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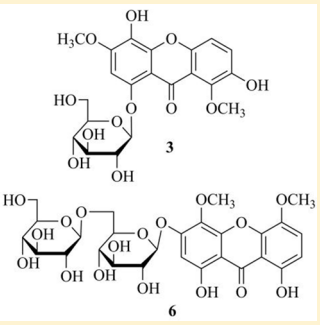
Xanthone Glycoside Constituents of *Swertia kouitchensis* with α-Glucosidase Inhibitory Activity

Luo-Sheng Wan, Qiu-Xia Min, Yong-Long Wang, Yao-Dong Yue, and Jia-Chun Chen*

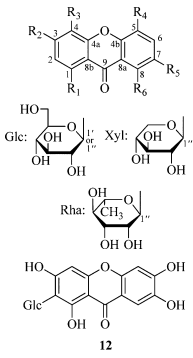
Hubei Key Laboratory of Natural Medicinal Chemistry and Resource Evaluation, Pharmaceutical Science Department of Tongji Medical School, Huazhong University of Science and Technology, Wuhan 430030, People's Republic of China

Supporting Information

ABSTRACT: Ten new xanthone glycosides, kouitchensides A–J (**1**–**10**), and 11 known analogues were isolated from an *n*-butanol fraction of *Swertia kouitchensis*. The structures of these glycosides were determined on the basis of extensive spectroscopic data interpretation and comparison with data reported in the literature. In an in vitro test, compounds **2**, **4**, **5**, **6**, **11**, **12**, and **13** (IC_{50} values in the range 126 to 451 μM) displayed more potent inhibitory effects against α-glucosidase activity than the positive control, acarbose (IC_{50} value of 627 μM).



Swertia kouitchensis Franch. (Gentianaceae), widely distributed in mainland China, has been used as a treatment for hepatitis and diabetes.[1] Previous work has also found that this plant can control postprandial hyperglycemia by inhibiting α-glucosidase activity.[2] In order to find new inhibitors from *S. kouitchensis*, α-glucosidase was used as a target to guide the chemical investigation of this plant. It was found that an *n*-butanol-soluble fraction of *S. kouitchensis* extract showed inhibitory activity against α-glucosidase (Table S1, Supporting Information). Following purification of this fraction, 10 new xanthone glycosides, kouitchensides A–J (**1**–**10**), and 11 known analogues were found. Xanthones and their derivatives have been studied extensively for their inhibitory effects against α-glucosidase.[3−6] Herein, the isolation and identification of compounds **1**–**10** and the inhibitory activities of all compounds isolated against α-glucosidase are reported.



	R_1	R_2	R_3	R_4	R_5	R_6
1	*O*-glc(6-1)-xyl	OCH_3	OCH_3	H	OH	OCH_3
2	*O*-glc(6-1)-xyl	OCH_3	OCH_3	H	OCH_3	OCH_3
3	*O*-Glc	OCH_3	OH	H	OH	OCH_3
3a	OH	OCH_3	OH	H	OH	OCH_3
4	*O*-glc(6-1)-xyl	OCH_3	H	OCH_3	H	OCH_3
5	*O*-glc(6-1)-xyl	OCH_3	H	OCH_3	OCH_3	OCH_3
6	OH	*O*-glc(6-1)-xyl	OCH_3	OCH_3	H	OH
7	*O*-glc(6-1)-glc	OCH_3	H	OCH_3	H	H
8	*O*-glc(6-1)-glc	OCH_3	H	OCH_3	H	OH
9	OH	OCH_3	H	H	*O*-glc(2-1)-rha	OH
10	OH	OCH_3	H	H	*O*-rha	*O*-glc
11	OH	OCH_3	H	OH	H	*O*-glc
12						
13	*O*-glc(6-1)-xyl	OCH_3	H	H	OCH_3	OH

RESULTS AND DISCUSSION

The *n*-butanol fraction of *S. kouitchensis* was subjected to column chromatography to yield 10 new compounds (**1**–**10**). The IR spectra of these compounds showed characteristic carbonyl and hydroxy groups in the ranges 1618–1650 and 3200–3435 cm^{-1}, respectively, and the UV absorption bands were in the ranges 226–269 and 312–379 nm, typical of a xanthone chromophore.[7]

Kouitchenside A (**1**) gave a molecular formula of $C_{27}H_{32}O_{16}$ by HRESIMS (*m*/*z* 611.1648 $[M - H]^-$). After acid hydrolysis, **1** gave D-xylose and D-glucose (see Experimental Section).[8] The ^1H NMR and ^{13}C NMR data (Table 1) of **1** were similar to those reported for 1,7-dihydroxy-3,4,8-trimethoxyxanthone,[9] except for signals associated with two additional sugar residues. Moreover, when compared to 1,7-dihydroxy-3,4,8-trimethoxyxanthone, the carbonyl carbon C-9 in **1** displayed an upfield shift of about 5 ppm in the ^{13}C NMR spectrum, along with the absence of a signal for a chelated hydroxy group in the ^1H NMR spectrum, suggesting that the sugar unit replaced the hydroxy group at C-1.[10] The assumption was confirmed by an HMBC correlation of C-1 (δ_C 154.3) with the anomeric proton (δ_H 4.90) of the glucose unit. Further, the anomeric proton (δ_H 4.18) of the xylose moiety was long-range coupled with C′-6 (δ_C 69.0) of Glc. The relative configurations of the Glc and Xyl residues were both deduced to be β, based on the coupling constants and comparison of the NMR spectra with those of known compounds.[11] Thus, **1** was defined structurally as 1-*O*-[β-D-xylopyranosyl-(1→6)-β-D-glucopyranosyl]-7-hydroxy-3,4,8-trimethoxyxanthone.

The molecular formula of kouitchenside B (**2**) was determined as $C_{28}H_{34}O_{16}$ by HRESIMS (*m*/*z* 649.1749 $[M + Na]^+$). Its ^1H and ^{13}C NMR spectra (Table 1) were similar to those of compound **1**, except that an additional signal for a methoxy group at δ_H 3.86 replaced the hydroxy group signal at δ_H 9.49 (OH-7) in **1**, indicating that this additional methoxy group

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Table 1. ^{1}H and ^{13}C NMR Data of 1−3 and 3a in DMSO-d_6 (δ in ppm, J in Hz in parentheses)

	1		2		3		3a	
position	δ_H	δ_C	δ_H	δ_C	δ_H	δ_C	δ_H	δ_C
1		154.3		154.2		150.5	12.83, s, OH	154.8
2	6.94, s	98.0	6.92, s	97.8	7.07, s	99.4	6.49, s	94.3
3		156.8		156.9		151.8		155.1
4		130.9		130.7	9.11, s, OH	129.3	8.72, s, OH	125.2
4a		149.8		149.3		145.0		143.7
4b		148.6		149.8		148.8		149.6
5	7.22, d (9.1)	112.9	7.35, d (9.3)	112.6	7.20, d (9.1)	112.8	7.23, d (9.1)	113.3
6	7.31, d (9.1)	123.2	7.54, d (9.3)	119.8	7.32, d (9.1)	123.3	7.38, d (9.1)	124.4
7	9.49, s, OH	146.9		149.1	9.40, s, OH	146.6	9.55, s, OH	146.8
8		145.2		147.4		145.2		145.3
8a		117.0		117.1		116.8		114.6
8b		107.7		107.6		107.9		102.7
9		175.2		175.0		175.8		181.0
3-OCH_3	3.93, s	56.3	3.93, s	56.4	3.90, s	56.0	3.90, s	56.3
4-OCH_3	3.81, s	60.9	3.82, s	60.9				
7-OCH_3			3.86, s	56.6				
8-OCH_3	3.79, s	60.8	3.81, s	61.0	3.80,s	60.8	3.81, s	61.0
Glc-1′	4.90, d (7.6)	103.4	4.92, d (7.6)	103.1	4.73, d (5.0)	104.7		
2′	3.40, m	73.4[a]	3.41, m	73.3	3.40, m	73.6		
3′	3.32, m	75.8	3.34, m	75.9	3.31, m	76.1		
4′	3.25, m	69.6	3.24, m	69.6	3.16, m	70.2		
5′	3.63, m	76.1	3.63, m	76.1	3.39, m	77.7		
6′	4.03, m	69.0	4.03, m	69.0	3.77, m	61.1		
	3.62, m		3.62, m		3.50, m			
Xyl-1″	4.17, d (7.6)	104.2	4.16, d (7.6)	104.2				
2″	2.92, m	73.4[a]	3.92, m	73.4				
3″	3.08, m	76.7	3.09, m	76.8				
4″	3.16, m	70.0	3.17, m	70.0				
5″	3.66, m	65.7	3.67, m	65.7				
	3.01, m		3.00, m					

[a]Overlapped signals.

should be located at C-7 of the aglycone. This deduction was further supported by the HSQC and HMBC spectra, which showed the additional methoxy group (δ_C 56.6/δ_H 3.86) to have a long-range correlation with C-7 (δ_C 149.1). Thus, **2** was assigned as 1-*O*-[β-D-xylopyranosyl-(1→6)-β-D-glucopyranosyl)-3,4,7,8-tetramethoxyxanthone.

Kouitchenside C (**3**) gave a molecular formula of $C_{21}H_{22}O_{12}$, on the basis of its HRESIMS data (m/z 489.0991 $[M + Na]^+$). On acid hydrolysis, **3** gave D-glucose. Comparison of the spectroscopic data (Table 1) of **3** with those of **1** showed that they were superimposable in terms of the xanthone core, while the methoxy group (δ_H 3.81) at C-4 in **1** was replaced by a hydroxy group (δ_H 9.11) in **3**, and also signals associated with a Xyl residue were absent in **3**. In the HMBC spectrum, the anomeric proton of the Glc was correlated with C-1 (δ_C 150.5). From this information and from the coupling constant (J = 5.0 Hz) of the Glc anomeric proton, the structure of **3** was elucidated as 1-*O*-(β-D-glucopyranosyl)-4,7-dihydroxy-3,8-dimethoxyxanthone.

The xanthone aglycone (**3a**) of **3** was also found to be a new compound. The molecular formula of kouitchensone (**3a**), the acid hydrolysis product of **3**, was deduced as $C_{15}H_{12}O_7$ by HRESIMS (m/z 303.0511 $[M - H]^-$). Its NMR spectra (Table 1) were similar to the xanthone core of **3**, except that **3a** exhibited a chelated hydroxy group at δ_H 12.83 (1H, s, OH-1) and the signal at C-9 was shifted downfield from δ_C 175.8 (in **3**) to 181.0 (in **3a**), suggesting the presence of a chelated hydroxy group at C-1.[10] Accordingly, the structure of **3a** was deduced as 1,4,7-trihydroxy-3,8-dimethoxyxanthone.

Kouitchenside D (**4**) was assigned the molecular formula $C_{27}H_{32}O_{15}$ on the basis of its HRESIMS data (m/z 619.1640 $[M + Na]^+$). The NMR data (Table 2) of **4** were similar to those of 3,5,8-trimethoxyxanthone-1-*O*-glucopyranoside,[12] except for a group of signals from an additional xylose residue. In the HMBC spectrum, a cross-peak between the anomeric proton (δ_H 4.16) of Xyl and C′-6 (δ_C 68.7) of Glc indicated these two sugar residues to be connected in a 1→6 manner. The relative configuration of the Xyl residue was deduced as β from the coupling constant (J = 7.5 Hz). According to the data obtained, **4** was elucidated as 1-*O*-[β-D-xylopyranosyl-(1→6)-β-D-glucopyranosyl]-3,5,8-trimethoxyxanthone.

Kouitchenside E (**5**) gave a molecular formula of $C_{28}H_{34}O_{16}$ by HRESIMS (m/z 627.1932 $[M + H]^+$). Its ^{13}C NMR data (Table 2) were similar to those of **4** with the exception of a signal for an additional methoxy group, downfield shifts of C-5, C-7, and C-8a (2.7, 42.8, and 4.2 ppm, respectively), and upfield shifts of C-4b, C-6, and C-8 (6.9, 12.3, and 13.0 ppm, respectively). These observations suggested that this additional methoxy group is located at C-7, and this was confirmed by an HMBC correlation between the additional methoxy group (δ_H 3.89) and C-7 (δ_C 148.5). Thus, **5** could be proposed as 1-*O*-[β-D-xylopyranosyl-(1→6)-β-D-glucopyranosyl]-3,5,7,8-tetramethoxyxanthone.

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Table 2. ^{1}H and ^{13}C NMR Data of 4–6 in DMSO-d_6 (δ in ppm, J in Hz in parentheses)

	4		5		6	
position	δ_H	δ_C	δ_H	δ_C	δ_H	δ_C
1		158.8		158.9	11.20,[b] s, OH	157.0
2	6.75,[a] brs	100.5	6.76, d (2.3)	100.2	6.73, s	98.4
3		164.2		164.3		158.2
4	6.75,[a] brs	95.0	6.73, d (2.3)	94.8		129.1
4a		157.2		157.6		148.9
4b		145.8		138.9		144.9
5		141.3		144.0		139.9
6	7.34, d (9.1)	116.5	7.23, s	104.2	7.50, d (9.0)	121.8
7	6.84, d (9.1)	105.7		148.5	6.75, d (9.0)	109.3
8		152.5		139.5	11.62,[b] s, OH	153.0
8a		113.6		117.8		107.5
8b		108.0		107.5		102.7
9		174.3		174.4		184.3
3-OCH_3	3.87,[a] s	56.2	3.89,[a] s	56.1		
4-OCH_3					3.85, s	61.1
5-OCH_3	3.87,[a] s	56.4	3.96, s	56.5	3.91, s	57.2
7-OCH_3			3.89,[a] s	56.9		
8-OCH_3	3.80, s	56.1	3.74, s	60.9		
Glc-1′	4.89, d (7.2)	102.7	4.92, d (7.6)	102.4	5.10, d (7.0)	100.1
2′	3.37, m	73.4[a]	3.41, m	73.4[a]	3.34, m	73.1
3′	3.30, m	75.9	3.32, m	75.8	3.33, m	76.4
4′	3.24, m	69.5	3.25, m	69.5	3.24, m	69.5
5′	3.60, m	76.0	3.61, m	75.9	3.65, m	75.7
6′	3.94, m	68.7	3.96, m	68.6	3.92, m	68.5
	3.61, m		3.63, m		3.63, m	
Xyl-1″	4.16, d (7.5)	104.2	4.18, d (7.5)	104.1	4.16, d (7.5)	104.1
2″	2.95, m	73.4[a]	2.97, m	73.4[a]	2.98, m	73.3
3″	3.07, m	76.6	3.09, m	76.6	3.08, m	76.5
4″	3.20, m	69.7	3.23, m	69.7	3.30, m	69.4
5″	3.66, m	65.7	3.68, m	65.7	3.69, m	65.6
	2.97, m		3.00, m		2.97, m	

[a]Overlapped signals. [b]Signals may be interchanged.

The molecular formula of kouitchenside F (**6**) was determined as $C_{26}H_{30}O_{16}$ by HRESIMS (m/z 597.1483 $[M - H]^-$). After acid hydrolysis, **6** gave D-glucose and D-xylose. The NMR signals (Table 2) of **6** were similar to those of corymbiferin 3-*O*-β-D-glucopyranoside,[13] except for additional signals for a xylose residue and the downfield shift of C′-6 of the glucose unit (δ_C from 61.8 to 68.5), suggesting that the Xyl residue is located at C′-6 of Glc. This inference was supported by the correlation between the anomeric proton (δ_H 4.16) of Xyl and C′-6 (δ_C 68.5) of Glc in the HMBC spectrum. From this information, in addition to the coupling constant (J = 7.6 Hz) of the Xyl anomeric proton, **6** was assigned as 3-*O*-[β-D-xylopyranosyl-(1→6)-β-D-glucopyranosyl]-1,8-dihydroxy-4,5-dimethoxyxanthone.

Kouitchenside G (**7**) was obtained as a pale yellow powder. Its molecular formula was established as $C_{27}H_{32}O_{15}$ by HRESIMS (m/z 619.1632 $[M + Na]^+$). The NMR data (Table 3) of **7** were closely comparable to those of 1-*O*-(β-D-xylopyranosyl-(1→6)-β-D-glucopyranosyl)-3,5-dimethoxyxanthone,[14] except that the signals for a xylose residue were replaced by signals associated with a glucose residue. Its HMBC spectrum displayed long-range correlations between the anomeric proton (δ_H 5.00) of Glc-1 and C-1 (δ_C 159.2) of the aglycone and between the anomeric proton (δ_H 4.21) of Glc-2 and C′-6 (δ_C 68.9) of Glc-1. These indicated that the Glc-2 residue is linked to the Glc-1 residue by a (1→6) linkage. The coupling constant of the Glc-2 anomeric proton was found to be 7.5 Hz. Therefore, **7** was determined to be 1-*O*-[β-D-glucopyranosyl-(1→6)-β-D-glucopyranosyl]-3,5-dimethoxyxanthone.

The molecular formula of kouitchenside H (**8**) was determined to be $C_{27}H_{32}O_{16}$ by HRESIMS (m/z 611.1620 $[M - H]^-$). The NMR spectra (Table 3) of **8** were very similar to those of **7**, except for an additional chelated hydroxy group signal at δ_H 12.49 and a downfield shift of the C-9 (6.0 ppm) signal, indicating that a hydroxy group is located at C-8.[10] Upfield shifts were observed in C-5, C-7, and C-8a (8.7, 15.2, and 14.1 ppm, respectively), with a downfield shift for C-8 (37.1 ppm). Thus, **8** was defined as 1-*O*-[β-D-glucopyranosyl-(1→6)-β-D-glucopyranosyl]-8-hydroxy-3,5-dimethoxyxanthone.

The molecular formula of kouitchenside I (**9**) was established as $C_{26}H_{30}O_{15}$ by HRESIMS (m/z 605.1483 $[M + Na]^+$). On acid hydrolysis, **9** gave D-glucose and L-rhamnose. The NMR spectra (Table 3) of **9** were similar to those of 7-*O*-β-D-glucopyranosyl-1,8-dihydroxy-3-methoxyxanthone,[15] except for a group of signals from an additional rhamnose residue and the downfield shift of C′-2 of a glucose residue (δ_C from 73.2 to 76.1). This suggested that the Rha residue is located at C′-2 of Glc. The assumption was supported by the HMBC spectrum, in which the Rha anomeric proton (δ_H 5.21) showed a correlation with C′-2 (δ_C 76.1) of the Glc unit. The relative configuration of the Rha residue was deduced to be α by comparison with literature ^{13}C NMR spectroscopic data.[16] Accordingly, the structure of **9** was

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Table 3. ^{1}H and ^{13}C NMR Data of 7−10 in DMSO-d_6 (δ in ppm, J in Hz in parentheses)

	7		8		9		10	
position	δ_H	δ_C	δ_H	δ_C	δ_H	δ_C	δ_H	δ_C
1		159.2		159.1	11.78,[a] s, OH	161.9	13.26, s, OH	162.9
2	6.86, brs	100.8	6.83, brs	99.5	6.38, brs	97.4	6.36, brs	97.0
3		164.8		165.7		167.2		166.2
4	6.84, brs	95.6	6.82, brs	94.9	6.60, brs	92.9	6.57, brs	92.0
4a		158.4		158.6		157.6		156.5
4b		144.6		144.0		150.0		151.6
5		147.8		139.1	6.94, d (9.0)	105.5	7.33, d (9.3)	113.3
6	7.42, d (7.8)	115.7	7.41, d (9.3)	119.8	7.58, d (9.0)	125.1	7.65, d (9.3)	126.4
7	7.33, t (7.9)	123.9	6.68, d (9.3)	108.7		139.7		146.1
8	7.63, d (7.8)	116.5	12.49, s, OH	153.6	11.47,[a] s, OH	150.0		145.5
8a		123.0		108.9		107.4		115.0
8b		106.8		105.3		101.8		103.4
9		174.5		180.5		184.1		180.5
3-OCH_3	3.90, s	56.3	3.93, s	56.3	3.88, s	56.3	3.87, s	56.1
5-OCH_3	3.95, s	56.2	3.88, s	56.7				
Glc-1′	5.00, d (7.6)	102.3	5.12, d (7.6)	100.7	5.09, d (7.7)	98.8	5.10, d (7.6)	103.4
2′	3.43, m	73.5	3.44, m	73.3	3.56, m	76.1	3.45, m	74.4
3′	3.33, m	76.0	3.34, m	76.3	3.30, m	76.9	3.22, m	76.6
4′	3.25, m	69.8	3.25, m	69.7	3.21, m	69.8	3.67, m	69.7
5′	3.71, m	75.8	3.74, m	75.6	3.45, m	77.6	3.08, m	77.4
6′	4.01, m	68.9	3.99, m	68.8	3.65, m	60.6	3.55, m	60.5
	3.66, m		3.64, m		3.45, m		3.46, m	
	Glc		Glc		Rha		Rha	
1″	4.21, d (7.6)	103.7	4.19, d (7.1)	103.6	5.21, brs	100.2	5.27, brs	101.3
2″	2.98, m	73.6	2.97, m	73.5	3.44, m	70.5	3.21, m	69.5
3″	3.13, m	76.8	3.13, m	76.7	3.71, m	70.6	3.70, m	70.4
4″	3.05, m	70.1	3.05, m	70.1	3.18, m	72.0	3.31, m	71.8
5″	3.06, m	77.0	3.06, m	76.9	3.95, m	68.3	3.99, m	70.2
6″	3.66, m	61.1	3.66, m	61.0	1.10, d (6.1)	18.0	1.18, d (6.1)	17.9
	3.40, m		3.41, m					

[a]Signals may be interchanged.

elucidated as 7-*O*-[α-L-rhamnopyranosyl-(1→2)-β-D-glucopyranosyl]-1,8-dihydroxy-3-methoxyxanthone.

Kouitchenside J (**10**) gave a molecular formula of $C_{26}H_{30}O_{15}$ from its HRESIMS data (m/z 605.1483 [M + Na]$^+$) and again afforded gave D-glucose and L-rhamnose on acid hydrolysis. The spectroscopic data (Table 3) of **10** were similar to those of 7-*O*-β-D-glucopyranosyl-1,8-dihydroxy-3-methoxyxanthone,[15] except for additional rhamnose residue signals and the absence of a signal for a chelated hydroxy group. In addition, an upfield shift of C-9 (3.4 ppm) signal was observed, suggesting that C-8 or C-1 is also substituted.[10] The downfield shifts of C-5, C-7, and C-8a (7.5, 6.1, and 7.7 ppm, respectively) and the upfield shift of C-8 (4.3 ppm) indicated that C-8 is substituted. Moreover, in the HMBC spectrum, the Glc anomeric proton (δ_H 5.10) was correlated with C-8 (δ_C 145.5), while the Rha anomeric proton (δ_H 5.27) was correlated with C-7 (δ_C 146.1). Thus, together with the comparison of the two sugar signals with those of **9**, compound **10** could be proposed as 7-*O*-(α-L-rhamnopyranosyl)-8-*O*-(β-D-glucopyranosyl)-1-hydroxy-3-methoxyxanthone.

The known compounds isolated were identified by comparison of their NMR data with literature data as swertianolin (**11**),[17] mangiferin (**12**),[18] 1-*O*-[β-D-xylopyranosyl-(1→6)-β-D-glucopyranosyl]-8-hydroxy-3,7-dimethoxyxanthone (**13**),[15] 1-*O*-[β-D-xylopyranosyl-(1→6)-β-D-glucopyranosyl]-3,5-dimethoxyxanthone (**14**),[14] 1-*O*-primeverosyl-3,7,8-trimethoxyxanthone (**15**),[19] 1-*O*-[β-D-glucopyranosyl-(1→6)-β-D-glucopyranosyl]-8-hydroxy-3,7-dimethoxyxanthone (**16**),[20] triptexanthoside D (**17**),[21] norswertianolin (**18**),[17] neolancerin (**19**),[22] 7-*O*-[α-L-rhamnopyranosyl-(1→2)-β-D-xylopyranosyl]-1,8-dihydroxy-3-methoxyxanthone (**20**),[23] and 7-*O*-[β-D-xylopyranosyl-(1→6)-β-D-glucopyranosyl]-1,8-dihydroxy-3-methoxyxanthone (**21**).[24]

All isolated compounds were evaluated for α-glucosidase inhibitory effects. The IC_{50} values, defined as the compound concentration that inhibits α-glucosidase activity by 50%, are summarized in Table 4. Among them, compounds **2**, **4**, **5**, **6**, **11**, **12**, and **13** (with IC_{50} values of 383, 360, 371, 184, 126, 296, and 451 μM, respectively) displayed more potent inhibitory effects than the positive control, acarbose (IC_{50} = 627 μM), with the latter comparable to a reported value.[25] Interestingly, on further analysis, it was observed that the presence of an *O*-glc(6−1)-xyl

Table 4. Inhibitory Effects of Compounds 1−13 and Acarbose against α-Glucosidase[a]

compound	IC_{50} (μM)	compound	IC_{50} (μM)
1	1503 ± 119	**8**	693 ± 47
2	383 ± 18	**9**	>1717
3	701 ± 51	**10**	714 ± 55
4	360 ± 39	**11**	126 ± 23
5	371 ± 22	**12**	296 ± 52
6	184 ± 23	**13**	451 ± 41
7	956 ± 35	acarbose	627 ± 28

[a]Each value represents the mean ± SD (n = 3).

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residue resulted in relatively more effective inhibitors than other diglycoside units. A hydroxy group located at C-1 or C-8 (compounds **6** and **11**) enhanced the inhibitory effects of the compounds, while a diglycoside residue located at C-7 (compounds **9**, **17**, **20**, and **21**) produced steric hindrance and lowered the inhibitory activity.

EXPERIMENTAL SECTION

General Experimental Procedures. Optical rotations were measured on an AA10R digital polarimeter. UV spectra were run on a Cary-50 UV−vis spectrophotometer. IR spectra were recorded on an Avater-360 FT-IR spectrophotometer with KBr pellets. 1D- and 2D-NMR spectra were recorded on a Bruker AV-400 spectrometer (400 MHz for ^{1}H and 100 MHz for ^{13}C, respectively). Chemical shifts are expressed in δ (ppm) and are referenced to the solvent peaks at δ_H 2.50 and δ_C 39.5 for DMSO-d_6, respectively, and coupling constants are in Hz. HRESIMS were measured by an Agilent 6520 Q-TOF LC-MS mass spectrometer for compounds **2**−**7**, **9**, and **10** and a Bruker micrOTOF-Q MS spectrometer for compounds **1**, **3a**, and **8**. Preparative HPLC was performed on a Hitachi Spectra Series HPLC system equipped with an L-2130 pump and a UV L-2400 detector in a YMC-ODS column (10 mm × 250 mm, 5 μm; flow rate at 2.0 mL/min; wavelength detection at 254 nm). GC analysis was carried out on an Agilent 7820A GC system using an HP-5 (30 m × 0.32 mm × 0.25 μm) column; detection FID; carrier gas N_2; injection temperature 250 °C, detection temperature 250 °C, column temperature 180 °C.

Plant Material. The whole plant of *S. kouitchensis* was collected in Enshi, Hubei Province, People's Republic of China, in October 2010, and identified by one of the authors (J.-C.C.). A voucher specimen (*S.k*-2010-1010) has been deposited in the University herbarium for future reference.

Extraction and Isolation. The chopped, dried whole plants of *S. kouitchensis* (15 kg) were refluxed with 120 L of 95% (v/v) EtOH−H_2O twice, two hours each time. After filtration, the filtrate was concentrated under reduced pressure to yield a brownish residue (3.0 kg). Part of the residue (2.5 kg) was suspended in water and partitioned successively with petroleum ether, CH_2Cl_2, EtOAc, and *n*-butanol, to afford five fractions.

The *n*-butanol fraction (890.0 g) was separated over a polyamide resin column, using an EtOH−H_2O gradient mobile phase, to give five fractions (A−E). Fraction B (10% EtOH−H_2O, 120 g) was purified by passage over Toyopearl HW-40, eluted with $CHCl_3$−MeOH (1:1), to give three subfractions (Ba−Bc). Subfraction Bb was further purified using ODS-A (MeOH−H_2O gradient mobile phase) and then by preparative HPLC (30% CH_3CN−H_2O) to yield compounds **1** (17 mg), **5** (21 mg), **7** (25 mg), **4** (9 mg), **2** (28 mg), **14** (13 mg), and **15** (41 mg).

Fraction C (20% EtOH−H_2O, 76 g) was subjected to separation over ODS-A using a MeOH−H_2O gradient mobile phase to give seven subfractions (Ca−Ch). Subfraction Cb was purified by preparative HPLC (27% CH_3CN−H_2O) to yield compounds **3** (18 mg) and **8** (25 mg). Subfraction Ce was separated over Sephadex LH-20 eluted with CH_2Cl_2−MeOH (1:1) to yield compounds **16** (21 mg) and **17** (14 mg). Subfraction Cf was purified by preparative HPLC (30% CH_3CN−H_2O) to give compound **6** (16 mg). Subfraction Cg was purified over Sephadex LH-20, eluted with CH_2Cl_2−MEOH (1:1), and then purified by preparative HPLC (30% CH_3CN−H_2O) to yield compounds **9** (20 mg) and **10** (13 mg).

Fraction D (30% EtOH−H_2O, 256 g) was suspended in MeOH (0.1 g/mL) and filtered to afford a sediment and the filtrate. The sediment (120 g) was subjected to purification by silica gel CC, using $CHCl_3$−MeOH (50:1−1:1) as mobile phase, to give compounds **11** (10.5 g) and **18** (16.8 g). In turn, the filtrate was subjected to passage over ODS-A using a MeOH−H_2O gradient system (0:100−100:0), to give six subfractions (Da−Df). Compound **12** (2.3 g) was recrystallized in MeOH from subfraction Da. Subfraction Db was purified over Sephadex LH-20 eluted with CH_2Cl_2−MeOH (1:1) to give compound **19** (176 mg). Subfraction De was purified by preparative HPLC (30% CH_3CN−H_2O) to give compounds **13** (23 mg), **21** (21 mg), and **20** (73 mg).

*Kouitchenside A (**1**):* yellowish gum; $[\alpha]^{25}_D$ −69.0 (0.1, MeOH); UV (MeOH) λ_{max} (log ε) 255 (4.21), 310 (3.75), 370 (3.35) nm; IR (KBr) ν_{max} 3369, 2932, 1619, 1589, 1311, 1064, 827 cm^{-1}; ^{1}H and ^{13}C NMR data, see Table 1; HRESIMS *m*/*z* [M − H]$^-$ 611.1648 (calcd for $C_{27}H_{31}O_{16}$, 611.1618).

*Kouitchenside B (**2**):* pale yellow, amorphous powder; $[\alpha]^{25}_D$ −43.9 (0.07, MeOH); UV (MeOH) λ_{max} (log ε) 230 (4.20), 255 (4.20), 310 (3.79), 360 (3.48) nm; IR (KBr) ν_{max} 3401, 2926, 1660, 1601, 1481, 1419, 1122, 1070, 797 cm^{-1}; ^{1}H and ^{13}C NMR data, see Table 1; HRESIMS *m*/*z* [M + Na]$^+$ 649.1749 (calcd for $C_{28}H_{34}O_{16}Na$, 649.1739).

*Kouitchenside C (**3**):* yellow, amorphous powder; $[\alpha]^{25}_D$ −52.1 (0.09, MeOH); UV (MeOH) λ_{max} (log ε) 240 (4.15), 265 (4.26), 320 (3.74) nm; IR (KBr) ν_{max} 3372, 2918, 1656, 1627, 1484, 1419, 1100, 823 cm^{-1}; ^{1}H and ^{13}C NMR data, see Table 1; HRESIMS *m*/*z* [M + Na]$^+$ 489.0991 (calcd for $C_{21}H_{22}O_{12}Na$, 489.1003).

Hydrolysis of Kouitchenside C (3) (ref 8). Compound **3** (10 mg) was refluxed with 2 N CF_3COOH in aqueous MeOH (25 mL) for 3 h at 60 °C. The reaction mixture was then evaporated to dryness with MeOH until neutral and diluted with H_2O (10 mL). After being extracted with EtOAc (3 × 10 mL), the EtOAc layer was concentrated to afford **3a**.

*Kouitchensone (**3a**):* brownish, amorphous powder; UV (MeOH) λ_{max} (log ε) 235 (4.22), 270 (4.35), 335 (3.80) nm; IR (KBr) ν_{max} 3367, 1652, 1608, 1477, 1328, 1212, 1101, 1055, 820 cm^{-1}; ^{1}H and ^{13}C NMR data, see Table 1; HRESIMS *m*/*z* [M − H]$^-$ 303.0511 (calcd for $C_{15}H_{11}O_7$, 303.0510).

*Kouitchenside D (**4**):* pale yellow, amorphous powder; $[\alpha]^{25}_D$ −57.3 (0.08, MeOH); UV (MeOH) λ_{max} (log ε) 245 (4.17), 275 (3.98), 305 (3.99), 360 (3.80) nm; IR (KBr) ν_{max} 3392, 2928, 1623, 1606, 1487, 1261, 1071, 806 cm^{-1}; ^{1}H and ^{13}C NMR data, see Table 2; HRESIMS *m*/*z* [M + Na]$^+$ 619.1640 (calcd for $C_{27}H_{32}O_{15}Na$, 619.1633).

*Kouitchenside E (**5**):* pale yellow, amorphous powder; $[\alpha]^{25}_D$ −48.5 (0.08, MeOH); UV (MeOH) λ_{max} (log ε) 230 (4.18), 250 (4.19), 300 (3.93), 370 (3.42) nm; IR (KBr) ν_{max} 3400, 2922, 1624, 1596, 1297, 1062, 812 cm^{-1}; ^{1}H and ^{13}C NMR data, see Table 2; HRESIMS *m*/*z* [M + H]$^+$ 627.1932 (calcd for $C_{28}H_{35}O_{16}$, 627.1920).

*Kouitchenside F (**6**):* brownish, amorphous powder; $[\alpha]^{25}_D$ −56.8 (0.20, MeOH); UV (MeOH) λ_{max} (log ε) 230 (4.11), 260 (4.25), 345 (3.82) nm; IR (KBr) ν_{max} 3401, 2930, 1631, 1582, 1493, 1273, 1070, 817 cm^{-1}; ^{1}H and ^{13}C NMR data, see Table 2; HRESIMS *m*/*z* [M − H]$^-$ 597.1483 (calcd for $C_{26}H_{29}O_{16}$, 597.1461).

*Kouitchenside G (**7**):* pale yellow, amorphous powder; $[\alpha]^{25}_D$ −61.0 (0.07, MeOH); UV (MeOH) λ_{max} (log ε) 245 (4.15), 299 (3.76), 340 (3.37) nm; IR (KBr) ν_{max} 3391, 2922, 1623, 1591, 1299, 1071, 771 cm^{-1}; ^{1}H and ^{13}C NMR data, see Table 3; HRESIMS *m*/*z* [M + Na]$^+$ 619.1632 (calcd for $C_{27}H_{32}O_{15}Na$, 619.1633).

*Kouitchenside H (**8**):* yellow, amorphous powder; $[\alpha]^{25}_D$ −44.9 (0.15, MeOH); UV (MeOH) λ_{max} (log ε) 240 (4.20), 280 (4.01), 310 (3.89) nm; IR (KBr) ν_{max} 3400, 1651, 1606, 1486, 1445, 1242, 1057, 817 cm^{-1}; ^{1}H and ^{13}C NMR data, see Table 3; HRESIMS *m*/*z* [M − H]$^-$ 611.1620 (calcd for $C_{27}H_{31}O_{16}$, 611.1618).

*Kouitchenside I (**9**):* yellow, amorphous powder; $[\alpha]^{25}_D$ −95.3 (0.10, MeOH); UV (MeOH) λ_{max} (log ε) 235 (4.19), 260 (4.23), 330 (3.95) nm; IR (KBr) ν_{max} 3367, 2929, 1663, 1635, 1504, 1275, 1047, 811 cm^{-1}; ^{1}H and ^{13}C NMR data, see Table 3; HRESIMS *m*/*z* [M + Na]$^+$ 605.1483 (calcd for $C_{26}H_{30}O_{15}Na$, 605.1477).

*Kouitchenside J (**10**):* yellow, amorphous powder; $[\alpha]^{25}_D$ −63.3 (0.10, MeOH); UV (MeOH) λ_{max} (log ε) 240 (4.18), 254 (4.21), 315 (3.95) nm; IR (KBr) ν_{max} 3404, 2921, 1651, 1601, 1472, 1272, 1060, 821 cm^{-1}; ^{1}H and ^{13}C NMR data, see Table 3; HRESIMS *m*/*z* [M + Na]$^+$ 605.1483 (calcd for $C_{26}H_{30}O_{15}Na$, 605.1477).

Acid Hydrolysis of Compounds 1−10 (ref 8). Compounds **1**, **2**, and **4**−**10** (each 5 mg) and **3** (10 mg) were refluxed with 2 N CF_3COOH in aqueous MeOH (25 mL) for 3 h at 60 °C. The reaction mixture was then evaporated to dryness with MeOH until neutral and diluted with H_2O (10 mL). After being extracted with EtOAc (3 × 10 mL), the aqueous layer was concentrated and compared with reference D-glucose, D-xylose, and L-rhamnose (Sigma-Aldrich, St. Louis, MO,

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USA) by TLC (silica gel with $CHCl_3$–MeOH–H_2O, 6:4:1). The residue was dissolved in pyridine (1.5 mL). Then 900 μL of HMDS–TMCS (hexamethyldisilazane–trimethylchlorosilane, 2:1) was added, and the mixture was stirred at 60 °C for 30 min. The supernatant was subjected to GC analysis. Derivatives of L-rhamnose (5.64 min), D-xylose (7.17 min), and D-glucose (13.33 min) were detected from **1**–**10**, separately.

Bioassay. Inhibitory α-glucosidase (from *Saccharomyces cerevisiae*; Sigma-Aldrich, St. Louis, MO, USA) activities were determined by using *p*-nitrophenyl-α-D-glucopyranoside (PNPG) as the substrate, according to a reported method with minor modifications.[25] Briefly, 20 μL of enzyme solution [0.6 U/mL α-glucosidase in 0.1 M potassium phosphate buffer (pH 6.8)] and 120 μL of the test compound in water containing 0.5% DMSO were mixed and preincubated for 15 min at 37 °C prior to initiation of the reaction by adding the substrate. After preincubation, 20 μL of PNPG solution [5.0 mM PNPG in 0.1 M potassium phosphate buffer (pH 6.8)] was added and then incubated together at 37 °C. After incubation, 80 μL 0.2 M Na_2CO_3 in 0.1 M potassium phosphate buffer was added to the test tube to stop the reaction. The amount of PNP released was quantified by using a UVmax kinetic microplate reader (Bio Tek, Synergy 2, Winooski, VT, USA) at 405 nm.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Structures of known compounds (**14**–**21**), IC_{50} values of extracts and known compounds (**14**–**21**), and copies of 1D-NMR, 2D-NMR, MS, and IR spectra for compounds **1**–**10** and **3a**. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author

*Tel/Fax: +86 27 83692793. E-mail: homespringchen@126.com.

Notes

The authors declare no competing financial interest.

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