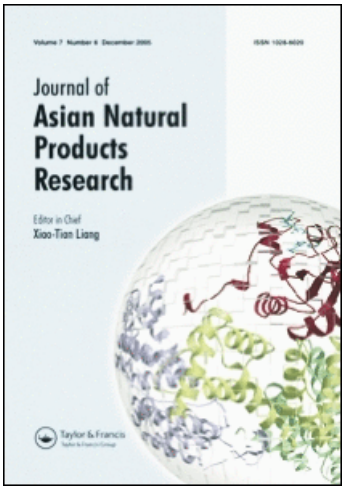

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Stilbene *C*-glucosides from *Cissus repens*

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Four new stilbene *C*-glucosides, namely *trans*-3-*O*-methyl-resveratrol-2-*C*-β-glucoside (**1**), *cis*-3-*O*-methyl-resveratrol-2-*C*-β-glucoside (**2**), *trans*-3-*O*-methyl-resveratrol-2-(2-*p*-coumaric)-*C*-β-glucoside (cissuside A) (**3**), and *trans*-3-*O*-methyl-resveratrol-2-(3-*p*-coumaric)-*C*-β-glucoside (cissuside B) (**4**), were isolated from the aerial parts of *Cissus repens*, along with known *trans*-resveratrol (**5**), *trans*-resveratrol-2-*C*-β-glucoside (**6**) and *cis*-resveratrol-2-*C*-β-glucoside (**7**). Their structures were established by spectroscopic methods. Stilbene *C*-glucosides were found in the genus *Cissus* for the first time.

Keywords: *Cissus repens*; Vitaceae; Stilbenes; *C*-Glucosides; Resveratrol; Cissuside

1. Introduction

Cissus repens Lamk. belongs to the family Vitaceae and is distributed in Southern China and Taiwan, Guizhou and Yunnan Province. The roots and stems of *C. repens* are used for snake bites, rheumatic pains and carbuncles in Chinese folk medicine, and the stems are also applied to the treatment of nephritis, long-term coughs and diarrhoea [1].

We are interested in the constituents of *C. repens*, and isolated a series of stilbene derivatives from the aerial parts of the plant, including four new stilbene *C*-glucosides (figure 1), namely *trans*-3-*O*-methyl-resveratrol-2-*C*-β-glucoside (**1**), *cis*-3-*O*-methyl-resveratrol-2-*C*-β-glucoside (**2**), *trans*-3-*O*-methyl-resveratrol-2-(2-*p*-coumaric)-*C*-β-glucoside (cissuside A) (**3**), and *trans*-3-*O*-methyl-resveratrol-2-(3-*p*-coumaric)-*C*-β-glucoside (cissuside B) (**4**), along with known *trans*-resveratrol (**5**) [2], *trans*-resveratrol-2-*C*-β-glucoside (**6**) [3] and *cis*-resveratrol-2-*C*-β-glucoside (**7**) [4]. Stilbene *C*-glucosides were found in the genus *Cissus* for the first time. Herein, we report the structural elucidation of the new compounds.

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2. Results and discussion

Compound **1** was obtained as a white amorphous powder and its molecular formula was deduced as $C_{21}H_{24}O_8$ by the ion peak at *m/z* 403.1396 $[M - H]^-$ in the HRESI-MS. The IR spectrum of **1** showed absorptions for hydroxyl group (3406 cm^{-1}) and aromatic group (1602 and 1513 cm^{-1}). In the ^1H NMR spectrum of **1**, the signals at δ 7.28 (d, 2H, $J = 8.3$ Hz, H-2′, 6′) and 6.68 (d, 2H, $J = 8.3$ Hz, H-3′, 5′) were owing to the existence of a 4-hydroxyphenyl group. Moreover, the signals at δ 7.80 (d, 1H, $J = 16.0$ Hz, H-7) and 6.71 (d, 1H, $J = 16.0$ Hz, H-8) were the characteristic of *trans* olefinic bonds. The spectral data of δ_H 4.97 (d, 1H, $J = 9.9$ Hz) and δ_C 81.8 (d), 80.2 (d), 75.7 (d), 74.7 (d), 71.7 (d), 62.8 (t) showed the presence of a *C*-β-glucosyl moiety [3]. Compound **1** was a methylated derivative of *trans*-resveratrol-2-*C*-β-glucoside by comparison of the ^1H NMR and ^{13}C NMR data of **1** with those in the literature [3,4]. The methoxyl was located at C-3 by the HMBC spectrum which displayed the cross peak between the methyl proton (δ_H 3.65) and the aromatic carbon (δ_C 160.8, C-3). Therefore, the structure of **1** was concluded to be *trans*-3-*O*-methyl-resveratrol-2-*C*-β-glucoside.

Compound **2** was obtained as a white amorphous powder and its molecular formula was deduced as $C_{21}H_{24}O_8$ by the ion peak at *m/z* 427.1372 $[M + Na]^+$ in the HRESI-MS. The IR spectrum of **2** showed absorptions for hydroxyl group (3406 cm^{-1}) and aromatic group (1603 and 1513 cm^{-1}). In the ^1H NMR spectrum of **2**, the signals at δ 7.08 (d, 2H, $J = 8.6$ Hz, H-2′, 6′) and 6.61 (d, 2H, $J = 8.6$ Hz, H-3′, 5′) were owing to the existence of a 4-hydroxyphenyl group. Unlike **1**, the signals at δ 6.76 (d, 1H, $J = 12.0$ Hz, H-8) and 6.41 (d, 1H, $J = 12.0$ Hz, H-7) were the characteristic of *cis* olefinic bonds. Compound **2** was a methylated derivative of *cis*-resveratrol-2-*C*-β-glucoside by comparison of the ^1H NMR and ^{13}C NMR data of **2** with those in the literature [4]. The methoxyl was located at C-3 by the HMBC spectrum which displayed the cross peak between the methyl proton (δ_H 3.74) and the aromatic carbon (δ_C 160.8, C-3). So, the structure of **2** was determined as *cis*-3-*O*-methyl-resveratrol-2-*C*-β-glucoside.

Compound **3** was obtained as a white amorphous powder and its molecular formula was deduced as $C_{30}H_{30}O_{10}$ by the ion peak at *m/z* 573.1755 $[M + Na]^+$ in the HRESI-MS. The IR spectrum of **3** showed absorptions for hydroxyl group (3418 cm^{-1}), carbonyl (1675 cm^{-1}) and aromatic group (1603 and 1513 cm^{-1}). In the ^1H NMR spectrum of **3**, the signals at δ7.41 (d, 2H, $J = 8.4$ Hz, H-2′, 6′), 6.77 (d, 2H, $J = 8.4$ Hz, H-3′, 5′), 7.55 (d, 2H, $J = 8.1$ Hz, H-2‴, 6‴) and 6.78 (d, 2H, $J = 8.1$ Hz, H-3‴, 5‴) were owing to the existence of two 4-hydroxyphenyl groups. The signals at δ 7.94 (d, 1H, $J = 16.2$ Hz, H-7), 6.78 (d, 1H, $J = 16.2$ Hz, H-8), 7.41 (d, 1H, $J = 16.0$ Hz, H-7‴), 6.05 (d, 1H, $J = 16.0$ Hz, H-8‴) showed the presence of two *trans* olefinic bonds in **3**. Comparison of the NMR data of **3** with those of **1** showed the presence of a *trans*-3-*O*-methyl-resveratrol-2-*C*-β-glucoside moiety in **3**. The remaining moiety contained a carbonyl, a *trans* olefinic bond and a 4-hydroxyphenyl group, which indicated that **3** bore a *p*-coumaric group. The linkage of the *p*-coumaric substituent to 2″-OH was established by the significant downfield shift of H-2″ (δ 5.35) of the glucose. This was further substantiated by the HMBC spectrum (figure 2), in which H-2″ was correlated to the ester carbonyl carbon (δ_C 167.8, C-9‴). Thus, the structure of **3** (cissuside A) was elucidated as *trans*-3-*O*-methyl-resveratrol-2-(2-*p*-coumaric)-*C*-β-glucoside.

Compound **4** was obtained as a white amorphous powder and its molecular formula was deduced as $C_{30}H_{30}O_{10}$ by the ion peak at *m/z* 573.1748 $[M + Na]^+$ in the HRESI-MS. The IR spectrum of **4** showed absorptions for hydroxyl group (3423 cm^{-1}), carbonyl (1690 cm^{-1}) and aromatic group (1603 and 1513 cm^{-1}). In the ^1H NMR spectrum of **4**, the signals at δ 7.40

(d, 2H, $J = 8.4$ Hz, H-2′, 6′), 6.77 (d, 2H, $J = 8.4$ Hz, H-3′, 5′), 7.37 (d, 2H, $J = 8.1$ Hz, H-2‴, 6‴) and 6.78 (d, 2H, $J = 8.1$ Hz, H-3‴, 5‴) were owing to the presence of two 4-hydroxyphenyl groups. The signals at δ 7.90 (d, 1H, $J = 16.2$ Hz, H-7), 6.79 (d, 1H, $J = 16.2$ Hz, H-8), 7.57 (d, 1H, $J = 16.0$ Hz, H-7‴), 6.37 (d, 1H, $J = 16.0$ Hz, H-8‴) showed the presence of two *trans* olefin bonds in **4**. Compound **4** was an analogue of **3** by comparison of the ^{1}H NMR and ^{13}C NMR data of **4** with those of **3**. However, the *p*-coumaric group of four was located at C-3″—OH by the significant downfield shift of H-3″ (δ 5.11) of the glucose and the HMBC spectrum (figure 2) which displayed the cross peak between H-3″ and the carbonyl carbon (δ_C 169.4, C-9‴). Accordingly, the structure of **4** (cissuside B) was concluded to be *trans*-3-*O*-methyl-resveratrol-2-(3-*p*-coumaric)-*C*-β-glucoside.

The structures of the known compounds (**5–7**) were identified by comparison of their spectral data with those reported in the literature.

The alcohol extract of *C. repens* and compounds **1** and **3** were tested for activity against Tobacco mosaic virus (TMV) by the conventional half-leaf method, but all of these samples were inactive.

3. Experimental

3.1 General experimental procedures

Column chromatography was performed over silica gel (200–300 and 300–400 mesh) and TLC on precoated plates with silica gel F_{254} (Qingdao Marine Chemical Ltd., China). 1D and 2D NMR spectra were recorded on Bruker AM-400 and DRX-500 spectrometers. MS were measured on a VG Auto Spec-3000 mass spectrometer. Optical rotations were determined on a Jasco DIP370 digital polarimeter. IR spectra were recorded on a Bio-Rad FTS-135 infrared spectrophotometer.

3.2 Plant material

The aerial parts of *Cissus repens* were collected from Xishuangbanna, Yunnan Province of China, in August 2004. The plant was identified by Professor De-Ding Tao (Kunming Institute of Botany, Chinese Academy of Sciences), and a voucher specimen is deposited at the State Key Laboratory of Phytochemistry and Plant Resources in West China, Kunming Institute of Botany, Chinese Academy of Sciences.

3.3 Extraction and isolation

The aerial parts of *Cissus repens* (3.0 kg) were extracted thrice with EtOH (95%). The solvent was evaporated to give a residue, which was suspended in water and participated with petrol, EtOAc and n-BuOH successively. The EtOAc extract (23.8 g) was fractionated by silica gel column chromatography ($CHCl_3$/MeOH, 10:1, 5:1 and 3:1) to afford four major fractions (I–IV).

Fraction I was purified by silica gel ($CHCl_3$/acetone, 3:1) and Sephadex LH-20 (acetone) column chromatography to give **5** (50 mg). Fraction II was purified by repeated silica gel column chromatography ($CHCl_3$/acetone, 1:1; petrol/EtOAc, 1:5) to give **3** (1 500 mg) and **4** (15 mg). Fraction III was purified by RP-18 (MeOH/H_2O, 30:70) and Sephadex LH-20 (MeOH) column chromatography to afford **1** (300 mg) and **2** (30 mg). Fraction IV was

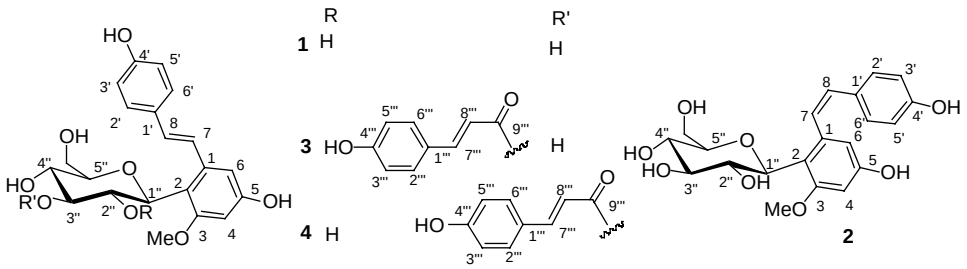

Figure 1. Structures of **1**–**4**.

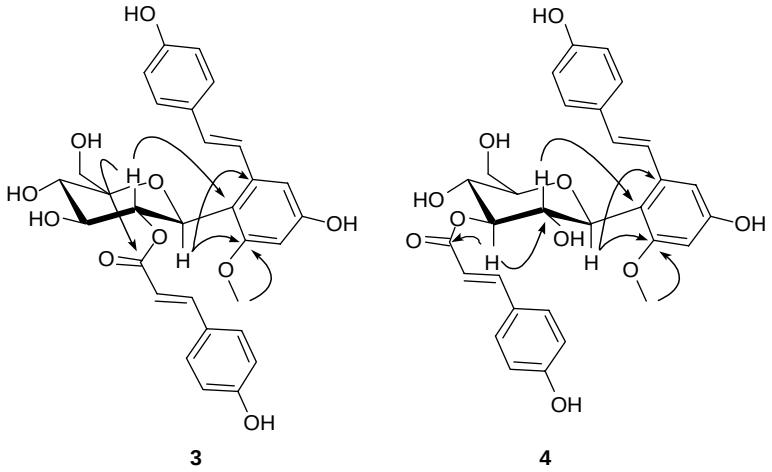

Figure 2. Significant HMBC correlations for **3** and **4**.

purified by repeated silica gel ($CHCl_3$/MeOH, 4:1) and Sephadex LH-20 (MeOH) column chromatography to yield **6** (300 mg) and **7** (30 mg).

3.3.1 *Trans*-3-*O*-methyl-resveratrol-2-*C*-β-glucoside (1). A white amorphous powder (MeOH); $[\alpha]_D^{23}$ + 52.2 (MeOH, *c* 0.83); UV λ_{max} (MeOH, nm, log ε): 305 (4.25), 220 (4.41); IR ν_{max} (KBr, cm^{-1}): 3406, 1602, 1513, 1079, 1018; ESI-MS *m/z* $[M - H]^-$ 403; HRESI-MS *m/z* $[M - H]^-$ 403.1396 (calcd for $C_{21}H_{23}O_8$, 403.1392); ^1H NMR and ^{13}C NMR, see table 1.

3.3.2 *cis*-3-*O*-Methyl-resveratrol-2-*C*-β-glucoside (2). A white amorphous powder (MeOH); $[\alpha]_D^{23}$ + 93.9 (MeOH, *c* 2.88); UV λ_{max} (MeOH, nm, log ε): 292 (4.17); IR ν_{max} (KBr, cm^{-1}): 3406, 1603, 1513, 1078, 1019; ESI-MS *m/z* $[M + H]^+$ 405; HRESI-MS *m/z* $[M + Na]^+$ 427.1372 (calcd for $C_{21}H_{24}O_8Na$, 427.1368); ^1H NMR and ^{13}C NMR, see table 1.

3.3.3 *trans*-3-*O*-Methyl-resveratrol-2-(2-*p*-coumaric)-*C*-β-glucoside (3). A white amorphous powder (MeOH); $[\alpha]_D^{23}$ −196.6 (MeOH; *c* 1.27); UV λ_{max} (MeOH; nm; log ε): 312 (4.64), 221 (4.58); IR ν_{max} (KBr; cm^{-1}): 3418, 1675, 1603, 1513, 1263, 1170; ESI-MS *m/z* $[M + H]^+$551; HRESI-MS *m/z* $[M + Na]^+$573.1755 (calcd for $C_{30}H_{30}O_{10}Na$, 573.1736); ^1H NMR and ^{13}C NMR, see table 2.

3.3.4 *trans*-3-*O*-Methyl-resveratrol-2-(3-*p*-coumaric)-*C*-β-glucoside (4). A white amorphous powder (MeOH); $[\alpha]_D^{23}$ −52.0 (MeOH; *c* 1.55); UV λ_{max} (MeOH; nm; log ε): 309 (4.62),

Table 1. ^{1}H NMR and ^{13}C NMR data of compounds **1** and **2**† (δ ppm, J Hz).

No.	***1***		***2***	
	δ_H	δ_C	δ_H	δ_C
1		141.3 s		141.0 s
2		116.8 s		117.3 s
3		160.8 s		160.8 s
4	6.27 (br s, 1H)	98.8 d	6.36 (d, 1H, 2.0)	99.2 d
5		158.8 s		158.5 s
6	6.60 (br s, 1H)	106.4 d	6.18 (d, 1H, 2.0)	109.6 d
7	7.80 (d, 1H, 16.0)	126.5 d	6.41 (d, 1H, 12.0)	128.6 d
8	6.71 (d, 1H, 16.0)	130.7 d	6.76 (d, 1H, 12.0)	130.0 d
1′		130.9 s		129.2 s
2′, 6′	7.28 (d, 2H, 8.3)	128.9 d	7.08 (d, 2H, 8.6)	131.6 d
3′, 5′	6.68 (d, 2H, 8.3)	116.4 d	6.61 (d, 2H, 8.6)	115.5 d
4′		158.0 s		157.2 s
1″	4.97 (d, 1H, 9.9)	75.7 d	5.05 (br, 1H)	75.0 d
2″	3.76 (m, 1H)	74.7 d	4.10 (br, 1H)	73.1 d
3″	3.38 (t, 1H, 9.0)	80.2 d	3.30 (br, 1H)	81.4 d
4″	3.48 (t, 1H, 9.0)	71.7 d	3.60 (br, 1H)	71.9 d
5″	3.30 (m, 1H)	81.8 d	3.44 (br, 1H)	80.4 d
6″	3.71 (m, 1H), 3.82 (m, 1H)	62.8 t	3.64 (m, 1H), 3.73 (m, 1H)	63.2 t
3-OMe	3.65 (s, 3H)	56.2 q	3.74 (s, 3H)	56.1 q

† NMR data of **1** measured in CD_3OD at 400 MHz for proton and 100 MHz for carbon and **2** in acetone-d_6 at 500 MHz for proton and 125 MHz for carbon.

Table 2. ^{1}H NMR and ^{13}C NMR data of compounds **3** and **4**† (δ ppm, J Hz).

No.	***3***		***4***	
	δ_H	δ_C	δ_H	δ_C
1		142.3 s		141.6 s
2		115.2 s		116.6 s
3		161.2 s		161.1 s
4	6.20 (d, 1H, 1.8)	98.4 d	6.36 (br s, 1H)	98.9 d
5		158.6 s		159.2 s
6	6.61 (d, 1H, 1.8)	106.6 d	6.66 (br s, 1H)	106.7 d
7	7.94 (d, 1H, 16.2)	126.2 d	7.90 (d, 1H, 16.2)	126.7 d
8	6.78 (d, 1H, 16.2)	131.3 d	6.79 (d, 1H, 16.2)	131.1 d
1′		131.2 s		131.1 s
2′, 6′	7.41 (d, 2H, 8.4)	129.1 d	7.40 (d, 2H, 8.4)	129.0 d
3′, 5′	6.77 (d, 2H, 8.4)	116.4 d	6.77 (d, 2H, 8.4)	116.8 d
4′		158.2 s		158.4 s
1″	5.24 (d, 1H, 9.5)	74.0 d	5.15 (d, 1H, 9.3)	76.0 d
2″	5.35 (t, 1H, 9.5)	75.8 d	4.02 (t, 1H, 9.3)	73.0 d
3″	3.65 (t, 1H, 9.5)	78.0 d	5.11 (d, 1H, 9.3)	81.4 d
4″	3.62 (t, 1H, 9.5)	71.8 d	3.77 (m, 1H)	70.2 d
5″	3.42 (m, 1H)	82.4 d	3.48 (d, 1H, 7.2)	82.0 d
6″	3.82 (m, 1H), 3.94 (m, 1H)	62.8 t	3.91 (m, 1H), 3.92 (m, 1H)	62.6 t
1‴		127.1 s		129.0 s
2‴, 6‴	7.55 (d, 2H, 8.1)	131.0 d	7.37 (d, 2H, 8.1)	131.1 d
3‴, 5‴	6.78 (d, 2H, 8.1)	116.8 d	6.78 (d, 2H, 8.1)	116.6 d
4‴		162.2 s		160.9 s
7‴	7.41 (d, 1H, 16.0)	146.1 d	7.57 (d, 1H, 16.0)	146.4 d
8‴	6.05 (d, 1H, 16.0)	115.1 d	6.37 (d, 1H, 16.0)	115.7 d
9‴		167.8 s		169.4 s
3-OMe	3.70 (s, 3H)	56.4 q	3.85 (s, 3H)	56.3 q

† NMR data measured in CD_3OD at 400 MHz for proton and 100 MHz for carbon.

220 (4.70); IR ν_{max} (KBr; cm^{-1}): 3423, 1690, 1603, 1513, 1262, 1169; ESI-MS *m/z* $[M + Na]^+$573; HRESI-MS *m/z* $[M + Na]^+$573.1748 (calcd for $C_{30}H_{30}O_{10}Na$, 573.1736); ^1H NMR and ^{13}C NMR, see table 2.

Acknowledgements

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