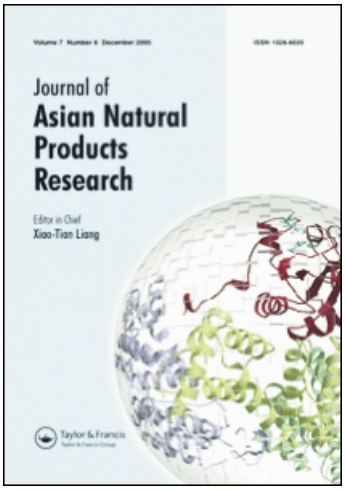

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Two new alkyl glycosides from *Clerodendranthus spicatus*

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Two new alkyl glycosides from *Clerodendranthus spicatus*

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Two new alkyl glycosides, 3-*O*-β-D-apifuranosyl-(1 → 6)-*O*-β-D-glucopyranosyl-(3*S*)-oct-1-*en*-3-ol (**1**, clerspide A) and 3-*O*-β-D-apifuranosyl-(1 → 6)-[β-D-xylopyranosyl-(1 → 2)]-*O*-β-D-glucopyranosyl-(3*S*)-oct-1-*en*-3-ol (**2**, clerspide B), have been isolated from the whole plants of *Clerodendranthus spicatus* (Labiatae). Their structures were established on the basis of spectroscopic analyses and chemical method.

Keywords: *Clerodendranthus spicatus*; Labiatae; alkyl glycoside; clerspides A and B

1. Introduction

Clerodendranthus spicatus is a herb widely distributed in India, Thailand, Indonesia, and the southeast of China. The whole plants of *C. spicatus* (Labiatae) have been used in Chinese folk medicine for the treatment of chronic nephritis [1]. However, little chemical investigation has been performed on *C. spicatus* [2]. In an effort to find new bioactive natural products from Chinese herbal medicines, constituents of *C. spicatus* were studied systematically. We herein report the isolation and structural characterization of two new alkyl glycosides, clerspides A (**1**) and B (**2**) (Figure 1), from the titled plant.

2. Results and discussion

Compound **1** was obtained as colorless gum with a molecular formula of $C_{19}H_{34}O_{10}$ according to its HRESIMS (*m/z* 445.2038, $[M + Na]^+$) and NMR analyses. In the ^{13}C NMR spectrum of **1**, 19 carbon signals including one methyl, eight methylenes, nine methines (one for sp^2 methine), and one quaternary carbon were observed. Two anomeric carbon signals at δ_C 103.7 (d) and 111.3 (d) indicated the existence of two sugar moieties in the structure of **1**. Acidic hydrolysis of **1** afforded glucose and apiose as its sugar moiety by co-TLC with authentic samples. Preliminary analyses of $^1H-^1H$ COSY and HSQC spectra revealed the fragment C-1–C-2–C-3–C-4–C-5–C-6–C-7–C-8– in its structure. In the HMBC spectrum of **1**, $^{13}C-^1H$ long-range correlations were observed at C-3/H-1, H-1′; C-1′/H-3; C-6′/H-1″; C-1″/H-6′; and C-4″/H-1″ (Figure 2). Thus, the planar structure of **1** can be established. The anomeric proton signal at δ_H 4.28 (1H, d, $J = 7.6$ Hz) revealed the glucose unit in the β-glycosidic linkage, and the apiose unit was also in the β-configuration from the ^{13}C NMR chemical shifts of apiose unit [**1**: 111.3 (C-1″), 78.5 (C-2″), 81.1 (C-3″), 75.5 (C-4″), 66.2 (C-5″); literature data: 110.9 (C-1″), 78.1 (C-2″), 80.5 (C-3″), 75.1 (C-4″), 65.8 (C-5″)] [3]. Enzymatic hydrolysis of **1** yielded oct-1-*en*-3-ol (**1a**). The absolute configuration of **1a** was identified to be 3*S* by comparing its optical rotation value of the aglycone with that reported in the literature {**1a**: $[\alpha]_D^{20} + 7.0$ (*c* 0.10,

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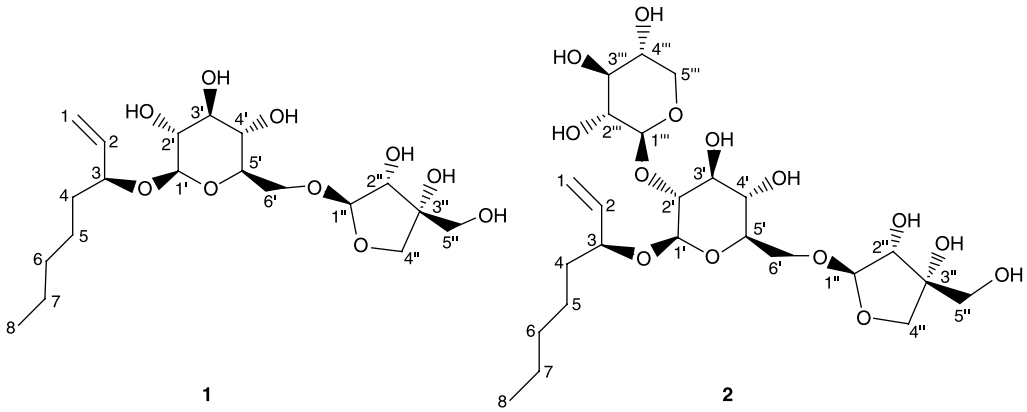

Figure 1. Structures of clerspides A (**1**) and B (**2**).

chloroform); (3*S*)-oct-1-*en*-3-ol: $[\alpha]_D^{19} + 10.1$ (*c* 0.67, chloroform)} [4]. The structure of **1** was finally characterized as 3-*O*-β-D-apifuranosyl-(1 → 6)-*O*-β-D-glucopyranosyl-(3*S*)-oct-1-*en*-3-ol. It is a new compound, named as clerspide A.

Compound **2** was obtained as colorless gum with a molecular formula of $C_{24}H_{42}O_{14}$ according to its HRESIMS (*m/z* 577.2431, $[M + Na]^+$) and NMR analyses. The IR spectrum of **2** exhibited strong absorption bands of hydroxyl (3400 cm^{-1}) and the double bond (1602 and 1516 cm^{-1}). Its ^1H and ^{13}C NMR spectra were very similar to those of **1** except one more set of carbohydrate signals, which indicated it to be an oct-1-*en*-3-yl glycoside with one more five-carbon sugar unit, compared with **1**. Acidic hydrolysis of **2** afforded glucose, apiose, and xylose as its sugar moiety by co-TLC with authentic samples. The planar structure of **2** was established on the basis of its HMBC spectrum, in which $^{13}C-^1H$ long-range correlation signals were observed at C-3/H-1, H-1′; C-1′/H-3; C-2′/H-1‴; C-6′/H-1″; C-1″/H-6′; and C-1‴/H-2′ (Figure 2). The two anomeric proton signals at δ_H 4.39 (1H, d, $J = 7.7$ Hz) and δ_H 4.49 (1H, d, $J = 7.2$ Hz) revealed the glucose and xylose moieties to be both in β-glycosidic linkage, while the apiose unit was identified to be in β-configuration according to the ^{13}C NMR chemical shifts of apiose moiety [**2**: 111.3 (C-1″), 78.4 (C-2″), 81.1 (C-3″), 75.4 (C-4″),

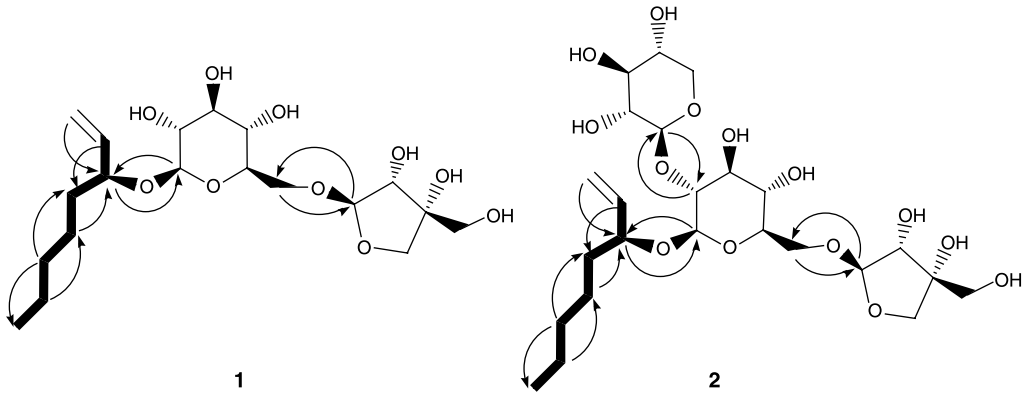

Figure 2. Key $^1H-^1H$ COSY (▬) and HMBC correlations of **1** and **2**.

66.0 (C-5″); literature data: 110.9 (C-1″), 78.1 (C-2″), 80.5 (C-3″), 75.1 (C-4″), 65.8 (C-5″)] [3]. Enzymatic hydrolysis of **2** yielded oct-1-*en*-3-ol. The absolute configuration of the aglycone of **2** was also determined to be 3*S* by comparing its optical rotation value with that in the literature [4]. Therefore, compound **2** was identified to be 3-*O*-β-D-apifuranosyl-(1 → 6)-[β-D-xylopyranosyl-(1 → 2)]-*O*-β-D-glucopyranosyl-(3*S*)-oct-1-*en*-3-ol. It is also a new compound, named as clerspide B.

3. Experimental

3.1 General experimental procedures

Optical rotations were measured with a Perkin-Elmer 241MC polarimeter. IR spectra were recorded using a Perkin-Elmer 577 spectrometer. LRESIMS were measured using a Finnigan LCQ-DECA instrument, HRESIMS data were obtained on a Mariner spectrometer, and LREIMS were obtained on a MAT-95 spectrometer. NMR spectra were run on Bruker AM 400 and Bruker AM 300 spectrometers with TMS as an internal standard. Preparative HPLC was carried out using a Varian SD-1 instrument, equipped with a Merck NW25 C18 column (10 μm, 20 mm × 250 mm), and a ProStar 320 UV/vis Detector. Column chromatographic separations were carried out using silica gel H60 (300–400 mesh) and Sephadex LH-20 (Pharmacia Biotech AB, Uppsala, Sweden) as packing materials. HSGF254 silica gel TLC plates (Yantai Chemical Industrial Institute, Yantai, China) and RP-18 WF_{254} TLC plates (Merck, Whitehouse Station, NJ, USA) were used for analytical TLC.

3.2 Plant material

The whole plants of *C. spicatus* were collected in the suburb of Guangzhou, Guangdong province, China, in May 2003, and identified by Professor Zexian Li of South China Institute of Botany, Chinese Academy of Sciences. A voucher specimen (No. SIMMW0309) is deposited in the herbarium of Shanghai Institute of Materia Medica, Chinese Academy of Sciences.

3.3 Extraction and isolation

Powdered air-dried whole plants of *C. spicatus* (3 kg) were percolated with 95% EtOH for three times (10 l × 3) at room temperature. The filtrate was concentrated to dryness *in vacuo* and then suspended in 20% EtOH. After the filtration of the precipitated chlorophyll and the evaporation of EtOH from the filtrate, the aqueous residue was extracted with chloroform and *n*-butanol (1 l × 3) successively to give chloroform fraction (6.5 g) and *n*-butanol fraction (40.5 g), respectively. The *n*-butanol extract (40.5 g) was separated by a silica gel H60 column eluted with chloroform–methanol gradient to give fractions B1 (3.65 g), B2 (5.90 g), B3 (6.62 g), B4 (6.15 g), and B5 (8.80 g). Fraction B4 (6.15 g) was subjected to a Sephadex LH-20 column eluted with 95% ethanol to give fractions B41 (150 mg), B42 (750 mg), B43 (3.75 g), and B44 (1.12 g). Fraction B42 (750 mg) was purified over a preparative HPLC column (2 cm i.d. × 25 cm, RP-18), eluted with a methanol–water gradient (20–50%, 10 ml/min, 1–90 min, 900 ml) to afford **2** (between 350 and 390 ml, 22.8 mg) and **1** (between 440 and 470 ml, 25.3 mg).

3.3.1 Clerspide A (*1*)

Colorless gum; $[\alpha]_D^{20}$ − 34.0 (*c* 0.24, methanol); IR (KBr) ν_{max} (cm^{-1}): 3442, 2931, 2092, 1648, 1384, 1054; ^1H and ^{13}C NMR spectral data: see Table 1; LRESIMS (positive-ion mode): *m/z* 445.2 $[M + Na]^+$; HRESIMS (positive-ion mode): *m/z* 445.2038 $[M + Na]^+$ (calcd for $C_{19}H_{34}O_{10}Na$, 445.2050).

3.3.2 Clerspide B (*2*)

Colorless gum; $[\alpha]_D^{20}$ − 40.5 (*c* 0.34, methanol); IR (KBr) ν_{max} (cm^{-1}): 3423, 2975, 2530, 2235, 2077, 1649, 1448, 1051; ^1H and

Table 1. ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectral data of **1** and **2** (CD_3OD).

	1		**2**	
No.	^{13}C	^{1}H	^{13}C	^{1}H
1	116.8, CH_2	a 5.10, dd (1.1, 17.5) b 5.08, dd (1.2, 10.1)	117.3, CH_2	a 5.10, dd (1.1, 17.5) b 5.07 dd (1.2, 10.2)
2	141.3, CH	5.82, ddd (6.4, 10.1, 17.5)	141.3, CH	5.81, ddd (6.4, 10.2, 17.5)
3	83.6, CH	4.08, dt (6.4, 13.0)	84.5, CH	4.06, dt (6.4, 13.0)
4	36.2, CH_2	1.65, m 1.50, m	36.3, CH_2	1.65, m 1.48, m
5	26.2, CH_2	1.40, m	26.2, CH_2	1.38, m
6	33.5, CH_2	1.25, m	33.6, CH_2	1.29, m
7	24.2, CH_2	1.32, m	24.2, CH_2	1.33, m
8	14.9, CH_3	0.90, t (6.9)	14.9, CH_3	0.95, t (7.2)
1′	103.7, CH	4.28, d (7.6)	102.3, CH	4.39, d (7.7)
2′	75.8, CH	3.21, dd (7.6, 9.1)	84.5, CH	3.40, dd (7.7, 9.0)
3′	78.6, CH	3.35, dd (9.1, 9.5)	78.5, CH	3.55, dd (9.0, 9.5)
4′	72.2, CH	3.30, dd (9.0, 9.5)	72.2, CH	3.29, dd (9.5, 8.9)
5′	77.3, CH	3.31, m	77.2, CH	3.30, m
6′	68.9, CH_2	3.90, dd (2.5, 11.0) 3.55, dd (6.0, 11.0)	68.8, CH_2	3.90, dd (2.6, 11.5) 3.52, dd (6.1, 11.5)
1″	111.3, CH	5.00, d (2.1)	111.3, CH	5.00, d (2.1)
2″	78.5, CH	3.89, d (2.0)	78.4, CH	3.85, d (2.0)
3″	81.1, C		81.1, C	
4″	75.5, CH_2	3.95, d (9.8) 3.75, d (9.8)	75.4, CH_2	3.94, d (9.7) 3.74, d (9.7)
5″	66.2, CH_2	3.57, s	66.0, CH_2	3.59, s
1‴			106.9, CH	4.49, d (7.2)
2‴			76.5, CH	3.20, m
3‴			77.9, CH	3.34, m
4‴			71.9, CH	3.46, m
5‴			67.8, CH_2	3.84, m 3.16, m

^{13}C NMR spectral data: see Table 1; LRESIMS (positive-ion mode): *m/z* 577.2 $[M + Na]^+$; HRESIMS (positive-ion mode): *m/z* 577.2431 $[M + Na]^+$ (calcd for $C_{24}H_{42}O_{14}Na$, 577.2472).

3.3.3 *Oct-1*-en-*3-ol* (***1a***)

Colorless oil; $[\alpha]_D^{20} + 7.0$ (*c* 0.10, chloroform); ^{1}H NMR ($CDCl_3$, 300 MHz): δ 5.20 (1H, dd, $J = 17.2$, 1.0 Hz, H-1a), 5.10 (1H, dd, $J = 1.1$, 10.1 Hz, H-1b), 5.80 (1H, ddd, $J = 6.5$, 10.0, 17.1 Hz, H-2), 4.11 (1H, dt, $J = 6.5$, 12.8 Hz, H-3), 1.20–1.50 (8H, m, H-4–H-7), 0.91 (3H, t, $J = 7.0$ Hz, H-8); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 114.2 (C-1), 141.5 (C-2), 73.0 (C-3), 36.9 (C-4), 25.0 (C-5), 31.7 (C-6), 22.5 (C-7), 13.8 (C-8); LREIMS: *m/z* 128 $[M]^+$.

3.4 *Acidic hydrolysis of compounds 1 and 2*

A solution of **1** (5 mg) dissolved in 50% methanol (5 ml) containing 5% HCl was heated in a boiling water bath for 3 h. After cooling, the reaction mixtures were neutralized with 10% Na_2CO_3 and then extracted with EtOAc. The aqueous residue was checked by TLC together with authentic sugar samples ($CHCl_3$–*n*-BuOH–HOAc–H_2O, 1.5:6:1:1, glucose, $R_f = 0.33$; apiose, $R_f = 0.45$).

Compound **2** (10 mg) was hydrolyzed in the same way as that of **1**, and the aqueous residue was checked by TLC together with authentic sugar samples ($CHCl_3$–*n*-BuOH–HOAc–H_2O, 1.5:6:1:1, glucose, $R_f = 0.33$; apiose, $R_f = 0.45$; xylose, $R_f = 0.51$).

3.5 Enzymatic hydrolysis of compounds 1 and 2

Compound **1** (15 mg) and β-cellulase (40 mg; Lizhu Dongfeng Bio-Tech Co. Ltd, Shanghai, China) were dissolved in 10 ml of 20% MeOH and kept at 37°C for 3 days. The product was extracted with EtOAc, and the extract was evaporated and chromatographed over a Sephadex LH-20 column with EtOH as eluent to give **1a** (2.1 mg), which was identified as 1-octen-3-ol by comparison of its ^1H and ^{13}C NMR spectra with data in the literature [5], and its specific rotation was $[\alpha]_D^{19} + 7.0$ (*c* 0.10, chloroform). Compound **2** (15 mg) was hydrolyzed in the same way above to give 1-octen-3-ol as its aglycone (1.8 mg), and its specific rotation was $[\alpha]_D^{20} + 9.0$ (*c* 0.09, chloroform) [4].

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