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SESQUITERPENE LACTONE GLYCOSIDES AND IONONE DERIVATIVE GLYCOSIDES FROM *SONCHUS ASPER*

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Key Word Index—*Sonchus asper*; Compositae; sesquiterpene glycoside; sonchuside; ionone derivative glycoside; sonchuionoside.

Abstract—Five new sesquiterpene glycosides, sonchusides E–I, and three new ionone derivative glycosides, sonchuionosides A–C, together with a known sesquiterpene glycoside, sonchuside D, and a known ionone derivative glycoside, icariside B_1 have been isolated from *Sonchus asper*. The structures of the new compounds were established on the basis of chemical and spectral data.

INTRODUCTION

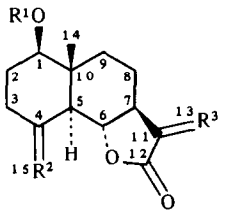
The sesquiterpene glycosides show considerable biological activity in a survival test [1]. In the course of a search for sesquiterpene glycosides in the Compositae, we have examined *Sonchus asper* and isolated five new sesquiterpene glycosides and three new ionone derivative glycosides together with previously known compounds. The identification of these compounds is described in this paper.

RESULTS AND DISCUSSION

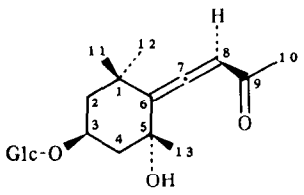
A known sesquiterpene glycoside, sonchuside D (**1**) [2], and a known ionone derivative glycoside, icariside B_1 (**7**) [3], were identified by comparing the ^{1}H and ^{13}C NMR with those of authentic materials.

The ^{1}H NMR spectrum of sonchuside E (**2**) exhibited exocyclic α-methylene-γ-lactone signals at δ5.26 and 6.05, an aldehyde proton signal at δ9.70, an angular methyl signal at δ0.91 and an anomeric proton signal at δ4.87. In the ^{13}C NMR spectrum, 21 signals, including six signals due to a glucopyranosyl moiety, were observed. These data suggested that **2** had a eudesmanolide-type skeleton. Enzymatic hydrolysis afforded **2a** as an aglycone, **2a** was assumed to be sonchucarpolide, which had been isolated from genus *Sonchus*, and this was identified by comparison of their ^{1}H NMR and MS spectra with reported data [4]. Thus, the structure of sonchuside E was decided to be **2**.

The ^{13}C NMR spectrum of sonchuside F (**3**) was similar to that of **2** except for the absence of the aldehyde carbon signal of C-15 and the appearance of a hydroxymethyl carbon signal at δ65.4. Enzymatic hydrolysis of **3**



	R^1	R^2	R^3
1	Glc	CH_2	CH_2
2	Glc	H,αCHO	CH_2
2a	H	H,αCHO	CH_2
3	Glc	H,αCH_2OH	CH_2
3a	H	H,αCH_2OH	CH_2
4	Glc	H,αCHO	H,αMe
4a	H	H,αCHO	H,αMe
5	Glc	H,αCH_2OH	H,αMe
5a	H	H,αCH_2OH	H,αMe
6	H	H,αCH_2O-Glc	H,αMe



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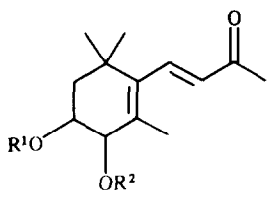

	R^1	R^2
8	H	Glc
8a	H	H
9	H	Glc—^{5}—Api
10	Glc	H

afforded **3a**, which was identified as 15-hydroxy-4β,15-dihydroreynosin by comparison of their ^{1}H NMR and MS spectra with reported data [5]. In the ^{13}C NMR spectrum of **2**, the C-2 (δ28.6) and C-10 (δ41.8) signals were shifted upfield by 2.2 and 0.8 ppm, respectively, and the C-1 (δ84.4) signal was shifted downfield by 6.5 ppm compared with those of **3a**. These results led us to conclude the structure of sonchuside F to be **3**.

The ^{1}H NMR spectrum of sonchuside G (**4**) was similar to that of **2** except for the absence of the exocyclic methylene proton signals of C-13 and the appearance of a doublet methyl signal at δ1.11. From these data, **4** was assumed to be a reduction product of **2**, and this was supported by ^{13}C NMR data. Enzymatic hydrolysis of **4** afforded **4a**, which was identified as 11β,13-dihydrosonchucarpolide by comparing their ^{1}H NMR and MS spectra [4].

Sonchuside H (**5**) showed ^{1}H and ^{13}C NMR spectra which were similar to those of **3**. Compound **5** was assumed to be a reduction product of **3**. Enzymatic hydrolysis of **5** afforded **5a**, which was identified as 15-hydroxy-4β,15,11β,13-tetrahydroreynosin by comparing their ^{1}H NMR and MS spectra [5]. In the ^{13}C NMR spectrum of **5**, the signals showed glycosylation shifts at C-1, C-2 and C-10 as compared with those of **5a**.

Sonchuside I (**6**) showed ^{1}H and ^{13}C NMR spectra which were similar to those of **5**. Enzymatic hydrolysis of **6** afforded **5a** as an algycone. In the ^{13}C NMR spectrum of **6**, the signals showed glycosylation shifts at C-4 and C-15 as compared with those of **5a**. Thus, the structure of sonchuside I was decided to be **6**.

In the ^{13}C NMR spectrum of sonchuionoside A (**8**), 19 signals, including six signals due to a glucopyranosyl moiety, were observed. Enzymatic hydrolysis of **8** afforded **8a** as an aglycone. Comparing the ^{13}C NMR signals with those of β-ionone [6] and the aglycone of icariside B$_6$ [7], suggesting that **8a** had hydroxy groups at C-3 and C-4. From the coupling constants [δ1.78 (1H, *dd*, J=12, 4 Hz, H-2 eq), 2.27 (1H, *t*, J=12 Hz, H-2 ax), 4.18 (1H, *dt*, J=12, 4 Hz, H-3), 4.30 (1H, *d*, J=4 Hz, H-4)], it is suggested that two hydroxy groups have *cis* configuration. But the absolute configurations of these two hydroxy groups are not known. In the ^{13}C NMR spectrum of **8**, the C-3 (δ66.1) and C-5 (δ131.5) signals were shifted upfield by 0.7 and 1.8 ppm, respectively, and the C-4 (δ84.3) signal was shifted downfield by 12.5 ppm compared with those of **8a**. In NOE experiment, irradiation of the anomeric proton signal increased the intensity of the H-4 [δ4.34 (*d*, J=4 Hz)] signal. Thus, the structure of sonchuionoside A was decided to be **8** exclusive of the stereochemistry at C-3 and C-4.

Sonchuionoside B (**9**) showed a ^{1}H NMR spectrum which was similar to that of **8**. The ^{13}C NMR spectrum was also similar to that of **8** but five additional signals were observed, which were assigned to an apiofuranosyl residue. Enzymatic hydrolysis of **9** afforded **8a** as an aglycone, and in the ^{13}C NMR spectrum of **9**, the signals showed glycosylation shifts as compared with those of **8**; C-6 of glucose (α-position) at δ69.3 (Δ +6.8) and C-5 of glucose (β-position) at δ76.9 (Δ −1.8). These results led us to conclude the structure of sonchuionoside B to be **9**, exclusive of the stereochemistry to C-3 and C-4.

Sonchuionoside C (**10**) showed six signals of a glucopyranosyl residue and 13 signals assignable to the aglycone moiety in the ^{13}C NMR spectrum. Enzymatic hydrolysis of **10** gave **8a**. In the ^{13}C NMR spectrum of **10**, the signals showed glycosylation shifts at C-2, C-3 and C-4 as compared with those of **8a**. Thus, the structure of sonchuionoside C was decided to be **10**, exclusive of the stereochemistry at C-3 and C-4.

EXPERIMENTAL

^{1}H and ^{13}C NMR spectra were recorded at 89.55 and 22.5 MHz, respectively and 399.65 MHz, TMS was used as an int. standard.

Plant material. Whole plants of *Sonchus asper* Vill. were collected in Darsano, Karachi, Pakistan. Plants were identified by Prof. S. I. Ali and Prof. M. Qaiser, and a voucher specimen has been deposited in the Herbarium, University of Shizuoka.

Extraction and isolation. Dried whole plants (3.5 kg) were extd twice with MeOH under reflux. The ext was concd under red. pres. and the residue was suspended in H_2O. This suspension was extracted with Et_2O. The H_2O layer was passed through an Amberlite XAD-2 column and the MeOH eluate concd under red. pres. The residue (35 g) was rechromatographed on a silica gel column with $CHCl_3$–MeOH (19:1) to give 20 mg **1**, 520 mg **2**, 113 mg **3**, 50 mg **4**, 31 mg **5**, 15 mg **6**, 5 mg **7**, 6 mg **8**, 5 mg **9** and 5 mg **10**.

Sonchuside E (**2**). Amorphous powder. (Found: C, 56.56; H, 6.98. $C_{21}H_{30}O_9 \cdot H_2O$ requires: C, 56.75; H, 7.26%). $[\alpha]_D^{22}$ −27.6° (H_2O; *c* 0.49). CD (H_2O; *c* 0.49) [θ] (nm): −3 700 (252). ^{1}H NMR (400 MHz, C_5D_5N): δ0.91 (3H, *s*, H_3-14), 1.80 (1H, *t*, J=11 Hz, H-5), 3.68 (1H, *dd*, J=11, 5 Hz, H-1), 3.77 (1H, *t*, J=11 Hz, H-6), 4.87 (1H, *d*, J=7 Hz, anomeric proton), 5.26 (1H, *d*, J=3.1 Hz, H-13a), 6.05 (1H, *d*, J=3.4 Hz, H-13b), 9.70 (1H, *d*, J=4 Hz, H-15). ^{15}C NMR: Table 1.

Sonchuside F (**3**). Amorphous powder. (Found: C, 56.38; H, 7.61. $C_{21}H_{32}O_9 \cdot H_2O$ requires: C, 56.49; H, 7.68%). $[\alpha]_D^{23}$ −5.6° (MeOH; *c* 0.63). CD (MeOH; *c* 0.32) [θ] (nm): −2600 (252). ^{1}H NMR (C_5D_5N): δ0.93 (3H, *s*, H_3-14), 4.84 (1H, *d*, J=8 Hz, anomeric proton), 5.22 (1H, *d*, J=3.2 Hz, H-13a), 6.04 (1H, *d*, J=3.6 Hz, H-13b). ^{13}C NMR: Table 1.

Sonchuside G (**4**). Amorphous powder. (Found: C, 53.33; H, 7.66. $C_{21}H_{32}O_9 \cdot 5/2H_2O$ requires: C, 53.27; H, 7.88%). $[\alpha]_D^{22}$ −37.9° (H_2O; *c* 1.82). ^{1}H NMR (C_5D_5N): δ0.92 (3H, *s*, H_3-14), 1.11 (3H, *d*, J=7 Hz, H_3-13), 4.82 (1H, *d*, J=8 Hz, anomeric proton), 9.66 (1H, *d*, J=4 Hz, H-15). ^{13}C NMR: Table 1.

Sonchuside H (**5**). Amorphous powder. (Found: C, 55.01; H, 7.87. $C_{21}H_{34}O_9 \cdot 3/2H_2O$ requires: C, 55.12; 8.15%). $[\alpha]_D^{23}$ −38.1° (MeOH; *c* 0.21). ^{1}H NMR (C_5D_5N): δ0.95 (3H, *s*, H_3-14), 1.09 (3H, *d*, J=7 Hz, H_3-13), 4.85 (1H, *d*, J=8 Hz, anomeric proton). ^{13}C NMR: Table 1.

Sonchuside I (**6**). Amorphous powder, FABMS *m/z* (rel. int.): 431 $[M+H]^+$ (75), 415 (8), 369 (10), 269 (100). $[\alpha]_D^{22}$ −31.0° (MeOH; *c* 0.50). ^{1}H NMR (C_5D_5N): δ1.02 (3H, *s*, H_3-14), 1.13 (3H, *d*, J=7 Hz, H_3-13), 3.41 (1H, *dd*, J=10, 5 Hz, H-1), 4.94 (1H, *d*, J=8 Hz, anomeric proton). ^{13}C NMR: Table 1.

Sonchuionoside A (**8**). Amorphous powder. FABMS *m/z* (rel. int.): 425 $[M+K]^+$ (5), 409 $[M+Na]^+$ (80), 387 $[M+H]^+$ (7), 329 (10), 307 (30). $[\alpha]_D^{23}$ −42.7° (MeOH; *c* 0.62). UV λ_{max}^{MeOH} nm (log ε): 279 (3.75). ^{1}H NMR (C_5D_5N): δ1.00, 1.03 (each 3H, *s*, H_3-11/H_3-12), 2.08 (3H, *s*, H_3-13), 2.24 (3H, *s*, H_3-10), 4.09 (1H, *dt*, J=12, 4 Hz, H-3), 4.34 (1H, *d*, J=4 Hz, H-4), 4.98 (1H, *d*, J=8 Hz, anomeric proton), 6.06 (1H, *d*, J=17 Hz, H-8), 7.16 (1H, *d*, J=17 Hz, H-7). ^{13}C NMR: Table 1.

Sonchusionoside B (**9**). Amorphous powder. FABMS *m/z* (rel. int.): 541 $[M+Na]^+$ (20), 519 $[M+H]^+$ (40), 387 (7), 369 (5). $[\alpha]_D^{23}$ −77.8° (MeOH; *c* 0.45). UV λ_{max}^{MeOH} nm (log ε): 279 (3.86). ^{1}H NMR (C_5D_5N): δ0.99, 0.99 (each 3H, *s*, H_3-11/H_3-12), 2.04 (3H, *s*, H_3-13), 2.23 (3H, *s*, H_3-10), 4.91 (1H, *d*, J=8 Hz, anomeric proton of glucose), 4.77 (1H, *d*, J=3 Hz, H-2 of apiose), 5.62 (1H,

Table 1. ^{13}C NMR spectral data

C	2	2a	3	3a	4	4a	5	6	8	8a	9	10
Aglycone moiety												
1	83.2	76.9	84.4	77.9	83.2	76.8	84.5	78.6	37.1	37.0	37.2	36.9
2	25.5	29.2	28.6	30.8	25.5	29.4	28.6	30.7	43.1	42.4	43.0	39.9
3	24.7	24.9	26.8	28.9	24.6	24.9	26.8	29.3	66.1	66.8	66.3	74.4
4	48.7	48.7	39.0	39.1	48.9	48.8[a]	39.1	37.0	84.3	71.8	84.4	68.9
5	50.1	48.9	50.8	50.8	48.9	49.0[a]	49.8	49.8	131.5	133.3	131.4	132.7
6	81.9	83.2	83.7	83.7	81.5	81.6	83.2	83.1	139.7	138.8	139.7	139.4
7	49.2	50.0	50.1	50.0	52.7	52.8	53.3	53.4	141.8	142.3	141.8	142.0
8	21.5	23.2	21.6	21.8	22.9	23.1	23.1	23.4	133.9	133.6	133.9	133.9
9	36.8	37.3	37.2	37.3	37.1	37.3	37.5	37.7	197.3	197.4	197.3	197.4
10	40.9	41.9	41.8	42.6	41.3	41.8	41.7	42.7	27.3[b]	27.4[c]	27.3[d]	27.4[e]
11	140.1	140.0	140.3	140.4	40.9	41.3	40.9	40.9	27.4[b]	27.7[c]	27.5[d]	27.6[e]
12	169.9	170.9	170.8	170.5	178.4	178.3	179.4	179.3	30.0[b]	30.0[c]	30.0[d]	30.0[e]
13	117.1	116.8	116.6	116.1	12.7	12.6	12.7	12.7	19.9	20.1	19.9	20.2
14	12.9	12.2	13.4	12.6	12.8	12.1	13.4	12.7				
15	203.2	203.3	65.4	65.4	203.1	203.2	65.4	73.6				
Sugar moiety												
Glc 1	102.3		102.2		102.2		102.2	104.8	106.8		106.7	101.9
2	75.1		75.2		75.1		75.3	75.5	75.0		74.9	75.5
3	78.5		78.3		78.3		78.3	78.0	78.4		78.3	78.7
4	72.1		72.1		72.1		72.1	72.0	71.5		71.9	71.8
5	78.7		78.6		78.6		78.7	78.0	78.7		76.9	78.8
6	63.3		63.3		63.3		63.3	63.0	62.5		69.3	62.9
Api 1											111.3	
2											77.7	
3											80.5	
4											75.3	
5											65.8	

Run at 22.5 MHz in pyridine-d_5.
[a–e] Assignment may be interchanged in each column.

d, $J = 3$ Hz, anomeric proton of apiose), 6.04 (1H, *d*, $J = 17$ Hz, H-8), 7.14 (1H, *d*, $J = 17$ Hz, H-7). ^{13}C NMR: Table 1.

Sonchuionoside C (**10**). Amorphous powder. FABMS *m/z* (rel. int.): 409 $[M + Na]^+$ (60), 353 (15), 339 (15). $[\alpha]_D^{21} -65.2°$ (MeOH; *c* 0.46). UV λ_{max}^{MeOH} nm (log ε): 278 (3.59). ^{1}H NMR (C_5D_5N): δ0.92, 1.00 (each 3H, *s*, H_3-11/H_3-12); 2.00 (3H, *s*, H_3-13), 2.28 (3H, *s*, H_3-10), 5.15 (1H, *d*, $J = 8$ Hz, anomeric proton), 6.23 (1H, *d*, $J = 17$ Hz, H-8), 7.26 (1H, *d*, $J = 17$ Hz, H-7). ^{13}C NMR: Table 1.

Enzymatic hydrolysis of **2–6**. A soln of **2** (30 mg) in H_2O (3 ml) was treated with cellulase (Sigma type II) (30 mg) at room temp. for 3 hr, then the reaction mixture was extracted with EtOAc 3 times. The extract was purified by HPLC to give **2a** (17.5 mg). **3** (18 mg), **4** (10 mg), **5** (9 mg) and **6** (5 mg) were hydrolysed in the same way to give **3a** (8 mg), **4a** (4 mg), **5a** (4 mg) and **5a** (2 mg), respectively. Sonchucarpolide (**2a**), colourless gum. EIMS *m/z* (rel. int.): 264 $[M]^+$ (trace), 236 (1), 210 (2), 149 (14), 44 (100). ^{1}H NMR (C_6D_6): δ0.47 (3H, *s*, H_3-14), 2.67 (1H, *dd*, $J = 11$, 5 Hz, H-1), 3.20 (1H, *t*, $J = 11$ Hz, H-6), 4.77 (1H, *d*, $J = 3.8$ Hz, H-13a), 5.88 (1H, *d*, $J = 4.0$ Hz, H-13b), 9.49 (1H, *d*, $J = 4$ Hz, H-15). ^{13}C NMR: Table 1. 15-Hydroxy-4β,15-dihydroreynosin (**3a**), colourless oil. EIMS *m/z* (rel. int.): 266 $[M]^+$ (trace), 248 (1), 236 (2), 85 (100). ^{1}H NMR ($CDCl_3$): δ0.92 (3H, *s*, H_3-14), 3.38 (1H, *dd*, $J = 11$, 5 Hz, H-1), 3.55 (1H, *dd*, $J = 12$, 8 Hz, H-15a), 3.70 (1H, *dd*, $J = 12$, 4 Hz, H-15b), 3.90 (1H, *t*, $J = 11$ Hz, H-6), 5.40 (1H, *d*, $J = 3.9$ Hz, H-13a), 6.06 (1H, *d*, $J = 4.1$ Hz, H-13b). ^{13}C NMR: Table 1. 11β,13-Dihydrosonchucarpolide (**4a**), colourless gum. EIMS *m/z* (rel. int.): 266 $[M]^+$ (trace), 238 (8), 220 (16), 210 (56), 147 (100). ^{1}H NMR ($CDCl_3$): δ0.98 (3H, *s*, H_3-14), 1.21 (3H, *d*, $J = 7$ Hz, H_3-13), 3.35 (1H, *dd*, $J = 10$, 5 Hz, H-1), 3.84 (1H, *t*, $J = 11$ Hz, H-6), 9.53 (1H, *d*, $J = 4$ Hz, H-15). ^{13}C NMR: Table 1. 15-Hydroxy-4β,15,11β,13-tetrahydroreynosin (**5a**), colourless oil. EIMS *m/z* (rel. int.): 268 $[M]^+$ (trace), 250 (1), 238 (5), 210 (10). ^{1}H NMR ($CDCl_3$): δ0.95 (3H, *s*, H_3-14), 1.22 (3H, *d*, $J = 7$ Hz, H_3-13), 3.31 (1H, *dd*, $J = 10$, 5 Hz, H-1), 3.58 (1H, *dd*, $J = 11$, 8 Hz, H-15a), 3.72 (1H, *dd*, $J = 11$, 4 Hz, H-15b), 3.92 (1H, *t*, $J = 11$ Hz, H-6).

Enzymatic hydrolysis of **8–10**. **8** (5 mg) was dissolved in H_2O (1 ml) and the soln treated with cellulase (10 mg) at room temp. for 5 hr with stirring. The soln was passed through an Amberlite XAD-2 column and the MeOH eluate purified by HPLC to give **8a** (4 mg). **9** (2 mg) and **10** (5 mg) were hydrolysed in the same way to give same aglycone **8a** (1 mg) and (3 mg), respectively; **8a**, colourless gum. EIMS *m/z* (rel. int.): 224 $[M]^+$ (10), 206 (25), 191 (62), 123 (100), 83 (80). $[\alpha]_D^{21} -116.7°$ (MeOH; *c* 0.06). ^{1}H NMR (400 MHz, C_5D_5N): δ1.04, 1.11 (each 3H, *s*, H_3-11/H_3-12), 2.07 (3H, *s*, H_3-13), 2.32 (3H, *s*, H_3-10), 1.78 (1H, *dd*, $J = 12$, 4 Hz, H-2 eq), 2.27 (1H, *t*, $J = 12$ Hz, H-2 ax), 4.18 (1H, *dt*, $J = 12$, 4 Hz, H-3), 4.30 (1H, *d*, $J = 4$ Hz, H-4), 6.32 (1H, *d*, $J = 17$ Hz, H-8), 7.39 (1H, *d*, $J = 17$ Hz, H-7). ^{13}C NMR: Table 1.

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