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Guaianolides and lignans from the aerial parts of *Centaurea ptosimopappa*

Sezgin Çelik [a], Sergio Rosselli [b], Antonella M. Maggio [b], Rosa Angela Raccuglia [b], Ismet Uysal [a], Wanda Kisiel [c], Klaudia Michalska [c], Maurizio Bruno [b,*]

[a] *Çanakkale Onsekiz Mart University, Science & Literature Faculty, Biology Department, 17100 Çanakkale, Turkey*
[b] *Dipartimento Chimica Organica, Università di Palermo, Viale delle Scienze, Parco d'Orleans II, 90128 Palermo, Italy*
[c] *Department of Phytochemistry, Institute of Pharmacology, Polish Academy of Sciences, PL-31-343 Krakow, Poland*

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1. Subject and source

The genus *Centaurea* L. (Asteraceae, tribe Cardueae, subtribe Centaureinae) comprises ca. 600 species distributed in Asia, Europa, North Africa and America (Hickey and King, 1981; Heywood, 1979). Turkish flora numbers 187 species, 114 of which being endemic (Davis, 1975; Davis et al., 1988; Wagenitz et al., 1988; Guner et al., 2000; Duran and Duman, 2000; Turkoglu et al., 2003).

Centaurea ptosimopappa Hayek is an endemic species distributed in the Mediterranean and South-Eastern Anatolian regions of Turkey; widespread and locally frequent in the Amanos and Casus mountains (Davis, 1975; Reeves and Adigüzel, 2004). Aerial parts of *C. ptosimopappa* were collected in Hatay, the Amanos Mountain above Dörtyol (Turkey), 850–950 m above sea level in June 2003 (36° 51′ N, 36° 13′ E). Voucher specimens (Celik 2148–2153) are deposited at the Department of Biology, Çanakkale Onsekiz Mart University.

2. Previous work

Previous chemical studies seem to indicate that patterns of sesquiterpene lactone are systematically important within the genus *Centaurea*. Other secondary metabolites present in plants of this taxon include triterpenes, steroids, hydrocarbons, polyacetylenes, flavonoids, anthocyanins, lignans and alkaloids (Al-Easa and Rizk, 1992). As part of our ongoing chemical investigation of *Centaurea* species of the Mediterranean area (Bruno et al., 1998, 2001, 2002; Senatore et al., 2003), we have examined the aerial parts of the hitherto unstudied *C. ptosimopappa*.

* Corresponding author. Tel.: +39 091 596 905; fax: +39 091 596 825.
E-mail address: bruno@dicpm.unipa.it (M. Bruno).

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3. Present study

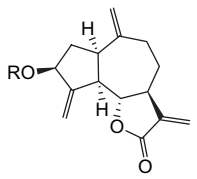
Dry aerial parts (2.8 kg), finely powdered, were extracted three times with acetone (3 × 10 L) at room temperature for one week. After filtration, the solvent was removed under reduced pressure to yield a residue (90 g) which was chromatographed on a silica gel column (Merck Art. 9025, 0.063–0.200 mm, 60 × 700 mm) eluted with petroleum ether with increasing amounts of EtOAc, 500 mL fractions being collected as follows: 1–10 (petroleum ether), 11–20 (petroleum ether–EtOAc, 4:1), 21–30 (petroleum ether–EtOAc, 3:2), 31–40 (petroleum ether–EtOAc, 2:3), 41–50 (petroleum ether–EtOAc, 1:4), 51–60 (EtOAc), 61–70 (EtOAc–MeOH, 9:1).

Fractions 31–40 were rechromatographed on a silica gel column (Merck Art. 9025, 0.063–0.200 mm, 30 × 400 mm), eluting with CH_2Cl_2 with increasing amounts of MeOH (49:1 → 9:1) to give a subfraction that was allowed to crystallize (petroleum ether–EtOAc, 1:1) giving 600 mg of zaluzanin D (**1**).

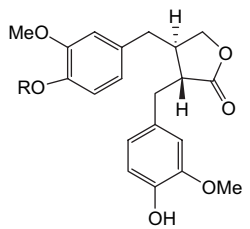
Fractions 41–50 were rechromatographed on a silica gel column (Merck Art. 9025, 0.063–0.200 mm, 30 × 400 mm), eluting with petroleum ether with increasing amounts of EtOAc (3:2 → 1:4) to give two subfractions. The first one was further purified to give 400 mg of zaluzanin C (**2**). The second one furnished 4 mg of arctigenin (**3**) after purification by prep. TLC (Merck Art. 5553, CH_3COCH_3–$CHCl_3$, 1:9, Rf 0.72).

Fractions 51–60 were rechromatographed on a silica gel column (Merck Art. 9025, 0.063–0.200 mm, 30 × 400 mm), using the same solvent system as described above to give two subfractions. The first one was purified by prep. TLC, as mentioned above, to give 1 mg of matairesinol (**4**, Rf 0.45). The second one was processed by semi-prep. RP HPLC on a Delta-Pack C-18 column (particle size 15 mm 25 × 100 mm) coupled to a dual wavelength UV/vis detector operating at 210 and 260 nm, using an H_2O–MeOH (11:9) mixture at flow rate of 3.0 ml/min, giving janerin (**5**, 1 mg, Rt 48.9), chlorojanerin (**6**, 1 mg, Rt 43.9), cynaropicrin (**7**, 5 mg, Rt 96.9) and a mixture containing **11** (Rt 31.0). The mixture could be further separated by semiprep. RP HPLC (H_2O–MeOH, 7:3) to yield

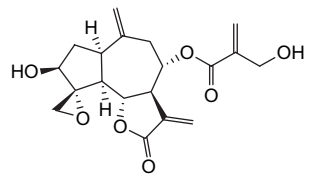
Structures of compounds **1–12**



1 R= Ac
2 R= H



3 R= H
4 R= Me



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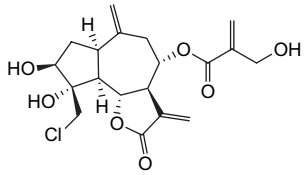

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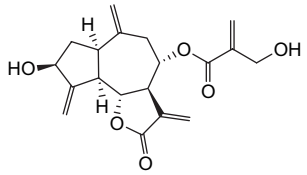

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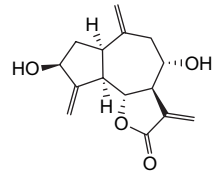

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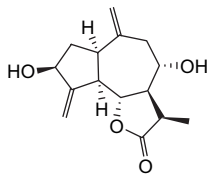

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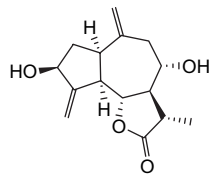

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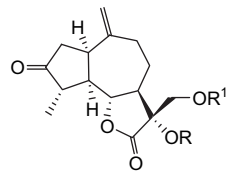

11 R= R^1= H
12 R= R^1= Ac

deacylcynaropicrin (**8**, 2 mg), 11α,13-dihydro-deacylcynaropicrin (**9**, 1 mg), 11β,13-dihydro-deacylcynaropicrin (**10**, 1 mg) and 4β,15-dihydro-3-dehydro-solstitialin A (**11**, 5 mg), the last one contamined with **8**.

The structures of the isolated compounds were readily identified by comparing their physical and spectral data (melting points, NMR-spectra, mass spectra) with those reported for zaluzanin D (**1**), zaluzanin C (**2**) (Ando et al., 1989), arctigenin (**3**), matairesinol (**4**) (Rahman et al., 1990), janerin (**5**), chlorojanerin (**6**) (Gonzalez et al., 1977), cynaropicrin (**7**), deacylcynaropicrin (**8**) (Rustaiyan et al., 1981), 11α,13-dihydro-deacylcynaropicrin (**9**) (Bohlmann and Chen, 1982), 11β,13-dihydro-deacylcynaropicrin (**10**) (Singhal et al., 1982). The identity of 4β,15-dihydro-3-dehydro-solstitialin A (**11**) was confirmed after acetylation which yielded 4β,15-dihydro-3-dehydro-solstitialin A diacetate (Rustaiyan et al., 1981).

4. Chemotaxonomic and biological significance

Our chemical studies of the aerial parts of *C. ptosimopappa* have led to the isolation of nine guaiane-type sesquiterpene lactones (**1**, **2**, **5**–**11**) and two butyrolactone lignans (**3**, **4**). The guaianolides zaluzanin D (**1**) and zaluzanin C (**2**) are major constituents of the plant material accompanied by minor quantities of the remaining compounds. This is the first report on the presence of zaluzanin D in *Centaurea* species. Zaluzanin C has been found in *Cheirolophus sempervirens* (L.) Pomel (Marco et al., 1994), a species formerly belonging to the section Cheirolophus (Cass.) of the genus *Centaurea* (Hellwig, 2004). Compounds **1** and **2**, first reported from *Zaluzania* species (Romo de Vivar et al., 1967; Dominguez et al., 1975), are also present in other plant genera, e.g. *Zinnia* (Romo et al., 1971), *Podachaenium* (Bohlmann and Le Van, 1977), *Conocephalum* (Asakawa and Takemoto, 1979), *Gochnatia* (Bohlmann et al., 1984), *Cynara* (Omar et al., 1984) and *Scalesia* (Spring et al., 1999).

C. ptosimopappa belongs to the section Ptosimopappus O. Hoffm., endemic to Turkey. The only other *Centaurea* species of this section is *Centaurea ptosimopappoides* Wagenitz, which, although quite similar, shows some morphological differences (Table 1). The minor constituents of *C. ptosimopappa* include cynaropicrin (**7**) and its deacyl derivatives, also found in *C. ptosimopappoides* (Oksuz and Serin, 1997). It follows, therefore, that both species produce cynaropicrin-like guaianolides and are chemotaxonomically related.

The section Ptosimopappus can be morphologically distinguished from the closely related section Microlophus (Cass.) DC by their differing of achenes, pappus-hairs and involucres. Three members of the later section have been examined. The guaianolides janerin (**5**) and cynaropicrin (**7**) have been reported from *Centaurea babylonica* L. (Bruno et al., 2005) and *Centaurea thracica* (Janka) Hayek (Nowak et al., 1986), respectively, and cynaropicrin (**7**), deacylcynaropicrin (**8**) and 4β,15-dihydro-3-dehydro-solstitialin A (**11**) from *Centaurea behen* L. (Rustaiyan et al., 1981).

The major guaianolides zaluzanin D (**1**) and zaluzanin C (**2**) isolated from *C. ptosimopappa* have been shown to exhibit a variety of biological activities. Zaluzanin D (**1**) displays antifungal activity against plant pathogenic fungi (Krishna Kumari et al., 2003) as well as zaluzanin C (**2**) (Wedge et al., 2000). Allelopathic activity (Macias et al., 1992) has been reported for zaluzanin C (**2**).

Finally, cynaropicrin (**7**) has been proved to be a potent feeding deterrent against several species of Lepidoptera (Bhattacharyya et al., 1995).

Table 1
Morphological characteristics of the section *Ptosimopappus*

Centaurea ptosimopappa Hayek	*Centaurea ptosimopappoides* Wagenitz
Shrub, 1–1.80 m	Subshrub, 30–50 cm
Leaves firm, almost leathery, glabrous on both surfaces, wooly at margin	Leaves firm, with slightly prominent lateral nerves, glabrous on both surface, slightly tomentose at magrin, entire
Leaves lanceolate–spathulate to obovate	Leaves lanceolate, basal and lower petiolate
Involucrum 18–25 × 8–16 mm	Involucrum 18–22 × 9–11 mm
Achen 4–5 mm, pappus deciduous and 4–6 mm	Achen 5–7 mm, pappus deciduous and 5–8 mm
Involucrum 18–25 × 8–16 mm	Involucrum 18–22 × 9–11 mm
Flowers yellow	Flowers yellow

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