Pergamon

SCIENCE DIRECT®

Bioorganic & Medicinal Chemistry 11 (2003) 703–708

BIOORGANIC & MEDICINAL CHEMISTRY

Biologically Active Phenols from *Saussurea medusa*

Cheng-Qi Fan and Jian-Min Yue*

State Key Laboratory of Drug Research, Institute of Materia Medica, Shanghai Institutes for Biological Sciences, Chinese Academy of Sciences, 294 Taiyuan Road, Shanghai, 200031, PR China

Received 16 August 2002; accepted 28 September 2002

Abstract—Sixteen phenolic compounds were isolated from the polar fraction of *Saussurea medusa* and were structurally elucidated by chemical evidences and spectral methods. These compounds include two new lignan glucosides, namely medusasides A (**1**) and B (**2**), and fourteen known phenolic compounds (**3**–**16**). One major compound, apigenin 7-*O*-[α-L-rhamnopyranosyl-(1→6)-β-D-glucopyranoside] (**6**) showed remarkable activity to attenuate the scopolamine induced memory deficit of mice. Compound **6** and another major one, quercetin (**8**) also exhibited moderate cell protecting activities against hydrogen peroxide (H_2O_2) induced PC12 cell damage.

Introduction

The whole plants of the *Saussurea* genus (Asteraceae) were used in the both of traditional Chinese medicine and Tibet folklore medicine for the cure of rheumatic arthritis, dysmenorrhea and gynopathy. A series of compounds with a variety of biological activities have been reported from the genus of *Saussurea*.[1–3] From the plant *S. medusa* Maxim, nine flavonoids and flavonoid glycosides have been reported,[4,5] and one flavonoid glycoside A_1 was tested for effects on CNS of mouse.[6] Here, we present the isolation and identification of two new lignan glucosides, namely medusasides A (**1**) and B (**2**), together with 14 known phenolic compounds from the polar fraction of *S. medusa*. One major compound, apigenin 7-*O*-[α-L- rhamnopyranosyl-(1→6)-β-D-glucopyranoside] (**6**) showed remarkable activity to attenuate the scopolamine induced memory deficit of mice by the animal model of mouse behavioral tests in the water maze. The compounds **4**, **6**–**9** and **14** with relatively rich quantity were tested for cell protecting activity against hydrogen peroxide (H_2O_2) induced PC12 cell damage, only compound **6** and another major one, quercetin (**8**) exhibited moderate cell protecting activity.

Results and Discussion

Structure elucidation of the new compounds 1 and 2

Compound **1** was obtained as an amorphous powder. The possible molecular formula of **1** was inferred to be $C_{26}H_{34}O_{12}$ from its quasi-molecular ions at *m*/*z* 561.3 $[M+Na]^+$ in positive ion mode ESI-MS and at *m*/*z* 537.2 $[M-H]^-$ in negative ion mode ESI-MS, and the ^{13}C NMR (with DEPT) spectral data (Table 1). The molecular composition of $C_{26}H_{34}O_{12}$ was finally confirmed by HREIMS at *m*/*z* 376.1525 ($C_{20}H_{24}O_7$, calculated: 376.1522) [M-glc (162)]$^+$. Hydroxyl groups, carbonyl group and aromatic ring(s) could be existed in the structure of compound **1** judged from the absorption bands at 3406 (OH), 1655, 1591 and 1516 cm^{-1} in its IR spectrum. In the ^{13}C NMR, 12 carbon signals were appeared at the down field, four of which at δ_C 146.2, 149.2, 149.3 and 153.6 were oxygenated, suggesting the presence of two benzene rings. One carbon signal atδ_C 203.5 showed the possible presence of a conjugated ketone group. Two methoxyl groups and a glucopyranosyl moiety were also distinguished in the structure of **1** on the basis of ^1H and ^{13}C NMR spectra, and the remaining carbon signals were observed as three methylenes (two of them were oxygenated) and two methines. The above-mentioned data proposed that compound **1** was most likely a lignan glucoside. The key carbon signals for two methines at δ_C 43.1 (C-8) and 50.1 (C-8′) and the coupling patterns of key proton signals of H-8 and H-8′ indicated that the aglycone of compound **1** was diphenylbutane type lignan[7] and confirmed by HMBC spectrum. In the HMBC spectrum, the correlations were observed among H-8 at δ_H 2.20 with C-7 (δ_C 37.0), C-9 (δ_C 70.5) and C-8′ (δ_C 51.0), and among H-8′ at δ_H 2.18 with C-7′ (δ_C 203.5), C-9′ (δ_C 62.0) and C-8 (43.1). In the ^1H NMR spectrum of **1**, the coupling patterns of the aromatic proton signals at δ_H 6.62 (d, $J=1.8$ Hz), 6.55 (d, $J=8.1$ Hz) and 6.51 (dd, $J=1.8$, 8.1 Hz), and aromatic proton signals at δ_H 7.26

*Corresponding author. Tel.: +86-21-6431-1833; fax: +86-21-6437-0269; e-mail: jmyue@mail.shcnc.ac.cn

0968-0896/03/$ - see front matter © 2002 Elsevier Science Ltd. All rights reserved.
PII: S0968-0896(02)00470-4

Table 1. ^{1}H (400 MHz) and ^{13}C (100 MHz) NMR of **1** (CD_3OD, δ in ppm)

	^{1}H	^{13}C		^{1}H	^{13}C
1		131.3	4′		153.6
2	6.62,d,1.8	114.5	5′	6.61,d,8.4	116.0
3		149.2	6′	7.18,dd,1.8,8.4	125.4
4		146.2	7′		203.5
5	6.55,d,8.1	116.3	8′	2.18,m	50.1
6	6.51,dd,1.8,8.1	123.5	9′	3.86,dd,7.7,11.0	62.0
7	2.89,dd,7.7,13.6	37.0		3.72,dd,3.8,11.0	
	2.73,dd,6.8,13.6		3′-OMe	3.67, s	56.7
8	2.20,m	43.1	Glc-1	4.04, d, 7.7	105.0
9	3.30,dd,5.6,10.2	70.5	Glc-2	3.06,m	75.5
	3.76,dd,4.8,10.2		Glc-3	3.15,m	78.4
3-OMe	3.62,s	56.7	Glc-4	3.15,m	71.9
1′		133.3	Glc-5	3.06,m	78.2
2′	7.26,d,1.8	112.7	Glc-6	3.66,m	63.0
3′		149.3		3.50,dd,5.5,11.7	

(d, $J=1.8$ Hz), 6.61 (d, $J=8.4$ Hz) and 7.18 (dd, $J=1.8$, 8.4 Hz), suggested the presence of two 1,3,4-trisubstituted benzene rings. In the NOESY spectrum, The NOE correlations between 3-OMe at δ_H 3.62 and H-2 at δ_H 6.62 (d, $J=1.8$ Hz), and between 3′-OMe at δ_H 3.67 and H-2′ at δ_H 7.26 (d, $J=1.8$ Hz) strongly indicated the two methoxyl groups were connected to the C-3 and C-3′, respectively. The glucose moiety assigned as β-configuration on the basis of the coupling constant of the anomeric proton at δ_H 4.04 (d, $J=7.7$ Hz) was attached to the C-9 judged from the correlation signals between C-9 and the anomeric proton in HMBC spectrum, and the NOE correlation between H-9 and the anomeric proton in NOESY spectrum. The structure of compound **1** was thus elucidated to be 4-*O*-(β-D-glucopyranosyl)-2-hydroxymethyl-3-[(4-hydroxy-3-methoxyphenyl)methyl]-1-(4-hydroxy-3-methoxyphenyl)butan-1-one (Fig. 1). The complete assignments of the proton and the carbon signals of compound **1** were achieved by 1D NMR and 2D NMR (^{1}H-^{1}H COSY, HMQC, HMBC and NOESY) spectra (Table 1).

Compound **2** was obtained as an amorphous powder. Its negative ion mode ESI-MS showed a quasi-molecular ion at m/z 537.3 $[M–H]^-$ and a significant fragment at m/z 374.9 $[M–H\text{-}162]^-$. A quasi-molecular ion at m/z 561.3 $[M+Na]^+$ and a remarkable fragment at m/z 399.1 $[M+Na\text{-}162]^+$ were also observed in its positive ion mode ESI-MS. The molecular formula of **2** was then deduced to be $C_{26}H_{34}O_{12}$ on the basis of a combination of ESI-MS and ^{13}C NMR (DEPT) (Table 2), and confirmed by HREIMS at m/z 376.1530 ($C_{20}H_{24}O_7$, calcd: 376.1522) $[M\text{-glc }(162)]^+$. Further analysis of its ^{1}H and ^{13}C NMR indicated the presence

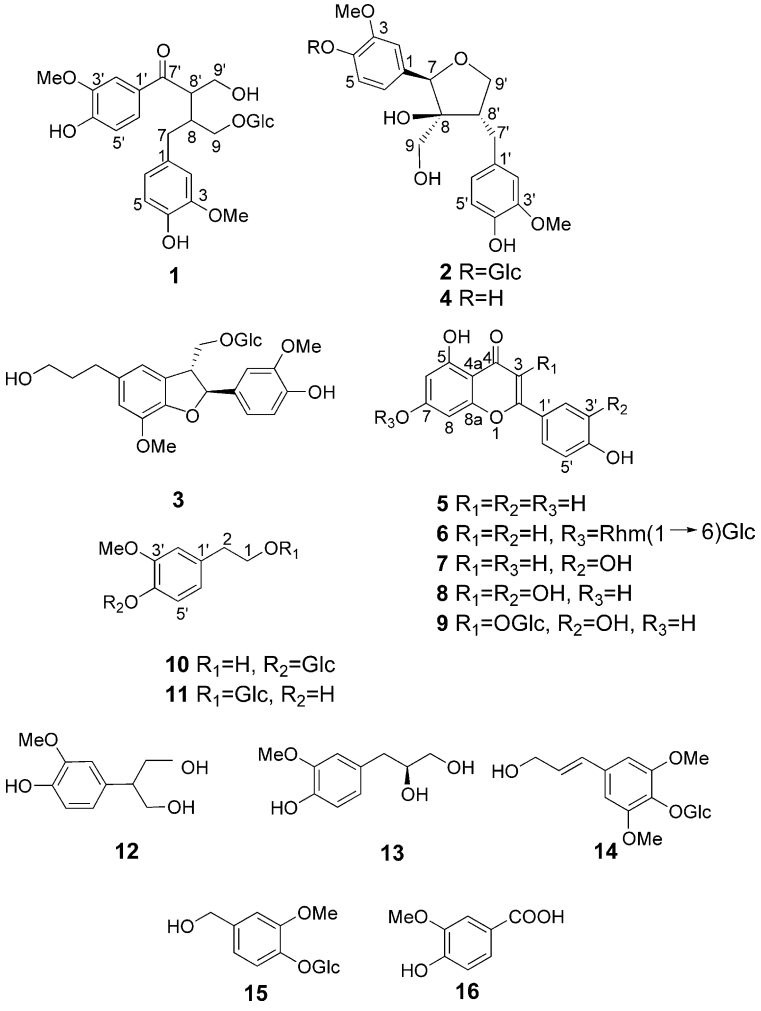

Figure 1. Structures of compounds **1**–**16**.

Table 2. ^{1}H (400 MHz) and ^{13}C (100 MHz) NMR of **2** (CD_3OD, δ in ppm)

	^{1}H	^{13}C		^{1}H	^{13}C
1		134.9	5′	6.92,d,7.9	116.5
2	7.23,d,1.9	113.9	6′	6.85,dd,1.8,7.9	122.6
3		150.7	7′	3.30,dd,3.2,12.9	35.2
4		147.8		2.70,dd,12.6,12.9	
5	7.33,d,8.4	117.8	8′	2.80,m	52.3
6	7.07,dd,1.8,8.4	123.5	9′	4.30,dd,6.6,8.4	62.0
7	5.07,s	85.7		3.90,overlapped	
8		83.6	3′-OMe	4.05,s	56.7
9	4.00,d,11.4	64.8	Glc-1	5.07, d, 7.3	103.3
	3.83,d,11.4		Glc-2	3.68,m	75.3
3-OMe	4.10,s	57.0	Glc-3	3.58,m	78.5
1′		133.6	Glc-4	3.58,m	71.7
2′	7.00,d,1.8	113.8	Glc-5	3.65,m	78.2
3′		149.4	Glc-6	3.90,m	62.9
4′		146.2		4.12,m	

of two 1,3,4-trisubstituted benzene rings, a glucopyranosyl moiety, two methoxyl groups, three methylenes (two oxygenated), two methines (including one oxygenated) and one oxygenated quaternary carbon in the structure of **2**. The ^{1}H NMR and ^{13}C NMR patterns of aglycone moiety of **2** showed great similarity with those of (−)-berchemol (**4**), which was also isolated from this plant. The oxygenated methine at δ_C 85.7 and a singlet proton δ_H 5.07 were respectively assigned to C-7 and H-7. An oxygenated methylene at δ_C 64.8, bearing two AB-type-coupling protons at δ_H 4.00, 3.83 (each 1H, d, $J = 11.4$ Hz, H-9) correlated with the quaternary carbon C-8 at δ_C 83.6 in the HMBC spectrum, was attributable to C-9. The carbon signals at δ 35.2, 52.3 and 72.4 were respectively assigned to C-7′, C-8′ and C-9′ according to the chemical shift and DEPT spectrum. The proton signals of H-7′, H-8′ and H-9′ were then respectively distinguished by the correlations with C-7′, C-8′ and C-9′ in the HMQC. A 7, 9′- epoxy linkage was indicated by the strong correlations among H-7 with C-8′ and C-9′ in the HMBC spectrum. A NOESY spectrum was performed to reveal the relative configuration of compound **2**. The key NOE correlations (Fig. 2) revealed that the aglycone of **2** had the same planar structure and relative configuration as that of (−)-berchemol.

The glucopyranosyl moiety was linked to C-4 with β-configuration was ascertained according to the ^{1}H NMR, HMBC and NOESY spectra. Acidic hydrolysis of compound **2** afforded D-glucose and (−)-berchemol (**4**), $[\alpha]_D^{20}$ −9.3° (*c* 0.081, MeOH) (reported value −7.9°, $c = 0.30$, in MeOH).[8] The structure of compound **2** was determined to be (−)-berchemol 4-*O*-β-D-glucopyranoside (Fig. 1), and its NMR data were assigned as in Table 2.

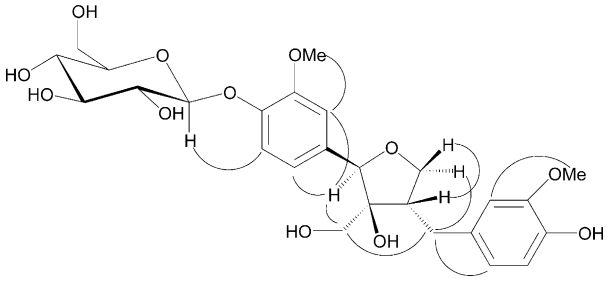

Figure 2. Main NOE correlations of compound **2**.

Structural identification of the known compounds 3–16

Among those of the known compounds, apigenin (**5**), luteolin (**7**), quercetin (**8**), quercetin 3-*O*-β-D-glucopyranoside (**9**) and vanillic acid (**16**) were identified by spectral data (^{1}H NMR and MS) and comparison with authentic samples (co-TLC). Dihydrodehydrodiconiferyl alcohol 9′-*O*-β-D-glucopyranoside (**3**),[9] (−)-berchemol (**4**),[8] 4-(2-hydroxyethyl)-2-methoxyphenyl β-D-glucopyranoside (**10**),[10] 2-(4- hydroxy-3-methoxyphenyl)propan-1,3-diol (**12**),[11] (2*S*)-3-(4-hydroxy-3-methoxy phenyl)propan-1,2-diol (**13**),[12] syringin (**14**)[13] and glucovanillyl alcohol (**15**)[14] were identified by comparison of their spectral data (^{1}H, ^{13}C NMR, MS and $[\alpha]_D$) with those reported. 2-(4-Hydroxy-3-methoxyphenyl)ethyl β-D-glucopyranoside **11** was identified by spectral data for the first time as a natural product, which was synthesized before.[15] Compound **6** was identified as apigenin 7-*O*-[α-L-rhamnopyranosyl-(1→6)-β-D-glucopyranoside] by comparison of ^{1}H and ^{13}C NMR spectral data with those of its isomer apigenin 7-*O*-[α-L-rhamnopyranosyl-(1→2)-β-D-glucopyranoside].[5] The glc-6 carbon signal in compound **6** was down-field shifted to 66.0 ppm in the ^{13}C NMR caused by the glucosylation, while that of the latter was appeared at 61.0 ppm (both in DMSO-d_6). The spectral data of compounds **6** and **11** were presented in the experimental part. Except for compounds **5**, **7** and **9**, all other known compounds were isolated from this plant for the first time.

Evaluation of biological activities

Effects on scopolamine-induced memory deficits of mice. In the course of our search for biologically active components from natural resources, the polar fraction of the EtOH extract of *S. medusa* showed a moderate activity to attenuate the scopolamine induced memory deficit by mouse behavioral tests in the water maze. After purification, one major compound **6** obtained from the polar fraction presented remarkable activity

to attenuate the scopolamine induced memory deficit in the same animal model. Oral administration of compound **6** at the dosages of 10, 15 and 20 mg/kg and then injection of scopolamine at the dose of 4.5 mg/kg for each group of mice 30 min later, the mice taking compound **6** in the tested groups obviously reduced the errors to enter non-exit and shortened the time to reach the platform than those injected only 4.5 mg/kg of scopolamine (Table 3).

Cell protective activities of major phenolics against H_2O_2-iduced PC12 cell damage

The major phenolic compounds **4**, **6**–**9** and **14** were tested for protecting activity against H_2O_2-induced damage in rat pheochromocytoma line PC12 cells. Two of them, apigenin 7-*O*-[α-L-rhamnopyranosyl-(1→6)-β-D-glucopyranoside] (**6**) and quercetin (**8**), showed moderate protective activities against H_2O_2-induced cell damage (Fig. 3).

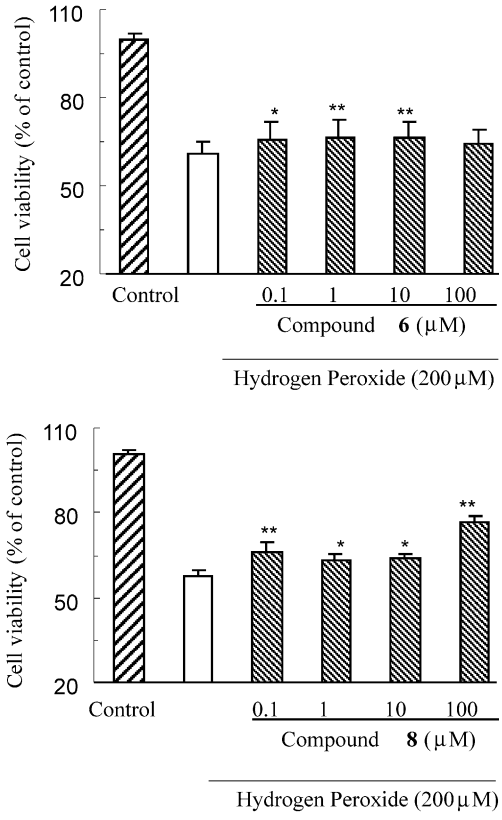

Figure 3. Effects of compounds **6** and **8** on cell viability. Cells were incubated with 200 μM H_2O_2 for 30 min and the cultures were further developed for another 6 h. Samples were added to the cultures 2 h prior to H_2O_2 addition. Cell viability was obtained by measuring the MTT reduction. Two independent experiments were carried out in triplicate. All data were expressed as percentage of control value. Statistical comparison was made by using one-way ANOVA, and followed by Duncan's test. The data were expressed as means ± SEM; $^*P<0.05$, $^{**}P<0.01$ vs H_2O_2 control group.

Experimental

General

Optical rotation $[\alpha]_D$ values were measured with a Perkin–Elmer polarimeter 341. UV spectra were recorded on a Shimadzu UV-210A spectrometer. IR spectra were performed on a Nicolet Magna 750 spectrometer with KBr discus. NMR spectra were obtained on a Brucker AM-400 MHz spectrometer. General ^1H NMR data were run at 400 MHz, and ^{13}C NMR were measured at 100.6 MHz. Chemical shifts are expressed in ppm relative to TMS. ESI-MS were recorded with a Finnigan LCQ^{DECA} mass spectrometer.

Plant material

The whole plant of *S. medusa* Maxim was collected in September 2000 in the Tibet Autonomous Region of China, and was identified by professor Zeng-Tao Wang of Shanghai Chinese Traditional Medical Unversity. A voucher specimen (No. Sm-2000-1Y) was deposited in Shanghai Institute of Materia Medica, Shanghai Institutes for Biological Sciences, Chinese Academy of Sciences, PR China.

Extaction and isolation

The dried whole plant of *S. medusa* (2.5 kg) was powdered and extracted by reflux in 95% EtOH for three times (2L×3), and the combined EtOH solution was evaporated to dryness under vacuum to give an extract (230 g). The extract was suspended in 1.0 L water and then extracted successively with dichloromethane and *n*-butanol to give fractions DM (60 g) and Bu (45 g),

Table 3. Effects on scopolamine-induced mice memory deficits of compound **6**

Sample combinations	Dose (mg/kg + mg/kg) po + ip	*N*	Time to find the platform	Number of entering non-exit
Saline + saline	/ + 4.5	12	15.8 ± 2.8	0.9 ± 0.3
Saline + scopolamine	/ + 4.5	16	51.4 ± 3.4[a]	7.5 ± 0.6[a]
Compound **6**	10 + 4.5	10	44.1 ± 5.6	4.8 ± 1.0[b]
+ scopolamine	15 + 4.5	10	36.7 ± 6.5	3.8 ± 1.0[c]
	20 + 4.5	10	43.8 ± 8.3	5.9 ± 1.4

N stands for the numbers of mice in the tested groups; data were expressed as means ± SEM. All mice were trained to follow a criterion of finding the platform within 20 min and the errors of entering non-exit were less than 2 (<2). The samples were orally administered 30 min prior to injection (ip) of scopolamine. The time to reach the platform and the numbers of entering non-exit were measured after 20 min.[16]

[a] $P<0.05$ vs saline + saline group.

[b] $P<0.05$ vs saline + scopolamine group.

[c] $P<0.01$ vs saline + scopolamine group.

respectively, and the aqueous part was condensed to give water-soluble fraction W (122 g).

The fraction Bu (45 g) was subjected to column chromatography (CC) on MCI GEL CHP 20P eluted with H_2O, 20% and 50% methanol in water, MeOH and acetone to give fractions 1–5. Fraction 5 was passed through a column of Sephadex LH-20 eluted with EtOH to give daucosterol. Fraction 4 was re-chromatographed on MCI GEL CHP 20P eluted with 70% methanol in water to give a major fraction 4a containing flavonoids and four other fractions 4b–4e. Fraction 4d was then subjected to CC on silica gel eluted with $CHCl_3$–MeOH (10:1) to give compound **4** (18 mg). Fraction 4a was subjected to CC on silica gel eluted with petroleum ether–EtOAc–formic acid (2:1:0.02) to give three parts and then passed through columns of Sephadex LH-20 eluted with EtOH to give compounds **5** (75 mg), **7** (134 mg) and **8** (55 mg). Fraction 4c was chromatographed on a reversed phase C18 silica gel eluted with 80% methanol in water to give compound **16** (83 mg). Part of fraction 3 was passed through a column of Sephadex LH-20 eluted with 70% ethanol in water to give two flavonoid glycosides, compound **6** (784 mg) and **9** (51 mg). Fraction 2 was re-chromatographed on a column of MCI GEL CHP 20P eluted with 10–50% methanol in water to obtain six fractions 2a–2f. Compounds **12** (13.5 mg) and **13** (6.5 mg) were obtained from fraction 2a by extensive column chromatography on reversed phase C18 silica gel eluted with 30–40% methanol in water. Fraction 2b was passed through a column of Sephadex LH-20 eluted with 70% ethanol in water and then subjected to CC on silica gel eluted with $CHCl_3$–MeOH (6:1) to give compound **15** (16 mg). Fraction 2c was subjected to CC on silica gel eluted with $CHCl_3$–MeOH (6:1) to give compound **14** (68 mg). Fraction 2d was passed through a column of Sephadex LH-20 eluted with 70% ethanol in water and then re-chromatographed on reversed phase C18 silica gel eluted with 40% methanol in water to give compounds **1** (15 mg) and **2** (12.5 mg). Fraction 2e was chromatographed on reversed phase C18 silica gel eluted with 40% methanol in water to give compound **3** (13 mg).

Medusaside A (1). White amorphous powder. $[\alpha]_D^{20}$ − 60.9° (*c* 0.755, MeOH); UV λ_{max} (MeOH) (log ε): 229 (4.08), 279 (3.85), 306 (3.68) nm; IR (KBr disc) ν = 3406 (OH), 2933 (C–H), 1655, 1591, 1516 (Ar–C=O), 1450, 1427 (C–H), 1275, 1161, 1076, 1031 (C–O) cm^{-1}; positive ESI-MS *m*/*z* (%): 561.3 $[M+Na]^+$ (100); negative ESI-MS *m*/*z* (%): 537.2 $[M-H]^-$ (100); EI–MS *m*/*z* (%): 376 $[M-glc]^+$(5), 358 $[M-glc-H_2O]^+$(8), 340 $[M-glc-2H_2O]^+$(12), 191 (20), 151 (48), 137 (100) and 98 (88); ^1H and ^{13}C NMR data: see Table 1.

Medusaside B (2). White amorphous powder. $[\alpha]_D^{20}$ −34.9° (*c* 0.53, MeOH); UV λ_{max} (MeOH) (log ε): 227 (3.89), 279 (3.43) nm; IR (KBr disc) ν = 3415 (OH), 2924 (C–H), 1601, 1514 (Ar), 1452, 1425 (C–H), 1269, 1070, 1032 (C–O) cm^{-1}; Positive ion mode ESI-MS *m*/*z* (%): 561.2 $[M+Na]^+$ (48), 399.1 $[M+Na\text{-}162]^+$ (100); Negative ion mode ESI-MS *m*/*z* (%): 537.3 $[M-H]^-$ (23), 489.0 (25), 374.9 $[M-H\text{-}162]^-$ (100), 345.0 (20) and 327.0 (37); EI-MS *m*/*z* (%): 376 $[M-glc]^+$(25), 153 (36), 137 (100) and 124 (34); ^1H and ^{13}C NMR data: see Table 2.

Acidic hydrolysis of 2. Compound **2** (6 mg) was added to 4 mL 5% H_2SO_4 in MeOH and refluxed for 4 h. The reaction mixture was neutralized with 5% $NaHCO_3$ and then worked up to give yellow residue. The residue was passed through a Sephadex LH-20 column eluted with EtOH to obtain glucose and (−)-berchemol (3.2 mg) which was identified by comparison of co-TLC and optical rotation $[\alpha]_D^{20}$ −9.3° (*c* 0.081, MeOH) with those of authentic sample.

Apigenin 7-*O*-[α-L-rhamnopyranosyl-(1→6)-β-D-glucopyranoside] (6). Yellow amorphous power. Positive ESI-MS *m*/*z* (%): 601.3 $[M+Na]^+$ (100), 579.3 $[M+H]^+$ (80), 433.3 $[M+H\text{-}146]^+$ (47), 271.5 $[M+H\text{-}146\text{-}162]^+$ (66); ^1H NMR data (400 MHz, DMSO-d_6) δ: 6.87 (1H, s, H-3), 6.45 (1H, s, H-6), 6.78 (1H, s, H-8), 6.98 (2H, d, *J* = 8.8 Hz, H-3′, 5′), 7.98 (2H, d, *J* = 8.8 Hz, H-2′, 6′), 5.08 (1H, d, *J* = 7.3 Hz, glc-1), 4.54 (1H, s, rhm-1), 1.08 (1H, s, rhm-6); ^{13}C NMR data (100 MHz, DMSO-d_6) δ: 164.4 (C-2), 103.1 (C-3), 182.0 (C-4), 105.4 (C-4a), 161.2 (C-5), 99.9 (C-6), 162.9 (C-7), 94.8 (C-8), 157.0 (C-8a), 121.1 (C-1′), 128.7 (C-2′, 6′), 161.2 (C-4′), 116.1 (C-3′, 5′), 99.5 (glc-1), 72.0 (glc-2), 76.2 (glc-3), 70.7 (glc-4), 75.6 (glc-5), 66.0 (glc-6), 100.5 (rhm-1), 70.3 (rhm-2), 69.5 (rhm-3), 73.1 (rhm-4), 68.3 (rhm-5) and 17.8 (rhm-6).

2-(4-Hydroxy-3-methoxyphenyl)ethyl β-D-glucopyranoside (11). White amorphous powder. Positive ESI-MS *m*/*z* (%): 353.3.2 $[M+Na]^+$ (100); negative ESI-MS *m*/*z* (%): 329.3 $[M-H]^-$ (100), 167.1 $[M-H\text{-}162]^-$ (30), 113.0 (95); ^1H NMR data (400 MHz, CD_3OD) δ: 3.55, 3.90 (2H, m, H-1), 2.67 (2H, m, H-2), 6.70 (1H, d, *J* = 1.8 Hz, H-2′), 6.53 (1H, d, *J* = 8.0 Hz, H-5′), 6.49 (1H, dd, *J* = 1.8, 8.0 Hz, H-6′), 3.66 (3H, s, H-OMe), 4.13 (1H, d, *J* = 7.7 Hz, glc-1), 3.00-3.18 (4H, m, glc-2, 3, 4, 5), 3.50, 3.70 (2H, m, glc-6); ^{13}C NMR data (100 MHz, CD_3OD) δ: 72.0 (C-1), 36.7 (C-2), 131.6 (C-1′), 113.8 (C-2′), 148.8 (C-3′), 145.9 (C-4′), 116.1 (C-5′), 122.4 (C-6′), 56.4 (C-OMe), 104.3 (glc-1), 75.1 (glc-2), 78.1 (glc-3), 71.7 (glc-4), 77.9 (glc-5), 62.8(glc-6).

Biology

Effects on scopolamine-induced memory deficits of mice. Effects on scopolamine-induced memory deficits of mice were carried out according to the procedure described in the literature.[16]

Tests of cell protective activities. Evaluation of cell protective activities of major phenols against H_2O_2-iduced PC12 cell damage was made according to the protocol reported in the literatures.[17]

Acknowledgements

Financial support of the National Scientific Foundation (for J. M. Yue, 30025044) and the Shanghai Municipal Scientific Foundation for Fundamental Research (for J.

M. Yue, 00JC14053) is gratefully acknowledged. We thank professor Xi-Can Tang of Shanghai Institute of Materia Medica for biological assays. We thank Professor Zeng-Tao Wang of Shanghai Chinese Traditional Medical University for identification of plant resource.

References and Notes

1. Jiangsu New Medical College. *Dictionary of Chinese Traditional Medicines*; Shanghai Scientific and Technologic Press: Shanghai, 1986; p. 2087.
2. Li, Y.; Jia, Z. J. *Phytochemistry* **1989**, *28*, 3395.
3. Yoshikawa, M.; Hatakeyama, S.; Inoue, Y.; Yamahara, J. *Chem. Pharm. Bull.* **1993**, *41*, 214.
4. Jia, Z. J.; Fei, H. M.; Li, Y.; Zhu, Z. Q. *Chemical Journal of Chinese Universities* **1986**, *7*, 789.
5. Jia, Z. J.; Gong, N. C.; Du, M. *Chemical Journal of Chinese Universities* **1990**, *11*, 202.
6. Cui, Z. Q.; Wang, L. B.; Zhang, W. Q.; Wang, D.; Wang, G. X.; Chen, Z. P.; Zhu, X. L. *Zhongcaoyao* **1995**, *26*, 247.
7. Soren, J.; Jesper, H.; Per, M. B. *Phytochemistry* **1993**, *33*, 523.
8. Fumiko, A.; Tatsuo, Y. *Chem. Pharm. Bull.* **1986**, *34*, 4340.
9. Nobuko, S.; Shin-ichi, N.; Ken-ichi, K.; Takao, I. *Chem. Pharm. Bull.* **1989**, *37*, 3311.
10. Kuo, Y. H.; Shue, M. J. *Journal of Chinese Chemical Society* **1991**, *38*, 65.
11. Perez, C.; Almonacid, L. N.; Trujillo, J. M.; Gonzalez, A. G.; Alonso, S. J.; Navarro, E. *Planta Medica* **1995**, *61*, 535.
12. Hiroe, K.; Sanae, H.; Yayoi, K.; Nobuji, N. *Phytochemistry* **1999**, *52*, 1307.
13. Sutarjadi, Th.M.M.; VanOs, F. H. L. *Phytochemistry* **1978**, *17*, 564.
14. Zhou, J.; Yang, Y. B.; Yang, C. R. *Hua Hsueh Hsueh Pao* **1980**, *38*, 162.
15. Kondo, R.; Iimori, T.; Imamura, H. *Mokuzai Gakkaishi* **1988**, *34*, 724.
16. Liu, J.; Zhang, H. Y.; Tang, X. C.; Wang, B.; He, X. C.; Bai, D. L. *Acta Pharmacologica Sinica* **1998**, *19*, 413.
17. Wang, R.; Xiao, X. Q.; Tang, X. C. *Neuroreport* **2001**, *12*, 2629.