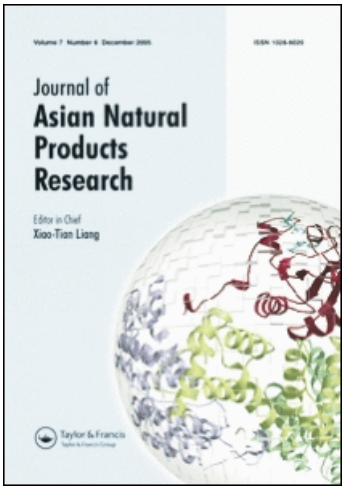

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Li-Ping Zhu[a]; Yuan Li[a]; Jing-Zhi Yang[a]; Li Zuo[a]; Dong-Ming Zhang[a]
[a] Institute of Materia Medica, Chinese Academy of Medical Sciences and Key Laboratory of Bioactive Substances and Resources Utilization of Chinese Herbal Medicine (Peking Union Medical College), Ministry of Education, Beijing, China

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Two new sesquiterpene lactones from *Sarcandra glabra*

Li-Ping Zhu, Yuan Li, Jing-Zhi Yang, Li Zuo and Dong-Ming Zhang*

Institute of Materia Medica, Chinese Academy of Medical Sciences and Key Laboratory of Bioactive Substances and Resources Utilization of Chinese Herbal Medicine (Peking Union Medical College), Ministry of Education, 1 Xiannongtan Street, Beijing 100050, China

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Two new sesquiterpene lactones (**1**) and (**2**), along with three known sesquiterpenes, atractylenolide β (**3**), chloranthalactone E (**4**), and (−)-istanbulin A (**5**), were isolated from the whole plant of *Sarcandra glabra*. The structures of two new compounds were established as 8β,9α-dihydroxyeudesman-4(15),7(11)-dien-8α,12-olide (**1**) and 8β,9α-dihydroxylindan-4(5),7 (11)-dien-8α,12-olide (**2**) on the basis of spectroscopic analysis. Compound **3** was isolated from this genus for the first time.

Keywords: *Sarcandra glabra*; chloranthaceae; sesquiterpene lactone; 8β,9α-dihydroxyeudesman-4(15),7(11)-dien-8α,12-olide; 8β,9α-dihydroxylindan-4(5),7(11)-dien-8α,12-olide

1. Introduction

Sarcandra glabra (Thunb.) Nakai [syn. *Chloranthus glaber* (Thunb.) Makino] (Chloranthaceae) grows in the southern part of China and Japan and in southeastern Asia. The whole plant has been used as an antibacterial and antitumor agent in China.[1] Several cycloeudesmanes, dihydrochalcones, and flavonoids were previously isolated from *C. glaber*.[1–5] In our search for bioactive compounds, two new sesquiterpene lactones (**1**) and (**2**) together with three known sesquiterpene lactones were isolated from the whole plant of *S. glabra*. This paper deals with the isolation and structure elucidation of the new compounds.

2. Results and discussion

Compound **1** was obtained as colourless needles. The molecular formula of **1** was determined as $C_{15}H_{20}O_4$ by HREIMS (*m/z*, 264.1342, $[M]^+$) and NMR analyses. The presence of hydroxyl and α,β-unsaturated lactone groups was indicated by its IR (ν 3520 and 1738 cm^{-1}, respectively) and UV (λ_{max} at 222 nm) spectra.[6,7] The ^1H NMR spectrum exhibited signals for two methyl groups at δ 1.06 (3H, s) and 1.74 (3H, d, $J = 1.2$ Hz), which are typical for Me-14 and Me-13 of eudesmanolides, along with one terminal double bond at δ 4.62 (1H, d, $J = 1.6$ Hz) and 4.83 (1H, d, $J = 1.6$ Hz) for H-15.[7] The ^{13}C NMR spectrum displayed 15 signals, of which the signals observed at δ 8.0 (C-13), 105.8 (C-8), 123.9 (C-11), 158.9 (C-7), and 173.6 (C-12) are characteristics of a 5-hydroxy-3-methyl-5-hydrofuran-2-one functional moiety of eudesmanolides.[7] The ^1H NMR patterns of **1** are similar to those of a known eudesmanolide, atractylenolide β (**3**),[6] except for a pair of signals at δ 3.62 (1H, d, $J = 4.4$ Hz, 9-H) and 4.29 (1H, d, $J = 4.4$ Hz, 9-OH) in **1** instead of the signals at 1.49 (1H, d, $J = 13.5$ Hz, 9-αH) and 2.22 (1H, d, $J = 13.5$ Hz, 9-βH) in **3**. After D_2O

*Corresponding author. Email: zhangdm@imm.ac.cn

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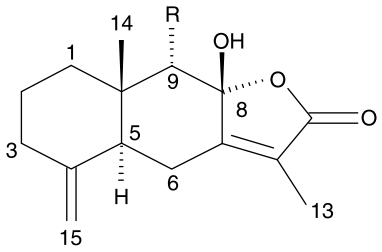
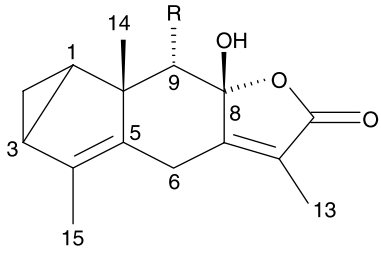


1 R=OH
3 R=H



2 R=OH
6 R=H

Figure 1. The structures of compounds **1**–**3** and **6**.

exchange, the signal at δ_H 4.29 disappeared and the doublet at δ_H 3.62 turned to a singlet, which indicated that **1** has a hydroxy group at C-9. In the HMBC spectrum of **1**, $^1H-^{13}C$ long-range correlations were observed for H-9/C-8, C-10, C-5, C-7, C-1, and C-14, which enabled the establishment of the site of 9-OH (Figure 2). The NOE correlations between H-14/H-1β, H-6β, H-9; H-5/H-3α, H-1α, H-6α; and H-9/H-14, H-1β indicated β-configurations for CH_3-14 and H-9, while H-5 was α-oriented (Figure 3). Thus, **1** was determined to be 8β,9α-dihydroxyeudesman-4(15), 7(11)-dien-8α,12-olide.

Compound **2** was obtained as white powder with a molecular formula of $C_{15}H_{18}O_4$, as determined by HREIMS (*m/z*, 262.1196, $[M]^+$) and NMR analyses. Its IR spectrum showed absorption bands of hydroxyl groups (3504 cm^{-1}) and an α,β-unsaturated lactone (1755 cm^{-1}).[6,7] Preliminary inspection of the ^1H NMR spectrum of **2** led to the identification of three methyl groups at δ 1.40, 1.76, and 1.81 for Me-14, Me-15, and Me-13, respectively. The ^1H NMR signals at δ 0.23 (1H, ddd, $J = 4.0, 4.0, 4.0$ Hz, *endo*-H on the cyclopropane ring) and 0.75 (1H, ddd, $J = 4.0, 8.0, 8.0$ Hz, *exo*-H on the cyclopropane ring) indicated the presence of a 1,2-disubstituted cyclopropane ring.[8] The ^{13}C NMR spectrum exhibited signals at δ 8.2 (C-13), 104.6 (C-8), 123.0 (C-11), 156.6 (C-7), and 172.6 (C-12), which confirmed the presence of a 5-hydroxy-3-methyl-5-hydrofuran-2-one functional moiety.[7] The ^1H NMR patterns of **2** are similar to those of compound **6**,[8] except for a singlet at δ 3.87 (1H, s) in **2** instead of a pair of doublets for H-9 at δ 1.79 (1H, d, $J = 14.0$ Hz) and 2.57 (1H, d, $J = 14.0$ Hz) in **6**, which indicated **2** has a hydroxyl group at C-9. In the HMBC spectrum of **2**, $^1H-^{13}C$ long-range correlations were observed for H-9/C-8, C-10, C-5, C-7, C-1, C-14; H-6/C-5, C-7, C-8, C-10, C-4, and C-11, which enabled the establishment of the site of 9-OH (Figure 2). The NOE correlation between H-14/H-2 *endo*, H-9; H-2 *endo*/H-14; and H-9/H-14 indicated β-configurations for CH_3-14 and H-9 (Figure 3). Thus, compound **2** was determined to be 8β,9α-dihydroxylindan-4(5),7(11)-dien-8α,12-olide.

Three known compounds were identified as atractylenolide β (**3**),[6] chloranthalactone E (**4**),[8] and (−)-istanbulin A (**5**),[9] respectively, by comparison of their spectral data with those reported in the literature. Among them, **3** was first reported from this genus.

3. Experimental

3.1 General experimental procedures

The optical rotations were determined on a Perkin–Elmer digital polarimeter. UV spectra were taken on a Shimadzu UV-300 spectrophotometer. IR spectra were recorded on an Nicolet 5700 spectrometer using the method of FT-IR Microscope Transmission. ^1H, ^{13}C NMR, HMQC, HMBC, and NOE spectra were run on INOVA-500 and MP-400 spectrometers, using solvent peaks as references. HREIMS was performed on an

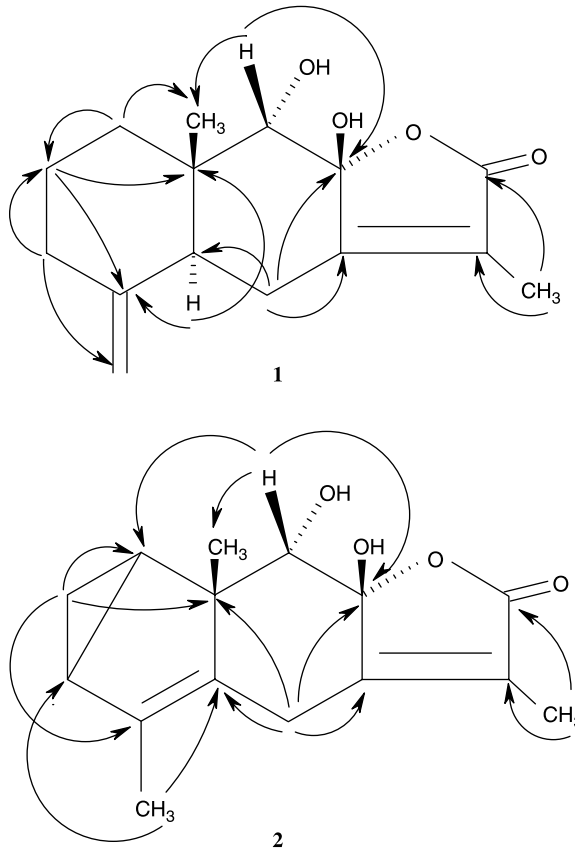


Figure 2. Key HMBC correlations of **1** and **2**.

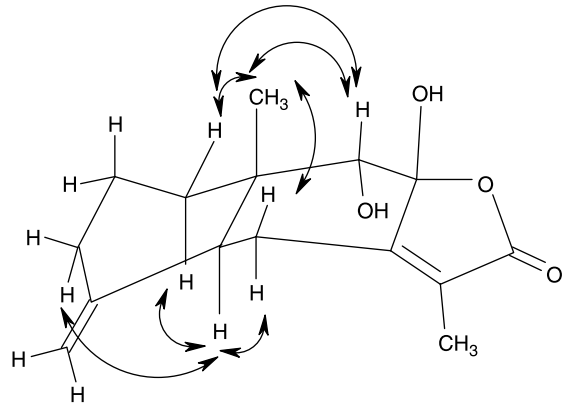
Autospec Ultima-Tof mass spectrometer. ESIMS was obtained using an Agilent 1100 series LC/MSD Trap SL mass spectrometer. Column chromatography was carried out on macroporous resin D101 (26–60 mesh, Tianjin Haiguang Chemistry Company, Tianjin, China), polyamide (60–90 mesh, Linjiang Chemistry Company, Jiangsu, China), silica gel (100–200, 200–300 mesh, Qingdao Marine Chemistry Company, Qingdao, China). Silica gel for TLC GF_{254} (Qingdao Marine Chemistry Company) was used for making silica gel plates.

3.2 Plant material

The plant was collected in Dayu County of Jiangxi Province in July 2004, and identified by Professor Yong-Ming Luo of the Faculty of Pharmacy, Jiangxi University of Traditional Chinese Medicine, Nanchang, China. A voucher specimen (No. 20040718) has been deposited at the herbarium of Institute of Materia Medica, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China.

3.3 Extraction and isolation

The whole air-dried and powdered plant (14.5 kg) of *S. glabra* was refluxed with 70% EtOH for three times. After evaporation of ethanol *in vacuo*, the aqueous residue was diluted with water. The filtrate was separated on macroporous resin D101 using water and 30, 70, and 95% EtOH–water successively to



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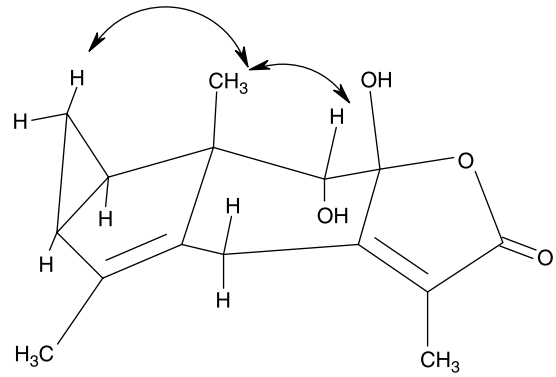

2

Figure 3. Key NOE correlations of **1** and **2**.

afford four fractions (A_1–A_4). Fraction A_3 (284 g) was subjected to a polyamide column eluted with water and 30, 60, and 95% EtOH–water successively to give four fractions (B_1–B_4). Fraction B_2 (47.9 g) was subjected to column chromatography on silica gel eluted with $CHCl_3$–MeOH (1:0–9:1) to afford 16 fractions (F_1–F_{16}). Fraction F_2 (2.3 g) was chromatographed on a silica gel column eluted with a gradient system of petroleum ether/-acetone (12:1–6:1) to give compound **3** (10 mg). Chromatography on silica gel column of fraction F_3 (442 mg) eluted with petroleum ether/acetone (6:1–1:1) yielded compound **5** (58 mg). Fraction F_4 (33 g) was chromatographed on silica gel and eluted with cyclohexane–EtOAc (6:1–1:1) to afford compounds **1** (30 mg) and **2** (34 mg). Chromatography on silica gel column of fraction F_5 (1.1 g) eluted with cyclohexane–EtOAc (6:1–1:1) furnished compound **4** (8 mg).

3.3.1 8β,9α-Dihydroxyeudesman-4(15),7(11)-dien-8α,12-olide (1)

Colorless needles. $[\alpha]_D^{20}$ + 174.4 (*c* 0.14, $CHCl_3$). UV (MeOH) λ_{max} (log ε): 202 (3.97), 222 (4.00) nm. IR (microscope) ν_{max}: 3521, 2929, 1739, 1649, 1434, 1377, 1132, 1074, 881 cm^{-1}. ^1H NMR (CD_3COCD_3, 400 MHz, MP-400) spectral data, see Table 1. ^{13}C NMR (CD_3COCD_3, 125 MHz, INOVA-500) spectral data, see Table 1. ESIMS *m/z* 287 $[M + Na]^+$.

Table 1. ^{1}H NMR and ^{13}C NMR spectral data for **1** (CD_3COCD_3) and **2** ($CDCl_3$).

	1		**2**	
No.	δ_H	δ_C	δ_H	δ_C
1	2.12 (α) m 1.23(β) ddd (3.2, 4.4, 13.2)	35.4	1.70 m	26.8
2	1.63 m	22.8	0.23 (*endo*) ddd (4.0, 4.0, 4.0) 0.75 (*exo*) ddd (4.0, 8.0, 8.0)	15.3
3	1.93 (α) m 2.31 (β) m	36.6	1.70 m	27.7
4		150.3		140.4
5	2.28 m	44.9		130.0
6	2.57 (α) dd (3.2, 12.8) 2.40 (β) ddd (1.2, 12.8, 12.8)	29.3	3.24 (α) d (14.0) 2.68 (β) d (14.0)	23.5
7		158.9		156.6
8		105.8		104.6
9	3.62 d (4.4)	78.5	3.87 s	79.2
10		41.5		52.3
11		123.9		123.0
12		173.6		172.6
13	1.74 d (1.2)	8.0	1.81 s	8.2
14	1.06 s	16.4	1.40 s	21.7
15	4.62 d (1.6) 4.83 d (1.6)	106.9	1.76 s	13.7
9-OH	4.29 d (4.4)			
8-OH	6.15 s			

HREIMS *m/z* 264.1342 $[M]^+$ (calcd for $C_{15}H_{20}O_4$, 264.1362).

3.3.2 8β,9α-Dihydroxylindan-4(5),7(11)-dien-8α,12-olide (2)

White powder. $[\alpha]_D^{20}$ − 61.9 (*c* 0.10, $CHCl_3$). UV (MeOH) λ_{max} (log ε): 212 (5.37), 266 (3.74) nm. IR (microscope) ν_{max}: 3504, 2972, 1755, 1686, 1443, 1378, 1162, 1072 cm^{-1}. ^{1}H NMR ($CDCl_3$, 500 MHz) spectral data, see Table 1. ^{13}C NMR ($CDCl_3$, 125 MHz) spectral data, see Table 1. ESIMS *m/z* 285 $[M + Na]^+$. HREIMS *m/z* 262.1196 $[M]^+$ (calcd for $C_{15}H_{18}O_4$, 262.1205).

Acknowledgements

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