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连翘果实中的三个新化合物

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摘要 利用大孔吸附树脂柱色谱、Sephdex LH-20 凝胶柱色谱以及半制备高效液相色谱等技术, 从连翘果实的乙醇提取物中分离得到三个新的化合物, 包括两个苯乙醇苷类衍生物 forsyside A (**1**), forsyside B (**2**)以及一个倍半萜 forsysacid A (**3**). 通过 UV, IR, HRESIMS, 一维 NMR 和二维 NMR 等波谱数据鉴定了它们的立体结构. 化合物 **1** 和 **3** 的绝对构型通过比较实验和计算圆二色谱的方法进行了确定, 化合物 **2** 的绝对构型通过激子手性法进行了确定. 此外, 对所有化合物的肝保护活性进行了研究, 其中化合物 **2** 在 10 μmol•L^{-1} 浓度下对 *N*-乙酰基−对氨基苯酚(APAP)引起的肝细胞损伤表现出较强的抑制作用.

关键词 连翘; 苯乙醇苷衍生物; 倍半萜; 肝保护活性

Three New Compounds from the Fruits of *Forsythia suspensa*

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Abstract Three new compounds including two phenylethanoid glycosides derivatives, forsyside A (**1**) and forsyside B (**2**), together with a sesquiterpene forsysacid A (**3**) were isolated from the EtOH extract of the fruits of *Forsythia suspensa*. Their structures were elucidated from analysis of UV, IR, HRESIMS, and 1D/2D NMR data. The absolute configurations of **1** and **3** were determined by quantum electronic circular dichroism (ECD) calculation, and compound **2** was determined by the ECD exciton chirality method. In addition, all compounds were evaluated for their hepatoprotective activity against *N*-acetyl-*p*-aminophenol-induced (APAP) HepG2 cell injury, and compound **2** showed significant activity at a concentration of 10 μmol•L^{-1}.

Keywords *Forsythia suspensa*; phenylethanoid glycosides derivative; sesquiterpene; hepatoprotective activity

1 Introduction

Forsythia suspensa belonging to the family Oleaceae is a small shrub widely distributed in China. The fruits of *F. suspensa* are widely used for the treatment of influenza, febrile disease, carbuncle toxin and anuria.[1] Previous investigations on the chemical constituents of the fruits of *F. suspensa* led to the isolation and identification of phenylethanoid glycosides, lignans, flavones, terpenoids and phenolic acids.[2-8] A wide array of pharmacological activities including anti-inflammatory, antioxidant, antibacterial, and neuroprotective properties have been reported for this plant.[9-13] Recent years, significant hepatoprotective activity of the extracts and components of the fruits of *Forsythia suspense* was revealed.[14-15] As part of ongoing effort to search for hepatoprotective compounds from *F. suspensa*, the chemical constituents of it were investigated in the present study. Herein, we report the isolation and structural elucidation of three new compounds including two phenylethanoid glycosides derivatives, forsyside A (**1**) and forsyside B (**2**), together with a sesquiterpene forsysacid A (**3**), from the fruits of *F. suspense* (Figure 1). All compounds were evaluated for their hepatoprotective activity against *N*-acetyl-*p*-aminophenol-induced HepG2 cell injury.

2 Results and discussion

Compound **1** was obtained as brown amorphous powder. It had a molecular formula of $C_{34}H_{40}O_{15}$ with an index of

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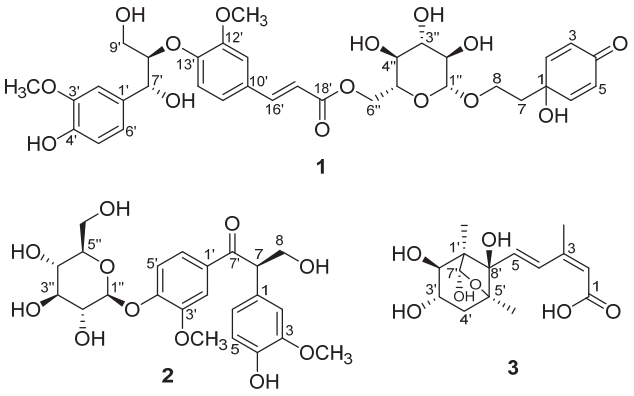

Figure 1 Chemical structures of **1**～**3**

hydrogen deficiency of 15 based on the HRESIMS ion at *m/z* 711.2264 (calcd for $C_{34}H_{40}O_{15}Na$ $[M+Na]^+$ 711.2259). The IR spectrum of **1** presented hydroxyl (3357 cm^{-1}), carbonyl (1702 and 1668 cm^{-1}), double bond (1628 cm^{-1}) and aromatic ring (1600 and 1512 cm^{-1}) groups. The ^1H NMR spectrum (Table 1) showed the resonances for two ABX systems [δ_H 7.37 (brs, H-11', 1H), 7.18 (brd, J=8.5 Hz, 1H, H-15'), 7.05 (d, J=8.5 Hz, 1H, H-14'), 6.95 (brs, H-2', 1H), 6.73 (brd, J=8.0 Hz, 1H, H-6') and 6.66 (d, J=8.0 Hz, 1H, H-5')], two *trans* olefinic protons [δ_H 7.56 (d, J=16.0 Hz, 1H, H-16') and 6.55 (d, J=16.0 Hz, 1H, H-17')], four additional olefinic protons [δ_H 6.89～6.97 (m, 2H, H-2,6) and 5.98～6.01 (m, 2H, H-3,5)], two oxygenated methines [δ_H 4.68 (overlap, H-7', 1H) and 4.36～4.40 (m, 1H, H-8')], one oxygenated methylene [δ_H 3.54～3.58 (m, 1H, H-9'a) and 3.22～3.27 (m, 1H, H-9'b)], and two methylenes [δ_H 1.89 (t, J=6.5 Hz, H-7, 2H), 3.73 (overlap, 1H, H-8a), and 3.45～3.50 (m, 1H, H-8b)]. Additionally, the presence of one anomeric proton at δ_H 4.14 (d, J=7.5 Hz, 1H, H-1") and multiple protons between δ_H 2.94 and 4.34 suggested the occurrence of a glucose moiety. In the ^{13}C NMR spectrum, 22 downfield carbons were identified as two carbonyl carbons, 12 aromatic carbons and six olefinic carbons. Ten oxygenated carbons included six glucose carbons, two methines carbons, one methylene carbon and one quaternary carbon. Comparison between the NMR data of **1** and the known compound forsythenside J suggested that these two compounds shared a similar skeleton except the substituent group of C-13'.[16] In forsythenside J, the substituent group of C-13' was feruloyl group. However, in the ^1H NMR spectrum of compound **1**, the remained ABX system, two oxygenated methines and one oxygenated methylene indicated the substituent group of C-13' was a phenyl-propanol group and it was confirmed by the HMBC correlations of H-8'/C-1', H-7'/C-9', H-7'/C-2', H-2'/C-4', H-5'/C-3', 3'- OCH_3/C-3' and H-8'/C-13' (Figure 2). The *d*-configuration of the glucose moiety was determined by gas chromatography (GC) analysis after acidic hydrolysis and chiral derivatization (retention time at 20.52 min). The relative configuration of H-7' and H-8' was confirmed as *threo* configuration according to the $\Delta\delta_{H9a\text{-}H9b}$ (0.31).[17] Thus, only 7'*S*,8'*S* or 7'*R*,8'*R* absolute configuration was feasible. Then, quantum chemical electronic circular dichroism (ECD) calculations were employed to confirm the absolute configuration. The systematic conformational analyses were carried out using molecular mechanics force field MMFF94 calculations. The optimized conformations were obtained at the B3LYP/6-31+G(d,p) level. At the B3LYP/6-31+G* level, their ECD spectra were calculated using time-dependent density functional theory (TDDFT). The overall calculated ECD spectra were generated by Boltzmann weighting of their lowest energy conformers. Throughout the entire range of wavelengths, the calculated spectrum of 7'*R*,8'*R* was consistent with **1** (Figure 3). Hence, the structure of compound **1** was established as 6-*O*-(4-((1*R*,2*R*)-1-(4-hydroxy-3-methoxyphenyl))propanetriol)-feruloyl-1-*O*-(2-(1-hydroxy-4-oxo-2,5-cyclohexadien-1-yl)ethyl)-*β*-*D*-glucopyranose and named forsyside A.

Compound **2** was obtained as a white amorphous powder. Its molecular formula was determined to be $C_{23}H_{28}O_{11}$ by the positive ion at *m/z* 481.1714 $[M+H]^+$ of HRESIMS. The ^1H NMR spectrum (Table 2) of **2** showed two ABX systems [δ_H 6.92 (d, J=1.5 Hz, 1H, H-2), 6.64 (d, J=8.0 Hz, 1H, H-5), 6.66 (dd, J=8.0, 1.5 Hz, 1H, H-6), 7.50 (d, J=1.5 Hz, 1H, H-2'), 7.11 (d, H-5', J=8.5 Hz), and 7.66 (dd, J=8.5, 1.5 Hz, 1H, H-6')], one oxygenated methylene [δ_H 4.09 (t, J=9.5 Hz, 1H, H-8a) and 3.51 (dd, J=9.5, 5.0 Hz, 1H, H-8b)], one methine [δ_H 4.80 (dd, J=9.5, 5.0 Hz,

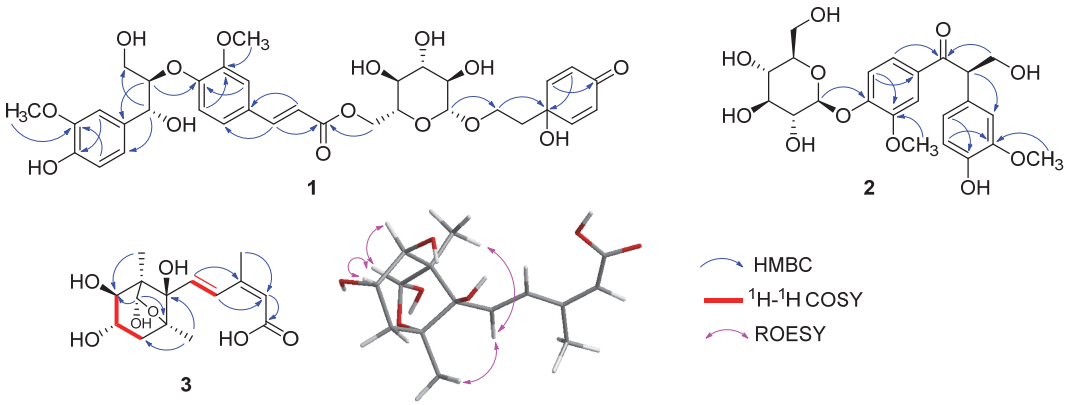

Figure 2 Key HMBC, ^1H-^1H COSY and ROESY correlations of **1**～**3**

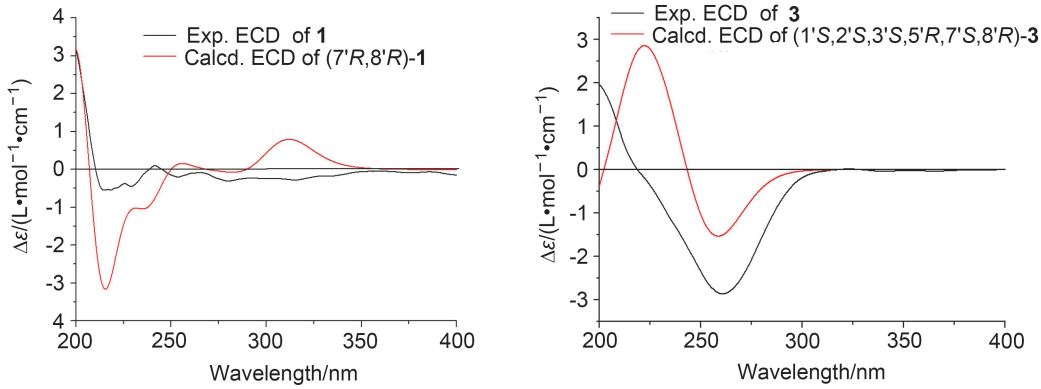

Figure 3 Experimental ECD and calculated ECD spectra of **1** and **3**

Table 1 ^{1}H NMR (500 MHz) and ^{13}C NMR (125 MHz) data of compound **1** in DMSO-d_6

Position	δ_H (J in Hz)	δ_C	Position	δ_H (J in Hz)	δ_C
1		67.3	10'		126.7
2	6.89～6.97 (m)	153.2	11'	7.37 (brs)	110.9
3	5.98～6.01 (m)	126.3	12'		149.6
4		185.3	13'		150.8
5	5.98～6.01 (m)	126.3	14'	7.05 (d, 8.5)	114.3
6	6.89～6.97 (m)	153.2	15'	7.18 (brd, 8.5)	122.9
7	1.89 (t, 6.5)	39.8	16'	7.56 (d, 16.0)	144.9
8	3.45～3.50 (m), 3.73 (overlap)	64.0	17'	6.55 (d, 16.0)	115.2
1'		132.8	18'		166.6
2'	6.95 (brs)	110.9	1"	4.14 (d, 7.5)	102.8
3'		147.0	2"	2.92～2.97 (m)	73.3
4'		145.5	3"	3.14 (overlap)	76.4
5'	6.66 (d, 8.0)	114.7	4"	3.12 (overlap)	69.9
6'	6.73 (brd, 8.0)	119.0	5"	3.35～3.39 (m)	73.6
7'	4.68 (overlap)	70.9	6"	4.15～4.18 (m), 4.34～4.36 (m)	63.6
8'	4.36～4.40 (m)	83.7	3'-OCH_3	3.71 (s)	55.4
9'	3.54～3.58 (m), 3.22～3.27 (m)	60.1	12'-OCH_3	3.82 (s)	55.7

Table 2 ^{1}H NMR (500 MHz) and ^{13}C NMR (125 MHz) data of compound **2** in DMSO-d_6

Position	δ_H (J in Hz)	δ_C	Position	δ_H (J in Hz)	δ_C
1		128.0	5'	7.11 (d, 8.5)	114.1
2	6.92 (d, 1.5)	112.4	6'	7.66 (dd, 8.5, 1.5)	122.8
3		147.6	7'		197.4
4		145.6	1"	5.01 (d, 7.5)	99.3
5	6.64 (d, 8.0)	115.5	2"	3.25 (overlap)	73.0
6	6.66 (dd, 8.0, 1.5)	120.4	3"	3.25 (overlap)	76.8
7	4.80 (dd, 9.5, 5.0)	54.0	4"	3.13～3.16 (m)	69.5
8	4.09 (t, 9.5), 3.51 (dd, 9.5, 5.0)	63.7	5"	3.33 (overlap)	77.1
1'		130.5	6"	3.64 (brd, 11.5), 3.43 (dd, 11.5, 5.5)	60.5
2'	7.50 (d, 1.5)	111.4	3-OCH_3	3.72 (s)	55.6
3'		148.6	3'-OCH_3	3.79 (s)	55.5
4'		150.4			

1H, H-7)] and two methoxy groups [δ_H 3.72 (s, 3-OCH_3, 3H) and 3.79 (s, 3'-OCH_3, 3H)]. The presence of multiple protons between δ_H 3.05 and 3.60 and the presence of an anomeric proton at δ_H 5.01 (d, J=7.5 Hz, 1H, H-1") suggested the occurrence of a glucose moiety. The ^{13}C NMR spectrum (Table 1) showed 23 carbon resonances including one carbonyl carbon, twelve aromatic carbons, one oxygenated methylene carbon, one methine carbon, two methoxy carbons and a set of glucose carbons. Comparison of the NMR data of aglycone moiety of **2** and the NMR data of the known compound evofolin B indicated that they shared same planar structure.[18] In the HMBC spectrum of **2**

(Figure 2), the correlation of H-1"/C-4' confirmed the glucose was attached at the C-4'. The glucose was confirmed as having a *D*-configuration by the same method as used above (retention time at 20.55 min). The *β*-configuration was deduced based on the coupling constant (J=7.5 Hz) of H-1". According to the Harada-Nakanishi nonempirical rule, the absolute configuration of **2** was determined by the ECD exciton chirality method.[19] The ECD spectrum of **2** showed the negative first Cotton effect at 267 nm and positive second Cotton effect at 233 nm (Figure 4), which is consistent with 7*R* configuration. Thus, the structure was confirmed as (*R*)-3-hydroxy-2-(4-hydroxy-3-methoxyphenyl)-1-(3-methoxy-4-glucosyloxy-phenyl)propan-1-one and named forsyside B.

Compound **3** was obtained as a white amorphous powder, and its molecular formula was $C_{15}H_{22}O_7$ based on HRESIMS at *m*/*z* 337.1256 (calcd for $C_{15}H_{22}O_7Na$ [M+Na]$^+$ 337.1258). The IR spectrum indicated the presence of hydroxy (3405 cm^{-1}), conjugated ketone (1691 cm^{-1}), and double bond (1603 cm^{-1}) groups. The ^{1}H NMR spectrum (Table 3) displayed three tertiary methyls at δ_H 0.88 (1'-CH_3), 1.06 (5'-CH_3), and 1.95 (3-CH_3), a methylene at δ_H 1.85 (dd, J=14.0, 8.0 Hz, H-4'a), 1.49 (dd, J=14.0, 10.0 Hz, H-4'b), three oxygenated methines at δ_H 3.36～3.40 (1H, m, H-3'), 3.26 (d, J=8.5 Hz, H-2', 1H), and 5.00 (s, H-7', 1H), and three olefinic protons at δ_H 5.67 (s, H-2, 1H), 6.07 (d, J=15.5 Hz, H-4, 1H), and 7.84 (d, J=15.5 Hz, H-5 1H,). The ^{13}C NMR spectrum (Table 3) showed 15 carbon signals. In the HMBC spectrum (Figure 2), correlations of 1'-CH_3/C-2', 1'-CH_3/C-7', 1'-CH_3/C-1', 1'-CH_3/C-8' and 5'-CH_3/C-4', 5'-CH_3/C-8', 5'-CH_3/C-5' indicated the presence of a 1,5-dimethyl-2,3,7,8-tetrahydroxy-6-oxabicyclo-[3,2,1]-octane skeleton. The correlations of H-2/C-1, H-2/C-4, H-5/C-3, 3-CH_3/C-2, and 3-CH_3/C-4 suggested the presence of a 3-methyl-2,4-pentadienoic acid moiety. In addition, the key correlation of H-4/C-8' and H-4/C-8' illustrated that the 3-methyl-2,4-pentadienoic acid moiety was attached at the C-8'. The coupling constant of $^3J_{2',3'}$ was 8.5 Hz indicated that the relative configuration of H-2′ and H-3' was *trans*. Moreover, according to the ROESY correlations of H-3'/H-7', 1'-CH_3/H-2', 1'-CH_3/H-5, and H-5/5'-CH_3 (Figure 2), the relative configuration of **3** was established. Finally, the absolute configuration of **3** was confirmed as 1'*S*,2'*S*,3'*S*,5'*R*,7'*S*,8'*R* by quantum chemical electronic circular dichroism (ECD) calculations (Figure 3). Thus, the structure of **3** was identified as (2*Z*,4*E*)-3-methyl-5-((1*S*,2*S*,3*S*,5*R*,7*S*,8*R*)-2,3,7,8-tetrahydroxy-1,5-dimethyl-6-oxabicyclo[3.2.1]octan-8-yl)penta-2,4-dienoic acid and named forsysacid A.

All of the compounds were assayed for their hepatoprotective activities. Compared with the control group, compound **2** showed significant hepatoprotective activity against *N*-acetyl-*p*-aminophenol (APAP)-induced HepG2 cell injury (Figure 5).

3 Conclusions

In the course of a search for bioactive compounds from *Forsythia suspensa*, two new phenylethanoid glycosides derivatives and a new sesquiterpene were obtained. All compounds were tested for their hepatoprotective effects,

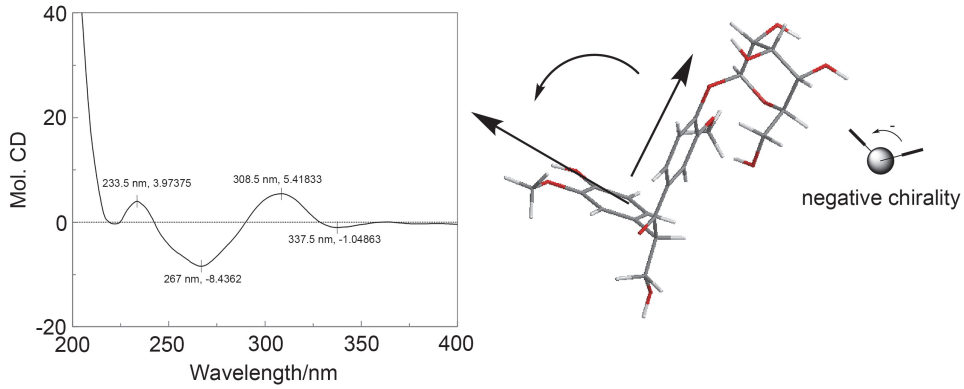

Figure 4 Absolute configurations of compound **2** as determined by the ECD exciton chirality method

Table 3 ^{1}H NMR (500 MHz) and ^{13}C NMR (125 MHz) data of compound **3** in DMSO-d_6

Position	δ_H (J in Hz)	δ_C	Position	δ_H (J in Hz)	δ_C
1		167.2	4'	1.85 (dd, 14.0, 8.0), 1.49 (dd, 14.0, 10.0)	42.0
2	5.67 (s)	119.3	5'		85.8
3		147.9	7'	5.00 (s)	97.4
4	6.07 (d, 15.5)	132.5	8'		81.9
5	7.84 (d, 15.5)	129.9	3-Me	1.95 (s)	20.7
1'		56.1	1'-Me	0.88 (s)	11.2
2'	3.26 (d, 8.5)	76.0	5'-Me	1.06 (s)	19.7
3'	3.36～3.40 (m)	70.6			

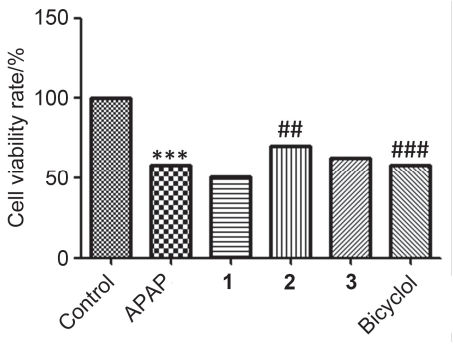

Figure 5 Hepatoprotective effects of all compounds (10 μmol•L^{-1}) (c_{APAP}=8 mmol•L^{-1}; $^{***}p<0.001$, $^{###}p<0.001$, $^{##}p<0.01$)

and it was observed that compound **2** had significant effect against *N*-acetyl-*p*-aminophenol-induced HepG2 cell injury at 10 μmol•L^{-1}. These results could contribute to the better understanding of the therapeutic usage of *Forsythia suspensa*.

4 Experimental section

4.1 General experimental procedures

The optical rotations, UV spectra, and ECD spectra were recorded with JASCO P-2000, V650 and J-815 spectrometers (JASCO, Easton, MD, USA), respectively. The infrared spectra were measured on a Nicolet 5700 spectrometer (Thermo Scientific, FL, USA). The NMR spectra were recorded with a Bruker 500 MHz nuclear magnetic resonance instrument (Bruker-Biospin, Billerica, MA, USA). HRESIMS reports were obtained from an Agilent 6520 HPLC-Q-TOF (Agilent Technologies, Waldbronn, Germany). Preparative HPLC separations were performed using a Shimadzu LC-10AT with an ODS-A column (250 mm×10 mm, 5 μm; YMC Corp., Kyoto, Japan). An Agilent 1200 series system with an Apollo C_{18} column (250 mm×4.6 mm, 5 μm; Alltech Corp., KY, USA) was used for HPLC-DAD analysis. Macroporous resin (Diaion HP-20, Mitsubishi Chemical Corp., Tokyo, Japan), RP-C18 (50 μm, YMC Corp., Kyoto, Japan), and Sephadex LH-20 (Pharmacia Fine Chemicals, Uppsala, Sweden) were used for column chromatography. The Agilent 7890A was used to carry on the GC analysis with a capillary column, HP-5 (60 m×0.32 mm, with a 1 μm film; Agilent Technologies Inc., CA, USA).

4.2 Plant material

The arid fruits of *Forsythia suspensa* were collected from Yuncheng City of Shanxi Province in PRC, in December 2011 and identified by Professor L. Ma. A voucher specimen (ID-S-2597) was deposited at the Institute of Materia Medica, Peking Union Medical College and Chinese Academy of Medical Sciences, Beijing, China.

4.3 Extraction and isolation

Powdered fruits of *Forsythia suspensa* (100.0 kg) was exhaustively extracted with 75% EtOH under reflux conditions. The solvent was evaporated by reduced pressure, and then, the residue (13 kg) was successively partitioned with petroleum ether, EtOAc and *n*-BuOH. The *n*-BuOH portion (4 kg) was then suspended in water (40 L) to obtain a water soluble layer, which was concentrated to yield an aqueous portion (1.5 kg). The portion was applied on a HP-20 column to give five fractions A～E through gradient elution with H_2O, 15% ethanol, 30% ethanol, 50% ethanol, and 95% ethanol, respectively. The fraction D (392.0 g) was separated on a HP-20 resin column eluting with a mixture gradient of MeOH-H_2O (*V*∶*V*, from 1∶4 to 9∶1) to obtain seven fractions (D1～D7). Fraction D5 was subjected to a Sephadex LH-20 with a gradient of increasing MeOH (0～100%) in H_2O and then separated by preparative HPLC to give **1** (9.0 mg, MeOH/H_2O, *V*∶*V*=45∶55, HOAc, 0.01%) and **3** (10.0 mg, MeOH/H_2O, *V*∶*V*=30∶70, HOAc, 0.01%). Fraction D6 was separated by column chromatography over a Sephadex LH-20 using H_2O as the eluent and was further purified by preparative HPLC (MeOH/H_2O, *V*∶*V*=40∶60, HOAc, 0.01%) to give **2** (7.0 mg).

6-*O*-(4-((1*R*,2*R*)-1-(4-Hydroxy-3-methoxyphenyl))propanetriol)-feruloyl-1-*O*-(2-(1-hydroxy-4-oxo-2,5-cyclohexadien-1-yl)ethyl)-*β*-d-glucopyranose (**1**): Brown amorphous powder. m.p. 235～236 ℃; $[\alpha]_D^{20}$ −52.9 (*c* 0.10, MeOH); UV (MeOH) λ_{max} [log *ε*/(L•mol^{-1}•cm^{-1})]: 230 (4.12), 287 (3.88), 323 (3.96) nm; ^{1}H NMR and ^{13}C NMR see Table 1; IR (KBr) ν_{max}: 3357, 2930, 1702, 1668, 1628, 1600, 1512, 1424, 1260, 1138, 1027 cm^{-1}; HRESIMS calcd for $C_{34}H_{40}O_{15}Na$ $[M+Na]^+$ 711.2259, found 711.2264.

(*R*)-3-Hydroxy-2-(4-hydroxy-3-methoxyphenyl)-1-(3-methoxy-4-glucosyloxy-phenyl)propan-1-one (**2**): White amorphous powder. m.p. 139～140 ℃; $[\alpha]_D^{20}$ +7.2 (*c* 0.10, MeOH); UV (MeOH) λ_{max} [log *ε*/(L•mol^{-1}•cm^{-1})]: 204 (4.56), 225 (4.35), 272 (4.09), 303 (3.89) nm; ^{1}H NMR and ^{13}C NMR see Table 2; IR (KBr) ν_{max}: 3387, 1666, 1593, 1514, 1418, 1269, 1076, 1046, 809 cm^{-1}; HRESIMS calcd for $C_{23}H_{29}O_{11}$ $[M+H]^+$ 481.1704, found 481.1714.

(2*Z*,4*E*)-3-Methyl-5-((1*S*,2*S*,3*S*,5*R*,7*S*,8*R*)-2,3,7,8-tetrahydroxy-1,5-dimethyl-6-oxabicyclo[3.2.1]octan-8-yl)-penta-2,4-dienoic acid (**3**): White amorphous powder. m.p. 240～241 ℃; $[\alpha]_D^{20}$ −19.8 (*c* 0.10, MeOH); UV (MeOH) λ_{max} [log *ε*/(L•mol^{-1}•cm^{-1})]: 256 (4.49) nm; ^{1}H NMR and ^{13}C NMR see Table 3; IR (KBr) ν_{max}: 3405, 1691, 1603, 1454, 1381, 1236 cm^{-1}; HRESIMS calcd for $C_{15}H_{22}O_7Na$ $[M+Na]^+$ 337.1258, found 337.1256.

4.4 Hepatoprotective activity

The HepG2 cell line was maintained in dulbecco's modified eagle medium (DMEM) containing 10% FBS and penicillin (100 U/mL)-streptomycin (100 μg/mL) and cultured at 37 ℃ (5% CO_2, 100% relative humidity). These cells were digested using 0.25% trypsin and then seeded into 96-well plates. After incubation for 12 h, the cells in the 96-well plates were treated with different samples (10 μmol•L^{-1}) and APAP (8 mmol•L^{-1}), and the samples were incubated for 48 h. Then, 100 μL of methyl thiazolyl te-

trazolium (MTT) reagent (0.5 mg/mL) was added to each well and incubated for 4 h. After removal of the media, 150 μL of dimethyl sulfoxide (DMSO) was added to solubilize the residuum. Finally, the absorbances were measured at 570 nm, using bicyclol as the positive control.

4.5 Determination of the absolute configurations of the glucose

Compound **1** (3 mg) was dissolved in 2 mol/L HCl and then the mixture was heated in 65 ℃ for 15 h. The mixture was then extracted three times with EtOAc, and the aqueous layer was freeze-dried to obtain residue. The residue was dissolved in anhydrous pyridine (2 mL), and l-cysteine methyl ester hydrochloride (4 mg) was added. Then the mixture was heated in a water bath (60 ℃) for 2 h. After the reaction solution was dried under vacuum, *N*-trimethylsilylimidazole (1 mL) was added, and the solution was heated in a water bath (60 ℃) for 1 h and extracted three times with H_2O/*n*-hexane. Then, the *n*-hexane layer was analyzed using GC under conditions as follows: injection temperature, 300 ℃; detector temperature (FID), 300 ℃; capillary column, HP-5 (60 m×0.32 mm, Dikma); start temperature, 200 ℃, raised to 260 ℃ at a rate of 10 ℃/min, and the final temperature maintained for 30 min; and N_2 used as the carrier gas.

Supporting Information 1D NMR, 2D NMR, HR-ESI-MS, UV, IR and CD spectra of compounds **1**～**3**. The Supporting Information is available free of charge via the Internet at http://sioc-journal.cn.

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