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Bioactive phenolics and terpenoids from *Manglietia insignis*

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ABSTRACT

Four new compounds, maninsigins A–D (**1**–**4**), including two new neolignans (**1**–**2**) and two new sesquiterpenes (**3**–**4**), as well as ten known compounds (**5**–**14**), were isolated from the leaves and stems of *Manglietia insignis*. Their structures were established on the basis of extensive spectroscopic analyses. In addition, some compounds were tested for their cytotoxic and neurite outgrowth-promoting activities, as well as their antagonistic activity toward FXR ligand.

1. Introduction

Magnolia officinalis Rehd. et Wils is a very important traditional medicine and has been used in the treatments of asthma, abdominal distention and pain, dyspepsia, and asthmatic cough [1,2]. Phytochemical studies have revealed a variety of lignans and alkaloids as chemical constituents of the plant. The lignans showed cytotoxic, anti-inflammatory, antioxidative, antagonistic, and antitumor activities, while the alkaloids exhibited antiplasmodial and free radicals restraining activities [3–8]. *Manglietia insignis* (Wall.) Bl. is widely distributed in the west of China and has been partly used as a substitute of *M. officinalis* in Yunnan and Sichuan provinces of China. Previous researches have shown that *M. insignis* also contained representative bioactive components as that of *M. officinalis*, such as magnolol and magnocurarine [9]. However, phytochemical research on *M. insignis* is quite limited so far. Aiming at discovering chemical constituents with significant bioactivities, we conducted the phytochemical investigation of the leaves and stems of *M. insignis*, which led to the isolation of four new compounds, maninsigins A–D (**1**–**4**) including two neolignans (**1**–**2**) and two sesquitepenoids (**3**–**4**), and ten known lignans (**5**–**14**) (Fig. 1). Herein, the isolation, structural elucidation, and biological activities of these compounds are described.

2. Experimental

2.1. General experimental procedures

Optical rotations were measured with a JASCO DIP-370 digital polarimeter. UV spectra were obtained using a Shimadzu UV-2401A spectrophotometer. A BioRad FtS-135 spectrophotometer was used for scanning IR spectroscopy with KBr pellets.

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1D and 2D NMR spectra were recorded on Bruker AM-400, DRX-500 and Bruker Avance III-600 MHz spectrometers. Unless otherwise specified, chemical shifts (δ) were expressed in ppm with reference to the solvent signals. High-resolution electrospray-ionization (HRESIMS) was performed on a VG Autospec-3000 spectrometer under 70 eV. Column chromatography was performed using a silica gel (200–300 mesh, Qing-dao Marine Chemical, Inc., Qingdao, China). Semi-preparative HPLC was performed on an Agilent 1100 liquid chromatography with a Zorbax SB-C_{18}, 9.4 mm × 25 cm, column. Fractions were monitored by TLC and spots were visualized by heating the silica gel plates sprayed with 10% H_2SO_4 in EtOH.

2.2. Plant material

The leaves and stems of *M. insignis* (Wall.) Bl. were collected in Kunming Botanic Garden, Yunnan Province, People's Republic of China, in August 2007. The specimen was identified by Prof. Xun Gong and a voucher specimen (No. KIB 2007-08-11) has been deposited at the State Key Laboratory of Phytochemistry and Plant Resources in West China, Kunming Institute of Botany, Chinese Academy of Sciences.

2.3. Extraction and isolation

The plant material of *M. insignis* (8.5 kg) was ground and exhaustively extracted with Me_2CO–H_2O (V/V = 7:3, 3 × 25 L) at room temperature. The solvent was evaporated in vacuo, and the crude extract was dissolved in H_2O and partitioned with EtOAc. The EtOAc portion (110 g) was chromatographed on a silica gel column (80–100 mesh, 15 × 120 cm, 0.6 kg) being eluted with $CHCl_3$–Me_2CO (1:0, 20:1, 10:1, 5:1, 2:1, 1:1, and 0:1, each 12 L) to afford fractions I–VII. Fraction III (9.2 g) was applied to RP-18 (3 × 40 cm), eluted with a MeOH–H_2O (40%–100%, each 8 L) gradient system, to afford five fractions. Fraction III-2 (1.3 g) was repeatedly chromatographed on a silica gel (a, 200–300 mesh, 3 × 35 cm, petroleum ether–Me_2CO, 12:1, 9:1, 6:1, and 2:1, each 0.9 L; b, 200–300 mesh, 1.5 × 35 cm, $CHCl_3$–Me_2CO, 30:1, 20:1, 15:1, 10:1, each 0.6 L) and Sephadex LH-20 (1.5 × 120 cm, MeOH) to yield **1** (9.0 mg), **4** (3.5 mg) and **6** (10.0 mg). Fraction III-3 (1.7 g) was chromatographed on a silica gel (a, 200–300 mesh, 3 × 35 cm, petroleum ether–Me_2CO, 18:1, 13:1, 8:1, 4:1 and 2:1, each 1.2 L; b, 200–300 mesh, 1.5 × 35 cm, $CHCl_3$–Me_2CO, 30:1, 20:1, 12:1, 6:1, each 0.8 L), further over an RP-18 column [1.5 × 35 cm, MeOH–H_2O, 56%, (4 L)], followed by Sephadex LH-20 (1.5 × 120 cm, MeOH) to yield **3** (3.5 mg), **5** (2.9 mg),

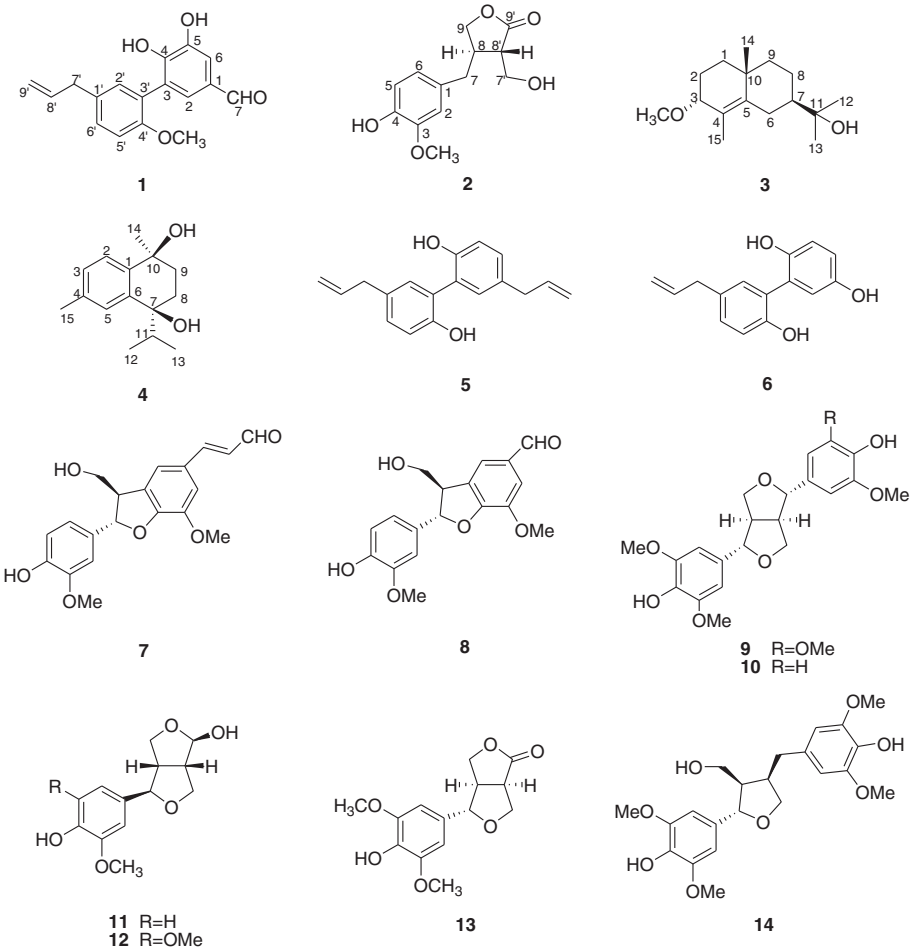

Fig. 1. The structures of compounds **1**–**14**.