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A New Neolignan Glycoside from the Leaves of *Acer truncatum*

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Abstract: A new neolignan glycoside, (7*R*,8*R*)-7,8-dihydro-9′-hydroxyl-3′-methoxyl-8-hydroxymethyl-7-(4-hydroxy-3-methoxyphenyl)-1′-benzofuranpropanol 9′-O-β-D-glucopyranoside (**1**) was isolated from the leaves of *Acer truncatum* along with (7*R*,8*R*)-7,8-dihydro-9′-hydroxyl-3′-methoxyl-8-hydroxymethyl-7-(4-O-α-L-rhamno-pyranosyloxy-3-methoxyphenyl)-1′-benzofuranpropanol (**2**), schizandriside (**3**), lyoniresinol (**4**), berchemol (**5**), (-)-pinoresinol-4-O-β-D-glucopyranoside (**6**), hecogenin (**7**), chlorogenic acid (**8**) and neochlorogenic acid (**9**). Their structures were elucidated on the basis of extensive spectroscopic data. The absolute configuration of compounds **1** was established by its CD spectrum. The antibacterial activities of compounds **1**-**7** were evaluated.

Keywords: *Acer truncatum*, Aceraceae, neolignan glycosides, antibacterial activity

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Introduction

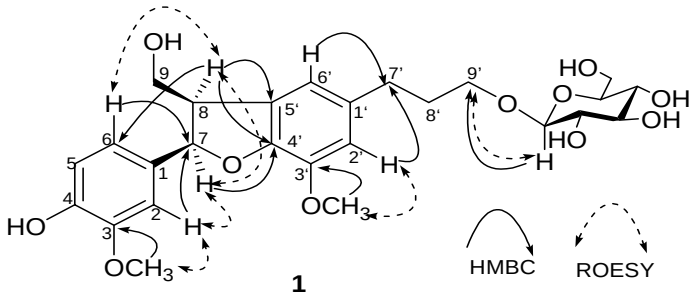
The genus *Acer* belongs to the family Aceraceae and there are more than 150 *Acer* flora species in China [1]. The roots of *Acer truncatum* (also known by the common names Shantung, Painted or

Purple-blow Maple) have been used as folk medicine to treat lumbago and its leaves have been used to prepare a sanitary tea [2]. In our previous reports on the phytochemical investigation of *A. truncatum*, we have described flavonoid glycosides [3], which had strong activity in thrombus, phenylpropanoids [4], egastigmanes [4] and sesquiterpenes [4]. During our ongoing investigations into the chemical constituents of this plant, the new neolignan glycoside (7*R*,8*R*)-7,8-dihydro-9′-hydroxyl-3′-methoxyl-8-hydroxymethyl-7-(4-hydroxy-3-methoxyphenyl)-1′-benzofuranpropanol 9′-O-β-D-glucopyranoside (**1**) and eight known compounds: (7*R*,8*R*)-7,8-dihydro-9′-hydroxyl-3′-methoxyl-8-hydroxymethyl-7-(4-O-α-L-rhamnopyranosyloxy-3-methoxyphenyl)-1′-benzofuranpropanol (**2**), schizandriside (**3**), lyoniresinol (**4**), berchemol (**5**), (-)-pinoresinol-4-O- β-D-glucopyranoside (**6**), hecogenin (**7**), chlorogenic acid (**8**) and neochlorogenic acid (**9**) were isolated from a water extract of *A. truncatum* leaves. The identification of the known compounds was supported by comparison with published data of related compounds [5-12]. Compounds **1**-**7** were evaluated for their antibacterial activities against *Escherichia coli, Staphylococcus aureus*, *Micrococcus luteus* and *Bacillus cereus*.

Results and Discussion

Compound **1**, a colorless amorphous powder, showed a $[M-H]^-$ ion peak at *m/z* 521.2039 in the negative ion HRESI-MS, indicating the molecular formula $C_{26}H_{34}O_{11}$. Its ^{1}H-NMR spectrum showed three ABX type phenyl protons at δ_H 6.76 (1H, d, J = 8.2 Hz, H-5), 6.81 (1H, d, J = 8.5 Hz, H-6), 6.93 (1H, d, J = 1.6 Hz, H-2)], two singlet signals at δ_H 6.72 (1H, s, H-2′) and 6.75 (1H, s, H-6′), two methoxy signals at δ_H 3.79 (3H, s) and 3.82 (3H, s), and two C_3 units at δ_H 5.48 (1H, d, J = 6.3 Hz, H-7), 3.45 (1H, m, H-8), 3.74 (1H, m, Ha-9), 3.80 (1H, m, Hb-9), and at δ_H 2.65 (2H, br t, J = 7.4 Hz, H-7′), 1.88 (2H, m, H-8′), 3.51 (1H, m, Ha-9′) and 3.92 (1H, m, Hb-9′). Furthermore, the ^{1}H- and ^{13}C-NMR spectral data (Table 1) indicated the presence of a β-glucopyranosyl moiety ($J_{1'',2''}$ = 7.8 Hz), which was in accordance with an $[M-H-162]^-$ peak observed at *m/z* 359 in the negative FAB-MS spectrum. In addition to two methoxyl carbons and the glucopyranosyl group signals, 18 skeletal carbon resonances appeared in the ^{13}C-NMR spectrum (Table 1). Significant HMBC correlations were also observed between H-7/C-4′ and H-8/C-5′. These spectral features indicated that **1** was a 7-aryl-8-hydroxymethyl-7,8-dihydrobenzofuranoid-type neolignan formed by two phenylpropanoid units [13-17]. The two methoxyl groups were located at C-3 and C-3′ and the β-glucopyranosyl group was connected at C-9′, based on the HMBC and ROESY correlations (Figure 1). The ^{1}H- and ^{13}C-NMR data of **1** were almost equivalent to those of glochidioboside [13], however, an obvious NOE was observed for H-7 [δ_H 5.48 (d, J = 6.3 Hz)] on irradiation at H-8 [δ_H 3.45 (m)] in the NOE experiment of **1**, which suggested that the substituents at C-7 and C-8 were is a *cis*- relative configuration. The absolute stereochemistry at C-7 and C-8 were assigned to be both *R*, on the basis of position Cotton effects at 243 nm and 294 nm and negative ones at 260 nm in its CD spectrum [17], Consequently, the structure of **1** was elucidated as (7*R*,8*R*)-7,8-dihydro-9′-hydroxyl-3′-methoxyl-8-hydroxymethyl-7-(4-hydroxy-3-methoxyphenyl)-1′-benzofuranpropanol 9′-O-β-D-glucopyranoside (**1**, Figure 1).

Figure 1. Selected HMBC and ROESY correlations of **1.**



1

Table 1. The ^{1}H- and ^{13}C-NMR Data of **1** (in CD_3OD).

Position	δ_H (*J* in Hz)	δ_C	Position	δ_H (*J* in Hz)	δ_C
1	-	134.8s	5′	-	129.9s
2	6.93 (d, 1.6)	110.6d	6′	6.75 (s)	118.0d
3	-	149.0s	7′	2.65 (t, 7.4)	32.9t
4	-	147.4s	8′	1.88 (m)	32.9t
5	6.76 (d, 8.2)	116.1d	9′	3.51 (m) 3.92 (m)	70.0t
6	6.81 (dd, 1.6, 8.2)	119.7d	1″	4.25 (d, 7.8)	104.4d
7	5.48 (d, 6.3)	88.9d	2″	3.23 (m)	75.1d
8	3.45 (m)	55.3d	3″	3.34 (m)	78.1d
9	3.80, 3.74 (2H, m)	65.0t	4″	3.32 (m)	71.6d
1′	-	136.8s	5″	3.26 (m)	77.8d
2′	6.72 (s)	114.2d	6″	3.67 (dd,11.7, 3.9) 3.87 (br.s)	62.7t
3′	-	145.1s	3-OMe	3.79 (s)	56.4q
4′	-	147.4s	3′-OMe	3.82 (s)	56.8q

Biological activity

Compounds **1-7** were tested for their antibacterial activities against *Escherichia coli*, *Staphylococcus aureus*, *Micrococcus luteus* and *Bacillus cereus* using the paper disk method. All stock cultures were grown on tryptic soy agar plates. Test strains were transferred to fresh tryptic soy broth before use and a disk containing only DMSO was used as negative control. The compounds were found to be inactive at concentrations of up to 50 μg/disk, except for schizandriside (**3**), which showed moderate antibacterial activity, affording inhibitory zone sizes of 11 mm against *Staphylococcus aureus* at a concentration of 2 μg/disk.

Conclusions

Nine phenolic constituents including a new neolignan glycoside were isolated from the leaves of *Acer truncatum*. Their structures were established on the basis of 1D- and 2D-NMR experiments, CD data and comparison with literature values. The antibacterial activities of pure compounds **1-7** was tested against four microbial species. Only schizandriside (**3**) showed moderate antibacterial activity against *S. aureus.*

Experimental

General

FAB mass spectra were obtained on a VG Auto spec-3000 spectrometer and high-resolution ESI mass spectra were recorded on an API Qstar Pulsar instrument. 1D- and 2D-NMR experiments were performed on Bruker AM-400 and DRX-500 instruments with TMS as internal standard. Chemical shifts (δ) were expressed in ppm with reference to the solvent signals; coupling constants (*J*) are given in Hertz (Hz). IR spectra were taken in KBr on a Bio-Rad FTS-135 infrared spectrophotometer. Optical rotations were measured in a JASCO DIP-370 digital polarimeter. UV spectra were measured using a Shimadzu UV-2401PC spectrophotometer. CD spectra were run on a JASCO J-810 instrument. Column chromatography (CC) was performed using 200-300 mesh silica gel (Qingdao Marine Chemical Inc., Qingdao, P.R. China), on silica gel H (10-40 μm, Qingdao Marine Chemical Inc.) and Lichroprep RP-18 (43-63 μm, Merck).

Plant material

Leaves of *A. truncatum* were collected in Kunming, Yunnan province, P. R. China, in August 2004. The plants were identified by Prof. Ting-Zhi Xu, Kunming Institute of Botany, Chinese Academy of Science.

Extraction and isolation

Air-dried leaves of *A. truncatum* (20 kg) were extracted with H_2O. The extract was evaporated *in vacuo* to give a black-brown gum, which was applied to ADS-7 porous resin and divided into four fractions: H_2O fraction, 30% EtOH fraction, 70% EtOH fraction, and 90% EtOH fraction. The 30% EtOH fraction (256 g) was subjected to CC (SiO_2, $CHCl_3$/MeOH 9:1→7:3) to afford fractions Fr.1-10, as judged by TLC. Fr. 2 (20 g) was further purified by CC (first SiO_2, petroleum ether/AcOEt, then RP-18 gel) to afford **7** (135 mg). Fr. 3 (12 g) was subjected to CC (SiO_2, petroleum ether/AcOEt) to afford **5** (20 mg). Fr. 4 (18 g) was subjected to CC (SiO_2, petroleum ether/AcOEt) to yield **4** (37 mg). Fr. 5 (19 g) was subjected to CC (SiO_2, $CHCl_3$/AcOEt) to yield **8** (13 mg) and **9** (10 mg). Fr. 7 (23 g) was subjected to CC (SiO_2, petroleum ether/AcOEt) to afford **6** (226 mg). Fr. 9 (20 g) was subjected to CC (first, SiO_2; $CHCl_3$/MeOH, then RP-18 gel) to afford **1** (37 mg), **2** (65 mg) and **3** (171 mg).

(7R,8R)-7,8-dihydro-9′-hydroxyl-3′-methoxyl-8-hydroxymethyl-7-(4-hydroxy-3-methoxyphenyl)-1′-benzofuranpropanol 9′-O-β-D-glucopyranoside (**1**): Colorless amorphous powder; $[\alpha]_D^{25}$ = –9.99 (MeOH, *c* 0.69); UV λ_{max} (log ε): 206 (4.76), 281 (3.82) nm; Negative FAB-MS: *m/z* 521 $[M-H]^-$, 359 $[M-H-162]^-$; HR-ESI-MS: *m/z* 521.2039 $[M-1]^-$ (calcd for $C_{26}H_{33}O_{11}$ 521.2022); IR ν_{max} (KBr): 3422, 2935, 2880, 1608, 1518, 1499 cm^{-1}; CD ($c = 2.08\times10^{-5}$ mol·L^{-1} in MeOH): $[\theta]_{294} + 1.7 \times 10^3$, $[\theta]_{260} - 0.7 \times 10^3$, $[\theta]_{243} + 6.7 \times 10^3$.; ^{1}H- and ^{13}C- NMR data see Table 1.

Antibacterial and antifungal activity [4]

Antibacterial activity was tested by the disk diffusion method with minor modifications. *E. coli*, *S. aureus*, *M. luteus* and *B. cereus* were subcultured in tryptic soy broth (TSB), incubated for 18 h at 37 °C and then the bacterial cells were suspended, according to the McFarland protocol, in saline solution to produce a suspension of about 10^{-5} CFU·mL^{-1}. An aliquot of this suspension (15 μL) was mixed with sterile tryptic soy agar (TSA, 15 mL) at 40 °C and poured onto an agar plate in a laminar flow cabinet. Each tested compound was dissolved in DMSO and added to a paper disk (6 mm diameter) that was dried and placed on the agar plate containing the bacterial cells (5 samples/disk plus control). A disk containing only DMSO was used as negative control. The susceptibility of the bacteria to the test compounds was determined by the formation of an inhibitory zone after 18 h of incubation at 37 °C. Experiments were run in triplicate, and the results were determined as mean values of the three measurements.

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