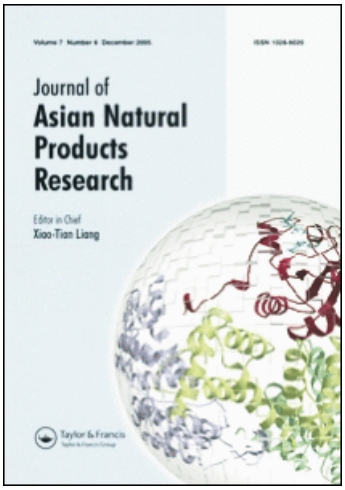

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Three new lignans from the seeds of *Saussurea involucrata*

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ORIGINAL ARTICLE

Three new lignans from the seeds of *Saussurea involucrata*

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Three new lignans, arctigenin-4-*O*-(6″-*O*-acetyl-β-D-glucoside) (**1**), arctigenin-4-*O*-(2″-*O*-acetyl-β-D-glucoside) (**2**), and arctigenin-4-*O*-(3″-*O*-acetyl-β-D-glucoside) (**3**), together with two known lignans, were isolated from the seeds of *Saussurea involucrata*. Their structures were established by spectroscopic methods, mainly 1D and 2D NMR, and mass spectral analysis.

Keywords: *Saussurea involucrata*; seeds; lignans; Asteraceae

1. Introduction

Saussurea involucrata (Kar. et Kir.) Sch. Bip. (Asteraceae) is a well-known traditional Chinese medicinal plant in Xinjiang Uighur Autonomous Region of China and is used for the treatment of rheumatic arthritis and gynopathy [1]. Focusing on the entire plant of *S. involucrata*, previous studies have already reported sesquiterpenes, flavonoids, coumarins, and other constituents from this species [2–9]. In our study, three new lignans, arctigenin-4-*O*-(6″-*O*-acetyl-β-D-glucoside) (**1**), arctigenin-4-*O*-(2″-*O*-acetyl-β-D-glucoside) (**2**), and arctigenin-4-*O*-(3″-*O*-acetyl-β-D-glucoside) (**3**) (Figure 1), together with two known lignans (artiin and arctigenin) which are first found in this plant, were isolated from the seeds of *S. involucrata*. This is the first chemical investigation on the seeds of *S. involucrata*. This paper describes the isolation and structural elucidation of the new compounds.

2. Results and discussion

Compound **1** was obtained as a yellow gum, and its molecular formula was determined as $C_{29}H_{36}O_{12}$ by the HR-ESI-MS ion at *m/z* 599.2083 $[M + Na]^+$. The IR spectrum exhibited the presence of carbonyl (1768, 1593 cm^{-1}) and aromatic (1516 cm^{-1}) functions. The ^1H and ^{13}C NMR spectral data (Table 1) of **1** were quite similar to those of arctiin [10], which suggested that **1** was a derivative of arctiin and had the same skeleton as that of arctiin. The most obvious difference between compound **1** and arctiin, after comparing their ^1H and ^{13}C NMR spectral data, was the presence of an acetyl group (δ_H 2.08, δ_C 20.9, 171.8) in compound **1**. The fragment peak in ESI-MS at *m/z* 355 $[M + H - (Glc—O—Ac)]^+$, together with the analogous ^1H and ^{13}C NMR spectral data of **1** and arctiin, indicated that the acetyl group was possibly linked to the glucose. Comparing with

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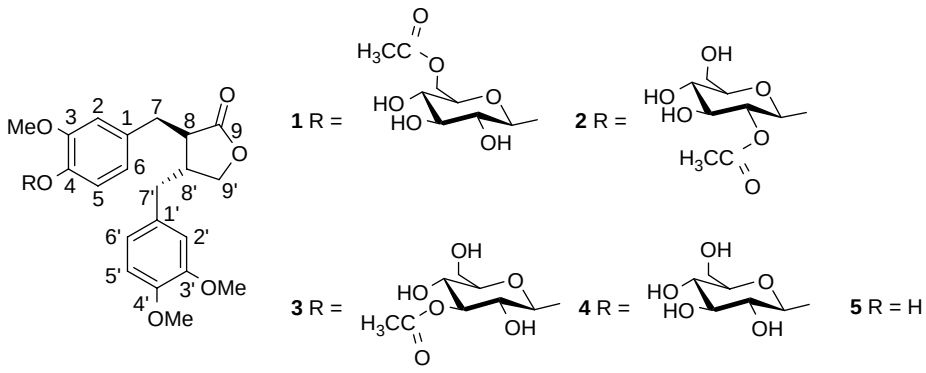

Figure 1. Chemical structures of compounds **1**–**5**.

arctiin, the C-6″ of compound **1** shifted from δ_C 61.8 to δ_C 63.1, whereas the C-5″ shifted from δ_C 76.2 to δ_C 74.3. This tiny but significant difference suggested that the location of the acetyl group was at C-6″ in compound **1**. Also, this could be verified by HMBC correlations: from H-6″ at δ_H 4.43 and 4.33 to the carbonyl carbon of the acetyl group (see Figure 2). It was reported that C-7 and C-7′ carbon signals always appeared at δ_C 34.5 ± 0.3 and 38.3 ± 0.7 in dibenzylsubsitituted butyrolactones with *trans*-configurations; however, in the *cis*-configuration, C-7 and C-7′ carbon signals were shielded by about 4–5 ppm [11,12]. The chemical shifts of C-7 ($\delta_C = 34.5$) and C-7′ ($\delta_C = 38.2$) suggested that compound **1** should be *trans*-configuration. For the arctigenin with *trans*-configuration, it was also reported that the optical rotation value +24.180 at 27°C indicated the 8(*S*) 8′(*R*) configuration, while the value −23.250 indicated the 8(*R*) 8′(*S*) configuration [13]. The optical rotation value of compound **1** $[\alpha]_D^{20}$ −45.9 enabled us to confirm that the configuration of compound **1** is 8(*R*) 8′(*S*). Therefore, the structure of **1** was deduced as arctigenin-4-*O*-(6″-*O*-acetyl-β-D-glucoside).

Compounds **2** and **3** were found to have very similar data to compound **1** by HR-ESI-MS, IR and ^{1}H and ^{13}C NMR spectra. Determined by HR-ESI-MS, the molecular formulae of these two compounds are the same as that of compound **1**, $C_{29}H_{36}O_{12}$ (*m/z* 599.2079 $[M + Na]^+$ for **2** and *m/z* 599.2095 $[M + Na]^+$ for **3**). The ^{1}H and ^{13}C NMR spectral data of compounds **2** and **3** also showed the presence of an acetyl group for each of them (δ_H 2.12, δ_C 21.0, 171.2 for **2** and δ_H 2.20, δ_C 21.1, 172.6 for **3**). Comparison of the ^{1}H and ^{13}C NMR spectral data of glucose moieties in compounds **2** and **3** with those in literatures suggested that the acetyl groups were located at C-2″ in compound **2** and C-3″ in compound **3** [14,15]. This conclusion was further confirmed by the HMBC correlations from H-2″ at δ_H 5.07 to the carbonyl carbon of the acetyl group in compound **2** (Figure 3) and from H-3″ at δ_H 4.99 to the carbonyl carbon of the acetyl group in compound **3** (Figure 4). Therefore, combined with the acetylation shifts [16] of C-1″, C-2″, and C-3″ in **2** and C-2″, C-3″, and C-4″ in **3**, compounds **2** and **3** were established as arctigenin-4-*O*-(2″-*O*-acetyl-β-D-glucoside) and arctigenin-4-*O*-(3″-*O*-acetyl-β-D-glucoside), respectively.

Compounds **4** (arctiin) and **5** (arctigenin) were identified by direct comparison of their spectral data with the literature [10].

It should be noted that no acetic acid or acetic anhydride was used during the process of extraction and isolation. So, we believe that these three new compounds are all derived from natural sources.

Table 1. ^{1}H and ^{13}C NMR spectral data of compounds **1**–**3** (*J*, Hz).

	1		**2**		**3**	
	^{1}H	^{13}C	^{1}H	^{13}C	^{1}H	^{13}C
1		134.4		133.9		134.7
2	6.68 (d, $J = 2.0$)	113.0	6.65 (d, $J = 2.0$)	113.8	6.69 (d, $J = 2.0$)	113.1
3		150.4		150.4		150.4
4		144.8		145.3		144.8
5	7.01 (d, $J = 8.0$)	120.1	7.01 (d, $J = 7.8$)	120.0	7.03 (d, $J = 8.0$)	120.1
6	6.62 (dd, $J = 8.0, 2.0$)	121.8	6.60 (dd, $J = 7.8, 2.0$)	121.7	6.62 (dd, $J = 8.0, 2.0$)	121.9
7	2.91 (dd, $J = 6.4, 13.0$)	34.5	2.98 (m)	34.6	2.93 (m)	34.6
	2.94 (dd, $J = 6.4, 13.0$)					
8	2.56 (overlapped)	46.4	2.56 (overlapped)	46.5	2.60 (overlapped)	46.5
9		178.5		178.5		178.5
1′		130.2		130.4		130.2
2′	6.48 (d, $J = 1.6$)	111.8	6.48 (d, $J = 2.0$)	112.1	6.48 (d, $J = 2.0$)	111.9
3′		148.9		149.1		149.0
4′		147.9		149.0		147.9
5′	6.75 (d, $J = 8.0$)	111.3	6.75 (d, $J = 8.0$)	111.6	6.76 (d, $J = 8.0$)	111.4
6′	6.55 (dd, $J = 8.0, 1.6$)	120.6	6.55 (dd, $J = 8.0, 2.0$)	120.7	6.55 (dd, $J = 8.0, 2.0$)	120.6
7′	2.56 (overlapped)	38.2	2.56 (overlapped)	38.2	2.60 (overlapped)	38.2
	2.63 (overlapped)		2.64 (overlapped)		2.64 (overlapped)	
8′	2.49 (m)	40.9	2.49 (m)	41.1	2.49 (m)	41.0
9′	3.89 (overlapped)	71.3	3.88 (overlapped)	71.2	3.95 (overlapped)	71.2
	4.17 (m)		4.30 (m)		4.20 (m)	
1″	4.70 (d, $J = 7.2$)	103.5	4.90 (d, $J = 7.8$)	100.7	4.75 (d, $J = 8.0$)	103.8
2″	3.65 (overlapped)	73.4	5.07 (m)	75.1	3.76 (overlapped)	71.8
3″	3.64 (overlapped)	75.8	3.72 (overlapped)	74.0	4.99 (m)	77.9
4″	3.49 (m)	69.6	3.71 (overlapped)	70.5	3.74 (overlapped)	69.0
5″	3.55 (m)	74.3	3.49 (m)	75.7	3.50 (m)	76.1
6″	4.33 (dd, $J = 12.0, 2.0$)	63.1	3.88 (overlapped)	61.9	3.76 (overlapped)	62.2
	4.43 (dd, $J = 12.0, 2.0$)		3.90 (overlapped)		3.91 (overlapped)	
3-OMe	3.85 (s)	55.9	3.84 (s)	56.0	3.86 (s)	55.9
3′-OMe	3.80 (s)	55.9	3.81 (s)	56.0	3.82 (s)	55.9

Table 1 – *continued*

	1		2		3	
	^{1}H	^{13}C	^{1}H	^{13}C	^{1}H	^{13}C
4′-OMe	3.78 (s)	55.9	3.73 (s)	55.9	3.80 (s)	55.8
Ac		171.8		171.2		172.6
	2.08 (s)	20.9	2.12 (s)	21.0	2.20 (s)	21.1

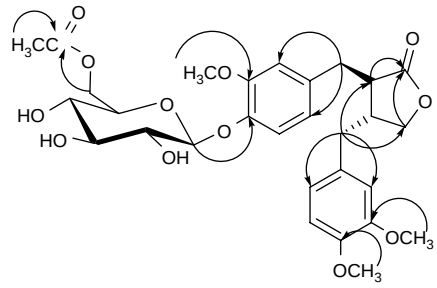

Figure 2. Key HMBC correlations of compound **1**.

3. Experimental

3.1 General experimental procedures

The $[\alpha]_D$ values were obtained in MeOH at 20°C using a Perkin-Elmer 341 digital polarimeter (Waltham, MA, USA). UV spectra were determined on a UV-2550 UV–vis spectrophotometer (Shimadzu, Kyoto, Japan). IR spectra were recorded on an EQUINOX-55 FT-IR spectrometer (Bruker, Karlsruhe, Germany) with KBr pellets. NMR spectra were recorded at 400 MHz for ^{1}H and 100 MHz for ^{13}C on a Varian INOVA-400 NMR spectrometer (Palo Alto, CA, USA) with TMS as the internal standard. HR-ESI-MS data were determined by a JEOL Accu TOF spectrometer (JMS-T100CS, JEOL, Tokyo, Japan). Silica gel (200–300 mesh; Qingdao Haiyang Chemical & Special Silica Gel Co., Ltd, Qingdao, China) was used for column chromatography. Sephadex LH-20 (GE, New York, NY, USA) was used for

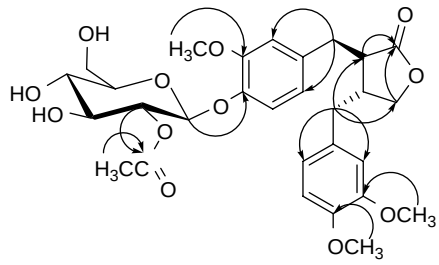

Figure 3. Key HMBC correlations of compound **2**.

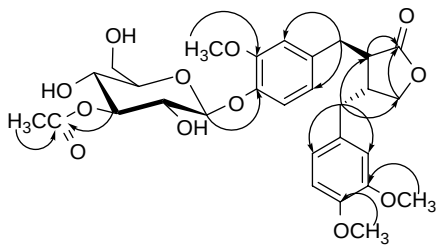

Figure 4. Key HMBC correlations of compound **3**.

molecular exclusion chromatography. Precoated Si gel GF254 plates (Yantai Jiangyou Silica Gel Co., Ltd, Yantai, China) were used for TLC tests.

3.2 Plant material

The seeds of *S. involucrata* were purchased from Hejing County, Xinjiang Uighur Autonomous Region, China. It was identified by Prof. Guanmian Shen (Xinjiang Institute of Ecology and Geography, Chinese Academy of Sciences). A voucher specimen has been deposited at the Xinjiang Technical Institute of Physics and Chemistry (No. SI080003), Chinese Academy of Sciences, China.

3.3 Extraction and isolation

The air-dried and powdered seeds of *S. involucrata* (1.0 kg) were extracted thrice with MeOH (4 liters for the first time and 2.5 liters for the second and third times) at room temperature for 4 days. The solvent was removed under reduced pressure to yield the crude extract (131 g). The extract (125 g) was suspended in water and extracted with $CHCl_3$ (3×500 ml). The $CHCl_3$ layer was concentrated *in vacuo* and the $CHCl_3$ extract (74.4 g, powder) was washed by petroleum ether (PE, 3 liters) to remove the PE-soluble constituents and yield the $CHCl_3$-soluble fraction (38.4 g). This fraction was subjected to column chromatography over silica gel (200–300 mesh) and eluted with a gradient $CHCl_3$–MeOH to afford five fractions (A–E). Fraction B (2.8 g) was separated on a silica gel column (200–300 mesh) with a gradient mixture of $CHCl_3$–MeOH (100:1–50:1) to give three subfractions. Compound **5** (8.3 mg, 60:1) was obtained from subfraction 3 (98.7 mg). Fraction D (11.3 g) was subjected to column chromatography over silica gel (200–300 mesh) with $CHCl_3$–MeOH (70:1–10:1) as the eluent to give four subfractions. Compound **1** (127 mg, 50:1) was obtained from subfraction 2 (153.9 mg). Subfraction 3 (137.6 mg) was purified by Sephadex LH-20 and eluted with $CHCl_3$–MeOH (1:1) to give compound **4** (111 mg) and a mixture (15.9 mg). The mixture was further purified by repeated silica gel column chromatography using $CHCl_3$–MeOH as the eluent to yield compounds **2** (4 mg, 30:1) and **3** (3 mg, 30:1).

3.3.1 *Arctigenin-4*-O-*(6″*-O-*acetyl-β-D-glucoside) (**1**)*

Yellow gum; $[\alpha]_D^{20}$ −45.9 ($c = 0.93$, MeOH); UV λ_{max} MeOH (nm): 201; IR (KBr) ν_{max} (cm^{-1}): 3448, 2921, 1769, 1516, 1266, 1025, 751; ^1H and ^{13}C NMR spectral data: see Table 1; HR-ESI-MS: *m/z* 599.2083 $[M + Na]^+$ (calcd for $C_{29}H_{36}O_{12}Na$, 599.2104).

3.3.2 *Arctigenin-4*-O-*(2″*-O-*acetyl-β-D-glucoside) (**2**)*

Light yellow oil; $[\alpha]_D^{20}$ −27.2 ($c = 0.33$, MeOH); UV λ_{max} MeOH (nm): 203; IR (KBr) ν_{max} (cm^{-1}): 3397, 2925, 1746, 1515, 1264, 1030, 759; ^1H and ^{13}C NMR spectral data: see Table 1; HR-ESI-MS: *m/z* 599.2079 $[M + Na]^+$ (calcd for $C_{29}H_{36}O_{12}Na$, 599.2104).

3.3.3 *Arctigenin-4*-O-*(3″*-O-*acetyl-β-D-glucoside) (**3**)*

Light yellow oil; $[\alpha]_D^{20}$ −32.7 ($c = 0.25$, MeOH); UV λ_{max} MeOH (nm): 202; IR

(KBr) ν_{max} (cm^{-1}): 3469, 2925, 1763, 1516, 1265, 1027, 757; ^1H and ^{13}C NMR spectral data: see Table 1; HR-ESI-MS: m/z 599.2095 $[M + Na]^+$ (calcd for $C_{29}H_{36}O_{12}Na$, 599.2104).

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