin (**219**) and centaurepensin (**224**) were screened against both standard and the isolated strain of *E. coli*, *P. aeruginosa*, *Enterococcus faecalis*, *S. aureus*, *C. albicans* and *Candida parapsilosis*. All lactones displayed moderate antibacterial activity (Gürbuz et al., 2006;Ozcelik et al., 2009).

The antimicrobial activities of chloroform extracts from the weeds *C. tweediei* and *Centaurea diffusa*, and the main SLs isolated from these species, onopordopicrin (**8**) and cnicin (**19**), respectively, were assayed. Results show that the chloroform extracts from both *Centaurea* species possess antibacterial activities against a panel of Gram+ and Gram− bacteria. Remarkable antibacterial activity against methicillin-resistant *S. aureus* was also measured (Bach et al., 2011).

Santamarin (**99**), alantolactone (**121**), pseudoivalin (**280**) were shown to have good antifungal activity against *Trichophyton mentagrophytes* and *Microsporum cookei*; 9α-hydroxypartenolide (**28**) only against *T. mentagrophytes* (Picman, 1984). Compounds **129**, **155** and **156** revealed good inhibitory activity against *Aspergillus niger*, *Aspergillus ochraceus*, *Cladosporium cladosporioides* and *Phomopsis helianthi* (Vajs et al., 1999).

The *in vitro* antifungal activity of compounds **8**, **14**, **15**, **19**, **20**, **22**, **24**, **36**, **75**, **80–82**, **94**, **103**, **107–109**, **111**, **137**, **138** was tested against nine fungal species, using the micro-dilution method. All the compounds tested showed great antifungal activity comparable and sometimes better than miconazole used as control (Skaltsa et al., 2000a; 2000b).

The activity against the fungus *Cunninghamella echinulata* of compounds **1**, **4**, **19** and **142** has been evaluated. Compounds **4** and **19** were inactive whereas **1** and **142** showed the same noticeable EC_{50} values (6 μg/mL) close to that of ketokonazole (1.5 μg/mL) used as reference drug (Barrero et al., 2000).

Costunolide (**1**), dehydrocostus lactone (**142**), zaluzanin C (**147**) and 3-desoxysolstitialin A (**180**) were tested for their fungicidal activity against the phytopathogenic fungi *Colletotrichum acutum*, *Colletotrichum fragariae*, *Colletotrichum gloesporioides*,*Fusarium oxysporum*,*Botrytis cinerea* and *Phomopsis* ssp. Active compounds in decreasing order of activity were **142**, **1** and **147**, whereas **180** was not active (Wedge et al., 2000).

The *in vitro* antifungal activity of four of the 10 sesquiterpenes isolated from *Centaurea deusta* was tested against nine fungal species (*Aspergillus* ssp., *Penicillum* ssp., *Trichoderma viride*, *C. cladosporioides*, *Alternaria alternata*). Compounds **24**, **81**, **95**, and **112** showed greater antifungal potential than miconazole except against *C. cladosporioides*. The antibacterial bioassays showed an activity only for compound **19** (Karioti et al., 2002). Nevertheless, this germacrane has also been proved to be active against the same previous nine fungi with a fungicidal potential higher

Table 13
Occurrence of sesquiterpenoids in taxa of the Subtribe Centaureinae.

Taxa	Section or Subgenus	Germacanes	Elemanes	Eudesmane	Guaianes	Other	Collection place
Only germacranes							
Aegialophila pumila (syn. *Centaurea aegialophila* Sect. *Aegialophila*)	Gr. 6	4, 19					Egypt
Centaurea affinis	Gr. 7, *Acrolophus*	4, 19					Serbia
C. aggregata	Gr. 7, *Acrolophus*	19					Polonia ??
C. alba	Gr. 7, *Phalolepis*	4, 19, 21, 24, 36					Spain
C. alba ssp. *caliacrae*	Gr. 7, *Phalolepis*	4					Bulgaria
C. alba ssp. *deusta*	Gr. 7, *Phalolepis*	4					Italy
C. alexandrina	Gr. 7, *Calcitrapa*	19					Egypt
C. aplopea	Gr. 7, *Acrolophus*	19					Italy
C. aplopea ssp *lunensis*	Gr. 7, *Acrolophus*	19					Italy
C. araneosa (a.n. *C. procurrens*)	Gr. 7,*Calcitrapa*	19					Egypt
C. arenaria	Gr. 7, *Acrolophus*	19					Hungary
C. arenaria ssp. *majorowii*	Gr. 7, *Acrolophus*	19					Ukraine
C. arenaria ssp. *odessana*	Gr. 7, *Acrolophus*	19					Germany
C. aspera ssp. *scorpiurifolia*	Gr. 7,*Seridia*	4, 5, 19, 21					Spain
C. attica ssp. *drakiensis*	Gr. 7, *Acrolophus*	19					Greece
C. attica ssp. *ossaea*	Gr. 7, *Acrolophus*	19					Greece
C. bombycina	Gr. 7, *Acrolophus*	4, 19, 24					Spain
C. calolepis	Gr. 7, *Acrolophus*	19					Turkey
C. calvescens	Gr. 7, *Acrolophus*	19					Germany
C. cineraria	Gr. 7, *Acrolophus*	19					Italy
C. cineraria var. *circae*	Gr. 7, *Acrolophus*	19					Italy
C. coronopifolia	Gr. 1, *Stizolphus*	31, 32, 34, 35					Turkey
C. crithmifolia	Gr. 7, *Acrolophus*	4					Italy
C. crocodylium	Gr. 6, *Crocodylium*	4, 19					Poland
C. cuneifolia ssp. *pallida*	Gr. 7, *Acrolophus*	19					Greece
C. derventana	Unresolved classification	4, 19, 21, 24					Serbia
C. diffusa ssp. *brevispina* = *C. bovina*	Gr. 7, *Acrolophus*	19					Greece
C. eriophora	Gr. 7, *Seridia*	4, 19					Poland, France
C. friderici	Gr. 7, *Acrolophus*	4					Italy
C. gigantea	*Cynaroides*	9, 13					Turkey
C. glaberima	Unresolved classification	19					Montenegro
C. glomerata	Unresolved classification	15, 17, 39, 43					Egypt
C. granatensis	Gr. 7, *Acrocentron*, syn. *Colymbada*	19					Spain
C. grisebachi ssp. *confusa*	Gr. 7,*Acrolophus*	19					Greece
C. iberica	Gr. 7, *Calcitrapa*	4, 19					Uzbekistan
C. kartschiana	Gr. 7, *Acrolophus*	19					Italy
C. leucophaea	Gr. 7, *Acrolophus*	19					Italy
C. lusitanica	Gr. 7, *Seridia*	3, 5, 19					Portugal
C. maculosa	Gr. 7, *Acrolophus*	19					USA
C. mantoudii	Gr. 7, *Acrolophus*	19					Greece
C. mariolensis	Gr. 7, *Acrolophus*	19, 21					Spain
C. maroccana (a.c.*C. sulphurea*)	Gr. 7, *Calcitrapa*	4, 19, 21, 36					Morocco
C. micranthos	Gr. 7, Acrolophus	19					?'
C. monticala	Gr. 7, *Acrolophus*	19, 21					Spain
C. ovina	Gr. 7, *Acrolophus*	19					Poland
C. pallescens	Gr. 7, *Acrolophus*	19					Egypt
C. pallidior	Gr. 7, *Acrolophus*	19					Greece
C. paniculata	Gr. 7, *Acrolophus*	4					France
C. pelia	Gr. 7, *Acrolophus*	19					Greece
C. polyacantha	Gr. 7, *Seridia*	53, 54					??
C. pontica	Gr. 7, *Calcitrapa*	4					Romania
C. pseudomaculosa	Gr. 7, Acrolophus	4, 19					Kazakhstan
C. raphanina ssp. *mixta*	Gr. 7, *Acrocentron*, syn. *Colymbada*	19					Greece
C. rhenana ssp. *savranica*	Gr. 7, *Acrolophus*	19					Greece
C. rocheliana	Gr. 7, *Jacea*	19					Rep. Czeka
C. rothmalerana	Gr. 7, *Acrolophus*	19					Portugal
C. seridis	Gr. 7, *Seridia*	53, 54, 57					Spain
C. sonchifolia	Gr. 7, *Seridia*	8, 53, 54					Spain, Greece
C. splendens	Gr. 7, *Phalolepis*	19					Montenegro
C. squarrosa	Gr. 7, *Acrolophus*	19					Uzbekistan
C. sulphurea	Gr. 7,*Solstitiaria*	19					Spain,
		19, 64, 66					Morocco Algeria

(continued on next page)

Table 13 (*continued*)

Taxa	Section or Subgenus	Germacanes	Elemanes	Eudesmane	Guaianes	Other	Collection place
C. transiens	Gr. 7, *Acrolophus*	19					Greece
C. tymphaea	Gr. 7, *Acrolophus*	19					Greece
C. thymphaea ssp. *brevispina*	Gr. 7, *Acrolophus*	19					Greece
C. vallesiaca	Gr. 7, *Acrolophus*	19					Italy
C. weldeniana	Gr. 7, *Jacea*	4					Italy
Stizolophus balsamita	Gr. 1	27, 29, 32, 33, 34, 35, 47, 56					Kazakhstan
Zoegea baldshuanica	Gr. 1	28					Poland
Germacranes and elemanes							
Centaurea aegialophila (a.n. *Aegialophila pumila*)	Gr. 6	19	69, 80				Cyprus
C. amara	Gr. 7, *Jacea*	10, 40	69, 84				Spain
C. aspera	Gr. 7, *Seridia*	4, 5, 8, 19, 21, 24, 36, 37, 38	94				Spain, France
C. aspera ssp. *stenophylla*	Gr. 7, *Seridia*	4, 5, 8, 11, 16, 18, 19, 21, 24, 38, 58	69, 84, 97				Spain
C. brugueriana	Gr. 7, *Tetramorphaea*	19	71				Iran
C. calcitrapa	Gr. 7, *Calcitrapa*	4, 19, 21, 36, 49	80, 84				Spain, Egypt
						285, 286	Argentina
C. castellana	Gr. 7, *Acrolophus*	19, 53	69, 87				Spain
C. cineraria ssp. *busambarensis*	Gr. 7, *Acrolophus*	19	69, 80				Sicily
C. cineraria ssp. *umbrosa*	Gr. 7, *Acrolophus*	19, 21	80				Sicily
C. cuneifolia	Gr. 7, *Acrolophus*	19	69, 80				Turkey
		19					Serbia
C. diffusa	Gr. 7, *Acrolophus*	19, 21	81, 83				Argentina
C. eryngioides	Gr. 7, *Acrocentron*, syn. *Colymbada*	8, 9, 19	75				Egypt
C. melitensis	Gr. 7, *Seridia*	4, 8, 9	76, 84, 90				Spain
C. napifolia	Gr. 7, *Seridia*	19, 21	69, 80, 81, 84				Sicily
C. nicaensis	Gr. 7, *Seridia*	8, 10, 19, 36, 40, 45	84, 91				Sicily, Algeria
C. paniculata ssp. *castellana*	Gr. 7, *Acrolophus*	19, 21	80				Spain
C. phrygia	Gr. 7, *Jacea*, *Lepteranthus*	16	79				Bulgaria
C. sphaerocephala	Gr. 7, *Seridia*	19, 21, 30, 53, 54	69, 81				Sicily
Cheirolophus intybaceus	Gr.1	4, 6, 7, 8, 15	75, 94				Spain
Cnicus benedictus	Gr. 7	4, 16, 19, 21, 53	80				
Germacranes, eudesmanes							
Centaurea kurdica	Gr. 7, *Cynaroides*	1, 2, 48		100			Turkey
C. stoebe	Gr. 7, *Acrolophus*	19					Serbia
		4, 19, 24		102			Germany ??
Phonus arborescens (a.n. *Carthamus arb.*)	Gr. 5	51, 52		139, 140, 141			Spain
Germacranes, elemanes, eudesmanes							
Centaurea achaia	Gr. 7, *Acrocentron*, syn. *Colymbada*	4, 7, 8, 13, 14, 15, 22, 36, 42	75, 82, 94	107, 108, 137			Greece
C. aspera ssp. *subinermis*	Gr. 7, *Seridia*	5, 38	69, 84, 92, 93	114, 116, 135			Spain
C. attica	Gr. 7, *Acrolophus*	19, 21	80, 95	109, 111, 138			Greece
C. deusta	Gr. 7, *Phalolepis*	19, 20, 21, 24	80, 81, 95, 96	111, 112			Greece
C. grisebachi	Gr. 7, *Acrolophus*	4, 19, 24	69, 80	103, 109, 110, 111, 112			Greece
C. malacitana	Gr. 7, *Seridia*	4, 5, 10, 18, 19, 21	69	109			Spain
C. moesiaca	Gr. 7, *Lepteranthus*	8, 16, 19, 20, 21, 24, 25, 26	80	109, 111			Bulgaria
C. orphanidea	Gr. 7, *Acrolophus*	4, 19, 21	80	103, 109, 111			Greece
C. paui	Gr. 7, *Acrolophus*	4, 19, 21, 24, 36, 59, 60, 61, 62, 64, 65, 67, 68	69, 70, 83, 85, 95	102			Spain
C. pullata	Gr. 7, *Melanoloma*	44, 45, 36, 46	69, 84, 89	115, 117, 118, 119			Algeria
C. spinosa	Gr. 7, *Acrolophus*	19, 21, 23	80, 83, 95	109, 110, 111, 113			Greece
C. thessala ssp. *drakiensis*	Gr. 7, *Acrolophus*	19, 21, 24	80, 81	103, 109			Greece
C. zuccariniana	Gr. 7, *Acrolophus*	19, 21	80	104			Greece
Neither germacranes nor guaianes							
Centaurea. cadmea	Gr. 7, *Phalolepis*			122			Turkey
C. granata	Gr. 7, *Jacea*			115			Algeria
C. hierapolitana	Gr. 7, *Phalolepis*		74, 77	130, 131			Turkey

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C. pamphilica	Unresolved classification		133		Turkey
C. phyllocephala	Gr. 7, *Tetramorphaea*	80, 81	109		Iraq
Only guaianes					
Acroptilon repens (syn. *Centaurea repens*)	Gr. 3			149, 151, 160, 162, 163, 176, 177, 205, 208, 209, 212, 214, 218, 219, 224, 233, 234, 255, 267	Caucasus Argentina
Amberboa divaricata	Gr. 2			162	India
A. muricata (syn. *Volutaria m.*, *Centaurea m.*)	Gr. 2			149, 162, 265, 269	Spain??
A. ramosa	Gr. 2			162, 188, 189, 190, 198, 217, 219, 220, 221, 236, 240, 260, 261, 262, 272, 273	Pakistan
A. tubuliflora	Gr. 2			149, 160, 162, 271	Egypt
Centaurea adjarica (a.n. *Psephellus simplicicaulis*)	Gr. 1, Psephellus			162, 169, 176, 207, 208, 209, 212, 213, 216, 218, 219, 222, 224, 229, 233, 243, 246	Poland
C. aegyptiaca	Gr. 7, *Calcitrapa*			149, 162, 199, 206, 208, 209, 214, 217, 218, 219, 222, 224, 227	Sinai
C. ainetensis (a.n. *C. eryngioides*)	Gr. 7, *Acrocentron*, syn. *Colymbada*			156	Lebanon
C. americana	Gr. 1, *Plectocephalus*			162	Mexico
C. babylonica, (a.n. *Centaurea behen*)	Gr. 7 or 1, *Microlophus*, aff. Sect. *Centaurium*			208, 209, 211, 212, 244, 246	Lebanon
C. behen (syn. *Centaurium behen*)	Gr. 7 or 1, *Microlophus*, aff. Sect. *Centaurium*			149, 160, 162, 183, 264, 277, 278	Iran
C. canariensis (a.n. *Cheirolophus canariensis*)	Gr. 1, *Cheirolophus*			149, 158, 160, 162	Canary Is.
C. clementei	Gr. 7, *Acrocentron*, syn. *Colymbada*			149, 162, 186, 187, 269, 279	Spain
C. collina	Gr. 7, *Acrocentron*, syn. *Colymbada*			149, 166, 190, 195	Spain
C. debeauxii ssp. *thuillieri*	Gr. 7, *Lepteranthus*			162	France
C. deflexa	*Cheirolepis*			149, 160, 162, 284	Turkey
C. depressa	Gr. 7, *Cyanus*			181, 183	Turkey
C. floccose	Gr. 7, *Cyanus*			144, 149	??
C. helenoides	Unresolved classification			162, 264	Turkey
C. hermannii	Unresolved classification			162, 208, 218, 219, 237, 241, 242, 243	Turkey
C. hololeuca	Unresolved classification			162, 208, 209, 240, 243, 244, 246, 256	Lebanon
C. hyrcanica	Gr. 7, *Jacea*			209, 212, 224	Russia??
C. imperialis	Gr. 7, *Cynaroides*			180, 181, 183, 224, 229, 252	Iran??
C. isaurica	Unresolved classification			208	Turkey
C. janeri	Gr. 7,*Jacea*			208, 219	Spain
C. kandavanensis	Gr. 7, *Acrocentron*, syn. *Colymbada*			150, 156	Iran
C. kotschyi	*Cheirolepis*			149, 162, 164, 167	Turkey
C. marshalliana (a.n. *Psephellus marshallianus*)	Gr. 1, *Psephellus*			208, 212, 219, 229	Russia
C. musimomum	Unresolved classification			160, 162, 164, 207, 208, 209, 218, 219, 224, 225, 258, 259, 276, 277, 278	Algeria
C. nicolai	Gr. 7, *Acrocentron*, syn. *Colymbada*			150, 152, 153, 155, 156	Montenegro
C. nigra	Gr. 7, *Jacea*, sect. *Lepteranthus*			224	Spain
C. pabotii	Unresolved classification			158, 165, 190	Iran
C. phaeopappoides (a.n. *Psephellus phaeopapp.*)	Gr. 1, *Psephellus*			162, 208, 219	Armenia
C. pseudosiniaca (a.n. *C. sinaica*)	Gr. 7, *Calcitrapa*			250, 251	S. Arabia

(*continued on next page*)

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Table 13 (*continued*)

Taxa	Section or Subgenus	Germacanes	Elemanes	Eudesmane	Guaianes	Other	Collection place
C. ptosimopappa	Gr. 7, *Ptosimopappus*				147, 148, 149, 162, 190, 199, 208, 219, 278		Turkey
C. ptosimopappoides	Gr. 7, *Ptosimopappus*				162, 190		Turkey
C. ragusina	Gr. 7, *Acrocentron*, syn. *Colymbada*				149, 160, 162		Egypt
C. ruthenica (a.n. *Rhaponticoides ruthenicus*)	Gr. 1, *Rhaponticoides*				264		Caucasus
C. sinaica	Gr. 7, *Calcitrapa*				200, 208, 219, 224, 275		Qatar
C. solstitialis ssp. *shouwii*	Gr. 7, *Solstitiaria*				160, 162, 277		Sicily
C. sventenii (a.n. *Cheirolophus sventenii*)	Gr. 1, *Cheirolophus*				149, 160, 162		Canary Is??
C. thracica	Gr. 7, *Microlophus*				162, 208, 219		Bulgaria
C. webbiana (a.n. *Cheirolophus webbianus*)	Gr. 1, *Cheirolophus*				270		Canary Is.
Centaurothamnus maximus	Gr. 6 *Rhaponticum*				162, 208, 219		S. Arabia
Chartolepis biebersteinii (a.n. *Centaurea pterocaula*)	Gr. 7, *Chartolepis*				162, 208, 209, 212, 219, 224, 238		Caucasus
C. glastifolia (a.n. *Centaurea glastifolia*)	Gr. 7, *Chartolepis*				160, 162, 169, 207, 208, 209, 212, 218, 219, 223, 224, 225, 229, 238, 241, 245, 246, 249, 254, 264		Caucasus, Turkey
C. intermedia (a.n. *Centaurea chartolepis*)	Gr. 7, *Chartolepis*				162, 264		Caucasus
C. pterocaula (a.n. *Centaurea pterocaula*)	Gr. 7, *Chartolepis*				162, 208, 209, 212, 219, 224, 229, 238, 264		Caucasus
Cheirolophus junoniaus	Gr.1				149, 158, 162, 190		Canary Is.
C. metlesicsii	Gr.1				158, 159, 190, 191, 199		Spain
C. teydis	Gr.1				158, 160, 162, 190		Canary Is.
C. uliginosus	Gr.1				149, 160, 162, 190, 193, 194		Spain
Grossheimia macrocephala (a.n. *Centaurea m.*)	Gr. 7				149, 157, 160, 162, 263, 264, 269		Russia
G. ossica (a.n. *Centaurea polyphylla*)	Gr. 7				264		Georgia
Leuzea longifolia	Gr. 3				201, 202, 203, 204		Portugal
L. rhapontica ssp. *helenipholia*	Gr. 3				162, 208, 219		Poland??
L. rhaponticoides	Gr. 3				162, 208, 219		Poland??
Psephellus carthalinicus	Gr. 1				161,162, 164, 208, 209, 212, 224		Romania
P. colchicus	Gr. 1				161,162, 164, 208, 209, 212, 224		Germania
P. daghestanicus	Gr. 1				161,162, 164, 208, 209, 212, 224		France
P. dealbatus	Gr. 1				161,162, 164, 208, 209, 212, 224		Italy
P. declinatus	Gr. 1				161, 162, 164		Bielorussia
P. hypoleucus	Gr. 1				161, 162, 164		Romania
P. karabaghensis	Gr. 1				161,162, 164, 208, 209, 212, 224		Armenia
P. leucophyllus	Gr. 1				161, 162, 164		Romania
P. nogmovii	Gr. 1				161,162, 164, 208, 209, 212, 224		?????
P. somcheticus	Gr. 1				161,162, 164, 208, 209, 212, 224		Hungary
P. taochius	Gr. 1				161, 164, 208, 209, 212, 224		Hungary
P. zangezuri	Gr. 1				161,162, 164, 208, 209, 212, 224		Belgium
Rhaponticum pulchrum	Gr. 3				160, 162, 176, 207, 208, 219, 233, 240, 243		Biolorussia
R. serratuloides	Gr. 3				162, 176, 212, 224, 239, 246, 248, 257		Kazakhstan
Serratula strangulata	Gr. 4				224, 226		China
Stemmamarca carthamoides	Unresolved classification				162, 176, 208, 219, 233		Poland??
S. rhapontica	Unresolved classification				162, 208, 219		??
Tricholepis glaberrima	Unresolved classification				162, 190		North India
Guaianes, germacranes							
Amberboa lippii	Gr. 2	19			264, 269, 275		Canary Is.
Centaurea africana (a. n. *Rhaponticoides a.*)	Gr. 1, *Rhaponticoides*	19			162		Algeria

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C. bella (a.n. *Psephellus bellus*)	Gr. 1, *Psephellus* syn. Sect. *Hyalinella*	50			161, 162, 169, 172, 173, 174, 175, 176, 178, 179, 207, 208, 209, 212, 213, 216, 218, 219, 222, 224, 229, 233, 243, 246, 253		Germany
C. exarata	Gr. 7,*Acrolophus*	19			162		Spain
C. incana	Gr. 7,*Acrolophus*	8					Morocco
					207, 208, 210, 212, 223, 238		Algeria
C. scabiosa	Gr. 7, *Acrocentron*, syn. *Colymbada*	55					Rep Czeka
					162, 209, 264		Siberia
C. scoparia	Gr. 7, Pseudophaeopappus	8			149, 162, 168, 169, 170, 171, 197, 199, 206, 208, 213, 217, 218, 219, 224, 229, 230, 231, 232, 235, 240, 243		Egypt
C. solstitialis	Gr. 7, *Solstitiaria*	32, 55					Georgia
					149, 161, 162, 164, 181, 182, 183, 190, 206, 207, 208, 209, 210, 212, 218, 219, 222, 223, 224, 225, 229,		Argentina France, Bulgaria
Guaianes, eudesmanes							
Centaurea arguta (a.n. *Cheirolophus teydis*)	Gr. 1 *Cheirolophus*			127, 129	160, 162		Canary Is.
C. canariensis var. *subexpinnata* (a.n. *Cheirolophus canariensis* var. *subexpinnata*)	Gr. 1, *Cheirolophus*			128	143, 145, 146, 149, 160, 162, 184, 185, 188, 189, 190		Canary Is.
C. conifera (a.n. *Leuzea conifera*)	Gr. 3, *Leuzea*			132			Spain
					208, 209, 210, 219, 224, 225, 240, 244(245)		Sicily
C. hyssopifolia	Gr. 7, *Jacea*			106	162, 212, 217, 224, 227, 228		Spain
C. linifolia	Gr. 7, *Jacea*			106	149, 160, 162, 164, 212, 217, 218, 224, 227, 228, 246, 247		Spain
C. ornata	Gr. 7, *Acrocentron*, syn. *Colymbada*			99, 120	149, 162, 166, 264, 266		Spain
C. uniflora ssp. *nervosa*	Gr. 7, *Jacea*, sect. *Lepteranthus*			99, 100	208, 213, 215		Italy
Cheirolophus sempervirens	Gr.1			101, 126, 128	143, 147, 158, 162		Portugal
Raponticum uniflorum	Gr. 3			134	160, 162, 224		China
Serratula latifolia	Gr. 4			121, 122, 124	280, 281, 282, 283	287	Iran
Guaianes, germacrane, eudesmanes							
Centaurea acaulis	Gr. 7, *Acrocentron*, syn. *Colymbada*	1		98, 99	148, 150, 154		Algeria
C. tweediei (a.n. *Plectocephalus tweediei*)	Gr. 1, *Plectocephalu s*	8, 63		105, 136	268		Argentina
Cheirolophus x *hortigenus*	Gr.1	7, 8		108, 126	143, 147, 149, 160, 162		Spain
C. mauritanicus	Gr.1	6		123, 124, 125	149, 158, 162, 165, 190, 191, 192		Morocco
Guaianes, germacrane, elemanes							
Centaurea. arbutifolia (a.n. *Cheirolophus arb.*)	Gr. 1 *Cheirolophus*	12, 41	78, 88		158		Canary Is.
C. salonitana	Gr. 7, *Acrocentron*, syn. *Colymbada*	4, 57					Bulgaria, Serbia
					150, 152, 156, 158, 161, 164, 190, 200		Greece, Turkey
			69, 86				Turkey
C. tagananensis (a.n. *Cheirolophus tagananensis*)	Gr. 1, *Cheirolophus*	8	75, 84		149, 162		Canary Is.
Guaianes, elemanes							
C. chilensis (a.n. *Plectocephalus chilensis*)	Gr. 1, *Plectocephalus*				142, 143, 144, 149, 196		Chile
			72, 73				Chile

Gr. = group; a.n. = accepted name.

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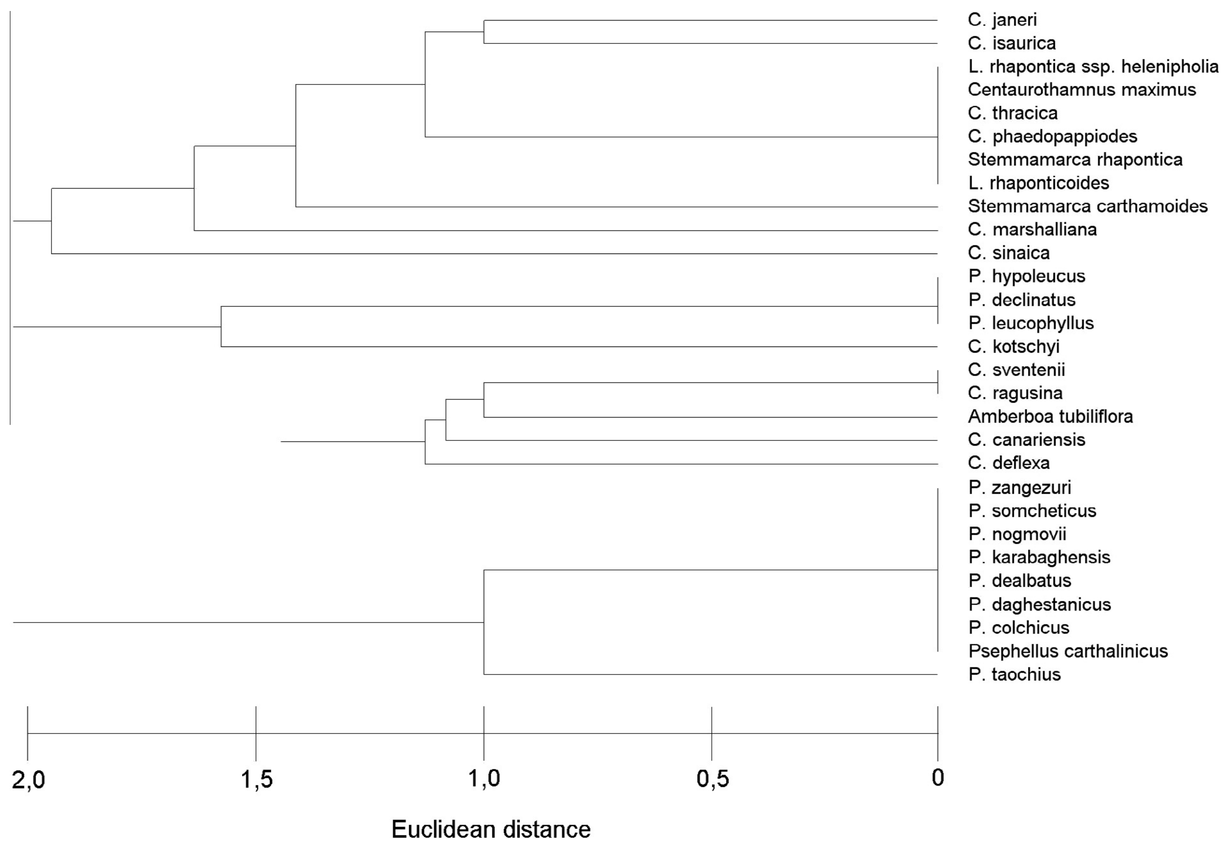

Fig. 3. Clusters based on presence/absence of single sesquiterpene in the *Psephellus*.

than miconazole (Panagouleas et al., 2003) and to inhibit mycelia growth of *B. cinerea* and *Fusarium moniliforme* (Adekenov et al., 1986a).

Alantolactone (**121**) was examined for activity against 16 species of fungi. At 10 μg/mL, the lactone strongly inhibited the growth of *M. cookei*, *T. mentagrophytes*, and *Trichothecium roseum* (Picman, 1983b). At the MIC of 1–5 ppm, it significantly inhibited growth of four isolates of *Fusarium graminearum* and two of each of *Verticillium albo-atrum* and *Leptosphaeria maculans* (Picman and Schneider, 1993). Furthermore, it completely inhibited the growth of *T. mentagrophytes*, *Microsporum canis*, *Paecilomyces liacinus* and *Rhizotonia* at 30, 40, 70, and 80 μg/mL, respectively. Complete inhibition of spore germination of *Fusarium*was recorded at 400 μg/mL (Wahab et al., 1981).

The antifungal activity of costunolide (**1**) was assessed using the mycelial radial growth inhibition technique against six plant pathogenic fungi (*A. alternata*, *Helminthosporium* spp., *Nigrospora* spp., *F. oxysporum*, *F. culmorium* and *Rhizocotonia solani*). Costunolide showed the strongest antifungal activity against three fungi, *Nigrospora* spp., *R. solani*, and *Helminthosporium* spp. with EC_{50} values of 0.48, 2.92, and 2.96 μg/mL, respectively (Ahmed and Abdelgaleil, 2005). Dehydrocostus lactone (**142**), isolated from a dichloromethane extract of the Portuguese liverwort *Targionia lorbeeriana*, presented antifungal activity against *Cladosporium cucumerinum* and *C. albicans*(Neves et al., 1999).

The antifungal sesquiterpene acid, isocostic acid (**123**), was isolated from *Inula viscosa* leaves, exhibited antifungal activity against six species of dermatophytes, but was devoid of antibacterial activity. The mouse oral LD_{50} values for it were 1 g/kg, with a favorable therapeutic index of 100 (Shtacher and Kashman, 1970).

Phytochemical investigation of *Vernonia arborea* resulted in the isolation of zaluzanin D (**148**). It showed 100% inhibition in mycelia growth of *R. solani*, the effect being ca. 75% with *Curvularia lunata* and *B. cinerea* at 200-ppm concentration (Kunari et al., 2003).

4.2. Antiprotozoal

Cynaropicrin (**162**), isolated from *Moquinia kingii* was evaluated *in vitro* against *Trypanosoma cruzi* trypomastigotes and the IC_{50} values for trypanocidal activity was 93.5 μg/mL (Schinor et al., 2004).

Stizolin (**27**), alantolactone (**121**), cynaropicrin (**162**), repin (**209**), acroptilin (**212**) and centaurepensin (**224**) showed strong protozoacidal activity *in vitro* (active at 0.24–7.8 μg/mL) against *Entamoeba histolytica* and *Trichomonas vaginalis*. The presence of an exocyclic methylene ring conjugated with the lactone carbonyl, the presence of an acetyl group on the ring, or oxidation of a hydroxyl group to a keto group generally increased the protozoacidal activity of the sesquiterpenes (Rubinchik et al., 1976).

The AcOEt extract of the bark of *Michelia alba* D.C. (Magnoliaceae) exhibited killing activity against *T. cruzi*. A bioassay-guided purification afforded several trypanocidal constituents, among which costunolide (**1**) and santamarine (**99**). The minimum lethal concentrations of these compounds against epimastigotes of *T. cruzi* were 7 μM and 25 μM, respectively (Asaruddin et al., 2003). Also dehydrocostus lactone (**142**) and zaluzanin D (**148**) showed lethal activity against epimastigotes of *T. cruzi* at concentrations of 6.3 and 2.5 μM, respectively (Uchiyama et al., 2002).

Costunolide (**1**), β-cyclocostunolide (**98**) and dehydrocostus lactone (**142**) showed significant antitrypanosomal activity against *T. brucei* with EC_{50} of 0.066, 0.18 and 0.21 μg/mL, respectively, several-fold more potent than the antitrypanosomal drugs eflornithine and suramin (Otoguro et al., 2011).

The essential oil of *Echinops kebericho*, containing as major constituent dehydrocostus lactone (**142**), exerted strong antileishmanial activity activity against two *Leishmania*

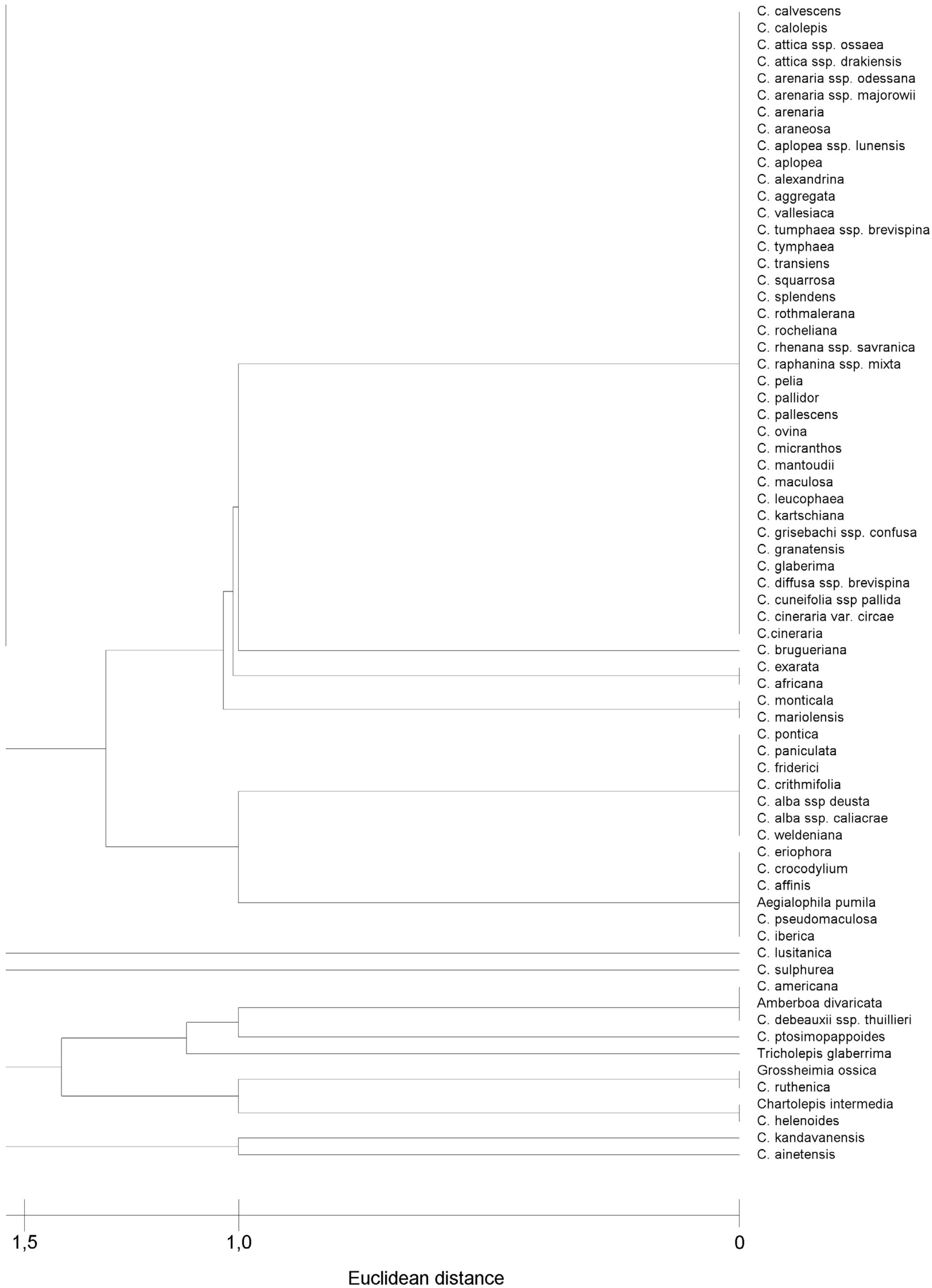

Fig. 4. Clusters of *Acrolophus* based on presence/absence of single sesquiterpene.

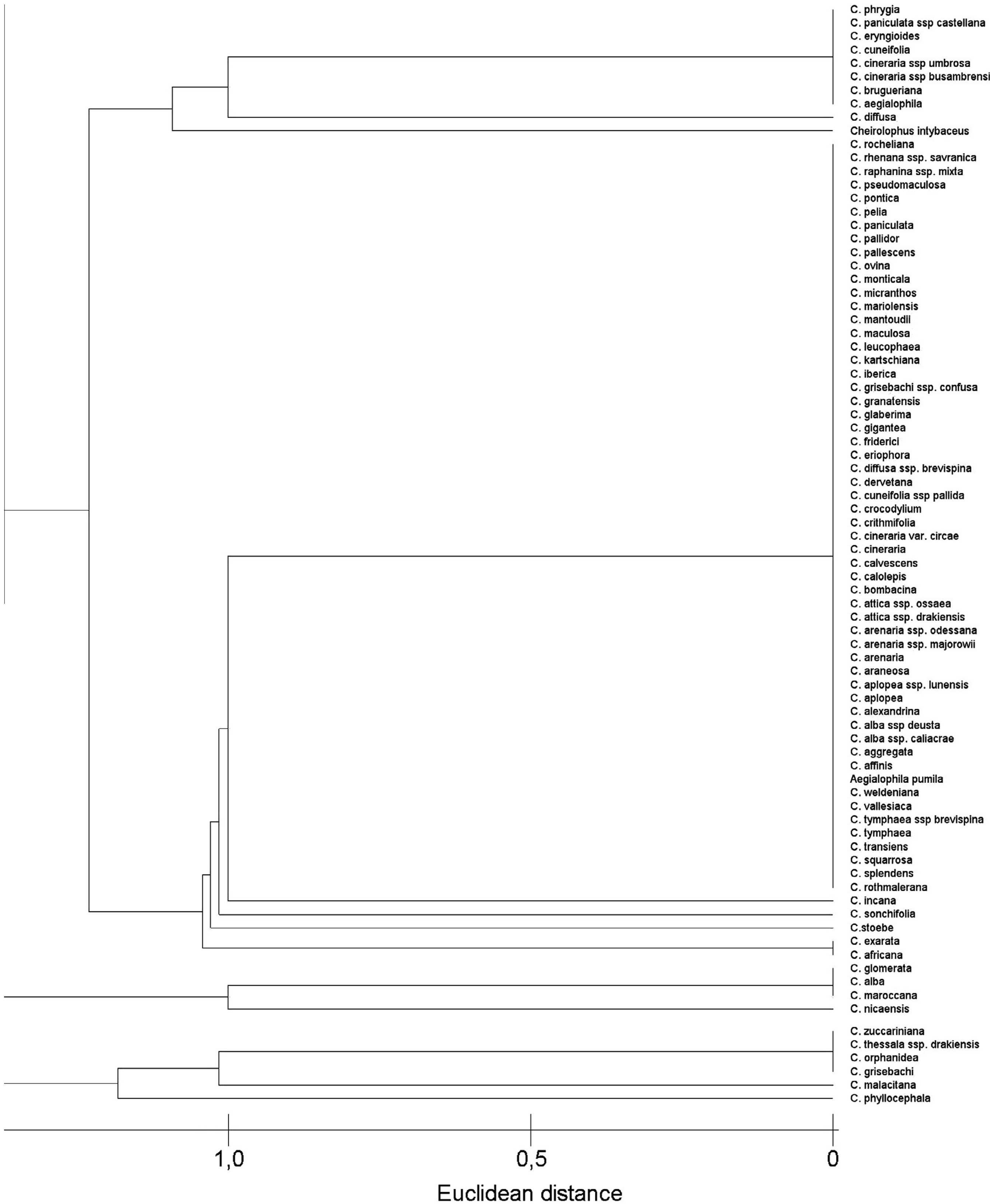

Fig. 5. Clusters based on presence/absence of structurally similar sesquiterpenes part A.

strains (*Leishmania aethiopica* and *Leishmania donovani*) that was even higher than that of amphotericin B (Tariku et al., 2011).

Costunolide (**1**), isolated from the essential oils from heartwood and sapwood of *Eremanthus elaeagnus*, *Vanillosmopsis erythropappa* and *Moquinea velutina* was effective against infestation by *Schisto-*

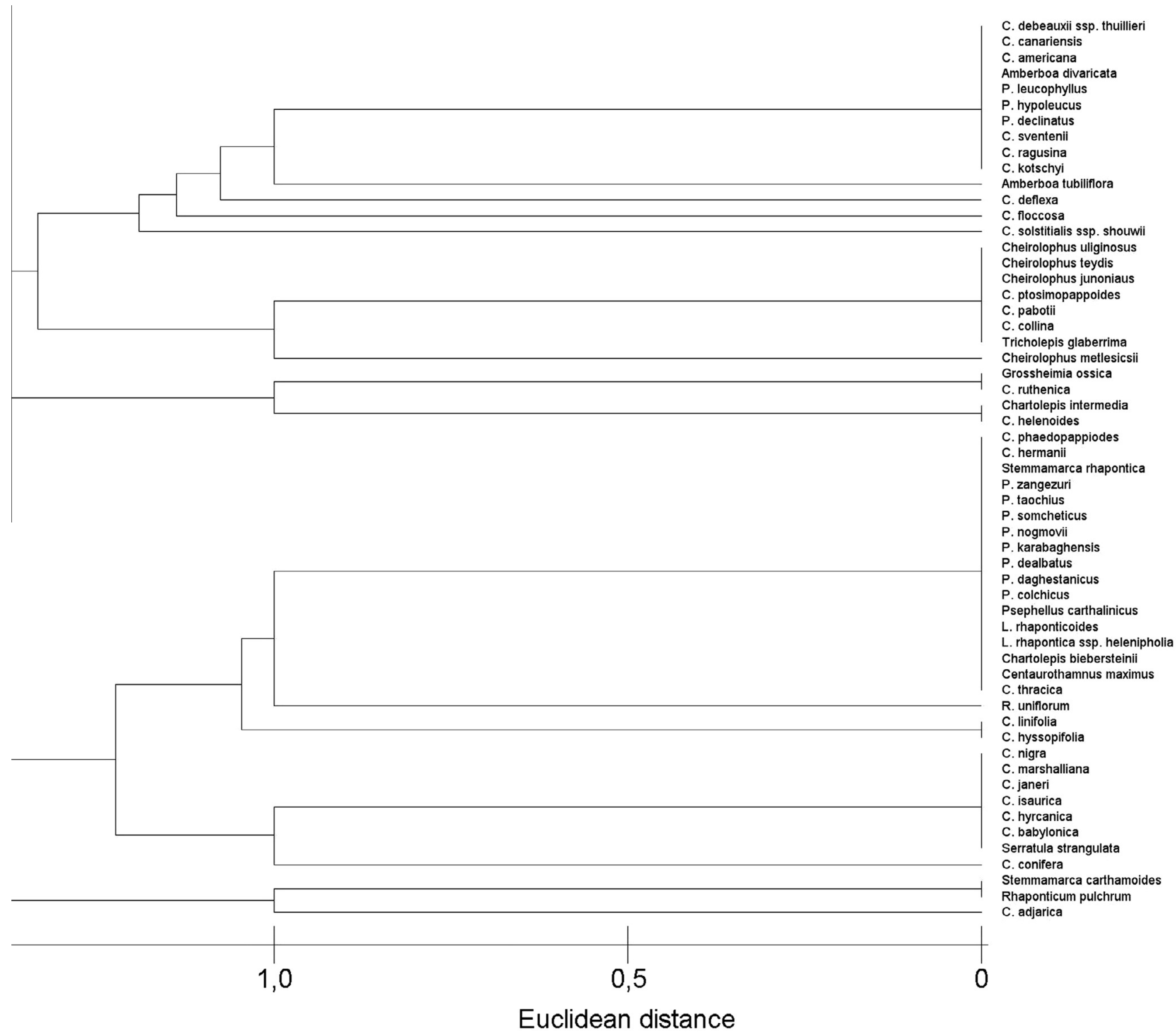

Fig. 6. Clusters based on presence/absence of structurally similar sesquiterpenes part B.

soma mansoni when topically applied to the skin (Baker et al., 1973).

In the course of searching for antiprotozoal agents from terrestrial plants, costunolide (**1**) was isolated from *Magnolia sororum* using bioassay-guided fractionation methods. It exhibited activity (IC_{50} = 9.4 μM) *in vitro* against the *Leishmania mexicana* parasite but not against *T. cruzi* and *Monkey vero* (Sanchez et al., 2007).

Cnicin (**19**), reynosin (**100**), alantolactone (**121**), ivalin (**122**) and carabrone (**287**) were tested *in vitro*against four major protozoan pathogens, *T. brucei rhodesiense*, *T. cruzi*, *L. donovani* as well as *Plasmodium falciparum*. Cnicin displayed high anti-parasitic activity against *T. brucei rhodesiense* (IC_{50} = 1.3 μM), while alantolactone was moderately active against all the four pathogens (Schmidt et al., 2009).

Extracts from *C. scabiosa* L. aerial parts revealed evident antiopisthorchiasis activity. The most effective was the extract contained greater amount of SLs (cynaropicrin (**162**), repin (**209**) and grosheimin (**264**) than other extracts (Kaminskii et al., 2010a,b).

12-Carboxy-3,11(13)-eudesmadiene (**123**), isolated from the above-ground portions of *I. viscosa*, showed anthelmintic activity against *Hymenolepis nana* var. *fraterna* and *Syphacia obvelata* *in vitro*. However, its activity against these parasites in mice was poor, due to considerable absorption in the digestive tract before reaching the intestinal site of parasitization (Azoulay et al., 1986).

4.3. Anti-inflammatory

SLs are known to possess a considerable anti-inflammatory activity in different inflammation models. They inhibit the transcription factor NF-κB, involved in the synthesis of inflammatory mediators, such as cytokines and chemokines, probably by alkylating cysteine in the DNA binding domain of the p65 subunit.

Cynaropicrin (**162**), santamarine (**99**) and reynosin (**100**) showed potent dose-dependent inhibitory effect on the production of tumor necrosis factor-α (TNF-α) with an IC_{50} of TNF-α production were 2.86 μg/mL (8.24 μM), 26.2 μg/mL (105 μM), and 21.7 μg/mL (87.4 μM), respectively. In the case of cynaropicrin (**162**) the result was better than dbcAMP and prednisolone used as controls. Treatment with sulfydryl (SH) compounds such as L-cysteine, dithiothreitol, and 2-mercaptoethanol abrogated the inhibitory effect of cynaropicrin on TNF-α production showing that the bioactive moiety is the unsaturated lactone (Cho et al., 2000, 1998).

Cynaropicrin (**162**), aguerin B (**160**) and grosheimin (**264**) showed a remarkable inhibitory effect on inducible nitric oxide synthase with IC_{50} values in the range 1.5–9.5 μg/mL (Blunder et al., 2008). Cynaropicrin (**162**) displayed immunomodulatory effects on the production of cytokine and nitric oxide from macrophages/monocytes. It has been demonstrated that cynaropicrin may be a potent functional regulator of CD29 and CD98 via interrupting extracellular signal-regulated kinase (ERK) activation which may be linked to cytoskeleton rearrangement, suggesting further application to CD29- and CD98-mediated diseases such as virus-induced chronic inflammation, and invasion, migration, and metastasis of leukocyte (Cho et al., 2004a).

An investigation on a set of 103 different SLs representing six structural groups (44 germacranolides, 16 heliangolides, 22 guaianolides, 9 pseudoguaianolides, 2 hypocretenolides, 10 eudesmanolides) for their NF-κB inhibiting properties was carried out and the resulting IC_{100}-values were submitted to a QSAR study. These studies indicated that the SLs more active possessed a rigid skeleton (furanoheliangolides and guaianolides), whereas in the case of flexible skeletons (germacranolides, such as germacrolides and melampolides), inhibition might be mostly determined by the number and type of α, β-unsaturated carbonyl structural elements (Siedle et al., 2004).

A review on the roles of NF-κB in inflammation, photoaging, and other diseases, on the inhibition of NF-κB by artichoke extract, the identification of cynaropicrin (**162**) as an active ingredient of artichoke extract and the prevention of pigmentation and photoaging, and decrease of open pores of the skin by lotions containing artichoke extracts in humans has been reported (Banno, 2011).

Investigation of *Podachaenium eminens* afforded several SLs from which costunolide (**1**) and santamarin (**99**) are new for this plant. The isolated compounds were studied for their anti-inflammatory activity using NF-κB as a molecular target. NF-κB is involved in the synthesis of inflammatory mediators, such as cytokines and chemokines. The compounds completely inhibited NF-κB DNA binding in an electrophoretic mobility shift assay at concentrations of 50 and 200 μM, respectively, without showing any cytotoxic effects (Castro et al., 2000).

Nitric oxide (NO), derived from L-arginine, is produced by two types (constitutive and inducible) of nitric oxide synthase (NOS: cNOS and iNOS). The NO produced in large amount by the iNOS is known to be responsible for inflammation, the vasodilation, and hypotension observed in septic shock, and cancer metastasis. Inhibitors of the overproduction of NO may thus be useful candidates for the treatment of inflammatory diseases. Dehydrocostuslactone (**142**) showed significant inhibitory activities on the production of NO and release of TNF-α with IC_{50} values lower than 1 μM (Zhao et al., 2008).

Costunolide (**1**), santamarine (**99**), reynosin (**100**), dehydrocostus lactone (**142**) and zaluzanin C (**147**) were found to inhibit NO production in lipopolysaccharide (LPS)-activated mouse peritoneal macrophages (IC_{50} = 1.2–3.8 μM). Furthermore, costunolide and dehydrocostus lactone inhibited iNOS in accordance with induction of heat shock protein 72 (HSP 72) (Matsuda et al., 2000a, 2003; De Marino et al., 2005).

Costunolide (**1**), isolated from *Magnolia grandiflora*, was found to inhibit NO production by down-regulating iNOS expression, at least, in part through the inhibition of IκBs′ phosphorylation and degradation, which are essential for the activation of NF-κB (Koo et al., 2001). Furthermore, costunolide (**1**) showed an ability to inhibit expression of multiple neuroinflammatory mediators of NFκB and MAPK activation. Further investigation of this novel role of costunolide may aid in developing better therapeutic strategies for treatment of neuroinflammatory diseases (Rayan et al., 2011).

The antipyretic and anti-inflammatory effects of costunolide (**1**) were investigated. The oral administration of costunolide inhibited carrageenan (Cg)-induced paw edema (ID_{50} 0.18 (0.12–0.27) mg/kg) and was effective in abolishing lipopolysaccharide (LPS)-induced fever (0.15 mg/kg) (Kassuya et al., 2009).

It was shown that the suppression of NO production by dehydrocostus lactone (**142**) is mediated by the inhibitory action on the i-NOS gene expression through the inactivation of NF-κB and this sesquiterpene lactone can act as a pharmacological inhibitor of the NF-κB activation (3.0 μM better than pyrrolidine dithiocarbamate used as control) (Jin et al., 2000).

In order to elucidate the mechanism for the anti-inflammatory activity of santamarin (**99**), its ability to interfere with the activation of the transcription factor NF-κB was studied. Santamarin (**99**) showed a moderate inhibitory activity (Lyss et al., 2000).

Alantolactone (**121**), isolated from the roots of *Inula racemosa* (Asteraceae), was screened for its inflammatory activity against carrageenan induced paw edema and hepatoprotective activity *in vitro* against galactosamine and thioacetamide and *in vivo* against carbon tetrachloride, paracetamol and rifampicin induced hepatotoxicities in albino rats. It showed significant anti-inflammatory and hepatoprotective activities similar to that of silymarin (Kurma and Mishra, 1997).

Cynaropicrin (**162**) and 13-acetyl solstitialin A (**183**), both present in the aerial parts of the yellow star thistle (*C. solstitialis*) have toxic potential in cell cultures of substantia nigra of the rat. The specificity of action towards cells of the substantia nigra remains to be proved, and a toxic action in the midbrain may contribute to the nigro-pallidal encephalomalacia, caused by the ingestion of the yellow star thistle by horses (Wang et al., 1991;Cheng et al., 1992).

The mixture of elemanolides **72** and **73** from *C. chilensis* showed anti-inflammatory activity when tested against carrageenan-induced edema in the guinea pig hindpaw (Negrete et al., 1993) and desacylcynaropicrin (**149**) isolated from the aerial parts of *Cyclolepis genistoides* produced a significant inhibition of carrageenan-induced inflammation at doses of 75 and 100 mg/kg, respectively (Sosa et al., 2011). Cnicin (**19**) showed an anti-inflammatory activity in the rat paw edema screen which was nearly equivalent to that of indomethacin (Schneider and Lachner, 1987).

Compounds **196** and **199** were evaluated for their inhibitory effects against cyclooxygenases-1 and 2 *in vitro*. Compound **199**showed moderate COX-1-inhibiting activity with IC_{50} value of 78.8 μM, comparable to that of representative anti-inflammatory drug aspirin with an IC_{50} value of 77.2 μM. Both compounds displayed potent COX-2 inhibitory activities with IC_{50} values of 28.7 and 57.9 μM, respectively, in comparison with that of aspirin with an IC_{50} value of 87.6 μM (Wang et al., 2009).

4.4. Antitumor and cytotoxic

Several guianolides have been the object of many antitumor and cytotoxic studies. For example, cynaropicrin (**162**) has been shown to have cytotoxic effect against several types of cell lines such as macrophages, eosinophils, fibroblasts and lymphocytes. Cynaropicrin potently inhibited the proliferation of leukocyte cancer cell lines, such as U937, Eol-1 and Jurkat T cells, but some other cells such as Chang liver cells and human fibroblast cell lines were not strongly suppressed by cynaropicrin treatment. The cytotoxic effect of cynaropicrin was due to inducing apoptosis and cell cycle arrest at G1/S phase, according to flow-cytometric, DNA fragmentation and morphological analyses using U937 cells (Cho et al., 2004b).

The same compound (**162**) along with desacylcynaropicrin (**149**) and aguerin B (**160**) a were evaluated *in vitro* for cytotoxic activity against human cancer cell lines, comprising SK-OV-3, LOX-IMVI, A549, MCF-7, PC-3 and HCT-15 by the sulforhodamine B (SRB) assay method. Compounds **160** and cynaropicrin (**162**) showed the most potent cytotoxic activity against MCF-7 (IC_{50}: 1.1 μg/mL) and HCT-15 cells (IC_{50}: 0.9 μg/mL and 1.4 μg/mL, respectively), whereas compound **149** showed a moderate activity (IC_{50}: 17.1 μg/mL) only against the HCT-15 cell line (Ha et al., 2003).

The biological investigation on the anti-proliferative activity of aguerin B (**160**) and the nor-guaianolide **284** was carried out against human pancreatic and colon cancer cells. Of the two compounds, only aguerin B (**160**) was shown to induce apoptotic cell death, confirming the role as pro-apoptotic moiety of the α-methylene-γ-lactone ring present in **160** but not in **284** (Chicca et al., 2011).

Desacylcynaropicrin (**149**), cynaropicrin (**162**), chlorojanerin (**219**), chlorohyssopifolin A (**224**) and chlorohyssopifolin E (**227**) have been tested for cytotoxic activities against human cervix epitheloid carcinoma cell lines (HeLa) and human hepatoma cell lines (SMMC-7721). The best activity was found for compound **162** with IC_{50} of 13.0 and 8.7 μg/mL, respectively (Ren et al., 2007).

The cytotoxicity of some of the above compounds (**149**, **160**, **162**) along with **169** and **190** was tested by SRB bioassay method against five cultured human tumor cells (A549, SK-OV-3, SK-MEL-2, XF-498, HCT-15). **160** and **162** showed non-specific significant cytotoxicity against these human tumor cell lines (**160**: 0.23–1.72 μg/mL and **162**: 0.29–1.37 μg/mL) comparable and sometimes better than etoposide and doxorubicin used as comparison drugs (Choi et al., 2005).

Cytotoxic studies with VERO cell cultures treated with deacylcynaropicrin (**149**), cynaropicrin (**162**), and grossheimin (**264**) indicated that the IC_{50} values for the last two compounds were 5.5 and 4.2 μg/L, respectively (Piacentini et al., 1986, 1987).

Compounds **149** and **162** showed very potent cytotoxic activity against tumor cell line P388 (murine leukemia), more than the natural anticancer agent pseudolaric acid B used as positive control, at the IC_{50} levels of 0.36 and 0.01 μM, respectively (Zha and Hou, 2008). They were also tested against human cancer cell lines of malignant melanoma (SK-MEL), epidermoid (KB), ductal (BT-549) and ovarian (SK-OV-3) carcinomas for cynaropicrin (**162**), janerin (**208**) and chlorojanerin (**219**), showing *in vitro* cytotoxic activity with IC_{50} values of 2–6 μg/mL (Muhammad et al., 2003).

Grosshemin (**264**) and the germacranolide cnicin (**19**) had cytostatic action on HeLa cells with ID_{50} of 2.5 μg/mL and 0.1 μg/mL, respectively. Dihydroestafiatone (**270**), on the other hand, showed poor cytostatic action (Gonzalez et al., 1978a). Compounds **224**, **217**, **212**, **228**, **227**, **162**, and **149** were also tested for cytostatic action on HeLa cells: the first four exhibited an ID_{50} in the range 0.25–0.5 μg/mL (Gonzalez et al., 1980b). Furthermore, grosshemin (**264**) inhibited the growth of malignant HeLa cultures. The effect of the compound on an *in vitro* lymphocyte culture showed that it inhibited cell division at the metaphase stage (Bialecki et al., 1973). Grosshemin (**264**) also inhibited sarcoma 180, Pliss's lymphosarcoma and Ehrlich solid tumor (Adekenov et al., 1986b).

The cytotoxic activity of the guaianolides **208**, **209**, **211**, **212**, **224**, **244** and **246** against tumor cell replication (A549, MCF-7, 1A9, KB, KB-V, HCT-8, SK-MEL-2) was reported. Repin (**209**), chlorohyssopifolin C (**212**) and chlorohyssopifolin A (**224**) showed significant antitumor potency (Bruno et al., 2005c). Repin (**209**) showed also significant activity toward chick embryo sensory neurons and a causal relationship between repin and the necrosis of the neural cells in substantia nigra of horses leading to equine nigrostriatal encephalomalacia (ENE) disease has been suggested (Stevens et al., 1990). To understand the mechanism whereby ingestion of *Centaurea repens* induces ENE and a Parkinson's disease (PD)-like disorder, repin cytotoxicity was examined. Repin was found to be highly cytotoxic to both Pc12 cells and mouse astrocytes in a dose- and time-dependent way. The cytotoxic effects were accompanied by depletion of glutathione, a rise in the level of reactive oxygen species and damage to cellular membranes (Robles et al., 1997). Both A- an B-ring modifications of the electrophilic exocyclic methylene group and the epoxy-ester moiety were performed, further demonstrating the importance of these functional group contributions to toxicity (Anand et al., 2003; Tukov et al., 2004).

Zaluzanin C (**147**) showed a significant cytotoxicity against several tumor cell lines A549, SK-OV-3, SK-MEL-2, XF498, HCT15 (Choi et al., 2006), GTB, HL60 (Zidorn et al., 2004) and P-388 lymphocytic leukemia (Jolad et al., 1974), a moderate cytotoxicity against three tumor cell lines (HepG2, HeLa, OVACAR-3) (Sun et al., 2003), and revealed relatively high cytotoxicities on human colon carcinoma cell lines and lung adenocarcinoma cell lines (Ahn et al., 2006). Furthermore, it showed significant cell growth inhibitory activity against murine lymphocytic leukemia (P388) *in vitro* (Ando et al., 1982), and a capacity to inhibit protein synthesis in intact HeLa cells preferentially to DNA and RNA synthesis. On the other hand dihydroestafiatone (**270**) showed poor cytostatic action on HeLa cells (Gonzalez et al., 1978a). Zaluzanin C (**147**) inhibits the proliferation of T and B lymphocytes of mice *in vitro*exhibiting cytotoxicity at concentration of 10 μM or lower (Chen et al., 2006).

Compounds **142**, **147** and **190** isolated from *Ainsliaea macrocephala* were tested for inhibitory activity against the production of nitric oxide in RAW 264.7 cells stimulated by LPS, as well as for cytotoxicity against RAW 264.7 macrophages. Zaluzanin C (**147**) strongly inhibited the production of nitric oxide with an IC_{50} value of 2.5 μM, and simultaneously showed low cytotoxicity against RAW 264.7 macrophages. The other two compounds had moderate activity (Wu et al., 2011).

The molecular mechanism underlying the suppression of lipopolysaccharide (LPS)/interferon-γ (IFN-γ)-induced nitric oxide (NO) and prostaglandin (PGE2) production was investigated in RAW 264.7 macrophages treated with sesquiterpene lactone, zaluzanin-C (**147**). It decreased NO production in LPS/IFN-γ-stimulated RAW 264.7 macrophages with an IC_{50} of about 6.6 μM and 3.8 μM, respectively. In addition, these compounds inhibited the synthesis of PGE2 in LPS/IFN-γ-treated RAW 264.7 macrophages. Furthermore, treatment with zaluzanin C (**147**) resulted in a decrease in inducible NO synthase (iNOS) and cyclooxygenase-2 (COX-2) protein and mRNA expression levels (Shin et al., 2005).

Salograviolide A (**156**) was found reduced the growth of colon cancer cell lines (El-Najjar et al., 2008) and to exert significant growth inhibitory effects on neoplastic cells. At concentrations that were not cytotoxic to primary keratinocytes, it preferentially inhibited the proliferation of papilloma and squamous cell carcinoma (SCC) cell lines without significantly affecting the growth of normal cells (Ghantous et al., 2008). Furthermore it was shown to reverse the effects observed by interleukin-I on cyclooxygenase-2 levels in NF-kB translocation in intestinal epithelial cells. It reduces the level of inflammatory cytokines and the level of inflammation in the animal model (Al-Saghir et al., 2009).

Also several sesquiterpenoids with a different skeleton rather than guaiane have been studied for their cytotoxic and antitumor activities.

Cnicin (**19**) showed cytotoxic activity against KB with ED_{50} = 3.4 μg/mL (Vanhaelen-Fastre, 1972), against TXL-5 mice lymphoma cells with ID_{50} = 6 μg/mL (El-Marsy et al., 1984) and showed moderate antiproliferative effects against HeLa, and A431 human tumor cell lines (Csapi et al., 2010). The cytotoxic activities of some cnicin (**19**) and salonitenolide (**4**) derivatives were determined against A549 and MCF-7 tumor cell lines. Cnicin was selectively cytotoxic against the MCF-7 breast cancer cell line with IC_{50} = 4.2 μM (Rosselli et al., 2010).

The cytotoxic activities of chloroform extracts from the weeds *C. tweediei* and *C. diffusa*, and the main SLs isolated from these species, onopordopicrin (**8**) and cnicin (**19**), respectively, were assayed. Both the extracts and the purified SLs show high cytotoxicity against human-derived macrophages (Bach et al., 2011). Onopordopicrin (**8**) also showed cytotoxic activity against KB cell line (Lonergan et al., 1992).

The *in vitro* cytotoxic activity of germacranes **4**, **5**, **8**, **19**, **20** and elemanes **69**, **75** was investigated against P388, A549 (human non small lung cancer) and HT29 (human colon cancer). As expected for compounds with an α-methylene-γ-lactone group, they have cytotoxic activity with IC_{50} values ranging from 2 to 10 μg/mL. The additional α, β-unsaturated ester group present in **8**, **19**, **20** and **75** increases the activity two or three times (Barrero et al., 1995).

Also germacranes **19**, **20**, elemanes **75**, **80**, **94**, and eudesmanes **103**, **104**, **111**, **112** were examined for their *in vitro* cytotoxic/cytostatic activity against five human cell lines (i.e. DLD1, SF268, MCF-7, H460, OVCAR3). Compounds **75** and **80** were found to be the most active and exhibited a considerable growth-inhibiting activity against most of the cell lines tested (Koukoulitsa et al., 2002). Cnicin (**19**), salitenolide (**4**) and the elemanes **66**, **70**, **80**, **83** were tested against nine cancer cell lines. **19** was active against 1A9, KB and KB-VIN. **83** showed good activity for all the lines except A549, and **66** and **70** were shown to be the best with $IC_{50} < 1$ μM (Bruno et al., 2005b). Cnicin (**19**) showed inhibition of NF-κB and inhibition of iNOS activity with IC_{50} values of 1.8 and 6.5 μM, respectively. Cytotoxic activity of cnicin (**19**) was observed toward pig epithelial (LLC-PK11), human malignant melanoma (SK-MEL) and human ductal carcinoma (BT-549) (Baykan Erel et al., 2011).

It has been suggested that deregulation of activin signaling contributes to tumor formation. Data suggested that alantolactone (**121**) induced activin/SMAD3 signaling in human colon adenocarcinoma HCT-8 cells and that it performs its antitumor effect by interrupting the interaction between Cripto-1 and the activin receptor type IIA in the activin signaling pathway (Shi et al., 2011). Furthermore, it showed antiproliferative activities against MK-1, HeLa, and B16F10 cell lines with GI_{50} in the range 4.7–6.9 μM (Konishi et al., 2002). Alantolactone (**121**) was also identified from the roots of *Inula helenium* L. and its inhibitory effects on human non-small cell lung cancer (NSCLC) A549 cells was examinated. The antiproliferative effect of alantolactone on A549 cells was investigated via MTT [3′-(4,5dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium bromide] assay and its apoptosis-inducing effect was determined by Hoechst staining and flow cytometry. Alantolactone was found to significantly inhibit the proliferation of A549 cells and to induce morphological changes typical for apoptosis (Zong et al., 2011).

9-α-Hydroxyparthenolide (**28**), isolated from *Anvillea garcini*, has shown activity in both the 9 KB cell culture and P388 mouse leukemia test systems (Tyson et al., 1981). Compound **28** was evaluated by an *in vitro* disease-oriented antitumor screen, which determinates cytotoxic effects against a panel of approximately 60 human tumor cell lines. The best results were obtained for NCI-H522 (non-small cell lung) and CCRF-CEM (leukemia) with ED_{50} of 0.5 μg/mL and 0.84 μg/mL, respectively (Sattar et al., 1996). Other authors tested the same compound against five other human cancer lines showing an IC_{50} of 2 μg/mL for A549, H116 and PSN1 (El Hassany et al., 2004).

The *in vitro* cytotoxic activities of 8α-(4′acetoxy-angeloyl)-salonitenolide (**18**) and malacitanolide (**109**) were assayed towards P388 and Schabel mouse lymphomas and toward the A549 (lung carcinoma), HT-29 (colon carcinoma) and MEL-28 (melanoma) human cell lines. Compound **18** showed an $IC_{50} = 2.5$ μg/mL against both mouse lymphomas and an $IC_{50} = 5$ μg/mL towards the three human cell lines whereas **109** showed an $IC_{50} = 0.12$ μg/mL in all cases (Barrero et al., 1997a).

Stizolicin (**32**), solstitialin A (**181**) and xanthinin (**288**) demonstrated a limited antitumor action *in vivo* on two types of tumor: L-1210 leukemia and P388 leukemia (Naidenova et al., 1988).

A moderate cytotoxic activity of compound **83** was also shown against SF268 and OVCAR3 tumor cell lines (Saroglou et al., 2005).

Compounds **9** and **13** were shown to have a good cytotoxic activity against colon cancer cell line CaCo-2 with IC_{50} values of 8.5 and 26.4 μM, respectively (Shoeb et al., 2007a).

Ivalin (**122**) showed cytotoxic activity ($ED_{50} < 10$ μM) against A549, SK-OV-3, SK-MEL-2 XF-498 and HCT-15 tumor cell lines comparable to that of cisplatin. Carabrone (**287**) was less active (Lee et al., 2002). A very good cytotoxic activity was observed for ivalin (**122**) against P388, KB-3 and KB-V1 with ED_{50} in the range 0.14–1.8 μg/mL (Topçu et al., 1993).

A large number of papers have been published on the biological properties of costunolide (**1**) and dehydrocostuslactone (**142**).

Costunolide (**1**), isolated from the root of *Saussurea lappa*, was investigated for its effects of on the induction of apoptosis in HL-60 human leukemia cells (Kim et al., 2010) and its putative pathways of action. Using apoptosis analysis, measurement of reactive oxygen species (ROS), and assessment of mitochondrial membrane potentials, it was shown that costunolide is a potent inducer of apoptosis, and facilitates its activity via ROS generation, thereby inducing mitochondrial permeability transition (MPT) and cytochrome c release to the cytosol. ROS production, mitochondrial alteration, and subsequent apoptotic cell death in costunolide-treated cells were blocked by the antioxidant N-acetylcysteine (NAC) (Lee et al., 2001). Furthermore costunolide (**1**) was found to induce apoptotic cell death in a dose-dependent manner by nucleosomal DNA ladder and flow cytometric analysis. Immunoblot analysis showed that the level of the anti-apoptotic protein, Bcl-2, was decreased, whereas the cleavage of poly-(ADP-ribose) polymerase was activated. Furthermore, the N-acetyl-L-cysteine antioxidant effectively prevented costunolide-induced cytotoxicity. These results suggested that costunolide-induced cell death is mediated by reactive oxygen species (Park HJ et al., 2001). Other results indicate that costunolide-induced c-Jun N-terminal kinase (JNK) activation acts downstream of ROS but upstream of Bcl-2, and suggest that ROS-mediated JNK activation plays a key role in costunolide-induced apoptosis. Moreover, the administration of costunolide (i.p. once a day for 7 d) significantly suppressed tumor growth and increased survival in 3LLLewis lung carcinoma-bearing model (Choi and Lee, 2009).

Costunolide (**1**), isolated from the stem bark of *Magnolia sieboldii*, demonstrated a significant inhibition upon the farnesylation process of human lamin-B by farnesyl-proteintransferase (FPTase), in a dose dependent manner *in vitro* (IC_{50} value was calculated as 20 μM). It was also found to exhibit an inhibition upon the proliferation of human tumor cell cultures, i.e., A549 (non small cell lung), SK-OV-3 (ovary), SK-MEL-2 (melanoma), XF498 (central nerve system) and HCT-15 (colon), *in vitro* (Park SH et al., 2001). Costunolide (**1**) also inhibits the killing activity of cytotoxic T lymphocytes through preventing the increase in tyrosine phosphorylation in response to the crosslinking of T-cell receptors (Taniguchi et al., 1995).

Costunolide (**1**) demonstrated inhibitory effect on the protein and mRNA expression of interleukin-1 β (IL-1 β) in LPS-stimulated RAW 264.7 cells. Costunolide was also shown to suppress the transcriptional activity of the IL-1 β promoter. Moreover, costunolide inhibited the activity of AP-1 transcription factor, and the phosphorylation of MAPKs, including SAPK/JNK and p38 MAP kinase. The inhibitory effect of costunolide on AP-1 activity was also confirmed by an electrophoretic mobility shift assay. These results demonstrated that costunolide inhibits IL-1 β gene expression by

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blocking the activation of MAPKs and DNA binding of AP-1 in LPS-stimulated RAW 264.7 cells (Kang et al., 2004).

It has been also suggested that costunolide (**1**) induces apoptosis in human promonocytic leukemia U937 cells by depleting the intracellular thiols. Costunolide treatment rapidly depleted the intracellular reduced glutathione (GSH) and protein thiols, and this preceded the occurrence of apoptosis. Pretreatment with sulfhydryl compounds such as GSH, N-acetyl-L-cysteine, dithiothreitol and 2-mercaptoethanol almost completely blocked the costunolide-induced apoptosis, highlighting the significance of the intracellular thiol level in the process. Furthermore, overexpression of Bcl-2 also significantly attenuated the effects of costunolide. The apoptosis-inducing activity of costunolide is likely to depend on the exomethylene moiety because derivatives, in which this group was reduced, such as dihydrocostunolide and saussurea lactone, did not deplete the cellular thiols and showed no apoptotic activity. In this study it has been demonstrated that the costunolide-induced apoptosis depends on intracellular thiols contents, which are modulated by Bcl-2 (Choi et al., 2002a). Other studies were carried out on the induction mechanism of apoptosis by costunolide in a human B cell leukemia NALM-6 cell culture system and the data suggested that one of the costunolide-induced apoptotic mechanisms is that the receptor-mediated pathway precedes the mitochondria-dependent pathway, caused by the inhibition of telomerase activity via suppression of telomerase reverse transcriptase (hTERT) in NALM-6 cells (Kanno et al., 2008). Also, in the case of MCF-7 and MDA-MB-231 cells, their growth inhibition seem to be mediated at least in part by a significant reduction in telomerase activity (Choi et al., 2005).

In the cell adhesion inhibitory activity test against B16-F1 mouse melanoma cell, costunolide (**1**) showed significant activities, with IC_{50} of 0.9 μg/mL. In the cytotoxicity test against several human tumor cells, costunolide had an IC_{50} values of below 0.3 μg/mL against all the tested cell lines except for UACC62. It exhibited a stronger activity against HCT15 and UO-31 cell lines than a positive control, adriamycin (Jang et al., 1998b).

Costunolide (**1**) showed effective antiproliferative activity against hormone dependent (LNCaP) and independent (PC-3 and DU-145) prostate cancer cells (ATCC) by SRB assay, clonogenic test and flow cytometric analalysis of carboxyfluorescein succinimidyl ester labeling. In PC-3 cells, data showed that costunolide induced a rapid overload of nuclear Ca^{2+}, DNA damage response and ATR phosphorylation (Hsu et al., 2011). It also had cytotoxic properties against MCF-7, NCI-H460, and SF-268 cancer cell lines *in vitro* (Chang et al., 2010), P-388, L-1210 leukemia and SNU-5 stomach cancer cells (Kim et al., 1999) and against human A549, SK-OV-3, SK-MEL-2, and HCT15 tumor cells (Park et al., 2010). Costunolide (**1**) and the guainolide zaluzanin D (**147**) displayed strong growth inhibitory effect against human promyelotic leukemia HL-60 cells by induction of chromatin condensation in the HL-60 cells (Hibasami et al., 2003).

Costunolide (**1**) has been reported to exhibit potent chemopreventive effects on carcinogenesis. Modifying effects of costunolide on intestinal carcinogenesis were examined in a rat model using azoxymethane (AOM). The results suggest that the natural sesquiterpene could be a promising chemopreventive agent for human intestinal neoplasia (Mori et al., 1994). Effects of costunolide on cellular activation induced by a tumor-promoting phorbol ester 12-O-tetradecanoylphorbol-13-acetate (TPA) were investigated: iNOS promoter-dependent reporter gene activity was significantly increased by TPA, and the TPA-induced increase of the reporter gene activity was efficiently reduced by costunolide, with an IC_{50} of approximatively 2 μM (Fukuda et al., 2001).

It was found that costunolide (**1**) selectively inhibits angiogenic factors including basic fibroblast growth factor (bFGF) and vascular endothelial growth factor (VEGF)-induced endothelial cells proliferation and migration. From these results, it has been suggested that costunolide would inhibit angiogenesis by blockade of angiogenic factors signaling pathway (Jeong et al., 2001, 2002).

Costunolide (**1**) could reduce the viability and arrest cell cycling at mitosis in hepatoma cells. Logical exploration of this mitosis-arresting activity for cancer therapeutics shows costunolide enhanced the killing effect of radiotherapy against human hepatocellular carcinoma (HCC) cells (Liu et al., 2011).

Investigations on the effect of costunolide (**1**) on cellular differentiation in the human promyelocytic leukemia HL-60 cell culture system were carried out. Costunolide markedly increased the degree of HL-60 leukemia cell differentiation when simultaneously combined with 5 nM 1,25-dihydroxyvitamin D3 (1,25-(OH)2D3). The results indicate that PKC, PI3-K, ERK and NF-κB may be involved in 1,25-(OH)2D3-mediated cell differentiation enhanced by costunolide (Choi et al., 2002b; Kim et al., 2002).

Investigations of the anticancer effect of dehydrocostus lactone (**142**) on human breast cancer cells (MCF7) (Kuo et al., 2009), human ovarian cancer cells (SK-OV-3) (Choi and Ahn, 2009), human prostate cancer cells (DU145) (Kim et al., 2008), human non-small cell lung cancer cell lines (A549, NCI-H460 and NCI-H520) (Hung et al., 2010), HeLa, T-98, HLE and HMV-1 cells (Chen et al., 2011) and HepG2 and PLC/PRF/5 cells (hepatocellular carcinoma) (Hsu YL et al., 2009) were carried out. Compound **142** was shown to inhibit cell proliferation by inducing cells to undergo cell cycle arrest and apoptosis.

Dehydrocostus lactone (**142**) inhibited the proliferation of human lung cancer A549 cells in a time- and dose-dependent manner. The cytometric analysis showed that the A549 cells were arrested at the sub-G1 phase by the treatment of dehydrocostus lactone. The evidence of the activation of caspase-9 and -3 verified that the death of A549 cells was through the apoptosis pathway. Dehydrocostus lactone also exhibited strong cytotoxicity on MDA-MB-231 (breast cancer) and HepG2 (hepatoma) cells (Hsu HF et al., 2009). Dehydrocostus lactone (**142**), isolated from the medicinal plant, *Saussurea lappa*, inhibited the production of NO in lipopolysaccharide (LPS)-activated RAW 264.7 cells by suppressing inducible NO synthase enzyme expression (Lee et al., 1999).

The anti-proliferative activity of dehydrocostus lactone (**142**) was investigated in human breast cancer (MDA-MB-231, MDA-MB-453 and SK-BR-3) and ovarian cancer (SK-OV-3 and OVCAR3) cell lines using the MTT assay. In the cells, exposure to dehydrocostus lactone resulted in a dose-dependent decline in cell proliferation. The IC_{50} value was found to be 21.5, 43.2, 25.6, 15.9 and 10.8 μM in MDA-MB-231, MDA-MB-453, SK-BR-3, SK-OV-3 and OVCAR3 cells, respectively. Dehydrocostus lactone exerted its anti-proliferative effects by inducing cell cycle arrest and apoptosis. Cell cycle distribution and apoptosis were analyzed using flow cytometry in cell lines exposed to 10 μM dehydrocostus lactone for 48 h (Choi and Kim, 2010).

It was demonstrated that dehydrocostus lactone (**142**), the major sesquiterpene lactone isolated from the roots of *Saussurea lappa*, inhibits NF-κB activation by preventing TNF-α-induced degradation and phosphorylation of its inhibitory protein I-κBα in human leukemia HL-60 cells and that **142** renders HL-60 cells susceptible to TNF-α-induced apoptosis by enhancing caspase-8 and caspase-3 activities (Oh et al., 2004).

Costunolide (**1**) and dehydrocostus lactone (**142**) both showed strong suppressive effect on the expression of the hepatitis B surface antigen (HBsAg) in human hepatoma Hep3B cells, but had little effect on the viability of the cells. Both costunolide and dehydrocostus lactone suppressed the HBsAg production by Hep3B cells in a dose-dependent manner with IC_{50} of 1.0 and 2.0 μM, respectively (Chen et al., 1995).

Dehydrocostus lactone (**142**) and costunolide (**1**) exhibited potent dose- and time-dependent cytotoxicity with CD_{50} values in

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the range 1.6–3.5 μg/mL against HepG2, OVCAR-3 and HeLa human cancer cell lines whereas zaluzanin C (**147**), santamarin (**99**) and reynosin (**100**) which are less lipophilic due to the presence of an hydroxyl group, showed lower cytotoxicity (Sun et al., 2003).

Costunolide (**1**), santamarine (**99**), reynosin (**100**) obtained through bioactivity-directed isolation from a methanol extract of the fruits of *Laurus nobilis* were found to be highly cytotoxic against the A2780 ovarian cancer cell line (Barla et al., 2007). Furthermore, cytotoxicity testing of the sesquiterpene lactone reynosin (**100**) against the KB cancer cell line (ATCC CCL17) revealed IC_{50} values of 2.7 μg/mL (Hilmi et al., 2003).

Dehydrocostus lactone (**142**), santamarine (**99**) and β-cyclocostunolide (**98**) showed effects on inhibited proliferation of human stomach cancer cells MGC-803, human pharyngeal cancer cells KB, human lung cancer cells NCI-H460, and human colon cancer cells HT-29 cultured for 72 h (IC_{50} < 10.0 mg/mL), and had weak effect on inhibiting proliferation of human liver cancer cells HepG-2 cultured for 72 h (IC_{50} = 16.3, 48.7, and 16.1 mg/mL, respectively) (Tang et al., 2010).

Cyathocline purpurea has been traditionally used to treat various diseases including cancers for many years and santamarine (**99**), one of its main constituents, inhibited the growth of L1210 murine leukemia, CCRF-CEM human leukemia, KB human nasopharyngeal carcinoma, LS174T human colon adenocarcinoma and MCF 7 human breast adenocarcinoma cells *in vitro*, with IC_{50} in the range of 0.16–1.3 μg/mL. In the L1210 model, santamarine inhibited cell growth, colony formation and [3H]-thymidine incorporation in time- and concentration-dependent manners. The mechanism of the cytotoxicity of santamarine towards L1210 cells could be related to alkylation of the sulfhydryl enzymes involved in nucleic acids and protein synthesis, as previously found for other SLs with the α-methylene-γ-lactone moiety. Santamarine (**99**) induced apoptosis of L1210 cells via activation of caspase 3 (Ma et al., 2009) and had moderate inhibitory effect on topoisomerases (Zhang et al., 2007). Santamarine (**99**) has been used as cytotoxic anticancer agent that is selective to mouse leucocythemia cell (L1210), human leucocythemia cell (CCRF-CEM), human nasopharyngeal carcinoma cell (KB), human mammary gland cancer cell (MCF-7), and human colon cancer cell (LS174T). The IC_{50} is 0.41, 0.59, 0.16, 0.92 and 0.53 μg/mL to the above tumor cells respectively, and the anticancer activity is in direct proportion to santamarine concentration and action time. The anticancer mechanism of santamarine relates to the inhibition of tubulin. Santamarine leads to tumor cell necrosis, not apoptosis (Li, 2005). Santamarin (**99**) and reynosin (**100**) have been reported to exhibit cytotoxic activity against the human lung carcinoma cell line GLC4 and the colorectal cancer cell line COLO 320 with IC_{50} in the range 7.4–10.7 μM (Goren et al., 1996).

4.5. Antiviral

Chlorohyssopifol A (**224**) and rhaposerin (**248**) suppressed reproduction of influenza virus by more than 50% at 5 μM concentration. Compound **224** decreased the infecting ability of virus of Newcastle disease (Berdin et al., 1999).

Antiviral properties of 13-acetyl solstitialin A (**183**), chlorojanerin (**219**) and centaurepensin (**224**) were screened against Herpes simplex type-1 (representative of DNA virus) and Parainfluenza (representative of RNA virus) were employed for the determination of antiviral activity. 13-acetyl solstitialin A (**183**) had significant activity against DNA virus over a wide range of concentration (16 μg/mL–6×10^{-5} μg/mL) (Gürbuz et al., 2006;Ozcelik et al., 2009).

4.6. Effects on insects

Grosheimin (**264**), and repin (**209**), administered in 0.1 mg/g doses to *Tenebrio molitor* larvae, inhibited its growth and showed antifeedant activity. Growth inhibition was due not only to reduced food intake but also to decreased absorption of digested food constituents and metabolic disorders (Rosinski et al., 1988). Also stizolin (**27**), 9α-hydroxypartenolide (**28**), stizolicin (**32**), aguerin B (**160**) and chlorojanerin (**219**) showed good antifeedant properties against *Sitophilus granaries*, *Trogoderma granarium* and *Tribolium confusum*, while janerin (**208**) and cynaropicrin (**162**) inhibited feeding of the latter species only (Cis et al., 2006;Bloszyk, 1988).

Cynaropicrin (**162**) was proved to be a potent feeding deterrent on testing against 4th instar larvae of Bihar hairy caterpillar, *Diacrisia obliqua* and the eri-silkworm *Philosamia ricini* (Bhattacharyya et al., 1996).

The antifeedant activity of compounds, **162**, **208**, **209**, **212**, **219**,**222**,**224**, **240**, **243**, **244** and **246** were tested against larvae of *Spodoptera littoralis*. The chlorine-containing guaianes, **217**, **219** and **246** showed significant activity at 100 ppm (Rosselli et al., 2006a).

Shiromool (**52**) showed significant antifeedant activity against the larvae of *S. littoralis* whereas compound **51** was inactive (Barrero et al., 1999).

Cnicin (**19**) exhibited significant mortality against the Formosan subterranean termite, *Coptotermes formosanus*, one of the most devastating termite pests (Meepagala et al., 2006) and was shown to be a disrupter of insect metamorphosis and modifier of reduced glutathione synthesis (Maymò et al., 1999). Furthermore, the effects of cnicin (**19**) on the ovopositional response and larval development of generalist and specialist insect herbivores were investigated as well as the toxicity on the larvae of *S. littoralis* (Landau et al., 1994).

Compounds **64** and **83** produce altering effects on the metamorphosis of the grasshopper *Locusta migratoria* when topically applied to the nymphs (Castillo et al., 1998).

Several SLs were examined for their nematocidal activity against root-knot nematode as a function of their structure. Maximum nematocidal activity was associated with an α-methylene-γ-lactone moiety, e.g., alantolactone (**121**) (97% mortality) (Mahajan et al., 1986).

HPLC-bioactivity-guided fractionations led to the isolation of costic acid (**124**) showing repellent activity against subterranean termite *C. formosanus* (Watanabe et al., 2005). Furthermore costic acid (**124**) had selective cytotoxic effects toward insect-derived Sf9 cells (Gonzalez-Coloma et al., 2005).

The larvicidal activities of alantolactone (**121**), isolated from the roots of *I. helenium*, against 3rd and 4th instars of *Aedes albopictus* (Diptera: Culicidae) and *Paratanytarsus grimmii* (Diptera: Chironomidae), were examined. It showed LC_{50} values of 2.7 μg/mL for *A. albopictus* and 5.1 μg/mL for *P. grimmii*, respectively (Konishi et al., 2008). It also had larvicidal activity against *Aedes aegypti* (Cantrell et al., 2010) and insect feeding deterrent properties (Picman et al., 1978).

Also dehydrocostus lactone (**142**), isolated from the dichloromethane extract of the Portuguese liverwort *T. lorbeeriana*, presented larvicidal activity against *A. aegypti* (Gonzalez-Coloma et al., 2005).

Costunolide (**1**), isolated from the fruits of *Magnolia salicifolia* exhibited 100% mortality on 4th instar *A. aegypti* at 15 ppm, in 24 h (Kelm et al., 1997).

Studies showed the insect repellent activity found in *Saussurea lappa* rhizomes to be due to dehydrocostus lactone (**142**) (Malik and Naqvi, 1984).

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4.7. Effects on plants

The SLs repin (**209**), acroptilin (**212**), solstitiolide (**222**), and centaurepensin (**224**) caused increased lettuce root elongation at 10 ppm and inhibited it at higher concentrations (Stevens and Merrill, 1985). Cnicin (**19**) and onopordopicrin (**8**) drastically reduced the germination of lettuce and honey weed. Furthermore cnicin (**19**) at 0.1 mg/g concentration selectively inhibited some soil microorganisms (Cabral et al., 2008) and was shown to have germination and growth inhibitor properties (Kelsey and Locken, 1987; Locken and Kelsey, 1987). Stizolin (**27**) has been tested on inhibition of seed germination of wheat and showed an excellent phytotoxic activity (Starykh and Konovalov, 1997). Costunolide (**1**) and dehydrocostus lactone (**142**) caused inhibition of radicle growth of seedlings of *Amaranthus hypochondriacus* (Mata et al., 2002). A structure–activity study to evaluate the effect of the *trans*,*trans*-germacranolide sesquiterpene lactone, costunolide (**1**), and some derivatives (in a range of 100–0.001 μM) on the growth and germination of several mono- and dicotyledon target species, was accomplished. These compounds appeared to have a selective effect on the radicle growth of monocotyledons at levels comparable to those of Logran (Macias et al., 1999a). Zaluzanin C (**147**) was shown to inhibit root and shoot growth in lettuce, tomatoes and cress (Macias et al., 1999b, 2010).

4.8. Other activities

In the nitric oxide release inhibitory experiments, costunolide (**1**) exhibited strong inhibition with an IC_{50} value of 0.2 μg/mL (0.86 μM). In the ACAT (acyl CoA: cholesterol acyltransferase) inhibitory assay, costunolide exhibited strong inhibition, with an IC_{50} value of 17 μg/mL (73.3 μM) (Jang et al., 1999).

A study demonstrated that dehydrocostus lactone (**142**) can protect osteoblasts against H_2O_2-induced cellular dysfunction. The results also suggest that **142** may be valuable as a protective agent against oxidative damage in osteoblasts (Choi et al., 2009) and, furthermore, it protects osteoblastic MC3T3-E1 cells from antimycin A induced cell damage through the improved mitochondrial function (Choi, 2011). The effect of costunolide (**1**) on the function of osteoblastic MC3T3-E1 cells was studied. Costunolide significantly increased the growth of MC3T3-E1 cells and caused a significant elevation of alkyl phosphatase (ALP) activity, collagen content, and mineralization in the cells ($P < 0.05$). These data indicate that the enhancement of osteoblast function by costunolide may result in the prevention for osteoporosis (Lee and Choi, 2011).

The molecular mechanism of inhibitory action of dehydrocostus lactone (**142**) and costunolide (**1**) towards the activation of signal transducer and activator of transcription 3 (STAT3) was studied. In human THP-1 cell line, they inhibit IL-6-elicited tyrosine phosphorylation of STAT3 and its DNA binding activity with EC_{50} of 10 μM with concomitant down-regulation of the phosphorylation of the tyrosine Janus kinases JAK1, JAK2 and Tyk2. Furthermore, these compounds that contain an $\alpha - \beta$-unsaturated carbonyl moiety and function as potent Michael reaction acceptor, induced a rapid drop in intracellular glutathione (GSH) concentration by direct interaction with it, thereby triggering S-glutathionylation of STAT3. It was concluded that SLs **142** and **1** are able to induce redox-dependent post-translational modification of cysteine residues of STAT3 protein in order to regulate its function (Butturini et al., 2011).

Costunolide (**1**) and dehydrocostus lactone (**142**), the active principle from the leaves of *Laurus nobilis*, were shown to inhibit selectively ethanol absorption rather than glucose absorption and to have a gastroprotective effect on acidified ethanol-induced gastric mucosal (Yoshikawa et al., 2000) lesions in rats (Matsuda et al., 2000b). The inhibitory mechanism of costunolide was investigated (Matsuda et al., 2002). In other studies through bioassay-guided separation from methanolic extract of the leaves of *Laurus nobilis*, costunolide (**1**), dehydrocostus lactone (**142**), and santamarine (**99**) were isolated as the active constituents that inhibited the elevation of blood ethanol level in ethanol-loaded rat; the α-methylene-γ-butyrolactone moiety was found to be essential for the preventive effect on ethanol absorption (Matsuda et al., 1999). Costunolide (**1**) and dehydrocostus lactone (**142**) showed strong cholagogic effect (Wang et al., 2001).

It has been shown that artichoke leaf extract is effective against acute gastritis and its beneficial effect is due to that of cynaropicrin (**162**) (Ishida et al., 2010).

A study of the cytoprotective activity of several guaianolides was undertaken. Ludartin (**262**) was found to exhibit good protection (Giordano et al., 1990). The structural activity relationship of the antiulcerogenic activity and the mechanism of action were investigated. It has been ascertained that a sterically unhindered Michael acceptor is an essential requirement for the activity, interacting with the thiol containing compounds of the gastric mucosa (Giordano et al., 1992).

The main components of *C. solstitialis* ssp. *solstitialis* responsible for its significant anti-ulcerogenic activity were determined as solstitialin A (**181**), 13-acetyl solstitialin A (**183**) and chlorojanerin (**219**) (Yesilada et al., 2004;Gürbüz and Yesilada, 2007).

Saussurea root has been used in Oriental medicine as sedative, as well as in incense. Dehydrocostus lactone (**142**) and costunolide (**1**) were isolated from this root and found to have sedative and analgesic effects on the central nervous system. The sedative effects of these two compounds were found to be caused by anti-dopaminergic and partly anti-serotonergic effects (Okukawa et al., 2000): they also increased hexobarbital sleeping time and decreased body temperature, nociception, and spontaneous locomotor activity (Okugawa et al., 1996).

The analgesic effect of 8α-(3′-hydroxy-4′-acetoxy-2′-methylene-butanoyloxy)-4-*epi*-sonchucarpolide (**111**), isolated from *C. grisebachi*, and of 8α-O-(4′-hydroxy-2′-methylenebutanoyloxy)-11β,13-dihydrosonchucarpolide (**118**), isolated from *C. pullata*, was studied in mice. The results showed significant decreasing in pain at 30 min post treatment with a dose of 10 mg/kg (Djeddi et al., 2008c). Solstitialin A (**181**) and 13-acetyl solstitialin A (**183**) were defined as the active components responsible of the antinociceptive and antipyretic properties *C. solstitialis* and *C. depressa* (Akkol et al., 2009).

It has been demonstrated that the α-methylene-γ-butyrolactone structural unit of dehydrocostus lactone (**142**) is the moiety responsible for increasing cellular resistance to oxidant injury in HepG2 cells, presumably through Nrf2/ARE-dependent HO-1 expression (Jeong et al., 2007).

The hexane fraction of *I. helenium* showed the potential to induce detoxifying enzymes such as quinine reductase (QR) and glutathione S-transferase in a dose-dependent manner. Its potential to induce the reported activity, suggested an antioxidant response element-mediated mechanism of action in the induction of phase II detoxifying enzymes. Alantolactone (**121**) isolated from this fraction significantly induced QR activity in both Hepa1c1c7 and BPRc1 cells (Im et al., 2007) and was shown to be a more effective antioxidant than α-tocopherol or ubiquinone (Mir-Babaev and Sereda, 1987).

Alantolactone (**121**) caused a dose-dependent induction of antioxidant enzymes including QR, GST, γ-glutamylcysteine synthase, glutathione reductase, and heme oxygenase 1 in hepa1c1c7 mouse hepatoma cells. The compound increased the luciferase activity of HepG2–19 cells, transfectants carrying antioxidant response element (ARE)-luciferase gene, in a dose-dependent manner, suggesting ARE-mediated transcriptional activation of antioxidant enzymes. Alantolactone also stimulated the nuclear accumulation

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of Nrf2 that was inhibited by phosphatidylinositol 3-kinase (PI3K) inhibitors. In conclusion, alantolactone appears to induce detoxifying enzymes via activation of PI3K and JNK signaling pathways, leading to translocation of Nrf2, and subsequent interaction between Nrf2 and ARE in the encoding genes (Seo et al., 2008).

Grosheimin (**264**), isolated from the medicinal plants of *Youngia japonica*, exhibited strong antiallergic and antioxidant activities (Yae et al., 2009).

Costunolide (**1**) and reynosin (**100**), isolated from *Saussureae* Radix, showed potent inhibitory effects on the IBMX-induced melanogenesis, in dose-dependent manners, with IC_{50} values of 3 and 2.5 μg/mL, respectively (Choi et al., 2008). Costunolide (**1**) inhibited contractions of the aorta induced by KCl but exerted less effect on those induced by norepinephrine, indicating the possible Ca antagonistic action of costunolide. Dehydrocostus lactone (**142**) caused similar inhibitor effects but its specificity of KCl-induced contraction was less than costunolide (Shoji et al., 1984).

The oxygen functional groups at the 3- and 8-positions and exo-methylene moiety in α-methylene-γ-butyrolactone ring were found to be essential for the anti-hyperlipidemic activity of guaiane-type sesquiterpene. In fact cynaropicrin (**162**), aguerin B (**160**) and grosheimin (**264**) significantly suppressed serum TG elevation at 50 and 100 mg/kg during the early stage (2 h after olive oil administration), whereas dehydrocostus lactone (**142**) and 11β, 13-dihydro-deacylcynaropicrin (**190**) had a weaker activity (Shimoda et al., 2003).

In vitro protein synthesis was blocked by zaluzanin C (**147**) and the study of the effects of the drug on resolved model systems indicates that it inhibits enzymic translocation of peptidyl-tRNA specifically (Santamaria et al., 1984). The Acyl-CoA cholesterol acyltransferase (ACAT), diacylglycerol acyltransferase (DGAT) and farnesyl-protein transferase (FPTase) inhibitory effects of the roots of *Ixeris dentata* forma *albida* were investigated and one of the active compounds was identified as zaluzanin C (**147**) (Bang et al., 2004). The inhibition of ATP synthesis, proton uptake, and electron transport (basal, phosphorylating, and uncoupled) from water to methylviologen by zaluzanin C (**147**) indicates that it acts as an electron transport inhibitor. The studies concluded that the site of inhibition by zaluzanin C is located at the oxygen evolution level (Lotina-Hennsen et al., 1992).

An inhibitor of CINC-1 (cytokine-induced neutrophil chemoattractant-1) induction in LPS-stimulated rat kidney epithelioid NRK-52E cells was purified from the roots of *Sassurea lappa*, a herbal medicine used in Korean traditional prescriptions for gastric intestinal diseases by a variety of column chromatography procedures. The inhibitor was identified as reynosin (**100**). It exhibited a dose-dependent inhibition on CINC-1 induction in LPS-stimulated NRK-52E cells, where 50% of inhibitory effect was shown at the concentration of about 1 μM (Jung et al., 1998). Furthermore, reynosin (**100**) displayed considerable inhibition against platelet aggregation induced by AA, ADP, or PAF (Wang et al., 2000).

A study describing the antispasmodic activity of some fractions and cynaropicrin (**162**), a sesquiterpene lactone from *Cynara scolymus*, cultivated in Brazil, against guinea-pig ileum contracted by acetylcholine was carried out. The dichloromethane fraction showed the most promising biological effects, with an IC_{50} of 0.93 (0.49–1.77) μg/mL. Its main active component, the sesquiterpene lactone cynaropicrin, exhibited potent activity, with IC_{50} of 0.065 (0.049–0.086) μg/mL, being about 14-fold more active than dichloromethane fraction and having similar potency to that of papaverine, a well-known antispasmodic agent (Emendoerfer et al., 2005).

A characteristic smooth muscle inhibitory profile is demonstrated by the α-methylenebutyrolactone cynaropicrin (**162**), but not by a compound lacking this functional group (solstitialin 13-acetate, **183**) (Hay et al., 1994).

Repin (**209**), on intraperitoneal injection, produces a dose-dependent and highly significant hypothermia in naive rats (Akbar et al., 1995).

Several SLs isolated from different Asteraceae species from north-western Argentina were investigated for their inhibitory action on the estrogen biosynthesis. Ludartin (**262**) was found to inhibit the aromatase enzyme activity in human placental microsomes and it was competitive inhibitor with an apparent K_i of 23 μM (Blanco et al., 1997).

Compounds **220** and **221** displayed promising inhibitory potential against enzyme urease in a concentration-dependent fashion (Khan et al., 2004a).

Compounds **190**, **198**, **217**, **219**, **236** and **240** showed inhibitory potential against butyrylcholinoesterase, the best one being chlorojanerin (**219**) with IC_{50} values of 15 μg/mL (Khan et al., 2005a).

5. Conclusions

This subtribe Centaureinae appears taxonomically very complex. It is worth to keep in mind that, in the numerous papers reviewed, the correct botanic identification plays a pivotal role. Moreover, the correct assessment of the taxa in their sections is a further problem in order to draw any chemotaxonomic classification.

The elaboration of the collected data allows to define groups of taxa with a consistent chemical composition reflecting a botanic relationship, i.e. *Psephellus* and *Acrolophus* sections. Other similarities or differences can be found, i.e. *Cheirolophus intybaceus* showing a complete different profile with respect to the other species of genus *Cheirolophus* or *C. calcitrapa*, *C. incana*, *C. salonitana* and *C. solstitialis* that have a very different composition depending on the collection place. Clearly, all the information arising from the statistical approach of the qualitative content of sesquiterpenes in the taxa, both single product and structural similarity products methods, should be evaluated for any botanical consistency.

As it is possible to observe, the main biological properties ascribed to sesquiterpenes are the antibacterial, anti-inflammatory and antitumor activities. In this context, a lot of publications regarding custonolide (**1**) and cynaropicrin (**162**), have shown a high potential towards these activities.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.phytochem.2013.07.002.

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