

## Anti-inflammatory iridoids from the stems of *Cistanche deserticola* cultured in Tarim Desert

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**[ABSTRACT]** In order to determine the chemical constituents of *Cistanche deserticola* cultured in Tarim desert, a systematically phytochemical investigation was carried out. The constituents were isolated by silica gel, Sephadex LH-20, MCI gel, ODS column chromatography, and semi-preparative HPLC. Their structures were determined on the basis of MS and NMR spectroscopic analyses, by chemical methods, and/or comparison with literature data. The anti-inflammatory activities of the isolates were evaluated for their inhibitory effects on the lipopolysaccharide (LPS)-induced nitric oxide (NO) production in BV-2 mouse microglial cells. Nine iridoids were isolated and identified as cistadesertoside A (**1**), cistanin (**2**), cistachlorin (**3**), 6-deoxycatalpol (**4**), glucoside (**5**), kankanoside A (**6**), ajugol (**7**), bartsioside (**8**), and 8-*epi*-loganic acid (**9**). Compound **9** exhibited potent inhibition on the NO production with an IC<sub>50</sub> value being 5.2 μmol·L<sup>-1</sup>, comparable to the positive control quercetin (4.3 μmol·L<sup>-1</sup>). Compound **1** was a new iridoid, and compounds **5**, **6**, and **8** were isolated from this species for the first time.

**[KEY WORDS]** *Cistanche deserticola*; Iridoids; Structure elucidation; Anti-inflammatory activity

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### Introduction

*Cistanches* Herba (Roucongong in Chinese) belonging to the Orobanchaceae family, is mainly distributed in the North Africa, Arabia, and Asian countries [1]. As a well-known tonic in traditional Chinese medicine (TCM), the stems of *C. deserticola* and *C. tubulosa* have long been used in China and Japan for the treatment of kidney deficiency, female infertility, morbid leucorrhea, neurasthenia, and senile constipation [2-3]. Previous phytochemical investigations have

indicated the presence of phenylethanoid glycosides (PhGs), iridoids, lignans, and polysaccharides in the *Cistanche* species [4], and some of the isolates presented neuroprotective, hepatoprotective, anti-inflammatory, anti-bacterial, anti-viral, and antioxidant effects [5-6].

In the late 1990s, in order to protect Tazhong Oilfield and control the desert, the sand-fixation plant *Haloxylon ammodendron* (C. A. Mey.) Bunge, the host of *C. deserticola*, was introduced from the north to the south of Xinjiang, and large quantities of *C. deserticola* were cultured. The climate conditions and growth environment in the south are very different from that in the north of Xinjiang. Whether the chemical constituents of *C. deserticola* cultured in the southern Xinjiang vary or not is not clear. In order to determine the chemical constituents of *C. deserticola* cultured in Tarim Desert, a systematically phytochemical investigation was carried out in the present study. Herein, the isolation and structural elucidation of a new iridoid glycoside (**1**) together with eight known analogues (**2–9**) are reported, along with their anti-inflammatory activities.

### Results and Discussion

The 85% aqueous ethanol extract of the stems of *C. de*

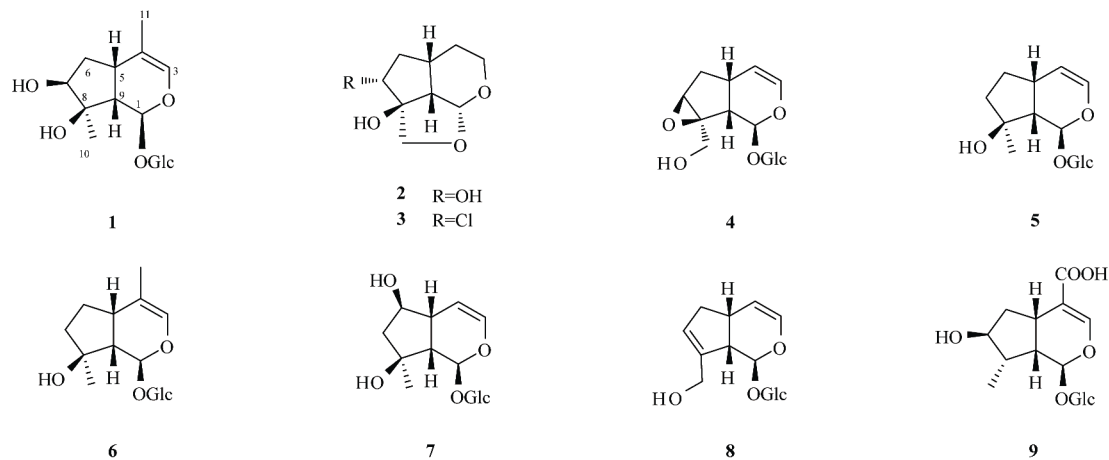
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Glc:  $\beta$ -D-glucopyranosyl

Fig. 1 Structures of compounds 1–9 from the stems of *C. deserticola*

*serticola* was suspended in H<sub>2</sub>O (10 L) and extracted with EtOAc (10 L  $\times$  3) and *n*-BuOH successively. The EtOAc and *n*-BuOH extracts were subjected to silica gel, Sephadex LH-20, MCI gel, and ODS column chromatography (CC), and semi-preparative HPLC to afford one new (**1**) and eight known iridoids (**2**–**9**) (Fig. 1).

Compound **1** was isolated as a white amorphous powder with negative optical rotation ( $[\alpha]_D^{20}$   $-118.0$ ,  $c$  0.1, MeOH). Its IR spectrum showed strong absorption bands at around 3 393  $\text{cm}^{-1}$  ascribable to the hydroxy groups. It has a molecular formula of C<sub>16</sub>H<sub>26</sub>O<sub>9</sub> determined by the quasi-molecular ion at  $m/z$  385.148 5 [M + Na]<sup>+</sup> (Calcd. for C<sub>16</sub>H<sub>26</sub>O<sub>9</sub>Na, 385.146 9) and  $m/z$  401.122 8 [M + K]<sup>+</sup> (Calcd. for C<sub>16</sub>H<sub>26</sub>O<sub>9</sub>K, 401.120 8) in the (+)-HR-ESIMS and supported by the <sup>13</sup>C NMR data (Table 1), indicating 4 degrees of unsaturation. Acid hydrolysis of compound **1** with 2 mol·L<sup>-1</sup> of trifluoroacetic acid afforded D-glucose, which was identified by analysis of its silane derivatives by GC analysis. The relative configuration at the anomeric center of the glucosyl was assigned as  $\beta$  from the coupling constant of 8.0 Hz. The <sup>1</sup>H and <sup>13</sup>C NMR data (Table 1) of compound **1**, which were unambiguously assigned by various 2D NMR experiments, showed signals assignable to two methyls at  $\delta_{\text{H}}$  1.23 (3H, s, H-10) and 1.52 (3H, br s, H-11), one methylene at  $\delta_{\text{H}}$  1.70 (1H, dt,  $J = 13.5, 5.5$  Hz, H-6 $\alpha$ ), and 1.92–1.98 (1H, m, H-6 $\beta$ ), three methines at  $\delta_{\text{H}}$  2.47 (1H, br d,  $J = 10.5$  Hz, H-9), 2.67–2.72 (1H, m, H-5), and 3.62 (1H, t-like,  $J = 5.5$  Hz, H-7), and an  $\alpha, \beta$ -unsaturated acetal group  $\delta_{\text{H}}$  5.40 (1H, d,  $J = 2.0$  Hz, H-1), 5.92 (1H, br s, H-3), together with a  $\beta$ -D-glucopyranosyl anomeric proton at  $\delta_{\text{H}}$  4.61 (1H, d,  $J = 8.0$  Hz, H-1'). The <sup>1</sup>H and <sup>13</sup>C NMR data of compound **1** were very similar to those of kankanoside A (**6**) except for the obvious deshielded signals of H-7 [ $\delta_{\text{H}}$  3.62 (1H, t-like,  $J = 5.5$  Hz)] and C-7 ( $\delta_{\text{C}}$  79.8), indicating the hydroxylation of C-7 position [7]. This deduction was supported by analyses of the <sup>1</sup>H-<sup>1</sup>H COSY of H-1/H-9/H-5/H-6/H-7 and of the HMBC correlations from H-7 to C-5, C-6, C-8, C-9, and C-10 (Fig. 2). The other HMBC

correlations from H-1 to C-1', H-10 to C-7, C-8 and C-9, and from H-11 to C-3, C-4, and C-5 also supported the above elucidation.

The stereochemistry of compound **1** was determined by comparison of the chemical shifts and coupling constants with literature data and by analysis of the NOESY spectrum. The relationship of H-5 to H-9 was determined as *cis* from their coupling constant (10.5 Hz) [8–9]. For the most natural iridoids, the configurations of C-1-OH, H-5, and H-9 are  $\beta$ , and the <sup>13</sup>C NMR chemical shifts of C-1 and C-1' are generally at  $\delta_{\text{C}}$  93–98 and 97–101, respectively. While, for those of  $\alpha$ -configuration, the resonances of C-1 and C-1' are, on average, 5–6 downfield shifted [10–11]. The <sup>13</sup>C NMR data of com-

Table 1 <sup>1</sup>H NMR (500 MHz) and <sup>13</sup>C NMR (125 MHz) data of **1** ( $\delta$  in ppm,  $J$  in Hz)

Position	<b>1</b> <sup>a</sup>	
	$\delta_{\text{H}}$	$\delta_{\text{C}}$
1	5.40 (d, $J = 2.0$ )	94.1
3	5.92 (s)	134.2
4		115.8
5	2.67–2.72 (m)	32.0
6	1.70 (dt, $J = 13.5, 5.5$ ) 1.92–1.98 (m)	36.1
7	3.62 (t-like, $J = 5.5$ )	79.8
8		79.4
9	2.47 (br d, $J = 10.5$ )	49.8
10	1.23 (s)	22.2
11	1.52 (br s)	16.3
1'	4.61 (d, $J = 8.0$ )	99.5
2'	3.18 (dd, $J = 8.0, 9.0$ )	75.0
3'	3.36–3.38 (m)	78.2
4'	3.27 (dd, $J = 10.0, 7.5$ )	71.9
5'	3.35–3.36 (m)	78.3
6'	3.66 (dd, $J = 11.5, 5.5$ ) 3.88 (br d, $J = 11.5$ )	63.0

<sup>a</sup> Measured in CD<sub>3</sub>OD

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