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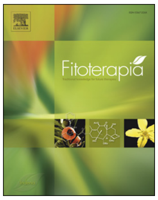

Triterpenoids with anti-tobacco mosaic virus activities from *Melia Toosendan*

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ABSTRACT

Four new triterpenoids, named Toosendansins A–D (**1**–**4**), along with nine known ones (**5**–**13**) were isolated from the fruits of *Melia toosendan* Sieb. et Zucc. Their structures were established on the basis of spectroscopic data. The isolation of compounds **1**–**12** were reported for the first time from this plant. All compounds were analyzed for the anti-Tobacco Mosaic Virus (TMV) activity and protective effect on H_2O_2-induced damage of SH-SY5Y cells. Compound **7** showed evident anti-TMV activity. Compounds **2** and **9** exhibited modest protection against H_2O_2-induced damage of SH-SY5Y cells.

1. Introduction

The plant family Meliaceae is rich in structurally diverse limonoids with a variety of potentially useful biological properties. Until now, about 1300 limonoids with more than 35 carbon frameworks had been isolated from four families (Meliaceae, Rutaceae, Simaroubaceae, and Cneoraceae) [1,2]. *Melia toosendan Sieb. et Zucc.* (Meliaceae) is mainly distributed in the southwest region of China. The fruits and bark are commonly used in Traditional Chinese Medicine for acesodyne and desinsection. In recent years, the chemical constituents of the fruits of *M. toosendan* have been studied extensively. Different types of limonoids including apoeuphors, meliacins, trichilinin, nimbolinin, C-19/C-29-bridged acetals, ring C-*seco* limonoids, highly oxidized C-*seco* limonoids, and spiro limonoids have been isolated [3,4]. Limonoids from the genus of *Melia* are attracting considerable interest because of their biological activities and variety of structures [5]. In this paper, we report the isolation, structural elucidation and bioactivity of three new limonoids (**1–3**) and a new triterpenoid (**4**), together with nine known ones (**5–13**). Among these compounds, compound **7** showed a significant inhibition effect against TMV, and compounds **2** and **9** revealed a modest protection effect to the H_2O_2-induced SH-SY5Y cell damage, which is beneficial to find new lead compound against virus diseases of plant or neuroprotective drug.

2. Experimental

2.1. General

All solvents used for extraction and isolation were distilled prior to use. Column chromatography (CC) was performed on silica gel (200–300 mesh and 300–400 mesh, Qingdao Haiyang Chem. Ind. Ltd. P. R. China), silica gel H (10–40 μm mesh, Qingdao), C18 reversed-phase silica gel (20–45 μm, Merck, Darmstadt, Germany), and Sephadex LH-20 (40–70 μm, Amersham Pharmacia Biotech AB, Uppsala, Sweden). TLC plates

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were precoated with silica gel GF254 (Qingdao Haiyang Chem. Ind. Ltd. PR China). The MPLC instrument included a Büchi Pump Module C-605 and a Büchi Pump Manager C-615. Optical rotations: JASCO DIP-370 Digital Polarimeter. IR Spectra: Bio-Rad FTS-135 spectrometer, KBr discs, in cm^{-1}. NMR spectra: Bruker AM-400 instrument (400/100 MHz) with TMS as an internal standard; chemical shifts δ in ppm rel. to residual aolvent signals, J in Hz. HR-ESI-MS: a VG Auto Spec-3000 spectrometer.

2.2. Plant material

The fruits of *Melia toosendan Sieb. et Zucc.* were collected in Guiyang, Guizhou Province, People's Republic of China, and were identified by Prof. Qing-wen Sun of Guiyang College of Traditional Chinese Medicine.

2.3. Extraction and isolation

The powder of dried fruits of *M. toosendan* (30.0 kg) was extracted three times with 95% EtOH (4 h, 3 h, 3 h). The extracts were combined, concentrated, and suspended in H_2O. Then the water layer was extracted with petroleum ether and EtOAc, successively. The EtOAc extracts (688 g) were subjected to silica gel column chromatography, eluted with $CHCl_3$/MeOH (from 100:0 to 0:100), yielding nine fractions (Fr. 1–9) with TLC detection. Fr. 4 was subjected to a reversed C18 column chromatograph (eluted with MeOH/H_2O from 5:5 to 1:0), yielding five subfractions (Fr. 4A1–Fr.

Table 1
^{1}H-NMR data of compounds **1–4** in $CDCl_3$.
(δ in ppm, J in Hz).

Position	**1**[a]	**2**[b]	**3**[a]	**4**[a]
1	4.78 (m)	4.87 (t, 1.2)	4.87 (t, 2.8)	1.50 (br.d) 2.07 (m)
2a	2.24 (m)	2.13 (m)	2.12 (dt, 16.4, 2.0)	2.31 (m)
2b		2.26 (dt, 16.0, 2.4)	2.28 (m)	2.77 (dt, 11.6, 5.6)
3	4.95 (m)	4.94 (m)	4.98 (t, 2.8)	–
4	–	–	–	–
5	2.85 (d, 12.4)	2.88 (d, 10.4)	2.78 (d, 12.8)	1.73 (t, 7.6)
6	4.01 (dd, 12.4, 3.2)	4.18 (dd, 10.0, 1.6)	4.14 (dd, 12.8, 3.2)	2.07 (m)
7	4.18 (d, 2.8)	6.01 (d, 1.6)	5.88 (d, 2.8)	5.32 (d, 2.8)
8	–	–	–	–
9	2.79 (dd, 8.4, 4.0)	3.23 (d, 8.4)	3.14 (d, 10.0)	2.31 (m)
10	–	–	–	–
11a	2.24 (m)	1.83 (d, 5.2)	1.84 (m)	1.57(m)
11b		1.61 (m)	1.56 (m)	
12	–	4.59 (m)	4.62 (m)	1.90 (m)
13	–	–	–	–
14	–	–	–	–
15	5.44 (t, 7.2)	4.87 (t, 1.2)	4.90 (d, 8.0)	1.57 (m)
16a	2.24 (m)	2.00 (m)	2.28 (m)	1.38(m)
16b		1.41 (d, 11.2)	1.57 (m)	
17	3.64 (d, 8.4)	3.17 (d, 7.6)	3.29 (d, 9.2)	2.07 (m)
18	1.31 (s)	1.79 (s)	1.78 (s)	0.86 (s)
19	1.00 (s)	1.01 (s)	1.02 (s)	1.02 (s)
20	–	–	–	2.07 (m)
21	7.27 (s)	7.18 (s)	7.25 (s)	4.75 (d, 3.2)
22a	6.31 (s)	6.33 (s)	6.40 (d, 1.2)	1.57 (m)
22b				1.90 (m)
23	7.33 (s)	7.25 (m)	7.31 (t, 1.6)	4.07 (dd, 15.6, 8.8)
24	–	–	–	3.61 (d, 8.8)
26	–	–	–	1.31 (s)
27	–	–	–	1.14 (s)
28a	3.70 (d, 8.0)	3.38 (d, 6.0)	3.47(d, 7.6)	1.12 (s)
28b	3.60 (d, 8.0)	3.48(d, 5.6)	3.54 (d, 7.6)	
29	1.25 (s)	1.17 (s)	1.19 (s)	1.05 (s)
30	1.68 (s)	1.49 (s)	1.47 (s)	1.04(s)
1′	–	–	–	–
2′	–	–	–	–
3′	6.91 (dd, 13.2, 6.0)	7.02 (d, 5.6)	6.91 (dd, 7.2, 1.6)	–
Me(2′)	1.91 (s)	2.08 (s)	1.91 (s)	1.47 (s)
Me(3′)	1.78 (s)	1.83 (d, 5.2)	1.84 (s)	1.37 (s)
OCH_3	–	3.01 (s)	3.06 (s)	3.34 (s)
OAc	–	1.89 (s)	1.96 (s)	–
$CO_2\underline{Me}$	3.25 (s)	–	–	–
R	6.75 (dd, 13.2, 6.0), 1.91 (s), 1.78 (s)	2 × 8.08 (d, 6.0), 2 × 7.40 (t, 8.0), 7.56 (t, 6.0)	7.01 (dd, 7.2, 1.2), 2.01 (s), 1.84 (s)	

[a] Data measured at 400 MHz.
[b] Data measured at 500 MHz.