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Albizosides D and E, two new cytotoxic triterpene saponins from *Albizia chinensis*

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ABSTRACT

Two oleanane-type triterpene saponins, named albizosides D and E (**1** and **2**), together with a known compound, Julibroside J_8 (**3**), were isolated from the stem bark of *Albizia chinensis*. The structures of compounds **1** and **2** were established by 1D, 2D NMR experiments, and chemical methods, and they showed moderate cytotoxic activity against a small panel of human tumor cell lines.

1. Introduction

The genus *Albizia* (Leguminosae) comprises about 150 species distributed throughout the world. Some species have been reported yielding a wide range of triterpenoid saponins.[1–5] In previous work, we described the isolation of three complex saponins albizosides A–C from the *n*-BuOH extract of stem barks of *Albizia chinensis* (Osb.) Merr.[6] Further investigation of the saponins of this plant afforded two new saponins, named albizosides D and E (**1** and **2**), together with one known compound, Julibroside J_8 (**3**). Herein, we report the isolation and structure elucidation of these triterpenoid saponins and the evaluation of the cytotoxic activities of saponins **1** and **2** against five human tumor cell lines.

2. Results and discussion

The *n*-BuOH-soluble fraction (200 g) was passed through a polyamide column, eluted with a gradient solvent system. The water eluate (55 g) was subjected to D_{101} macroporous resin column to give a crude saponin mixture. This crude saponin mixture fraction was chromatographed over an ODS column and repeatedly purified by preparative HPLC to afford two new complicated triterpenoid saponins, albizosides D and E (**1** and **2**), together with one known compound, Julibroside J_8 (**3**).

Albizoside D (**1**) was obtained as a white amorphous powder. QFTMS showed a $[M+Na]^+$ peak at *m*/*z* 2356.0350, in accordance with the composition, $C_{108}H_{172}O_{54}Na$. The IR spectrum showed carbonyl (1737 cm^{-1}) and α,β-unsaturated carbonyl (1696 cm^{-1}) groups absorption. On acid hydrolysis, **1** afforded an acacic acid lactone unit identified with an authentic sample, and the monosaccharides L-rhamnose, L-arabinose, D-fucose, D-xylose, D-glucose, and D-quinovose, which were identified by GC analysis of their trimethylsilyl thiazolidine derivatives.[7] The ^1H NMR spectrum of **1** displayed signals for 10 anomeric protons at δ 4.83 (d, *J* 7.8 Hz, H-Qui-1), 4.86 (d, *J* 7.8 Hz, H-Qui′-1), 4.87 (d, *J* 7.8 Hz, H-Glc_1-1), 4.96 (d, *J* 7.8 Hz, H-Fuc-1), 5.04 (d, *J* 7.2 Hz, H-Xyl-1), 5.33 (d, *J* 8.4 Hz, H-Glc″-1), 5.40 (d, *J* 7.8 Hz, H-Glc_2-1), 5.85 (br s, H-Rha-1), 6.04 (d, *J* 7.8 Hz, H-Glc′-1), and 6.26 [br s, H-Ara(*f*)-1], correlating with the carbon signals at δ 99.4, 99.4, 105.0, 103.5, 107.1, 105.8, 105.9, 101.9, 95.7, and 111.1, respectively, in the HSQC spectrum. Based on the coupling constants of the anomeric protons and the chemical shifts of the anomeric carbons, the anomeric configurations of the sugar moieties were determined as β for the glucose, xylose, fucose, and quinovose moieties and α for the rhamnose and arabinose moieties. Comparison of the ^{13}C NMR signals for aglycon of **1** with those of albizoside A,[6] the characteristic carbon resonances at δ 88.6 (C-3), δ 77.2 (C-21), δ 174.5 (C-28) of the aglycon moiety, suggested that **1** was a 21-acyl-3,28-bidesmoside of acacic acid. In addition, the ^1H NMR spectrum exhibited two olefinic proton signals at δ 7.02 (t, *J* 7.2 Hz) and 7.03 (t, *J* 7.2 Hz) and two groups of one-substituted olefin proton signals, one group at δ 6.19 (dd, *J* 18.0, 10.8 Hz), 5.40 (d, *J* 18.6 Hz), and 5.21 (d, *J* 10.8 Hz) and the other group at δ 6.20 (dd, *J* 18.0, 10.8 Hz), 5.42 (d, *J* 18.0 Hz),

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and 5.21 (d, *J* 10.8 Hz), indicating **1** had two units of monoterpenoid moieties. The assignments of the ^{1}H and ^{13}C NMR chemical shifts of **1** from 2D NMR experiments (HSQC and HMBC spectra) showed that all signals were superimposable with albizoside C[6] except for those of the oligosaccharide chain linked at C-3 of the aglycon, since the arabinopyranosyl residue in albizoside C was replaced by a fucopyranosyl residue in **1** (Tables 1–3). The spectroscopic data of the tetrasaccharide moiety at C-3 were identical to those of Julibroside I obtained from *Albizia julibrissin*.[8] In addition, comparison of the spectroscopic data of **1** with those of adiantifolloside C showed that the only difference between them was the terminal Xyl unit of the C-3 oligosaccharide chain in **1** instead of Ara(*p*) unit in adiantifolloside C.[5] Thus, the structure of **1** was determined as 21-*O*-{(2*E*,6*S*)-2-hydroxymethyl-6-methyl-6-*O*-[4-*O*-(2′*E*,6′*S*)-2′,6′-dimethyl-6′-*O*-β-D-quinovopyranosyl-2′,7′-octadienoyl-β-D-quinovopyranosyl]-2,7-octadienoyl}-3-*O*-{β-D-xylopyranosyl-(l→2)-β-D-fucopyranosyl-(1→6)-[β-D-glucopyranosyl-(1→2)]-β-D-glucopyranosyl} acacic acid 28-*O*-β-D-glucopyranosyl-(l→3)-[α-L-arabinofuranosyl-(l→4)]-α-L-rhamnopyranosyl-(l→2)-β-D-glucopyranosyl ester (Fig. 1).

Albizoside E (**2**) was isolated as an amorphous powder. Its molecular formula was deduced as $C_{117}H_{184}O_{56}$ from the QFTMS (*m*/*z* $[M+Na]^+$ 2508.1192, calcd for $C_{117}H_{184}O_{56}Na$ 2508.1443). Acid hydrolysis of **2** also gave an acacic acid lactone identified by co-TLC with an authentic sample, and the L-rhamnose, L-arabinose, D-xylose, D-glucose, and D-quinovose units were determined by GC analysis of their trimethylsilyl thiazolidine derivatives.[7] In the ^{1}H NMR spectrum, 10 anomeric protons were observed at δ 4.83 (d, *J* 7.2 Hz, H-Qui-1), 4.85 (d, *J* 7.8 Hz, H-Qui″-1), 4.89 (d, *J* 7.8 Hz, H-Glc$_1$-1), 4.98 (d, *J* 7.8 Hz, H-Qui′-1), 5.00 (overlapped, H-Xyl-1), 5.16 (d, *J* 4.0 Hz, H-Ara-1), 5.33 (overlapped, H-Glc″-1), 5.89 (br s, H-Rha-1), 6.05 (d, *J* 7.8 Hz, H-Glc′-1), and 6.27 [br s, H-Ara(*f*)-1], the corresponding carbon resonances at δ 99.4, 99.4, 106.9, 97.1, 106.3, 102.3, 105.8, 101.8, 95.8, and 111.1, respectively, according to the HSQC spectrum. Comparison of the spectroscopic data of **2** with those of Julibroside J_9[9] found that **2** possessed an additional monoterpene–quinovopyranosyl moiety (MT–Q). Furthermore, the ^{1}H and ^{13}C NMR resonances of **2** assigned from 2D NMR experiments were similar to albizoside A[6] which have three groups of monoterpene–quinovopyranosyl units. The only difference between **2** and albizoside A was the presence of arabinopyranosyl signals instead of fucopyranosyl signals in the C-3 oligosaccharide chain (Tables 1–3). Therefore, the structure of **2** was elucidated as 21-*O*-{(2*E*,6*S*)-2-hydroxymethyl-6-methyl-6-*O*-{4-*O*-(2′*E*,6′*S*)-2′,6′-dimethyl-6′-*O*-[2′-*O*-(2″*E*,6″*S*)-2″-hydroxymethyl-6″-methyl-6″-*O*-β-D-quinovopyranosyl-2″,7″-octadienoyl-β-D-quinovopyranosyl]-2′,7′-octadienoyl-β-D-quinovopyranosyl}-2,7-octadienoyl}-3-*O*-[β-D-xylopyranosyl-(l→2)-α-L-arabinopyranosyl-(1→6)-β-D-glucopyranosyl] acacic acid 28-*O*-β-D-glucopyranosyl-(l→3)-[α-L-arabinofuranosyl-(l→4)]-α-L-rhamnopyranosyl-(l→2)-β-D-glucopyranosyl ester (Fig. 1).

Compound **3** was identified by comparison with literature values as julibroside J_8,[10] 21-*O*-{(2*E*,6*S*)-2-hydroxymethyl-6-methyl-6-*O*-[4-*O*-(2′*E*,6′*S*)-2′,6′-dimethyl-6′-*O*-β-D-quinovopyranosyl-2′,7′-octadienoyl-β-D-quinovopyranosyl]-2,7-octadienoyl}-3-*O*-[β-D-xylopyranosyl-(l→2)-β-D-fucopyranosyl-(1→6)-β-D-glucopyranosyl] acacic acid 28-*O*-β-D-glucopyranosyl-(l→3)-[α-L-arabinofuranosyl-(l→4)]-α-L-rhamnopyranosyl-(l→2)-β-D-glucopyranosyl ester (Fig. 1).

Compounds **1** and **2** were tested for cytotoxicity on five human tumor cell lines (HCT-8, Bel-7402, BGC-823, A549, and A2780) using the MTT method. Both of them exhibited moderate cytotoxicity except compound **2** which showed no activity against HCT-8 (Table 4).

3. Experimental

3.1. General experimental procedures

Optical rotations were taken on a JASCO P-2000 polarimeter. UV spectra were measured on a JASCO V650 spectrophotometer. IR

Table 1
^{13}C NMR spectroscopic data of **1**–**3** (in pyridine-d_5)[a,b]

Position	**1**	**2**	**3**	Albizoside A[6]	Albizoside C[6]
Aglycon					
1	39.0	38.9	39.6	38.9	38.9
2	26.9	26.8	26.9	26.8	26.7
3	88.6	88.8	88.4	88.4	88.9
4	39.7	39.7	39.7	39.6	39.6
5	56.1	56.1	56.1	56.0	56.0
6	18.6	18.7	18.4	18.7	18.5
7	33.7	33.7	33.6	33.6	33.6
8	40.2	40.2	40.1	40.1	40.1
9	47.2	47.2	47.2	47.1	47.1
10	37.1	37.2	37.1	37.1	37.0
11	23.97	23.95	24.0	23.9	23.9
12	123.2	123.2	123.2	123.1	123.1
13	143.4	143.4	143.4	143.4	143.4
14	42.1	42.1	42.0	42.0	42.0
15	36.0	36.0	36.0	35.9	35.9
16	74.0	73.8	73.9	73.9	73.8
17	51.7	51.7	51.6	51.6	51.6
18	41.0	41.1	41.0	41.1	40.8
19	47.9	47.9	47.8	47.9	47.9
20	35.5	35.5	35.5	35.5	35.4
21	77.2	77.1	77.2	77.0	77.0
22	36.5	36.4	36.4	36.4	36.4
23	28.2	28.3	28.2	28.2	28.1
24	17.0	17.2	17.2	17.2	16.9
25	16.0	15.9	15.9	15.9	15.8
26	17.3	17.4	17.3	17.3	17.3
27	27.3	27.3	27.3	27.3	27.2
28	174.5	174.5	174.4	174.4	174.4
29	29.2	29.2	29.2	29.1	29.2
30	19.2	19.2	19.1	19.1	19.1
Sugar (C-28)					
Glc′1	95.7	95.8	95.7	95.7	95.7
2	76.9	76.9	76.9	77.0	76.9
3	78.0	78.0	78.0	78.0	78.0
4	71.3	71.3	71.3	71.2	71.2
5	79.2	79.2	79.1	79.1	79.1
6	62.0	62.0	62.0	62.0	61.9
Rha (1→2) Glc′					
1	101.9	101.8	101.8	101.8	101.8
2	70.5	70.6	70.5	70.5	70.4
3	82.1	82.1	82.0	82.1	82.0
4	79.1	79.1	79.0	79.0	79.0
5	69.3	69.2	69.2	69.2	69.2
6	19.0	18.96	18.9	18.7	18.8
Ara (1→4) Rha					
1	111.1	111.1	111.1	111.0	111.0
2	84.6	84.6	84.5	84.4	84.4
3	78.5	78.5	78.5	78.4	78.4
4	85.4	85.5	85.4	85.4	85.4
5	62.6	62.6	62.6	62.5	62.5
Glc″ (1→3)Rha					
1	105.8	105.8	105.8	105.7	105.7
2	75.4	75.4	75.4	75.4	75.5
3	78.2	78.4	78.2	78.0	78.2
4	71.8	71.8	71.8	71.8	71.8
5	78.3	78.4	78.3	78.2	78.4
6	62.8	62.8	62.8	62.7	62.68

[a] Assignments based on HSQC and HMBC experiments.
[b] Measured at 150 MHz for **1** and **2** and 125 MHz for **3**.