

Stilbene Glycoside Sulfates from *Polygonum cuspidatum*

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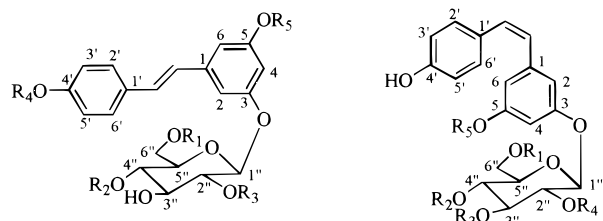
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Ten naturally occurring stilbene glycoside sulfates (**1–10**) were isolated from an aqueous extract of the root of *Polygonum cuspidatum*. Their structures were established based on chemical evidence and spectroscopic techniques, including 2D NMR methods.

The dried roots of *Polygonum cuspidatum* Sieb. et Zucc. (Polygonaceae) have been widely used in Chinese folk medicine for the treatment of suppurative dermatitis, gonorrhea, favus athlete's foot, and hyperlipemia. Many chemical components have been reported from the hydrophobic fraction of this plant, including anthraquinones,^{1–4} stilbenes,^{5–7} flavonoids,⁸ and other phenols.³

Stilbenes have aroused considerable interest for their bioactivities. Resveratrol and piceid have been reported to have lipid-lowering activity⁹ and to inhibit lipid peroxidation,¹⁰ arachidonate metabolism,^{11,12} and protein tyrosine kinase (PTK56^{lck}).⁷ Resveratrol also possesses antibacterial and antifungal effects⁶ as well as tumor chemopreventive activities,¹³ and piceid improves microcirculation.¹⁴

In a study of an aqueous acetone extract of the roots of *P. cuspidatum*, 10 naturally occurring stilbene glycoside sulfates (**1–10**) were isolated and identified. There has been no previous phytochemical work reported on the aqueous soluble components from this plant, and there has been no report in the literature on stilbenoid sulfates.



	R ₁	R ₂	R ₃	R ₄	R ₅		R ₁	R ₂	R ₃	R ₄	R ₅
1	SO ₃ M	H	H	H	H	6	SO ₃ M	H	H	H	H
2	H	SO ₃ M	H	H	H	7	H	SO ₃ M	H	H	H
3	H	H	SO ₃ M	H	H	8	H	H	SO ₃ M	H	H
4	H	H	H	SO ₃ M	H	9	H	H	H	SO ₃ M	H
5	H	H	H	H	SO ₃ M	10	H	H	H	H	SO ₃ M

M = Na⁺ or K⁺

Results and Discussion

The water-soluble fraction of an aqueous acetone extract of the dried roots of *P. cuspidatum* was subjected to column chromatography on Sephadex LH-20, MCI gel CHP20P, Cosmosil ODS, and Toyopearl HW-40F to give stilbene glycoside sulfates **1–10**. Their structures were elucidated by spectroscopic analysis and physicochemical evidences,

and their ¹H and ¹³C NMR data were unambiguously assigned by 2D NMR analysis.

Compound **1** was isolated as an amorphous powder. It exhibited FABMS ions at *m/z* 493, 508, 515, 531, and 547, indicating a molecular weight of 492 or 508, compatible with a molecular formula of C₂₀H₂₁O₁₁NaS or C₂₀H₂₁O₁₁-KS. This conclusion was consistent with atomic absorption data. A positive Molish test indicated that **1** might be a glycoside. The IR spectrum indicated the presence of hydroxyl (3405 cm⁻¹), double-bond (1606 cm⁻¹), aromatic (1589 and 1513 cm⁻¹), and -OSO₃⁻ (1254 and 1064 cm⁻¹) groups.^{15,16} The presence of S was confirmed by elemental analysis, while the presence of K⁺ was determined from atomic absorption analysis. The UV spectrum suggested that **1** possessed a stilbene skeleton.¹⁷ ¹H and ¹³C NMR data confirmed that **1** was a *trans*-resveratrol glycoside.^{7,18} Hydrolysis of **1** afforded D-glucose (determined by GC analysis); the anion SO₄²⁻, which was confirmed by precipitation with BaCl₂; and resveratrol, which was identified by comparison of IR and NMR data with literature.⁷ The ¹H and ¹³C NMR data indicated that the sugar was β-linked¹⁹ and that it was attached at C-3 according to an HMBC experiment. NOESY correlations observed between the anomeric proton and both H-2 and H-4 confirmed the linkage. The -OSO₃⁻ group was assigned to C-6'' due to the unusual downfield shifts of the H-6'' and C-6'' signals. Consequently, **1** was identified as a mixture of sodium and potassium *trans*-resveratrol-3-*O*-β-D-glucopyranoside-6''-sulfate.

Compounds **2** and **3** had similar UV, IR, FABMS, and atomic absorption data and gave the same hydrolysis products as **1**. In the ¹H and ¹³C NMR spectra, the downfield shifts of the H-4'' and C-4'' signals of **2** suggested that the -OSO₃⁻ group was attached at C-4'', while those of H-2'' and C-2'' of **3** indicated that the -OSO₃⁻ group was linked to C-2''. Consequently, **2** and **3** were identified as mixtures of sodium and potassium *trans*-resveratrol-3-*O*-β-D-glucopyranoside-4''-sulfate and *trans*-resveratrol-3-*O*-β-D-glucopyranoside-2''-sulfate.

Compounds **4** and **5** also had similar UV, IR, FABMS, and atomic absorption data and gave the same hydrolysis products as **1–3**. In the ¹H and ¹³C NMR spectra, H-3',-5' and C-3',-5' of **4** shifted downfield compared to those of **1**, and C-4' shifted upfield. While in **5**, the H-2, H-4, and H-6 signals were all downfield relative to those of **1**, and the C-2, C-4, and C-6 signals shifted downfield ranging from 4.3 to 5.9 ppm, and C-5 shifted upfield 4.2 ppm. As an electron withdrawing group, *O*-sulfate leads to a decreased electron density of ortho and para carbons and an increased electron density of the carbon carrying the sulfate group.¹⁵ Thus, the evidence above suggested that the -OSO₃⁻

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Table 1. ¹H NMR (400 MHz) Data (δ , J (Hz)) for Stilbene Glycoside Sulfates **1–5**

proton	1 ^a	2 ^a	3 ^a	4 ^b	5 ^a
2 (1H)	6.98 t (2.0)	7.00 t (2.0)	7.03 t (2.0)	6.78 t (2.1)	7.30 t (2.0)
4 (1H)	6.71 t (2.0)	6.69 t (2.0)	6.71 t (2.0)	6.48 t (2.1)	7.15 t (2.0)
6 (1H)	6.88 t (2.0)	6.87 t (2.0)	6.85 t (2.0)	6.68 t (2.1)	7.34 t (2.0)
2', 6' (2H)	7.62 d (8.6)	7.59 d (8.6)	7.57 d (8.7)	7.48 d (8.7)	7.56 d (8.6)
3', 5' (2H)	7.01 d (8.6)	7.01 d (8.6)	7.00 d (8.7)	7.29 d (8.7)	6.99 d (8.6)
α (1H)	7.08 d (16.4)	7.06 d (16.3)	7.04 d (16.3)	6.89 d (16.4)	7.12 d (16.3)
β (1H)	7.23 d (16.4)	7.24 d (16.3)	7.23 d (16.3)	7.00 d (16.4)	7.29 d (16.3)
glucose					
1'' (1H)	5.11 d (7.5)	5.16 d (7.9)	5.25 d (7.7)	4.98 d (7.6)	5.16 d (7.3)
2'' (1H)	3.69 ^c	3.78 dd (7.9, 9.0)	4.50 dd (7.7, 9.0)	3.56 ^c	3.68 dd (7.3, 9.0)
3'' (1H)	3.74 dd (8.9, 9.0)	4.00 dd (9.0, 9.2)	3.97 dd (9.0, 9.4)	3.63 dd (9.2, 8.7)	3.70 dd (9.0, 8.8)
4'' (1H)	3.67 dd (9.0, 9.5)	4.40 dd (9.2, 9.5)	3.74 dd (9.4, 9.6)	3.51 dd (8.7, 9.4)	3.63 dd (8.8, 9.2)
5'' (1H)	3.94 m	3.86 m	3.74 m	3.59 m	3.73 m
6''- α	4.56 dd (11.1, 1.8)	4.16 dd (12.6, 2.0)	4.14 (11.2, 1.8)	3.95 dd (12.5, 2.0)	4.12 dd (12.2, 2.0)
6''- β	4.38 dd (11.1, 5.8)	3.98 dd (12.6, 5.8)	3.94 ^c	3.76 dd (12.5, 5.7)	3.93 dd (12.2, 5.6)

^a Measured in CD₃OD + D₂O. ^b Measured in D₂O. ^c Obscured by other signals: coupling constants could not be accurately determined.

group was linked to C-4' in **4** and C-5 in **5**, and **4** and **5** were established as mixtures of sodium and potassium *trans*-resveratrol-3-*O*- β -D-glucopyranoside-4'-sulfate and *trans*-resveratrol-3-*O*- β -D-glucopyranoside-5-sulfate.

Compound **6** also had UV, IR, FABMS, and atomic absorption data similar to those of **1–5**. In the ¹H NMR spectra, the coupling constants of olefinic protons (12.0 Hz) indicated that **6** was a *cis*-stilbene. Acid hydrolysis of **6** afforded *cis*-resveratrol,⁷ D-glucose, and the anion SO₄²⁻. The downfield shifts of H-6'' and C-6'' of **6** suggested that the -OSO₃⁻ group was attached at C-6''. Thus, **6** was elucidated as a mixture of sodium and potassium *cis*-resveratrol-3-*O*- β -D-glucopyranoside-6''-sulfate.

Compounds **7**, **8**, and **9** showed similar UV, IR, FABMS, and atomic absorption data and gave the same hydrolysis products as **6**. The unusual downfield shifts of H-4'' and C-4'' of **7**, H-3'' and C-3'' of **8**, and H-2'' and C-2'' of **9** suggested that the -OSO₃⁻ group was attached to C-4'', C-3'', and C-2'', respectively. Consequently, **7**, **8**, and **9** were identified as mixtures of sodium and potassium *cis*-resveratrol-3-*O*- β -D-glucopyranoside-4''-sulfate, *cis*-resveratrol-3-*O*- β -D-glucopyranoside-3''-sulfate, and *cis*-resveratrol-3-*O*- β -D-glucopyranoside-2''-sulfate, respectively. Compound **7** is the *cis* isomer of **2**, while **9** is the *cis* isomer of **3**.

Compound **10** showed similar UV, IR, FABMS, and atomic spectral data and gave the same hydrolysis products as **6–9**. As in **5**, Compound **10** showed downfield shifts due to ortho and para effects of -OSO₃⁻. H-2, H-4, H-6, and the corresponding carbons shifted similarly compared to those of **5**. Therefore, the -OSO₃⁻ group was linked to C-5. Thus, **10** was identified as a mixture of sodium and potassium *cis*-resveratrol-3-*O*- β -D-glucopyranoside-5-sulfate, the *cis* isomer of **5**.

In the ¹H NMR spectra, the sugar moiety signals of **6–10** were somewhat different from those of **1–5** because of the *cis* double bond and the influence of the aromatic ring. Biological assays of **1–10** included cytotoxicity against human cancer cell lines KB, HeLa, and A549 *in vitro*,²¹ as well as antifungal effects against four yeasts²² and four filamentous fungi.²³ Only **2** showed moderate cytotoxicity against A549 (IC₅₀ = 80 μ g/mL). Compounds **1–10** showed no antifungal activity. In comparison with the reported antifungal activity of resveratrol,⁶ it can be inferred that the free 3-hydroxyl is essential for antifungal activity.

Experimental Section

General Experimental Procedures. Optical rotations were recorded in CH₃OH using a Perkin-Elmer 241 automatic digital polarimeter. ¹H, ¹³C NMR, ¹H-¹H COSY, HMQC, HMBC,

and NOESY spectra were recorded on a Bruker DRX-400 spectrometer (¹H 400 MHz and ¹³C 100 MHz) using CD₃OD + D₂O or D₂O as solvent. The carbon multiplicities were obtained by DEPT experiment. FABMS were obtained using a Finnigan MAT-90 instrument. UV was carried out on a Varian Cary 300 Bio instrument. IR was recorded on a Hitachi 275-50 IR spectrometer. Elemental analysis was carried out on an Elementar Vario EL instrument. Atomic absorption was recorded on a Hitachi Z-5000 spectrometer. Gas chromatography (GC) was run on a HP 1890 gas chromatograph. Sephadex LH-20 (Pharmacia), Toyopearl HW40F (Tosoh), MCI-gel CHP20P (Mitsubishi), and Cosmosil ODS (40-60 μ m, Nacalai Tesque, Inc.) were used for column chromatography.

Plant Material. The roots of *P. cuspidatum* Sieb. et Zucc. were collected from Sichuan Province, People's Republic of China, in October 1997, and were identified by the author. A voucher specimen (no. PC001) is deposited at Shanghai Institute of Materia Medica, Chinese Academy of Sciences, People's Republic of China.

Extraction and Isolation. The dried roots of the plant (10 kg) were extracted with 60% acetone 3 times at room temperature. The acetone was evaporated in vacuum to afford a hydrophobic substance that was precipitated and filtered. The water-soluble portion was concentrated to a suitable volume, then chromatographed on a Sephadex LH-20 column eluted with H₂O, aqueous MeOH (10%-70%), and 50% acetone, successively. The sugars eluted by water were discarded, and the remaining water and 10% MeOH eluates were subjected to MCI gel chromatography eluted with aqueous MeOH (10% to 60% gradient). The 20% aqueous MeOH eluate from the MCI column was repeatedly chromatographed on Cosmosil ODS (eluted with 30% MeOH) and Toyopearl HW-40F (eluted with 20% MeOH) to give **1** (30 mg), **2** (50 mg), **3** (65 mg), **4** (30 mg), **5** (40 mg), and **9** (20 mg), respectively. The 30-40% aqueous MeOH eluate from the MCI column was repeatedly chromatographed on ODS (eluted with 30% MeOH), MCI gel (eluted with 30-40% MeOH), and Toyopearl HW-40F (eluted with 30% MeOH) to give **6** (35 mg), **7** (18 mg), **8** (25 mg), and **10** (25 mg), respectively.

Compound 1: white amorphous powder; [α]_D²⁴ -105° (c 0.13 MeOH); UV (MeOH) λ_{\max} 215, 236 (sh), 306, 322; IR (KBr) ν_{\max} 3405, 1606, 1589, 1513, 1448, 1254, 1173, 1064, 995, 837 cm⁻¹; ¹H NMR and ¹³C NMR, see Tables 1 and 3; FABMS m/z 547, 531, 515, 508, 493; *anal.* C 47.14%, H 4.12%, S 6.23%, calcd for C₂₀H₂₁O₁₁SK, C 47.24%, H 4.16%, S 6.30%.

Compound 2: white amorphous powder; [α]_D²⁴ -59.5° (c 0.08 MeOH); UV (MeOH) λ_{\max} 212, 236 (sh), 306, 322 nm; IR (KBr) ν_{\max} 3423, 1606, 1589, 1513, 1444, 1256, 1078, 1028, 986 cm⁻¹; ¹H NMR and ¹³C NMR, data see Tables 1 and 3; FABMS m/z 547, 531, 515, 508, 493; *anal.* C 45.59%, H 4.38%, S 6.02%, calcd for C₂₀H₂₁O₁₁SK·H₂O, C 45.62%, H 4.40%, S 6.09%.

Compound 3: white amorphous powder; [α]_D²⁴ -60° (c 0.19 MeOH); UV (MeOH) λ_{\max} 215, 233 (sh), 306, 319 nm; IR (KBr)

Table 2. ¹H NMR (400 MHz) Data (δ , J (Hz)) for Stilbene Glycosidate Sulfates **6–10** Measured in D₂O

proton	6	7	8	9	10
2 (1H)	6.56 t (2.0)	6.53 t (2.0)	6.55 t (2.0)	6.55 t (2.1)	6.88 t (2.0)
4 (1H)	6.47 t (2.0)	6.45 t (2.0)	6.46 t (2.0)	6.48 t (2.1)	6.97 t (2.0)
6 (1H)	6.56 t (2.0)	6.53 t (2.0)	6.55 t (2.0)	6.55 t (2.1)	6.88 t (2.0)
2', 6' (2H)	7.21 d (8.5)	7.16 d (8.0)	7.19 d (8.4)	7.17 d (8.2)	7.18 d (8.1)
3', 5' (2H)	6.84 d (8.5)	6.80 d (8.0)	6.82 d (8.4)	6.80 d (8.2)	6.80 d (8.1)
α (1H)	6.51 d (12.0)	6.53 d (12.2)	6.49 d (12.2)	6.47 d (12.0)	6.52 d (12.1)
β (1H)	6.67 d (12.0)	6.61 d (12.2)	6.65 d (12.2)	6.62 d (12.0)	6.66 d (12.1)
glucose					
1'' (1H)	4.59 d (7.6)	4.58 d (7.9)	4.72 d (8.0)	4.68 d (7.9)	4.67 d (7.4)
2'' (1H)	3.50 ^a	3.55 dd (7.9, 8.8)	3.63 dd (8.0, 9.2)	4.21 dd (7.9, 8.6)	3.49 ^a
3'' (1H)	3.50 ^a	3.67 dd (8.8, 9.4)	4.28 dd (9.2, 9.1)	3.64 ^a	3.49 ^a
4'' (1H)	3.52 dd (9.0, 9.5)	4.21 dd (9.2, 9.4)	3.71 dd (9.1, 9.4)	3.56 dd (9.6, 9.3)	3.57 dd (9.0, 9.2)
5'' (1H)	3.37 m	3.20 m	3.25 m	3.17 m	3.22 m
6'' (2H)	4.16 m	3.76 m	3.76 m	3.67 m	3.70 m

^a Obscured by other signals: coupling constants could not be accurately determined.

Table 3. ¹³C NMR (100 MHz) Data (δ) for Stilbene Glycosidate Sulfates **1–10**

carbon	1 ^a	2 ^a	3 ^a	4 ^b	5 ^a	6 ^b	7 ^b	8 ^c	9 ^b	10 ^b
1	141.7 s	141.7 s	141.6 s	142.5 s	141.6 s	142.6 s	142.6 s	140.3 s	142.6 s	142.7 s
2	108.1 d	107.6 d	107.9 d	109.2 d	112.4 d	113.8 d	113.9 d	110.6 d	113.9 d	116.1 d
3	160.4 s	160.3 s	160.4 s	160.7 s	159.9 s	160.3 s	160.3 s	159.0 s	160.4 s	159.4 s
4	104.4 d	104.4 d	104.7 d	106.1 d	110.2 d	105.8 d	105.9 d	103.5 d	106.3 d	111.9 d
5	159.2 s	159.2 s	159.3 s	159.5 s	155.0 s	159.3 s	159.5 s	158.5 s	159.4 s	154.7 s
6	108.6 d	108.8 d	108.9 d	110.9 d	114.5 d	110.5 d	110.5 d	108.3 d	110.8 d	119.5 d
1'	130.7 s	130.7 s	130.7 s	137.4 s	130.5 s	132.2 s	132.1 s	128.8 s	132.1 s	131.8 s
2'	129.3 d	129.3 d	129.2 d	130.5 d	129.4 d	133.3 d	133.3 d	131.0 d	133.3 d	133.3 d
3'	116.8 d	116.8 d	116.8 d	124.4 d	116.8 d	117.9 d	117.9 d	116.0 d	118.0 d	118.0 d
4'	158.0 s	158.0 s	158.2 s	153.3 s	158.6 s	157.4 s	159.5 s	157.0 s	157.5 s	157.6 s
5'	116.8 d	116.8 d	116.8 d	124.4 d	116.8 d	117.9 d	117.9 d	116.0 d	118.0 d	118.0 d
6'	129.3 d	129.3 d	129.2 d	130.5 d	129.4 d	133.3 d	133.3 d	131.0 d	133.3 d	133.3 d
α	126.9 d	126.8 d	126.8 d	130.5 d	126.2 d	130.9 d	130.9 d	128.4 d	130.9 d	130.2 d
β	130.3 d	130.4 d	130.3 d	131.1 d	131.0 d	133.6 d	133.6 d	131.2 d	133.6 d	134.1 d
glucose										
1''	102.6 d	102.1 d	100.8 d	103.0 d	102.6 d	103.4 d	103.2 d	100.9 d	101.9 d	103.4 d
2''	74.8 d	74.2 d	81.5 d	75.6 d	75.1 d	75.1 d	75.1 d	72.4 d	82.5 d	75.4 d
3''	77.5 d	76.5 d	77.2 d	78.3 d	78.3 d	78.0 d	76.9 d	84.1 d	77.2 d	78.2 d
4''	71.2 d	78.0 d	71.3 d	72.2 d	71.5 d	71.3 d	78.7 d	68.8 d	71.4 d	71.6 d
5''	76.0 d	76.5 d	78.0 d	78.8 d	78.0 d	76.4 d	76.9 d	76.5 d	78.4 d	78.5 d
6''	68.3 t	62.4 t	62.0 t	63.3 t	62.6 t	69.0 t	62.7 t	60.8 t	62.7 t	62.7 t

^a Measured in CD₃OD + D₂O. ^b Measured in D₂O. ^c Measured in DMSO-*d*₆.

ν_{\max} 3406, 1609, 1539, 1514, 1447, 1258, 1173, 1072, 997 cm⁻¹; ¹H NMR and ¹³C NMR data, see Tables 1 and 3; FABMS *m/z* 547, 531, 515, 508, 493; *anal.* C 42.13%, H 5.00%, S 5.67%, calcd for C₂₀H₂₁O₁₁SK·7/2H₂O, C 42.03%, H 4.94%, S 5.61%.

Compound 4: white amorphous powder; [α]_D²⁵ -70.6° (c 0.08 MeOH); UV (MeOH) λ_{\max} 211, 229 (sh), 301, 312 nm; IR (KBr) ν_{\max} 3406, 1597; 1504, 1444, 1263, 1165, 1074, 1047, 871, 843 cm⁻¹; ¹H NMR and ¹³C NMR data, see Tables 1 and 3; FABMS *m/z* 547, 531, 515, 508, 493; *anal.* C 45.54%, H 4.46%, S 6.13%, calcd for C₂₀H₂₁O₁₁SK·H₂O, C 45.62%, H 4.40%, S 6.09%.

Compound 5: white amorphous powder; [α]_D²⁵ -67° (c 0.07, MeOH); UV (MeOH) λ_{\max} 207, 232 (sh), 305, 320 nm; IR (KBr) ν_{\max} 3400, 1605, 1514, 1446, 1263, 1173, 1080, 1053, 847, 806, 777 cm⁻¹; ¹H NMR and ¹³C NMR data, see Tables 1 and 3; FABMS *m/z* 547, 531, 515, 508, 493; *anal.* C 44.02%, H 4.58%, S 5.80%, calcd for C₂₀H₂₁O₁₁SK·2H₂O, C 44.11%, H 4.63%, S 5.89%.

Compound 6: white amorphous powder; [α]_D²⁵ -33.6° (c 0.25 MeOH); UV (MeOH) λ_{\max} 215, 233 (sh), 284 nm; IR (KBr) ν_{\max} 3396, 1608, 1512, 1444, 1252, 1173, 1065, 999 cm⁻¹; ¹H NMR and ¹³C NMR data, see Tables 2 and 3; FABMS *m/z* 547, 531, 515, 508, 493; *anal.* C 46.35%, H 4.70%, S 6.21%, calcd for C₂₀H₂₁O₁₁SK·3/2H₂O, C 46.24%, H 4.66%, S 6.17%.

Compound 7: white amorphous powder; [α]_D²⁵ -32.3° (c 0.18, MeOH); UV (MeOH) λ_{\max} 216, 232 (sh), 288, 322 (sh) nm; IR (KBr) ν_{\max} 3400, 1606, 1512, 1444, 1251, 1173, 1078, 982; ¹H NMR and ¹³C NMR data, see Tables 2 and 3; FABMS *m/z* 547, 531, 515, 508, 493; *anal.* C 45.70%, H 4.45%, S 6.01%, calcd for C₂₀H₂₁O₁₁SK·H₂O, C 45.62%, H 4.40%, S 6.09%.

Compound 8: white amorphous powder; [α]_D²⁵ -40.0° (c 0.20, MeOH); UV (MeOH) λ_{\max} 217, 235 (sh), 286, 322 (sh) nm; IR (KBr) ν_{\max} 3406, 1606, 1514, 1444, 1258, 1172, 1076, 1041, 999 cm⁻¹; ¹H NMR and ¹³C NMR data, see Tables 2 and 3; FABMS *m/z* 547, 531, 515, 508, 493; *anal.* C 44.20%, H 4.69%, S 5.96%, calcd for C₂₀H₂₁O₁₁SK·2H₂O, C 44.11%, H 4.63%, S 5.89%.

Compound 9: white amorphous powder; [α]_D²⁵ -44° (c 0.30 MeOH); UV (MeOH) λ_{\max} 217, 234 (sh), 290, 321 (sh) nm; IR (KBr) ν_{\max} 3415, 1606, 1514, 1444, 1256, 1173, 1072, 999 cm⁻¹; ¹H NMR and ¹³C NMR data, see Tables 2 and 3; FABMS *m/z* 547, 531, 515, 508, 493; *anal.* C 45.37%, H 4.80%, S 6.11%, calcd for C₂₀H₂₁O₁₁SK·2H₂O, C 45.46%, H 4.77%, S 6.07%.

Compound 10: white amorphous powder; [α]_D²⁵ -31° (c 0.40 MeOH); UV (MeOH) λ_{\max} 216, 232 (sh), 290, 322 (sh) nm; IR (KBr) ν_{\max} 3400, 1605, 1514, 1443, 1257, 1173, 1076, 1051. ¹H NMR and ¹³C NMR data, see Tables 2 and 3; FABMS *m/z* 547, 531, 515, 508, 493; *anal.* C 42.81%, H 4.79%, S 5.79%, calcd for C₂₀H₂₁O₁₁SK·3H₂O, C 42.70%, H 4.84%, and S 5.70%.

Acid Hydrolysis of Compounds 1–10. Solutions of **1–5** (6 mg each) in 2 N HCl were heated (90 °C) for 2 h, after removing HCl by evaporation in vacuum, the mixtures were diluted with H₂O and extracted with EtOAc. The EtOAc layer in each case was evaporated to dryness, and the residue was recrystallized in MeOH to afford *trans*-resveratrol, which was identified by comparison with an authentic sample (co-TLC, IR, and NMR⁷). The same treatment of compounds **6–10** (5 mg each) afforded *cis*-resveratrol, and its IR and NMR data was consistent with that in the literature.⁷ A sample of each aqueous layer (**1–10**) gave a positive sulfate test with BaCl₂.

Another sample of the each aqueous layer was neutralized with 1 N NaOH and was then subjected to TLC analysis on Kieselgel 60 F₂₅₄ (Merck) [using CHCl₃-MeOH-H₂O (30:12:9), 9 mL, and HOAc, 1 mL] and paper chromatography [using *n*-BuOH-HOAc-H₂O (4:1:5)] with standard sugars; in each case the presence of glucose was established. The rest of each aqueous layer was then passed through an Amberlite IRA-60E column, the aqueous eluate was concentrated and treated with thiazolidine as described previously.²⁰ Only the D-glucose derivative was detected by GC. (GC conditions: column, Supelco SPB-1, 0.25 mm × 27 m, column temperature 230 °C; carrier gas, N₂; *t*_R, D-glucose derivative, 17.9 min, and L-glucose derivative, 17.3 min).

Bioassay Procedures. Cytotoxicity was evaluated against human cancer cell lines KB, HeLa, and A549 using previously described 3-[4,5-dimethylthiazol-2-yl]-2,5-diphenyltetrazolium bromide or microculture tetrazolium (MTT) protocols.²¹ The antifungal activity *in vitro* against four yeasts (*Candida albicans*, *Cryptococcus neoformans*, *Candida parapsilosis*, *Candida tropicalis*) was tested according to the method proposed by the National Committee for Clinical and Laboratory Standard,²² and the method described by C. Hennequin²³ was adapted for the antifungal evaluation against four filamentous fungi (*Fonsecaea pedrosoi*, *Sporothrix schenckii*, *Aspergillus fumigatus*, *Trichophyton rubrum*).

References and Notes

- (1) Tsukida, K.; Yoneshige, M. *Yakugaku Zasshi* **1954**, *74*, 379–382.
- (2) Murakami, T.; Ikeda, K.; Takido, M. *Chem. Pharm. Bull.* **1968**, *16*, 2299–2300.
- (3) Kimura, Y.; Kozawa, M.; Baba, K.; Hata, K. *Planta Med.* **1983**, *48*, 164–168.
- (4) Yeh, S. F.; Chou, T.-C.; Liu, T.-S. *Planta Med.* **1998**, *64*, 413–414.
- (5) Nonomura, S.; Kanagawa, H.; Shin, H.; Makimoto, A. *Yakugaku Zasshi* **1963**, *83*, 988–990.
- (6) Kubo, M.; Kimura, Y.; Shin, H.; Haneda, T.; Tani, T.; Namba, K. *Shoyakugaku Zasshi* **1981**, *35*, 58–61.
- (7) Jayatilake, G.; Jayasuriya, H.; Lee, E.-S.; Koonchanok, N. M.; Geahlen, R. L.; Ashendei, C. L.; McLaughlin, J. L.; Chang, C.-J. *J. Nat. Prod.* **1993**, *56*, 1805–1810.
- (8) Kuznetsova, Z. P. *Vestsi Akad. Navuk BSSR, Ser. Biyal. Navuk* **1979**, *5*, 29–32.
- (9) Arichi, H.; Kimura, Y.; Okuda, H.; Baba, K.; Kozawa, M.; Arichi, S. *Chem. Pharm. Bull.* **1982**, *30*, 1766–1770.
- (10) Kimura, Y.; Ohminami, H.; Okuda, H.; Baba, K.; Kozawa, M.; Arichi, S. *Planta Medica* **1983**, *49*, 51–54.
- (11) Kimura, Y.; Okuda, H.; Arichi, S. *Bioch. Biophys. Acta* **1985**, *834*, 275–287.
- (12) Kimura, Y.; Okuda, H.; Kubo, M. *J. Ethnopharmacol.* **1995**, *45*, 131–139.
- (13) Jang, M.; Cai, L.; Udeani, G. O.; Slowing, K. V.; Thomas, C. F.; Beecher, C. W. W.; Fong, H. H. S.; Farnsworth, N. R.; Kinghorn, A. D.; Mehta, R. G.; Moon, R. C.; Pezzuto, J. M. *Science* **1997**, *275*, 218–220.
- (14) Luo, S.-F.; Jin, X.-Z.; Ye, J.-F.; Zhang, P.-W. *Chin. J. Pharmacol. Toxicol.* **1999**, *13*, 1–4.
- (15) Barron, D.; Varin, L.; Ibrahim, R. K.; Harborne, J. B.; Williams, C. A. *Phytochemistry* **1988**, *27*, 2375–2395.
- (16) Terashima, S.; Shimizu, M.; Nakayama, H.; Ishikura, M.; Ueda, Y.; Imai, K.; Suzu, A.; Morita, B. *Chem. Pharm. Bull.* **1990**, *38*, 2733–2736.
- (17) Hillis, W. E.; Ishikura, N. *J. Chromatogr.* **1968**, *32*, 323–336.
- (18) Nyemba, A. M.; Mpondo, T. N.; Kimbu, S. F.; Connolly, J. D. *Phytochemistry* **1995**, *39*, 895–898.
- (19) Agrawal, P. K. *Phytochemistry* **1992**, *31*, 3307–3330.
- (20) Miyase, T.; Saitoh, H.; Shiokawa, K.; Ueno, A. *Chem. Pharm. Bull.* **1995**, *43*, 466–472.
- (21) Leonce, S.; Perez, V.; Casabianca-Pignede, M.-R.; Anstett, M.; Bisagni, E.; Pierre, A.; Atassi, G. *Invest. New Drugs* **1996**, *14*, 169–180.
- (22) Krishnrao T. V.; Galgiani, J. N. *Antimicrob. Agents Chemother.* **1997**, *41*, 1957–1960.
- (23) Hennequin, C.; Benailly, N.; Silly, C.; Sorin, M.; Scheinmann, P.; Lenoir, G.; Gaillard, J. L.; Berche, P. *Antimicrob. Agents Chemother.* **1997**, *41*, 2064–2066.

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