A novel sesquiterpenoid glucoside from *Hedyosmum orientale*

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One novel sesquiterpenoid guaiane glucoside, hedyosmum F, and three known sesquiterpenoids, hedyosmum D–E and 7,10-epoxy-hedyosminolide were isolated from the aerial of *Hedyosmum orientale*. The structure of hedyosmum F was established on the basis of spectroscopic data, including IR, HR-ESI-MS, 1D and 2D NMR spectroscopy.

Keywords: *Hedyosmum orientale*, sesquiterpenoid, Chinese medicine

The Chloranthanceae family is composed by four genera, *i.e.*, *Sarcandra*, *Chloranthus*, *Hedyosmum*, and *Ascarina*.[1] In Eastern Asia, the Chloranthanceae are widely used in folk medicines as antiseptic, antispasmodic, and analgesis agents. Since 1971 when pelargonidin-3-rhamnosylglucoside was discovered from Chloranthanceae,[2] more than 130 compounds have been reported from this family.[3] These compounds can be divided into six classes: organic acids, amides, coumarins, sterols, terpenoids and flavonoids. Among these, half of the isolates were sesquiterpenes and sesquiterpene derivatives. Sesquiterpenes have been recognized as characteristic metabolites of this family.[3]

Hedyosmum orientale Merr. et Chun is the only species native to the south of China. Previous studies of the plant have resulted in the isolation of five new guaiane sesquiterpenoids, hedyosumins A–E.[4] In our present study, a novel sesquiterpenoid glucoside, hedyosmum F (**1**), was isolated from the aerial of *H. orientale*, together with three known compounds, hedyosmum D–E (**2**–**3**)[4] and 7, 10-epoxyhedyosminolide (**4**).[5] Compound **4** was obtained from this plant for first time. The structure of **1** was established by spectroscopic methods, especially 2D NMR (HMQC, HMBC, and NOESY). We report herein the isolation and structural determination of these sesquiterpenoids from *H. orientale*.

Hedyosmum F (**1**) was obtained as a colourless amorphous powder. The molecular formula of **1** was determined as $C_{21}H_{28}O_8$ by HR-ESI-MS at *m/z* 431.1689 $[M + Na]^+$ (Calcd 431.1682), implying the existence of eight degrees of unsaturation. The IR spectrum exhibited bands at 3400 and 1730 cm^{-1} due to hydroxyl and lactone groups, respectively.[6] The glycosidic nature of **1** was indicated by anomeric resonances [δ_H 4.59 (1H, d, J = 7.5 Hz); δ_C 98.3] (Table 1). The ^{1}H NMR spectrum of **1** revealed the presence of three tertiary methyl groups (δ 1.32, 1.86, and 1.87), two trisubstituted double bond signals at δ 5.43 (1H, m) and 6.23 (1H, m). It also showed signal due to an oxygenated methine at δ 4.93 (1H, dd, J = 11.0, 2.0), together with signals arising from the glucosyl moiety. The ^{13}C NMR spectrum of **1** exhibited the presence of 21 C-atoms comprising six quaternary, nine tertiary, three secondary C-atoms, and three methyl groups. These included six carbon signals assigned to the glucosyl moiety. One carbonyl and three double bonds were identified in **1** from their chemical shifts. Four out of the eight degrees of unsaturation were due to the carbonyl group and three double bonds, and the remaining four degrees of unsaturation were accounted for by four rings. The data mentioned above showed **1** was a guaiane-type sesquiterpenoid with glucosyl moiety.

After correlation of all the protons with their directly-bonded carbon partners via a HMQC spectrum, it was possible from the HMBC spectrum to deduce the planar structure of **1** (Figure 2). The HMBC correlations of H-13/C-6, H-13/C-7, H-13/C-11, and H-13/C-12 indicated the presence of an α, β, δ-unsaturated ketone, which was confirmed by the UV absorption band at 312 nm ($\log_e$ 3.2). The linkage of C-12 and C-8 by O-atoms to form a lactone was deduced from the HMBC correlation of H-8/C-12. The proton signal of C-15 (δ 1.32) was correlated with the C-10 and C-1 to support the linkage of C-1 and C-10. The glycosyl moiety was allocated to C-10 by the strong correlations between C-10 and H-1′. The planar structure of **1** was thus outlined.

The relative stereochemistry of **1** was completely established by the coupling constants in the ^{1}H NMR and the correlations in the NOESY spectra. The large coupling constant of H-1′ at δ 4.59 (1H, d, J = 7.5 Hz) showed the β-configuration of the sugar. In the NOESY spectrum, the proton signal for H-15 showed correlations with the signals of H-8 and H-2β,

Table 1 ^{1}H and ^{13}C NMR data of **1** at 400 MHz in CD_3OD

Carbon	δ_H J/Hz	δ_C	Carbon	δ_H J/Hz	δ_C
1	3.27 (1H, m)	54.2	12	–	42.9
2α	2.72 (1H, m)	35.4	13	1.86 (3H, s)	8.5
2β	2.68 (1H, m)				
3	5.43 (1H, m)	141.6	14	1.86 (3H, s)	13.0
4	–	141.7	15	1.32 (3H, s)	18.4
5	–	160.7	1′	4.59 (1H, d, 7.5)	98.3
6	6.23 (1H, s)	108.6	2′	3.17 (1H, t, 7.5)	75.2
7	–	158.7	3′	3.38 (1H, m)	78.2
8	4.93 (1H, dd, 11.0, 2.0)	79.7	4′	3.34 (1H, m)	71.8
9	2.88 (1H, 11.0, 7.0)	45.4	5′	3.32 (1H, m)	77.6
	2.00 (1H, t, 7.0)				
10	–	80.9	6′	3.85 (1H, dd, 13.0, 1,5)	62.8
				3.66 (1H, dd, 13.0, 5.0)	
11	–	122.5			

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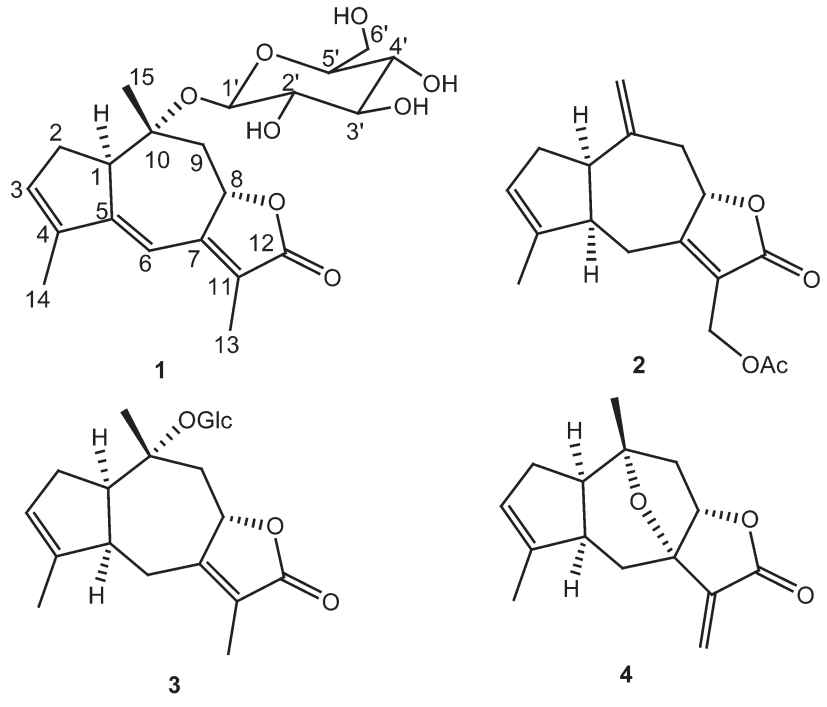

Fig. 1 Structure of compounds **1–4**.

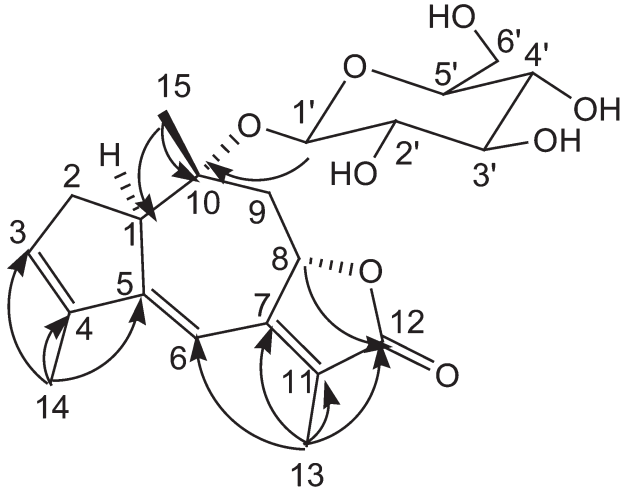

Fig. 2 Selected HMBC correlations of **1**.

indicating that H-15, H-8 and H-2β were on the same side of the molecule and designated as β-orientation, and as a consequence, H-2α was assigned an α-orientation. The correlation of H-2α/H-1 indicated the H-1 was in α-face. The ^{1}H, ^{13}C NMR spectral data and 2D NMR experiments support the assignment of structure **1** to the new compound which was named hedyosmum F.

Experimental

IR spectra were recorded on a Nicolet 6700 spectrometer with KBr disks. UV spectra were measured on a Shimadzu UV-2450 UV-visible spectrophotometer. Optical rotations: Rudolph Autopol IV polarimeter. NMR spectra were measured on a Bruker AM-500 apparatus with TMS as internal standard. δ in ppm *J* in Hz. ESI-MS: Agilent 6210 Lc/Tof mass spectrometer; in *m/z*. All solvents used were of analytical grade (Hangzhou Gaojing Fine Chemical Plant, Hangzhou, People's Republic of China). Silica gel (200–300 mesh) was used for column chromatography (CC)and pre-coated silica gel GF_{254} plates (Qingdao Marine Chemical Plant, Qingdao, People's Republic of China) were for TLC. MCI gel (CHP20P, 75-150 μm, Mitsubishi Chemical Industries Ltd.), and Toyopearl HW-40C gel (Tosoh Corporation) were used for column chromatography.

The aerial part of *H. orientale* was collected from Hainan Province of P. R. China and identified by Prof. Hai-Bo Bai of the College of City, Zhejiang University. A voucher specimen (ZJUT 20090715) has been deposited at Zhejiang University of Technology, P. R. China.

The air-dried powder of the aerial parts (5kg) of *H.orientale* was extracted with aq. 95% ethanol three times at room temperature. The ethanol extract was concentrated under reduced pressure to give a brown residue (800 g), which was then dissolved in 4L water to form a suspension. The mixture was extracted with $CHCl_3$ (6 × 1L) to give the $CHCl_3$-soluble fraction A (50g). Fraction A was subjected to a silica gel column chromatography eluted with petroleum ether-acetone (8:1 to 2:1) to give three major fractions 1–3. Fraction 3 was subjected to column chromatography (CC) containing MCI gel CHP 20P and eluted with MeOH-H_2O (0:10–5:5) to yield **4** (22.9 mg), **2** (5 mg). Fraction 2 was subjected to CC (MCI CHP20P gel; MeOH-H_2O 0:1→ 5:5) to give **3** (11 mg). Fraction 1 was purified by Toyopearl HW-40C eluted with MeOH to yield **1** (27 mg).

Hedyosumin F (**1**)**:** Colourless amorphous powder; $[\alpha]^{20}{}_{D} = -27.5°$ (*c* = 0.25, MeOH); UV (MeOH): 312 (3.2), 205 (2.7). IR (KBr): 3400, 2925, 1730, 1649, 1598, 1442, 1384, 1075, 1030 cm^{-1}; ^{1}H- and ^{13}C-NMR see Table 1. ESI-MS *m/z*: 431 $[M + Na]^+$ HR-ESI-MS *m/z:* 431.1689 $[M + Na]^+$ ($C_{21}H_{28}O_8Na$; Calcd 431.1682).

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