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Sesquiterpene lactone glucosides from *Sonchus asper*

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Abstract

From the methanolic extract of the roots of *Sonchus asper*, two new sesquiterpene glucosides, together with two known sesquiterpene glucosides and a known aglycone were isolated. Structures were identified as 11β,13-dihydrourospermal A, 15-*O*-β-D-glucopyranosyl-11β,13-dihydrourospermal A, 15-*O*-β-D-glucopyranosylurospermal A, 15-*O*-[6′-(*p*-hydroxyphenylacetyl)]-β-D-glucopyranosylurospermal A and 14-*O*-methylacetal-15-*O*-[6′-(*p*-hydroxyphenylacetyl)]-β-D-glucopyranosylurospermal A, by spectroscopic means. © 2000 Elsevier Science Ltd. All rights reserved.

Keywords: Sonchus asper; Asteraceae; Melampolides; Sesquiterpene glucosides; Urospermal A derivatives

1. Introduction

Sonchus asper (L.) Hill, (Asteraceae) is a cosmopolitan annual herb, less abundant in the tropics than in cool and temperate regions, native to the old and introduced into the new world (Taeckholm, 1974; Boulos & El-Hadidi, 1989). *Sonchus* species are known to contain sesquiterpene lactones mainly of the eudesmanolide type (Shimizu, Miyase, Ueno & Usmanghani, 1989; Mahmoud, El-Marsy, Amer, Ziesche & Bohlmann, 1983; Mahmoud, El-Marsy, Amer, Ziesche & Grenz, 1984; Miyase & Fukushima, 1987; Bermejo, Breton, Gonzales & Villar del Fresno, 1968; Bermejo, Breton, Fajaro & Gonzalez, 1968; Barrera, Breton, Fajaro & Gonzalez, 1967), in addition to the guaianolide jacquinelin (Bermejo, Breton & Gonzalez, 1966). Flavonoids were also reported in *Sonchus* species (Giner, Ubeda, Just, Serrano, Manez & Rios, 1993; Manez et al., 1994; Guirong, Jian, Xinxin, Suxian, Ligun & Xian, 1995; Guirong, Xinxin & Jian, 1996). In the course of a search for sesquiterpene glycosides in the Asteraceae, we have examined the roots of *Sonchus asper*. Aerial parts of *S. asper* have furnished glucosides of eudesmanolides (Shimizu et al., 1989).

2. Results and discussion

The methanolic extract of the roots of *Sonchus asper* afforded 5 sesquiterpene lactones, one aglycone (**1**) and four glycosides (**2–5**). All isolated compounds are derivatives of urospermal A (**6**), a melampolide type sesquiterpene lactone (Chart 1). This is the first report for the isolation of urospermal A derivatives from *Sonchus* species.

The identification of these sesquiterpene glycosides was accomplished by their spectral data (500 MHz ^{1}H- and ^{13}C-NMR, COSY, HMQC and NOESY and FAB mass spectral analysis) and confirmed by comparison

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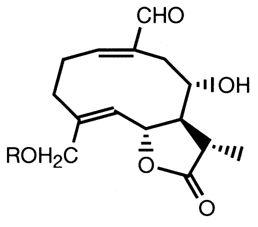
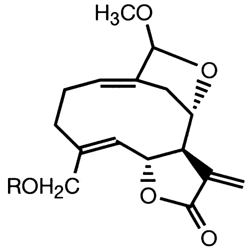


2 R = Glc



5 R = 6'-(p-hydroxy-phenylacetyl)Glc

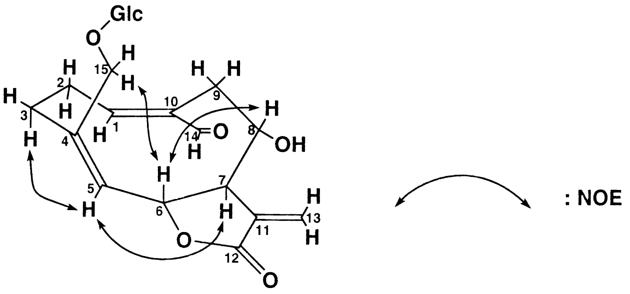


Fig. 1. Significant correlation in the NOESY spectrum of 3.

with published data (Rychlewska et al., 1986; Marco, Sanz-Cervera, Yuste & Oriola, 1994; Bentley, Buchanan, Halsall & Thaller, 1970; Bohlmann, Singh & Jakupovic, 1982; Amer, Salama, Bohlmann & Ziesche, 1984; Abdel Salam, Mahmoud, Ziesche & Bohlmann, 1982; Zdero & Bohlmann, 1990; Nishimura, Miyase, Ueno, Noro, Kuroyanagi & Fukushima, 1986; Macias & Fischer, 1992).

Compound **1**, $C_{15}H_{20}O_5$, EI-MS, *m*/*z* 281 $[M + 1]^+$, was identified as 11β,13-dihydrourospermal A (**1**), by comparing its spectral data, with those reported, isolated from the genera *Urospermum* and *Dicoma* (Rychlewska et al., 1986; Marco et al., 1994; Bentley et al., 1970; Bohlmann et al., 1982).

In the ^{1}H-NMR spectrum of **2** ($C_{21}H_{30}O_{10}$, FAB-MS, *m*/*z* 443 $[M + 1]^+$), the exocyclic methylene proton signals of H-13 were replaced by a methyl *doublet*

Table 1
^{1}H-NMR spectral data of compounds **1**–**5** (500 MHz, in CD_3OD)

Atom	**1**	**2**	**3**	**4**	**5**
1	6.81 (*ddd*, 10.0, 7.5, 1.7)	6.86 (*t*, 8.4)	6.88 (*t*, 8.6)	6.86 (*t*, 8.5)	5.56 (*br t*, 8.8)
2	2.51 (*m*)	2.53 (2H, *m*)	2.58 (2H, *m*)	2.53 (2H, *m*)	1.99 (*m*)
	2.57 (*m*)				2.30 (*m*)
3	2.00 (*td*, 12.6, 2.5)	2.05 (*m*)	2.06 (*m*)	2.02 (*br t*, 12.0)	1.97 (*m*)
	2.74 (*ddd*, 12.6, 5.6, 2.5)	2.70 (*m*)	2.72 (*m*)	2.59 (*m*)	2.48 (*m*)
5	5.02 (*d*, 10.5)	5.09 (*d*, 10.5)	5.17 (*d*, 10.5)	5.14 (*d*, 10.5)	5.11 (*d*, 10.0)
6	4.74 (*t*, 10.5)	4.88 (*t*, 10.5)	4.83 (*t*, 10.5)	4.81 (*t*, 10.5)	4.83 (*t*, 10.0)
7	1.58 (*q*, 10.5)	1.62 (*q*, 10.5)	2.50 (*t*, 10.5)	2.51 (*m*)	3.20 (*m*)
8	3.82 (*tdd*, 10.5, 5.6, 1.5)	3.92 (*m*)	4.07 (*m*)	4.05 (*br dd*, 10.5, 4.9)	4.39 (*br t*, 6.3)
9	2.42 (*br d*, 16.0)	2.34 (*br d*, 16.0)	2.39 (*d*, 16.5)	2.35 (*d*, 16.2)	2.33 (2H, *m*)
	2.69 (*dd*, 16.0, 5.6)	2.92 (*dd*, 16.0, 4.7)	2.91 (*dd*, 16.5, 5.0)	2.95 (*dd*, 16.2, 4.9)	
11	2.62 (*dq*, 10.5, 7.1)	2.65 (*dq*, 10.5, 6.8)			
13	1.40 (*d*, 7.1)	1.38 (*d*, 6.8)	6.28 (*br s*)	6.27 (*br s*)	5.87 (*d*, 3.2)
			6.47 (*br s*)	6.47 (*br s*)	6.21 (*d*, 3.2)
14	9.46 (*br s*)	9.46 (*s*)	9.46 (*s*)	9.44 (*s*)	5.29 (*s*)
15	4.32 (*dd*, 12.8, 2.6)	4.26 (*d*, 11.5)	4.26 (*d*, 11.3)	4.25 (2H, *s*)	4.18 (*d*, 12.6)
	4.39 (*br d*, 12.8)	4.55 (*d*, 11.5)	4.55 (*d*, 113)		4.49 (*br d*, 12.6)
OMe					3.47 (3H, *s*)
Glucose moiety					
1′		4.37 (*d*, 7.9)	4.35 (*d*, 7.9)	4.28 (*d*, 8.5)	4.27 (*d*, 7.9)
2′		3.28 (*t*, 7.9)	3.27 (*t*, 7.9)	3.23 (*t*, 8.5)	3.24 (*t*, 7.9)
3′		3.41 (*m*)	3.40 (*m*)	3.39 (*m*)	3.38 (*m*)
4′		3.40 (*m*)	3.40 (*m*)	3.29 (*t*, 8.5)	3.28 (*t*, 7.9)
5′		3.33 (*m*)	3.31 (*m*)	3.46 (*m*)	3.43 (*m*)
6′		3.77 (*dd*, 12.0, 5.1)	3.76 (*dd*, 12.0, 4.7)	4.28 (*m*)	4.27 (*m*)
		3.89 (*dd*, 12.0, 2.4)	3.88 (*dd*, 12.0, 2.4)	4.46 (*br d*, 12.0)	4.45 (*br d*, 12.2)
p-Hydroxyphenylacetyl moiety					
2″, 6″				6.75 (2H, *d*, 8.3)	6.76 (2H, *d*, 8.3)
3″, 5″				7.11 (2H, *d*, 8.3)	7.10 (2H, *d*, 8.3)
CH_2				3.57 (2H, *s*)	3.56 (2H, *s*)

at δ 1.38 ppm and a *quartet* at δ 1.62 ppm ($J_{7,6} = J_{7,8} = J_{7,11} = 10.5$ Hz) indicating that H-7 was α, while H-6, H-8 and H-11 were *β*. The other signals were similar to those of **1**. In addition, the anomeric proton as a *doublet* at δ 4.37 ppm ($J = 7.9$ Hz) and sugar protons at δ 3.28–3.89 ppm, indicated the presence of a β-glucoside. The ^{13}C-NMR spectral data of **2** showed 21 signals, including six signals due to the glucopyranoside moiety, indicated that **2** was the β-glucoside of **1** at C-15, this was confirmed by ^{1}H–^{1}H COSY and HMQC experiments. Hence, **2** was 15-*O*-β-D-glucopyranosyl-11β,13-dihydrourospermal A.

The ^{1}H-NMR spectrum of **3**, $C_{21}H_{28}O_{10}$, FAB-MS, *m*/*z* 441 $[M + 1]^{+}$, was very similar to that of **2**, but showed the presence of the exocyclic α-methylene-γ-lactone proton signals as *broad singlet* at δ 6.28 and 6.47 ppm (H-13), and a *triplet* at δ 2.50 ppm ($J = 10.5$ Hz, H-7). The stereochemistry of **3** was substantiated by NOE (Fig. 1), which showed effects between H-5 and H-7 as well as H-3 and between H-6 and H-8 as well as H-15. From the ^{13}C-NMR spectral data, **3** was 15-*O*-β-D-glucopyranosyl urospermal A, previously isolated from the roots of *Urospermum picroides* L. (Amer et al., 1984). His ^{13}C-NMR spectral data has not been reported previously.

The ^{1}H- and ^{13}C-NMR spectra of **4**, $C_{29}H_{34}O_{12}$, FAB-MS, *m*/*z* 575 $[M + 1]^{+}$, were very similar to those of **3**, but showed the presence of an additional *p*-hydroxyphenylacetate residue (^{1}H-NMR signals at δ 7.11 *d* of H-3″, H-5″, 6.75 *d* of H-2″, H-6″ and 3.57 *s*, 2H of Ph-CH$_2$), on H-6′, which was shifted down-field compared with **4**. Hence, it was identical with 15-*O*-[6′-(*p*-hydroxyphenyl-acetyl)]-β-D-gluco-pyranosyl urospermal A, previously isolated from the aerial parts of *Urospermum picroides* L. (Abdel Salam et al., 1982). The ^{13}C-NMR spectral data has not been reported previously.

The ^{1}H- and ^{13}C-NMR spectra of **5**, $C_{30}H_{36}O_{12}$,

Table 2
^{13}C-NMR spectral data of compounds **1**–**5** (125 MHz, in CD$_3$OD)

Atom	1	2	3	4	5
1	159.2 *d*	159.8 *d*	160.7 *d*	160.9 *d*	122.9 *d*
2	27.8 *t*	27.5 *t*	27.7 *t*	27.7 *t*	27.3 *t*
3	32.8 *t*	33.5 *t*	33.4 *t*	33.5 *t*	35.2 *t*
4	139.9 *s*	137.3 *s*	138.6 *s*	138.6 *s*	139.2 *s*[a]
5	128.1 *d*	129.3 *d*	128.4 *d*	128.2 *d*	128.1 *d*
6	75.7 *d*	75.9 *d*	75.9 *d*	76.0 *d*	75.8 *d*
7	56.1 *d*	55.6 *d*	51.1 *d*	51.0 *d*	52.5 *d*
8	71.5 *d*	70.9 *d*	69.5 *d*	69.5 *d*	78.3 *d*
9	33.1 *t*	32.5 *t*	32.6 *t*	32.3 *t*	33.1 *t*
10	144.7 *s*	144.4 *s*	144.0 *s*	143.8 *s*	140.8 *s*[a]
11	41.2 *d*	40.9 *d*	136.8 *s*	136.8 *s*	138.7 *s*[a]
12	179.1 *s*	179.7 *s*	170.9 *s*	170.9 *s*	170.5 *s*
13	16.4 *q*	15.9 *q*	124.7 *t*	124.4 *t*	119.7 *t*
14	199.3 *d*	199.8 *d*	200.0 *d*	200.1 *d*	104.7 *d*
15	61.1 *t*	68.1 *t*	68.2 *t*	68.1 *t*	68.4 *t*
OMe					56.0 *q*
Glucose moiely					
1′		102.7 *d*	102.8 *d*	102.3 *d*	102.6 *d*
2′		73.2 *d*	73.3 *d*	73.0 *d*	73.1 *d*
3′		76.6 *d*	76.6 *d*	76.5 *d*	76.2 *d*
4′		69.8 *d*	69.8 *d*	69.6 *d*	69.6 *d*
5′		75.9 *d*	75.9 *d*	73.7 *d*	73.8 *d*
6′		61.4 *t*	61.4 *t*	63.3 *t*	63.4 *t*
p-Hydroxyphenylacetyl moiety					
1″				124.4 *s*	124.5 *s*
2″, 6″				115.0 *d*	115.2 *d*
3″, 5″				129.9 *d*	130.0 *d*
4″				155.6 *s*	155.7 *s*
CH$_2$				40.0 *t*	40.1 *t*
CO				172.2 *s*	172.3 *s*

[a] May be exchangeable.

FAB-MS, *m/z* 589 [M + 1]$^+$, were very similar to those of **4**. However, the *singlet* of the aldehydic proton at *δ* 9.44 ppm was replaced by the *singlet* of a methoxy group at *δ* 3.47 ppm. The spectral data were thus very similar to those of the methyl acetal of urospermal A, from *Dicoma species* (Zdero & Bohlmann, 1990). Hence, **5** is 14-*O*-methylacetal-15-*O*-[6′-(*p*-hydroxyphenyl-acetyl)]-β-D-glucopyranosylurospermal A.

3. Experimental

EI-MS: 70 eV. ^{1}H- and ^{13}C-NMR 500 and 125 MHz, respectively. TLC: Merck Silica gel 60 F_{254} and RP-18 F_{254}S. CC: Merck Silica gel 60 (silica gel), Silica gel 60 silanized (RP-2), LiChroprep Si 60 (Si 60) and LiChroprep RP-8 (RP-8).

3.1. Plant material

The whole plant was collected in April 1996, in the public gardens, Giza, Cairo and identified by Prof. Dr. N. El-Hadidy. A voucher specimen has been deposited in the Herbarium, Faculty of Pharmacy, Cairo University.

3.2. Isolation of the lactones

The air-dried powdered roots (270 g) of *Sonchus asper*, were extracted with methanol (1.5 l × 3) and then evaporated to give the methanolic extract (30 g). The methanolic extract (30 g) was chromatographed over silica gel (360 g), eluted with chloroform and the polarity was increased with methanol, in fractions, each of 500 ml. The eluted fractions were combined into 3 main fractions (Frs. A–C).

Fr. A (620 mg, eluted with 15% MeOH/$CHCl_3$), was chromatographed on RP-2, using MeOH–H_2O (1:1) as eluent, to give frs. (169 mg), which was subjected to MPLC over RP-8, using MeOH–H_2O (4:6) as eluent, to afford compound **1** (6 mg). Fr. B (1.5 g, eluted with 20% MeOH/$CHCl_3$), was chromatographed on RP-2, using MeOH–H_2O (1:1) as eluent, to give frs. (170 mg), which was subjected to MPLC over Si 60, using $CHCl_3$–MeOH (9:1) as eluent, to afford compound **4** (14 mg) and compound **5** (9 mg). Fr. C (1.8 g, eluted with 20% MeOH/$CHCl_3$), was chromatographed on RP-2, using MeOH–H_2O (3:7) as eluent, to give frs. (220 mg), which was subjected to MPLC over Si 60, using $CHCl_3$–MeOH (85:15) as eluent, to afford compound **2** (4 mg) and compound **3** (11 mg).

- 11β,13-Dihydrourospermal A (**1**), Oil, ^{1}H-NMR: Table 1. ^{13}C-NMR: Table 2. EI-MS *m/z* 280 [M]$^+$.
- 15-*O*-β-D-Glucopyranosyl-11β,13-dihydrourospermal A (**2**), Oil, ^{1}H-NMR: Table 1. ^{13}C-NMR: Table 2. FAB-MS, *m/z* 443 [M + 1]$^+$.
- 15-*O*-β-D-Glucopyranosylurospermal A (**3**), Oil, ^{1}H-NMR: Table 1. ^{13}C-NMR: Table 2. FAB-MS, *m/z* 441 [M + 1]$^+$.
- 15-*O*-[6′-(*p*-Hydroxyphenylacetyl)]-β-D-glucopyranosylurospermal A (**4**), Oil, ^{1}H-NMR: Table 1. ^{13}C-NMR: Table 2. FAB-MS, *m/z* 575 [M + 1]$^+$.
- 14-*O*-Methylacetal-15-*O*-[6′-(*p*-hydroxyphenyl-acetyl)]-β-D-glucopyranosylurospermal A (**5**), Oil, ^{1}H-NMR: Table 1. ^{13}C-NMR: Table 2. FAB-MS, *m/z* 589 [M + 1]$^+$.

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