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GUAIANOLIDES FROM *CENTAUREA SCOPARIA*

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Key Word Index—*Centaurea scoparia*; Compositae; aerial parts; guaianolides.

Abstract—3β,8α-*O*-Di(4-hydroxytigloyl)-1αH,5αH,6βH,7αH-guai-4(15),10(14),11(13)-triene-6,12-olide; a new guaianolide, has been isolated from the aerial parts of *Centaurea scoparia* together with nine known ones. © 1997 Elsevier Science Ltd. All rights reserved

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INTRODUCTION

Plants belonging to the genus *Centaurea* are used in folk medicine for many purposes e.g. as a stimulant, tonic [1, 2] antidiabetic [3–5], diuretic [3] and antirheumatic [6, 7]. Moreover, some sesquiterpene lactones, chlorohyssopifolins A–D, cynaropicrin and deacylcynaropicrin, from this genus exhibit cytotoxic and cytostatic activity [8–10]. *Centaurea scoparia* Sieb. (Syn. = *Phaeopappus scoparia* Sieb.) is an annual or biannual herb growing in Sinai, Egypt [11]. A preliminary phytochemical screening of the aerial parts of this plant indicated the probable presence of sesquiterpene lactones and flavonoids [5]. Recently, several guaianolides, flavonoids and lignans have been isolated from the aerial parts of the same plant [12–15]. We report here on the isolation and characterization of a new guaianolide (**1**) from *C. scoparia* together with nine known compounds.

RESULTS AND DISCUSSION

The aerial parts of *C. scoparia* collected in 1993 were extracted with 90% ethanol, and those obtained in 1995 were extracted with water and then methanol. Repeated column chromatography of the chloroform soluble fraction of the 90% ethanol extract afforded four compounds (**2**, **6**–**8**), while investigation of the aqueous and MeOH extracts led to the isolation of seven compounds (**1**, **3**–**5**, **8**–**10**). The spectral data of nine compounds (**2**–**10**) were in accordance with those reported [10, 12, 16–25]. Cebellin F (**2**) is known from *C. bella* and *C. adjarica* (syn. *C. koenigi*) [10, 16], 8α,4′-(hydroxytiglinate)-8-desacyloxysubluteolide (**3**) from *Berkheya carlinopsis* Welw. ex Hoffm. ssp. *magalismontana* (H. Boll) Roessl. (the C-4 stereochemistry is given incorrectly) [17], 8-desacylrepin (**4**) from *Jurinea carduiformis* Boiss. (the C-4 stereochemistry is given incorrectly) [18], (1*S*,3*S*,5*R*,6*R*,7*R*,8*S*)-8-angelyloxy-3-hydroxyguai-3(15),10(14),11(13)-trien-6,12-olide (**5**) from *Vernonia nitidula* Less. [19], 8-desacetylcentaurepensin-8-*O*-(4-hydroxytiglinate) (**6**) from the plant under investigation [12], chlorohyssopifolin A (**7**) (i.e. centaurepesin) is a guaianolide frequently found in *Centaurea* species [20–22], 8α-hydroxy-11α,13-dihydrozaluzanin C (**8**) is a zaluzanin derivative previously isolated from *Ainsliaea fragrans* Champ. [23, 24], desacylcynaropicrin (**9**) is known from *C. behen* L. [25], and chlorohyssopifolin B (**10**) from *C. hyssopifolia* Vahl [20].

The structure of compound **1** followed from the ^{1}H and ^{13}C NMR spectral data (Table 1), and the EI-mass-spectrometry (*m*/*z* 458 $[M]^{+}$), and their comparison with those of **2**. The ^{1}H, ^{1}H COSY spectrum of **1** showed another spin system at δ 6.85, 4.43 and 1.86 which suggested the presence of an additional 4-hydroxytigloyl group. The downfield shift of C-3 (δ 5.62, δ_C 75.00) suggested possible acylation of its hydroxyl-group with 4-hydroxytiglic acid. This was further confirmed by long range correlations observed in the HMBC spectrum of **1**.

The relative stereochemistry of **1** was investigated by comparing the coupling constants of each proton (see Experimental) with those reported for related guaianolides [26] and by a NOESY experiment. The coupling constants involving H-6 (10.5, 9.2) with H-5 and H-7 suggested *trans*-diaxial dispositions of the protons at C-5 (α), C-6 (β) and C-7 (α), a feature

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Table 1. ^{13}C NMR spectral data (125 MHz) of compounds **1–5**

C	**1**	**2**	**3**	**4**	**5**
1	45.5 *d*	45.1 *d*	45.6 *d*	45.2 *d*	45.3 *d*
2	36.3 *t*	38.9 *t*	37.5 *t*	37.3 *t*	39.1 *t*
3	75.0 *d*	73.6 *d*	76.1 *d*	75.0 *d*	73.7 *d*
4	152.2 *s*	152.1 *s*	68.2 *s*	68.4 *s*	152.3 *s*
5	51.4 *d*	51.2 *d*	52.9 *d*	52.4 *d*	51.3 *d*
6	47.7 *d*	78.6 *d*	76.9 *d*	77.4 *d*	47.8 *d*
7	47.7 *d*	47.5 *d*	48.0 *d*	51.1 *d*	47.8 *d*
8	74.1 *d*	74.1 *d*	74.0 *d*	71.5 *d*	73.8 *d*
9	37.5 *t*	36.9 *t*	36.5 *t*	40.8 *t*	37.2 *t*
10	141.6 *s*	141.7 *s*	141.3 *s*	142.2 *s*	141.9 *s*
11	137.2 *s*	137.3 *s*	137.0 *s*	137.8 *s*	137.4 *s*
12	169.1 *s*	169.2 *s*	169.1 *s*	170.3 *s*	169.2 *s*
13	122.9 *t*	122.7 *t*	122.7 *t*	123.1 *t*	122.6 *t*
14	118.4 *t*	118.1 *t*	118.6 *t*	117.3 *t*	118.0 *t*
15	116.0 *t*	113.4 *t*	48.5 *t*	48.4 *t*	113.5 *t*
16	167.2 *s*	166.2 *s*	166.5 *s*		166.9 *s*
16′	166.4 *s*				
17	128.4 *s*	127.7 *s*	127.9 *s*		128.3 *s*
17′	128.0 *s*				
18	141.3 *d*	141.9 *d*	141.7 *d*		136.6 *d*
18′	140.6 *d*				
19	59.9 *t*	59.7 *t*	59.8 *t*		14.6 *q*
19′	59.8 *t*				
20	12.8 *q*	12.7 *q*	12.7 *q*		12.0 *q*
20′	12.8 *q*				

common to guaianolide lactones [27]. The NOESY spectrum showed significant spatial correlations: H-1 and H-5; H-3 and H-2α; H-5 and H-1, H-7; H-6 and H-8, H-9β; H-19 and Me-20, H-18; H-19′ and Me-20′, H-18′. These correlations confirmed the relative stereochemistry as shown in formula **1**.

From the foregoing findings, the structure of compound **1** was determined to be 3β,8α-*O*-di(4-hydroxytigloyl)-1αH,5αH,6βH,7αH-guai-4(15),10(14),11(13)-triene-6,12-olide.

EXPERIMENTAL

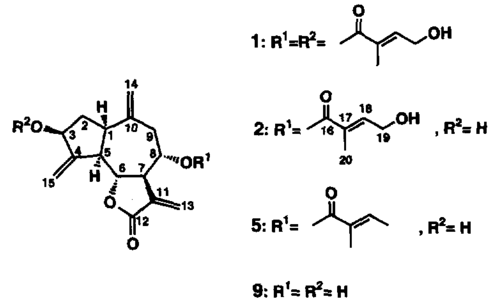
General. Mps: uncorr.; IR: KBr; ^1H and ^{13}C NMR: $CDCl_3$ unless otherwise stated; MS: 70 eV; TLC: Merck Silica gel 60 F_{254} and RP-18 F_{254} S; CC: Merck Silica gel 60, Silica gel 60 silanized (RP-2) and LiChroprep PR-8 (PR-8).

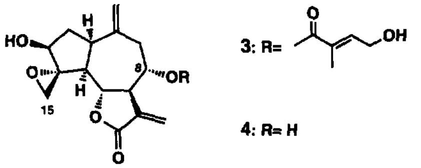
Plant material. The aerial parts of *Centaurea scoparia* Sieb. were collected during April–May (1993 and 1995) from flowering plants growing wild in Saint Katherine, Sinai, Egypt. The identity was confirmed by Prof. N. El-Hadidy, Professor of Plant Taxonomy, Faculty of Science, Cairo University. Voucher specimens are on deposit in the herbarium of the Department of Pharmacognosy, Faculty of Pharmacy, Cairo University, Cairo, Egypt.

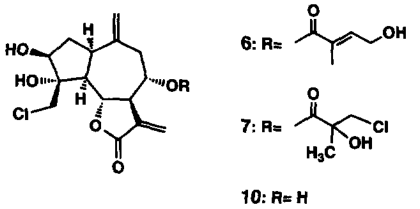
Extraction and isolation. The air-dried aerial parts (2 kg) of *C. scoparia* (collected in 1993) were powdered and extracted with 90% EtOH (4 × 10 l) at room temp. to give a crude extract (285 g). 90 g extract were suspended in hot H_2O (500 ml) and extracted successively with hexane (4 × 500 ml, 12.3 g), $CHCl_3$ (4 × 500 ml, 32.0 g), EtOAc (4 × 500 ml, 12.9 g) and BuOH (4 × 500 ml, 21.0 g).

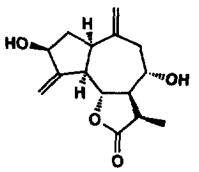
20 g of the $CHCl_3$-soluble fraction were applied to CC (silica gel 60, 600 g) and eluted with hexane followed by, $CHCl_3$ with increasing amounts of MeOH (2–30% MeOH). Nine frs (500 ml each) were collected. Fr. 5 (5 g) eluted with 7% MeOH in $CHCl_3$ was further chromatographed over silica gel 60 (150 g) and eluted with benzene–Me_2CO (85 : 15 to 75 : 25). Frs 11–16 (115 mg) were eluted with 16% Me_2CO in benzene, Frs 17–19 (230 mg) with 20% Me_2CO in benzene, Frs 20–24 (347 mg) with 20% Me_2CO in benzene, and Frs 25–28 (149 mg) with 25% Me_2CO in benzene. CC (RP-2) of these individual fractions followed by MPLC (RP-8) [elution with MeOH–H_2O (7 : 3)] afforded **2** (75 mg), **6** (35 mg), **7** (9 mg) and **8** (11 mg), respectively.

The aerial parts (1 kg) of *C. scoparia* (collected in 1995) were powdered and extracted, successively, with dist. water (3 × 3 l) and MeOH (3 × 3 l) at room temp. The water extract was concentrated to 300 ml and partitioned between $CHCl_3$ and EtOAc. The $CHCl_3$-soluble fraction was evaporated under red. pres. to give a residue. The residue (4 g) was applied to CC (silica gel, 150 g) and elution started with $CHCl_3$









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followed by increasing amounts of MeOH (2–10% MeOH). CC of fr. 3 (400 mg, eluted with 5% MeOH in $CHCl_3$) over RP-2 (elution with aq. MeOH) followed by MPLC (RP-8, elution with MeOH–H_2O 1 : 1) afforded **3** (35 mg). Similarly, fr. 6 (410 mg, eluted with 7.5% MeOH in $CHCl_3$) afforded **9** (40 mg), whereas fr. 8 (680 mg, eluted with 9% MeOH in $CHCl_3$) afforded **4** (35 mg) and **8** (6 mg). Similarly, the EtOAc-soluble fraction (3.6 g) was applied to CC (RP-2) followed by MPLC (silica gel, elution with benzene–Me_2CO, 8 : 2), afforded **10** (3 mg) and an additional amount of **4** (10 mg). The MeOH extract (35 g) was suspended in water and shaken with CH_2Cl_2. CC (silica gel) of the CH_2Cl_2-soluble fraction (17 g) afforded **1** (5 mg) and **5** (6 mg).

3β,8α-O-*Di*(4-*hydroxytigloyl*)-1α*H*,5α*H*,6β*H*,7α*H*-*guai*-4(15),10(14),11(13)-*triene*-6,12-*olide* (**1**). Oil, EI-MS *m*/*z*: 458 $[M]^+$ (99); ^1H NMR (500 MHz): δ 1.83 (1H, *ddd*, $J = 13.7, 10.7, 7.3$ Hz, H-2β), 1.86 (3H, *d*, $J = 1.3$ Hz, H-20), 1.90 (3H, *d*, $J = 1.3$ Hz, H-20′), 2.38 (1H, *dd*, $J = 14.5, 4.8$ Hz, H-9α), 2.41 (1H, *dt*, $J = 13.7, 7.7$ Hz, H-2α), 2.69 (1H, *dd*, $J = 14.5, 4.8$ Hz, H-9β), 2.89 (1H, *dd*, $J = 10.5, 7.7$ Hz, H-5), 3.05 (1H, *dt*, $J = 10.7, 7.7$ Hz, H-1), 3.22 (1H, *tt*, $J = 9.2, 3.2$ Hz, H-7), 4.19 (1H, *dd*, $J = 10.5, 9.2$ Hz, H-6), 4.38 (2H, *d*, $J = 6.0$ Hz, H-19), 4.43 (2H, *d*, $J = 6.0$ Hz, H-19′), 4.98 (1H, *br s*, H-14), 5.12 (1H, *dt*, $J = 9.2, 4.8$ Hz, H-8), 5.15 (1H, *br s*, H-14), 5.37 (1H, *br s*, H-15), 5.55 (1H, *br s*, H-15), 5.62 (1H, *d*, $J = 3.2$ Hz, H-13), 5.62 (1H, *m*, H-3), 6.24 (1H, *d*, $J = 3.2$ Hz, H-13), 6.85 (1H, *tq*, $J = 6.0, 1.3$ Hz, H-18), 6.92 (1H, *tq*, $J = 5.8, 1.3$ Hz, H-18); ^{13}C NMR: Table 1.

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