A NOVEL LIGNANOID AND NORBISABOLANE SESQUITERPENOIDS FROM *Glochidion puberum*

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*A novel lignanoid, named glochinin A (**1**), along with two known norbisabolane sesquiterpenoids, namely glochicoccin D (**2**) and phyllaemblic acid (**3**), were isolated from* Glochidion puberum. *Their structures were elucidated by spectral analysis.*

Key words: *Glochidion puberum*, lignanoid, glochinin A, norbisabolane sesquiterpenoid.

Glochidion puberum (L.) Hutch., widely distributed in China, is commonly used as folk medicine in the treatment of influenza, dysentery, impaludism, rheumatoid arthritis, and dyspepsia [1]. In order to find potentially bioactive secondary metabolites from the genus of *Glochidion*, we investigated this species, which led to the isolation of a novel lignanoid, glochinin A (**1**), along with two known norbisabolane sesquiterpenoids, glochicoccin D (**2**) [2] and phyllaemblic acid (**3**) [3]. These compounds were isolated from *Glochidion puberum* (L.) Hutch. for the first time. In this paper, we describe the structures of these compounds.

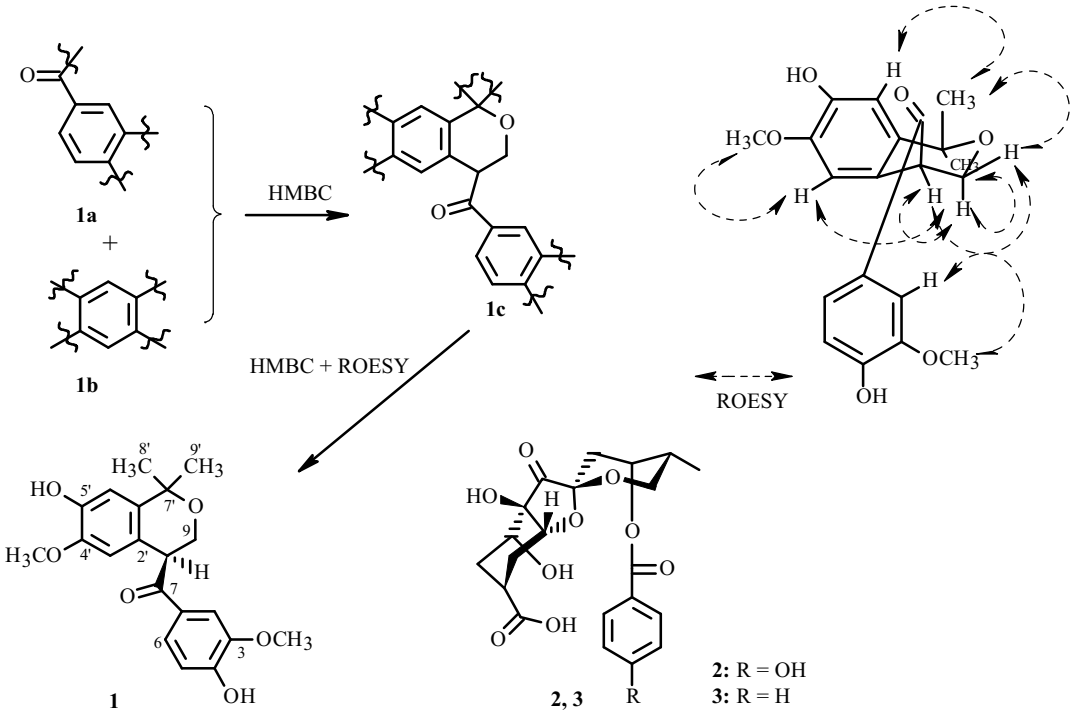

Fig. 1. Structure of **1**-**3** and ROESY Correlations of **1**.

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TABLE 1. ^{1}H NMR (500 MHz), ^{13}C NMR (125 MHz), and HMBC Spectral Data of **1** (pyridine-d_5, δ, ppm, J/Hz)

C atom	δ_H	δ_C	DEPT	HMBC (C/H)
1		129.2	C	
2	7.91 (d, J = 1.5)	112.2	CH	C-1, C-3, C-4, C-6, C-7
3		148.9	C	
4		153.6	C	
5	7.28 (d, J = 8.5)	116.2	CH	C-1, C-3, C-4, C-6
6	7.93 (dd, J = 8.5, 1.5)	124.5	CH	C-1, C-2, C-4, C-5, C-7
7		198.4	C	
8	5.07 (d, J = 4.4)	47.3	CH	C-7, C-9, C-1′, C-2′, C-3′
9	a: 4.38 (dd, J = 11.5, 4.4) b: 4.48 (d, J = 11.5)	63.5	CH_2	C-7, C-8, C-2′, C-7′
1′		137.0	C	
2′		123.6	C	
3′	6.83 s	112.7	CH	C-8, C-1′, C-2′, C-4′, C-5′
4′		147.5	C	
5′		147.3	C	
6′	7.18 s	113.7	CH	C-8, C-1′, C-2′, C-4′, C-5′
7′		75.2	C	
8′	1.58 s	29.3	CH_3	C-2′, C-7′, C-9′
9′	1.69 s	30.6	CH_3	C-2′, C-7′, C-8′
3-OMe	3.68 s	55.9	CH_3	C-3
4′-OMe	3.62 s	55.8	CH_3	C-4′

Glochinin A (1) was isolated as a white powder. Its molecular formula was determined to be $C_{20}H_{22}O_6$ by HRESIMS and NMR data. The ^{1}H NMR spectrum exhibited ABX coupling aromatic protons at δ 7.93 (J = 8.5, 1.5 Hz), 7.91 (J = 1.5 Hz), and 7.28 (J = 8.5 Hz)], two isolated aromatic protons at δ 7.18 and 6.83 ppm downfield, two methoxyl protons at δ 3.62 and 3.68 ppm, and two methyl protons at δ 1.58 and 1.69 ppm upfield. Its ^{13}C NMR and DEPT spectrum displayed one carbonyl carbon, eight quaternary carbons, six methines, one methane, and four methylenes (Table 1). Considering the fact that the chemical constituents isolated from the genus *Glochidion* belong mainly to lignans and triterpenes [4–9] and the NMR spectral data of **1** were quite distinct from those of the known skeletons, we first established the structure of **1** by extensive analysis of two-dimensional NMR spectral data.

In the HMBC spectrum (Table 1), the signals of H-2 (δ 7.91 ppm) correlated with C-6, C-1, C-3, C-4, and C-7, and the signals at δ 7.93 ppm (H-6) showed cross-peaks with C-2, C-5, C-1, C-4, and C-7. These observations, along with the proton spin system of H-5/H-6 deduced from ^{1}H–^{1}H COSY correlations, led to the establishment of partial structure **1a**.

Interpretation of HMBC data also showed the following correlations: both the proton signals at δ 6.83 ppm (H-3′) and 7.18 ppm (H-6′) showing cross-peaks with C-1′, C-2′, C-4′, C-5′, determined the existence of partial structure **1b** (Fig. 1). Furthermore, the HMBC cross-peaks of H-8/C-7, H-8/C-1′, H-8/C-2′ and H-8/C-3′, suggested C-8 located between C-7 and C-2′; the proton signals of H-6′, H-9b, and H-9a correlated with C-7′, and that of H-8 showed correlation with C-9, allowed the construction of **1c** (Fig. 1). The two methyl signals at δ 1.69 ppm (H-9′) and 1.58 ppm (H-8′) showed cross-peaks with C-1′ and C-7′, indicated two methyl groups located at C-7′. The NOESY correlations between the protons of a methoxyl group (δ 3.62 ppm), and H-3′ (δ 6.83 ppm), and HMBC cross-peaks of these protons with C-4′, indicated this methoxyl group (δ 55.8) located at C-4′. Similarly, the remaining methoxyl group (δ 55.9 ppm) located at C-3, and two hydroxyl groups located at C-4 and C-5′. Thus, the novel skeleton was established for glochinin A.

The equatorial orientation of H-8 was determined from the coupling constants with the two non-equivalent protons of C-9, and the ROESY experiment showed the correlations of H-8 (δ 5.07 ppm) with 4.38 ppm (H-9a). So the structure of **1** was elucidated as shown in Fig. 1 and named glochinin A. The absolute configuration cannot be confirmed since the yield of **1** was small.

EXPERIMENTAL

General Experimental Procedures. UV spectra were measured on a Shimadzu UV-2401 spectrometer (Kyoto, Japan). IR spectra were obtained on KBr pellets using a Bio-Rad FTS-135 spectrometer (Bio-Rad, Richmond, CA). The ^{1}H and ^{13}C NMR spectra were obtained on an INOVA-500 (Viarian, San Francisco, USA) with TMS as an internal standard. EIMS measurements were undertaken on a VG Autospec-3000 mass spectrometer (VG. Manchester, UK). TLC and column chromatography were performed on plates precoated with silica gel F_{254} and silica gel (200–300 mesh; Qingdao Marine Chemical Ltd., Qingdao, China), respectively. Solvents were distilled prior to use.

Plant Materials. The aerial parts of *G. puberum* were obtained from Dafang, Guizhou Province, People¢s Republic of China, in July 2005. The plant was identified by Pr. Q. D. Long, School of Pharmacy, Guiyang Medical University, GuiYang, where a voucher specimen (GMC No. 050721) was deposited.

Extraction and Isolation. The air-dried and roughly powdered *G. puberum* (6 kg) was extracted three times with 75% ethanol under reflux. After removal of the solvent by evaporation, the extracts were partitioned between H_2O and petroleum ether, EtOAc, and *n*-BuOH, successively. The EtOAc extract was chromatographed on a silica gel (100–200 mesh) column, eluting with a $CHCl_3$–MeOH mixture to afford 10 fractions. Fraction 2 was subjected to CC (1. SiO_2, $CHCl_3$–MeOH 40:1; 2. Sephadex LH-20, $CHCl_3$–MeOH 1:1) and further purified by preparative TLC to provide Glochinin A (3 mg). Fraction 8 was resubmitted to CC (1. SiO_2, $CHCl_3$–MeOH 9:1; 2. Sephadex LH-20, $CHCl_3$–MeOH 1:1) and further purified by preparative TLC to afford glochicoccin D (132 mg) and phyllaemblic acid (101 mg).

Glochinin A (1), white power, $[\alpha]_D^{24}$ –13.5° (*c* 0.37, MeOH); UV (MeOH, λ_{max}, nm): 281 (3.75), 228 (3.97), 208 (4.25); IR (KBr, cm^{-1}): 3421, 2971, 2934, 1708, 1666, 1591, 1513, 1463, 1425, 1364, 1278, 1157, 1077, 1031, 837, 800; ^{1}H NMR and ^{13}C NMR spectral data are given in Table1; EIMS *m/z* 358 $[M]^+$, 207, 189, 179, 151, 123; HRESIMS *m/z* 381.1316 $[M+Na]^+$ (calcd for $C_{20}H_{22}O_6$, 381.1314).

Glochicoccin D (2), colorless amorphous solid; IR, MS, ^{1}H NMR, and ^{13}C NMR spectral data were identical to those reported in the literature [2].

Phyllaemblic acid (3), colorless amorphous solid; IR (KBr, cm^{-1}): 3420, 2967, 2932, 1780, 1710, 1603, 1584, 1452, 1391, 1346, 1281, 1174, 1115, 1095, 1005, 951, 714; FAB-MS *m/z* 419 $[M–H]^+$; HRFAB-MS *m/z* 419.1316 $[M–H]^+$ (calcd for $C_{21}H_{23}O_9$, 419.1314); ^{1}H NMR and ^{13}C NMR spectral data were identical to those reported in the literature [3].

REFERENCES

1. *Flora Reipublicae Popularis Sinicae*, Delectis Florae Reipublicae Popularis Sinicae Edita, Beijing Science Press, Beijing, 1999.
2. H. T. Xiao, X. Y. Hao, X. W. Yang, Y. H. Wang, Y. Lu, Y. Zhang, S. Gao, H. P. He, and X. J. Hao, *Helv. Chim. Acta*, **90**, 164 (2007).
3. Y. J. Zhang, T. Tanaka, Y. Iwamoto, C. R. Yang, and I. Kouno, *Tetrhedron Lett*, **41**, 1781 (2000).
4. W. H. Hui and M. L. Fung, *J. Chem. Soc. C*, **13**, 1710 (1969).
5. R. Srivastava and D. K. Kulshreshtha, *Phytochemistry*, **27**, 3575 (1988).
6. H. Otsuka, E. Hirata, A. Takushi, T. Shinzato, M. Bando, M. Kido, and Y. Takeda, *Chem. Pharm. Bull*, **48**, 547 (2000).
7. H. Otsuka, E. Hirata, T. Shinzato, and Y. Takeda, *Chem. Pharm. Bull*, **48**, 1084 (2000).
8. H. Otsuka, H. Kijima, E. Hirata, T. Shinzato, A. Takushi, M. Bando, and Y. Takeda, *Chem. Pharm. Bull*, **51**, 286 (2003).
9. H. Otsuka., Y. Takeda., E. Hirata, T. Shinzato, A. Takushi, and M. Bando, *Chem. Pharm. Bull*, **52**, 591 (2004).