

# A new ursane and a new oleanane triterpene acids from the whole plant of *Spermacoce latifolia*



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## ABSTRACT

A phytochemical study on the whole plant of *Spermacoce latifolia* led to the isolation of a new ursane triterpene acid, 3 $\beta$ ,6 $\beta$ ,23-trihydroxy-urs-12,20(30)-dien-28-oic acid (**1**), and a new oleanane triterpene acid, 3 $\beta$ ,6 $\beta$ ,29-trihydroxy-olean-12-en-28-oic acid (**2**), together with seven known triterpenic acids (**3–9**). Their structures were established on the basis of detailed spectroscopic analysis, including one- and two-dimensional NMR, ESI-MS and HR-ESI-MS techniques. All the compounds were isolated from *S. latifolia* for the first time. Compounds **3**, **5**, **6** and **9** were found to show *in vitro* growth inhibitory activity against three assayed human cancer cell lines MCF-7, NCI-H460 and HepG-2 with IC<sub>50</sub> values from 9.53 to 80.20 mM. Compounds **1** and **3–9** were further revealed to show significantly *in vitro*  $\alpha$ -glucosidase inhibitory activity with IC<sub>50</sub> values from 0.009 to 0.422 mM, most of which were more potent than the reference compound acarbose (IC<sub>50</sub> 0.409 mM).

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## 1. Introduction

The *Spermacoce* genus, belonging to the family Rubiaceae, comprises about 250–300 species widespread in tropical and subtropical America, Africa, Asia, and Europe (Dessein et al., 2006). Some species in this genus play an important role in traditional medicine, including the treatment for malaria, diarrheal and other digestive problems, fever, hemorrhage, urinary and respiratory infections, headache and skin diseases (Conserva and Ferreira, 2012). Previous phytochemical studies have revealed some structurally diverse chemicals from *Spermacoce* species, including alkaloids, iridoids, flavonoids, terpenoids and phenolic compounds, some of which showed important bioactivities (Zamora-Martinez and Pola, 1992; Moreira et al., 2010; Vieira et al., 1999). *Spermacoce latifolia* Aubl. (Syn: *Borreria latifolia* (Aubl.) K. Schum.), native to South America, is known as an exotic invasive plant in

many tropical and subtropical countries of the world, including China (Hong et al., 2008). It was reported that the root juice of this plant can be used to treat malaria (Pereira et al., 2006; Manandlar, 1995). So far, only a few iridoid glycosides and a diterpenoid have been reported from this plant (Kohei et al., 2002). As one part of our work on searching for potentially new and bioactive natural products from invasive plants in China (Xu et al., 2014; Zhou et al., 2013), we carried out a phytochemical study on the whole plant of *S. latifolia*, by which a new ursane and a new oleanane triterpene acids (**1** and **2**), along with seven known triterpenic acids (**3–9**) (Fig. 1) were obtained. Herein we report the isolation and structure elucidation of these compounds, as well as their cytotoxic and  $\alpha$ -glucosidase inhibitory activities.

## 2. Results and discussion

Compound **1** was obtained as a white amorphous powder with molecular formula C<sub>30</sub>H<sub>46</sub>O<sub>5</sub> as determined by HR-ESI-MS, *m/z* 485.3262 [M – H]<sup>–</sup> (calcd. for C<sub>30</sub>H<sub>45</sub>O<sub>5</sub> 485.3272), which requires eight degrees of unsaturation. The <sup>1</sup>H NMR spectrum of **1** (Table 1) showed signals readily recognized for four tertiary methyl groups

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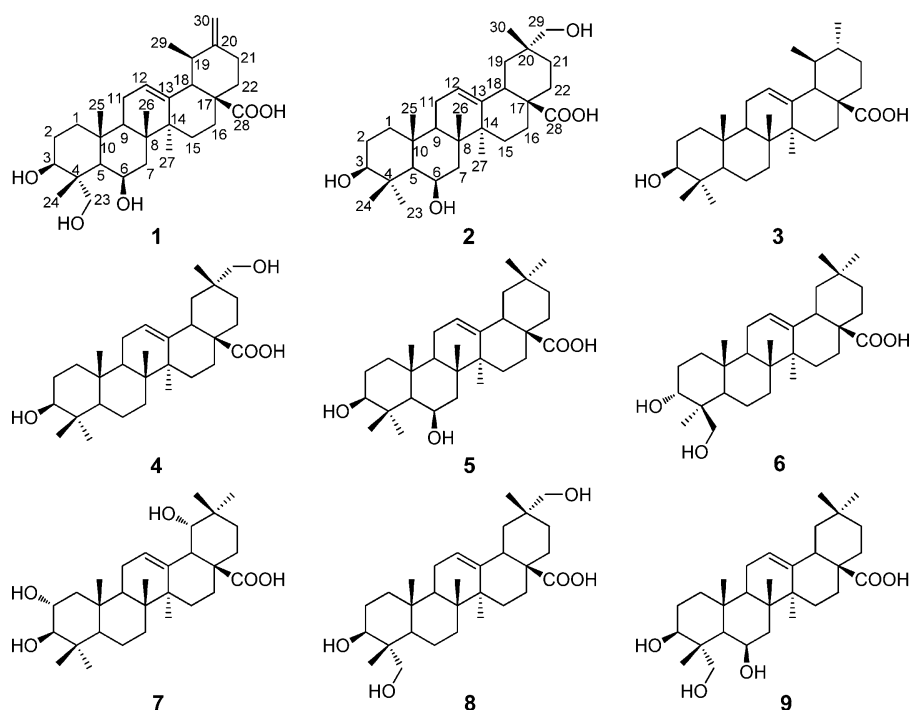


Fig. 1. Chemical structures of compounds 1–9.

at  $\delta_{\text{H}}$  1.34 (3H, s), 1.15 (3H, s), 1.11 (3H, s) and 1.06 (3H, s), and for a secondary methyl group at  $\delta_{\text{H}}$  1.02 (3H, d,  $J = 6.5$  Hz). Additionally, signals for an olefinic proton at  $\delta_{\text{H}}$  5.30 ( $t, J = 3.6$  Hz), a couple of vinyl protons at  $\delta_{\text{H}}$  4.68 (s) and 4.63 (s), two oxygenated methine protons at  $\delta_{\text{H}}$  4.39 (br s) and 3.56 (dd,  $J = 11.8, 4.3$  Hz), a pair of oxymethylene

protons at  $\delta_{\text{H}}$  3.60 and 3.47 (each d,  $J = 11.0$  Hz), and a doublet proton at  $\delta_{\text{H}}$  2.29 ( $J = 11.9$  Hz) were also observed. The  $^{13}\text{C}$  NMR and DEPT spectra (Table 1) of **1** supported the above analysis, which indicated the presence of five methyls ( $\delta_{\text{C}}$  14.1, 17.8, 19.0, 24.1 and 16.7), ten methylenes [including an oxygenated methylene at  $\delta_{\text{C}}$  66.7 (C-23) and an vinyl at  $\delta_{\text{C}}$  105.2 (C-30)], seven methines [including an olefinic methine at  $\delta_{\text{C}}$  127.5 (C-12) and two oxymethines at  $\delta_{\text{C}}$  73.7 (C-3) and 68.5 (C-6)], and eight quaternary carbons [including two olefinic quaternary carbons at  $\delta_{\text{C}}$  138.7 (C-13) and 154.5 (C-20), and a carboxyl carbon at  $\delta_{\text{C}}$  180.9 (C-28)]. These above findings accounted for three of the eight degrees of unsaturation, suggesting that **1** is a pentacyclic triterpenoid. Comparison of the NMR data (Table 1) of **1** with those of rhododendric acid A indicated that they were structurally closely related (Choi et al., 2012), with the only difference of the methylene group at C-6 in rhododendric acid A being replaced by a hydroxymethine group ( $\delta_{\text{C}}$  68.5) in **1**. This assignment was consistent with the molecular formula of **1** and in accord with the significant change of the chemical shift value for C-6 from  $\delta_{\text{C}}$  19.0 in rhododendric acid A to  $\delta_{\text{C}}$  68.5 in **1** (Choi et al., 2012). The location of the -OH group at C-6 was supported by significant HMBC correlations (Fig. 2) from  $\delta_{\text{H}}$  4.39 (H-6) to  $\delta_{\text{C}}$  44.2 (C-4),  $\delta_{\text{C}}$  49.2 (C-5) and  $\delta_{\text{C}}$  39.8 (C-8). The chemical shift values (Table 1) and HMBC correlations from  $\delta_{\text{H}}$  3.56 (H-3) to  $\delta_{\text{C}}$  41.8 (C-1), 44.2 (C-4), 66.7 (C-23) and 14.1 (C-24) supported that each of C-3 and C-23 was attached with a hydroxyl group. The coupling constant of H-3 ( $J_{\text{H-3}} = 11.8, 4.3$  Hz) and NOE correlations between  $\delta_{\text{H}}$  3.56 (H-3) and H-23 ( $\delta_{\text{H}}$  3.60 and 3.47), and between  $\delta_{\text{H}}$  1.06 (H-24) and  $\delta_{\text{H}}$  1.34 (H-25) (Fig. 3) supported the  $\beta$ -orientation of the hydroxyl group at C-3. The NOE correlation between  $\delta_{\text{H}}$  4.39 (H-6) and  $\delta_{\text{H}}$  1.18 (H-5) (Fig. 3) indicated the  $\beta$ -orientation of the hydroxyl group at C-6. In addition, The consistent NMR data (Table 1) from C-8 through C-20 and from C-26 through C-30 of **1** with those of rhododendric acid A (Choi et al., 2012) supported the same C/D/E ring system of **1** with rhododendric acid A, which was further supported by HMBC and NOESY spectral data of **1** (Figs. 2 and 3). Therefore, compound **1** was determined as 3 $\beta$ ,6 $\beta$ ,23-trihydroxy-urs-12,20(30)-dien-28-oic acid.

Compound **2** was obtained as white amorphous powder. Its HR-ESI-MS (negative mode) showed a pseudo-molecular ion peak

Table 1  
 $^1\text{H}$  and  $^{13}\text{C}$  NMR NMR data of compounds **1** and **2**.

No.	$\delta_{\text{C}}$ (1)	$\delta_{\text{H}}$ (1)	$\delta_{\text{C}}$ (2)	$\delta_{\text{H}}$ (2)
1	41.8 CH <sub>2</sub>	1.60 (m), 0.99 (m)	42.0 CH <sub>2</sub>	1.57 (m), 0.97 (m)
2	27.6 CH <sub>2</sub>	1.74 (m), 1.60 (m)	28.0 CH <sub>2</sub>	1.70 (m), 1.55 (m)
3	73.7 CH	3.56 (dd, 11.8, 4.3)	80.0 CH	3.08 (dd, 11.6, 3.9)
4	44.2 C	–	39.7 C	–
5	49.2 CH	1.18 (m)	57.1 CH	0.72 (br s)
6	68.5 CH	4.39 (br s)	68.7 CH	4.49 (br s)
7	40.4 CH <sub>2</sub>	1.84 (m), 1.63 (m)	41.6 CH <sub>2</sub>	1.67 (m), 1.51 (m)
8	39.8 C	–	40.7 C	–
9	49.2 CH	1.66 (m)	49.4 CH	1.61 (m)
10	37.3 C	–	37.6 C	–
11	24.4 CH <sub>2</sub>	2.04 (m), 2.00 (m)	24.5 CH <sub>2</sub>	2.00 (m), 1.93 (m)
12	127.5 CH	5.30 (t, 3.6)	124.0 CH	5.30 (t, 3.5)
13	138.7 C	–	144.4 C	–
14	43.8 C	–	43.3 C	–
15	29.2 CH <sub>2</sub>	2.01 (m), 1.15 (m)	28.8 CH <sub>2</sub>	1.84 (m), 1.08 (m)
16	25.4 CH <sub>2</sub>	2.23 (m), 1.75 (m)	24.1 CH <sub>2</sub>	1.61 (m)
17	48.7 C	–	47.9 C	–
18	56.6 CH	2.29 (d, 11.9)	41.9 CH	2.90 (dd, 13.7, 4.2)
19	38.5 CH	2.41 (m)	41.4 CH <sub>2</sub>	1.80 (m), 1.08 (m)
20	154.5 C	–	36.8 C	–
21	33.3 CH <sub>2</sub>	2.32 (m), 2.21 (m)	29.3 CH <sub>2</sub>	1.48 (m), 1.16 (m)
22	41.3 CH <sub>2</sub>	1.80 (m), 1.52 (m)	33.1 CH <sub>2</sub>	1.76 (m), 1.58 (m)
23	66.7 CH <sub>2</sub>	3.60 (d, 11.0), 3.47 (d, 11.0)	28.4 CH <sub>3</sub>	1.04 (s)
24	14.1 CH <sub>3</sub>	1.06 (s)	17.6 CH <sub>3</sub>	1.16 (s)
25	17.8 CH <sub>3</sub>	1.34 (s)	17.3 CH <sub>3</sub>	1.30 (s)
26	19.0 CH <sub>3</sub>	1.11 (s)	18.8 CH <sub>3</sub>	1.09 (s)
27	24.1 CH <sub>3</sub>	1.15 (s)	26.5 CH <sub>3</sub>	1.14 (s)
28	180.9 C	–	181.8 C	–
29	16.7 CH <sub>3</sub>	1.02 (d, 6.5)	74.4 CH <sub>2</sub>	3.19 (s)
30	105.2 CH <sub>2</sub>	4.68 (s), 4.63 (s)	19.5 CH <sub>3</sub>	0.94 (s)

Recorded in CD<sub>3</sub>OD;  $\delta$  in ppm and  $J$  in Hz.

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