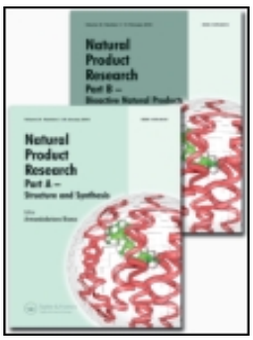

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Limonoids from the leaves of *Swietenia macrophylla*

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One new limonoid of the phragmalin type (**1**) named Swietenine J with nine known compounds methyl-6-β-hydroxy angolensate (**2**), 1-*O*-acetylkhayanolide A(**3**), Khayanolide E (**4**), Khayalactone (**5**), Khayanone (**6**), 1-*O*-Acetylkhayanolide B (**7**), 1-*O*-Deacetylkhayanolide E (**8**), Khayanolide A (**9**), Khayanolide B (**10**) were isolated from *Swietenia macrophylla*. The structure of **1** was elucidated on the basis of 1D and 2D- NMR spectroscopic analysis.

Keywords: *Swietenia macrophylla*; swieteniene J; limonoids; phragmalin type

1. Introduction

Swietenia macrophylla is an economically important timber tree native to west India, Malaysia, and southern China (Chen, Chen, & Lee, 1997; Mulholland, Parel, & Coombes, 2000). Its seeds have been applied as a folk medicine for the treatment of anti-tumor, anti-diabetes, and anti-inflammatory (Chen et al., 2010; Maiti, Dewanjee, Kundu, & Mandal, 2007). Previous chemical investigations on this species were focused on fruits and seeds (Chakrabartty, Connolly, McCrindle, Overton, & Schwarz, 1968; Chakravarty & Chatterjee, 1955; Chakrabartty & Chatterjee, 1957; Connolly, Henderson, McCrindle, Overton, & Bhacca, 1964; Dewanjee, Maiti, Das, Mandal, & Dey, 2009; Ghosh, Chakrabartty, & Chatterjee, 1960; Guha-Sircar & Chakravarty, 1951; Kojima, Isaka, & Ogihara, 1998; Mootoo et al., 1999; Tan et al., 2009; Taylor, & Taylor, 1983). In 2009, Lin et al. was focused on the twigs of this specie which collected from Sanya of Hainan Island, People's Republic of China (Lin et al., 2009).

In this report, we examined the methanolic extract of the dry leaves of *S. macrophylla* collected from China of Guangzhou and further isolated one new limonoid of the phragmalin type named Swietenine J (**1**) together with nine known compounds Methyl-6-β-hydroxy angolensate (**2**) (Narender, Khaliq, & Shweta, 2008), 1-*O*-Acetylkhayanolide A (**3**) (Nakatani, et al., 2001), Khayanolide E (**4**) (Olmo, et al., 1997), Khayalactone (**5**) (Tchuendem, Ayafor, Connolly, & Sterner, 1998), Khayanone (**6**) (Nakatani et al., 2001), 1-*O*-Acetylkhayanolide B (**7**) (Olmo et al., 1996), 1-*O*-Deacetylkhayanolide E (**8**) (Olmo et al., 1996), Khayanolide A (**9**) (Nakatani et al., 2000), Khayanolide B (**10**) (Olmo et al., 1996; Figure 1). Herein, we reported the isolation and structural elucidation of the new constituent. Meanwhile, all of the isolates were evaluated for their cytotoxicity against the human HL-60, SMMC-7721, A-549, MCF-7 and SW480 cell lines using the MTT assay.

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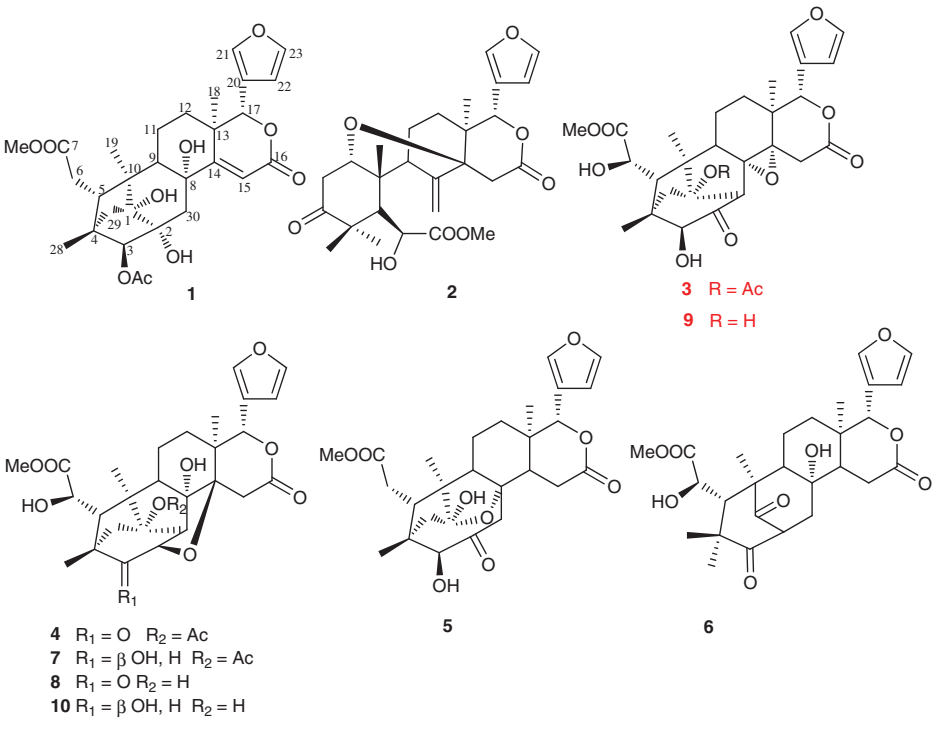

Figure 1. The structures of **1–9**.

Unfortunately, none of them demonstrated inhibitory activities against all tested cells with IC_{50} values of >40 μM.

2. Results and discussion

The molecular formula of compound **1**, $C_{29}H_{36}O_{10}$ (12 unsaturations), was determined by HRESIMS. From the ^{1}H and ^{13}C NMR spectra, six of the unsaturations were present as double bonds: three carbon-carbon (two of them as one furan ring), three CO (two esters and one acetyl). Therefore, the molecule is a hexacyclic compound. The NMR data of **1** also revealed that the presence of 5 × CH_3 (one methoxy), 5 × CH_2, 8 × CH (four olefinic) and 11 × C (two olefinic, one acetyl and two ester carbonyls).

All prontons directly bonded to carbon atoms were first assigned by the HMQC spectrum, and then the 2D NMR (^{1}H-^{1}H COSY, HMBC, and NOESY spectra; Figure 2) studies elucidated that **1** was a phragmalin type compound derived via a mexicanolide. Moreover, the H-6 methylene protons at δ 2.60 (d, $J = 16.2$ Hz, 1H) and 2.44 (dd, $J = 16.6$, 12.0 Hz, 1H) attached to a carbon adjacent to an ester carbonyl were coupled with the H-5 proton at δ 2.75 (d, $J = 11.8$ Hz), and the presence of this moiety and a characteristic H-17 at δ 6.01 strongly suggested that **1** was a rings B, D-seco limonoid. And the absence of signals due to two tertiary methyls to be at 4β (C-29), 8β (C-30) in the basic limonoid skeleton and the absence of the proton signals to be assigned to 29-methylene at 2.08, 1.92 (dd, $J = 10.4$, 10.5 Hz), supported that **1** was a phragmalin type such as Tabulalin (Nakatani et al., 2004). However, there were two methylenes and one methine in **1** instead of two methines (oxygenated carbons) and one oxygenated quaternary carbon in

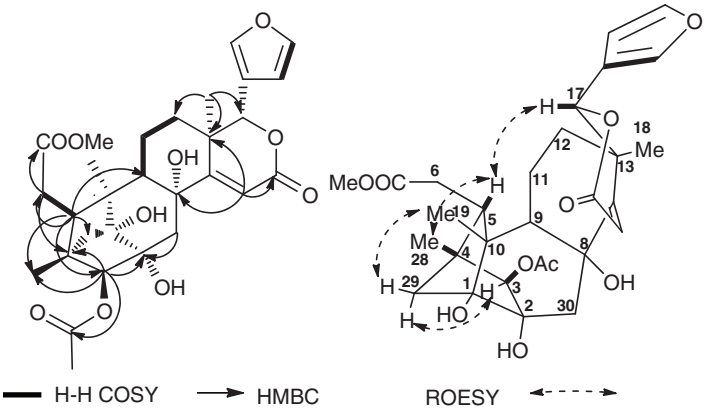

Figure 2. Selected HMBC, H-H COSY and key ROESY correlations of **1**.

Tabulalin. It was suggested that **1** was absence of three hydroxyls at C-30, C-9, C-12, respectively, by carefully comparing the ^{13}C NMR data of **1** with Tabulalin.

These findings were further proved by HMBC spectrum and ^{1}H-^{1}H COSY. In the HMBC spectrum of **1** (Figure 2), the observed long-range C-H correlations of the H-3 signal with ^{13}C NMR signals at δ 34.5 (CH_2), 88.0 (CH), 45.8 (C), 39.6 (CH_2), 19.7 (CH_3) and 15.6 (CH_3) led to their assignments as C-6, C-3, C-9, C-19 and C-28, respectively; the correlation of the H-3 with acetyl carbon signal (δ 171.0) indicated that acetyl was attached to C-3; the correlations of the H_2-30 (δ 2.68, 3.44) with C-2 (δ 76.9, s), of the H-15 (δ 7.00, s) with C-8 (δ 71.5 s), of the H-9 (δ 2.59) with C-5 (δ 37.9) further confirmed the locations of the hydroxyls. Meanwhile, in the ^{1}H-^{1}H COSY spectrum (Figure 2), the correlations of the H-9/H-11/H-12 suggested that there were absence of hydroxyls at C-30, C-9 and C-12 in **1** compared with in Tabulalin.

The observed NOE correlations (Figure 2) showed that **1** had the same relative stereochemistry as Tabulalin at positions C-1, C-2, C-3, C-4, C-5 and C-10. The cross-peaks of H-5 signal with H_3-28 and H-17 in the NOESY spectrum indicated that the β orientation for these protons and the folded conformation of **1**. The 29-methylene proton signals showed NOE correlations with the H-3 and 19-Me proton signals.

3. Experimental

3.1. *General experimental procedures*

Optical rotations were recorded on a HORIBA SEPA-300 digital polarimeter using a sodium lamp. IR spectra were measured using a Bio-Rad FTS-135 spectrometer. FABMS and HRESIMS were performed on a VG Auto Spec-3000 spectrometer. NMR Spectras were measured by Bruker AV-400 or DRX-500 instruments with chemical shifts δ in ppm rel. to Me_4Si, coupling constants J in Hz. Column chromatography was carried out on normal phase chromatographic (Qingdao Marine Chemical, China), sephadex LH-20 (Pharmacia Fine Chemical Co. Ltd.), RP-18 (Merk, Darmstadt, Germany).

3.2. *Plant material*

The dry leaves of *S. macrophylla* were collected from the Guangzhou, Guangdong province, China in August 2009, and identified by Prof. Shukun Chen. A voucher specimen, no. KIB 20091011, has been deposited at the State Key Laboratory of

Phytochemistry and Plant Resources in West China, Kunming Institute of Botany, Chinese Academy of Sciences.

3.3. *Extraction and isolation*

Dried leaves of *S. macrophylla* (5 kg) were extracted with MeOH. Removal of solvent in a vacuum gave the MeOH extract (120 g), which was partitioned in water and extracted with Petroleum Ether, ethyl acetate (AcOEt). The AcOEt layer was concentrated and the residue (50 g) was fractionated by column chromatography on normal-phase silica gel, eluted with gradient $CHCl_3$/MeOH (100 : 1, 60 : 1, 30 : 1, 15 : 1, 1 : 1) afforded five fractions (*Fr.1-Fr.5*). Compound **2** (83 mg) was isolated from *Fr.1* by using the chromatographic column on normal-phase silica gel column eluted with $CHCl_3$/MeOH (100:1); *Fr.2* was separated by reversed-phase silica gel column eluted with MeOH/ H_2O (45%–75%) to afford compounds **3** (22 mg), **4** (12 mg), **5** (41 mg) and **6** (10 mg); Compounds **1** (12 mg), **7** (31 mg), **8** (12 mg) and **9** (10 mg) were obtained from *Fr.3* by reversed-phase silica gel column eluted with MeOH/ H_2O (45–60%) as well as on Sephadex LH-20 column using MeOH as fluent. Compound **10** (35 mg) was got from the *Fr.4* by using the chromatographic column on normal-phase silica gel column eluted with $CHCl_3$/MeOH (20 : 1).

3.4. *Spectral data*

Swietenine J (**1**), $C_{29}H_{36}O_{10}$; white powder; $[\alpha]_D^{25} = +22.3^\circ$ (c 0.08 MeOH); positive FABMS: *m/z* 567 $[M+Na]^+$; HRESIMS: *m/z* 567.2209 $[M+Na]^+$ (calcd. 567.2206); IR (KBr) ν_{max}: 3600$^-$3300, 1742, 1724, 1633, 1375, 1239, 1100 cm^{-1}; ^1H NMR (C_5D_5N, 500 MHz) δ: 5.57 (1H, s, H-3), 2.75 (1H, br d, $J = 11.8$ Hz, H-5), 2.60 (1H, d, $J = 16.2$ Hz, H-6), 2.44 (1H, dd, $J = 16.6$ Hz, 12.0 Hz, H-6), 2.56$^-$2.60 (1H, m, H-9), 1.64$^-$1.68 (2H, m, H-11), 1.26$^-$1.28 (2H, m, H-12), 7.00 (1H, s, H-15), 6.02 (1H, s, H-17), 1.67 (3H, s, H-18), 1.34 (3H, s, H-19), 7.83 (1H, s, H-21), 6.72 (1H, br s, H-22), 7.72 (1H, br s, H-23), 0.93 (3H, s, H-28), 2.08, 1.92 (2H, dd, $J = 10.4$ Hz,10.5 Hz, H-29), 2.68, 3.44 (2H, 2m, H-30), 3.65 (3H, s, COO$\underline{CH_3}$), 2.18 (3H, s, 3-OCO$\underline{CH_3}$); ^{13}C NMR (C_5D_5N, 125 MHz) δ: 82.4 (C, C-1), 76.9 (C, C-2), 88.0 (CH, C-3), 44.8 (C, C-4), 37.9 (CH, C-5), 34.5 (CH_2, C-6), 174.8 (C, C-7), 71.5 (C, C-8), 45.8 (CH, C-9), 47.0 (C, C-10), 30.0 (CH_2, C-11), 29.9 (CH_2, C-12), 38.9 (C, C-13), 166.9 (C, C-14), 116.6 (CH, C-15), 166.6 (C, C-16), 80.8 (CH, C-17), 22.0 (CH_3, C-18), 19.7 (CH_3, C-19), 121.4 (C, C-20), 142.4 (CH, C-21), 111.1 (CH, C-22), 143.5 (CH, C-23), 15.6 (CH_3, C-28), 39.6 (CH_2, C-29), 40.9 (CH_2, C-30), 51.7 (COO$\underline{CH_3}$), 21.7 (3-OCO$\underline{CH_3}$), 171.0 (3-O$\underline{C}$OCH$_3$).

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