SHORT REPORT

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Two New Sesquiterpenoids from *Chloranthus henryi* Hemsl

Yuting Bian [1*], Fangyou Chen [1*], Weiming Huang [1*], Zhichao Chen [1*], Pengcheng Shuang [2] and Yongming Luo [1*]

[1]*School of Pharmacy, Jiangxi University of Traditional Chinese Medicine, Nanchang, Jiangxi 330004, P. R.China*

[2]*School of Chinese Materia Medica , Beijing University of Chinese Medicine, Beijing, 100029, P. R.China*

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Abstract: Two new Chloratene F (**1**) and Chlomultin G (**2**), along with eight known sesquiterpenes (**3**-**10**) and six other known compounds (**11**-**16**) were isolated from the whole plant of *Chloranthus henryi*. Their structures were elucidated by HR-ESI-MS, NMR spectroscopic. The absolute configuration of two new compounds were determined by the X-ray crystallographic. All the compounds were reported for the first time from this species.

Keywords: *Chloranthus henryi*; Chloratene F; Chlomultin G; sesquiterpene; absolute configuration.

1. Plant Source

The whole plant of *Chloranthus henryi* were collected from the Jinggang Mountain, Jiangxi Province, China, on November 2018, and identified by A. Prof Kezhong Deng, Jiangxi University of Traditional Chinese Medicine, Nanchang, China. The voucher specimen (No.20181126) was deposited in the herbarium of the Faculty of Pharmacy, Jiangxi University of Traditional Chinese Medicine.

2. Previous Studies

The *Chloranthus henryi* Hemsl is a *Chloranthus* Swartz plant of Chloranthaceae, which is mostly distributed in southwest China [1-2]. Its whole grass, root and rhizome are a kind of traditional Chinese medicine commonly were used to treat injury, promot blood, remove blood stasis and rheumatoid arthritis [3-5]. In recent years, pharmacological studies on the *Chloranthus henryi* have shown that most of the plants have good antibacterial and anti-tumor activities [6-8]. Related studies also show that sesquiterpenes rich in *Chloranthus henryi* are the main active components of their antibacterial and anti-tumor activities [9,10]. Thus, it is necessary to study sesquiterpene compounds.

* Corresponding author: E- Mail: loym999@126.com (Y. -M. Luo), Phone : +086-13970058758.
1964306673@qq.com (Y.Bian)

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3. Present Study

In the process of phytochemistry research on characteristic medicinal plants in Jiangxi Province [1-3]. We research *Chloranthus henryi* Hemsl, it is a *Chloranthus* Swartz plant of Chloranthaceae, We report on the structure elucidation of sixteen compounds (**1**-**16**) were isolated from the whole of *Chloranthus henryi* for the first time, including two new sesquiterpenoids Chloratene F (**1**) and Chlomultin G (**2**) (Figure 1).

The dried powder of the whole plants (23 kg) of *C. henryi* was extracted with 95% EtOH (3×100L) for 3 times, after combining the extract, the extract was decompressed and concentrated to no alcohol flavor, and the total extract was 1100 g. The total extract was eluted with petroleum ether, CH_2Cl_2, EtOAc and MeOH in turn by diatomite column chromatography. After vacuum concentration, the eluents obtained 156.3 g of petroleum ether, 394.2 g of CH_2Cl_2, 94.6 g of EtOAc and 454.9 g of MeOH. The CH_2Cl_2 extract (128 g) was chromatographed over an PRP 512A (MeOH/H_2O, 30%-95%) to yield four fractions (A-D). Fr.B (100g) was chromatographed over a silica gel CC eluted with petroleum ether-EtOAc in a gradient (30:1-0:1), to afford 5 fractions (B1-B5). Fr.B2 were purified by a silica gel column (CH_2Cl_2/MeOH, 50:1-0:1), and then a Sephadex LH-20 (MeOH) column to give **3** (9.0 mg), **4** (5.6 mg), **5** (7.8 mg), **7** (10.2 mg) and **13** (5.3 mg). Fr. B3 (6.9 g) was separated by silica-gel (CH_2Cl_2/MeOH, 50:1-0:1) as eluent, and then a ODS column chromatography eluted with MeOH/H_2O (50:50-80:20) to give three fractions (B3a-B3c). Fr.B3a was separated by preparative HPLC using MeOH/H_2O (65:35) to give **1** (7.0 mg), **2** (6.6 mg), **6** (8.8 mg), **8** (12.1 mg), **9** (11.0 mg) and **10** (7.4 mg). Fr.B3b (5.0 g) was separated by silica-gel (200-300 mesh) using CH_2Cl_2/MeOH (30:1-0:1), and by preparative HPLC (C_2H_3N/H_2O, 55:45) to obtain **11** (7.8 mg), 1**2** (10.6 mg) , **14** (9.4 mg), **15** (10.4 mg) and **16** (8.4 mg).

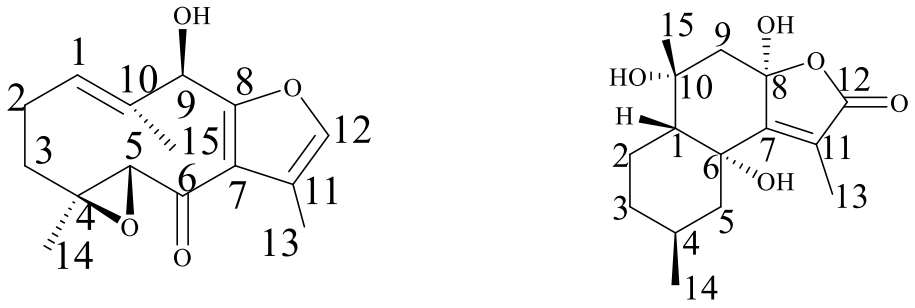


Figure 1. Structure of compounds **1** and **2** isolated from *C. henryi*

*Chloratene F (**1**)*: Colorless granular crystal (MeOH); $[\alpha]_D^{24}$ = – 8.32 (*c* = 0.46, MeOH), HR-ESI-MS *m/z* 285.1099 $[M+Na]^+$ (calcd for $C_{15}H_{18}O_4Na$, 285.1084); X-ray crystallography data: $C_{15}H_{18}O_4$, *M* = 261.28 g/mol, orthorhombic, $P2_1$, a = 7.9436(3) Å, b = 12.2385(3) Å, c = 13.8003(4) Å, V = 1341.63(7) Å3, Z = 4, T = 293.0 K, Dcalc = 1.294 g/cm^3, 2351 reflections independent, R_1 = 0.0376 and wR_2 = 0.0993. Flack parameter = 0.04 (14). (deposition number : CCDC 2053107); ^{1}H NMR (600 MHz, $CDCl_3$) and ^{13}C NMR (150 MHz, $CDCl_3$) data, see Table 1.

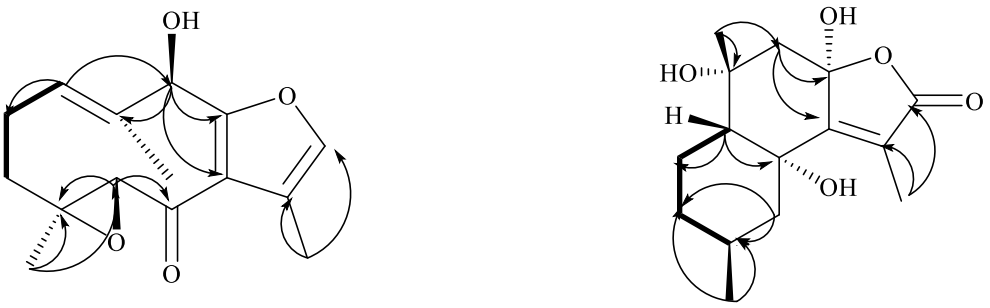
*Chlomultin G (**2**)*: Colorless granular crystal (MeOH); $[\alpha]_D^{24}$ = – 7.51 (*c* = 0.37, MeOH); HR-ESI-MS *m/z* 281.1394 $[M-H]^-$ (calcd for $C_{15}H_{21}O_5$, 281.1390); X-ray crystallography data: for $C_{15}H_{22}O_5$, *M* = 279.30 g/mol, orthorhombic, $P2_1$, a = 8.10670(10) Å, b = 10.69920(10) Å, c = 16.1887 (2) Å, V = 1404.13(3) Å3, Z = 4, T = 293 (2) K, Dcalc = 1.321 g/cm^3, 2559 reflections independent, R_1 = 0.0326 and wR_2 = 0.0892. Flack parameter = 0.10 (8). (deposition number : CCDC 2059824); ^{1}H NMR (600 MHz, $CDCl_3$) and ^{13}C NMR (150 MHz, $CDCl_3$) data, see Table 1.

Table 1. The NMR datas for **1** and **2** in $CDCl_3$ (δ in ppm, *J* in Hz)

NO.	1		2	
	δ_H, mult. (*J* in Hz)	**δ_C**	**δ_H, mult. (*J* in Hz)**	**δ_C**
1	6.04 (1H, m)	126.2	1.38 (1H, dd, *J* = 12.3, 3.7 Hz)	52.5
2a	2.59 (1H, m)	23.9	1.77 (1H, m)	22.1
2b	2.30 (1H, m)		1.90 (1H, m)	
3a	2.32 (1H, m)	38.1	1.01 (1H, m)	35.4
3b	1.33 (1H, m)		1.79 (1H, m)	
4	-	64.2	1.96 (1H, m)	28.0
5a	3.93 (1H, d, *J* = 1.0 Hz)	66.4	2.18 (1H, m)	46.5
5b			1.50 (1H, m)	
6	-	192.6	-	75.0
7	-	123.7	-	160.5
8	-	157.0	-	105.8
9a	5.30 (1H, s)	71.2	1.77 (1H, m)	51.3
9b			2.49 (1H, m)	
10	-	131.9	-	73.0
11	-	121.9	-	122.5
12	7.19 (1H, t, *J* = 1.2 Hz)	139.4	-	174.5
13	2.12 (1H, d, *J* = 1.3 Hz)	10.3	2.05 (3H, s)	10.3
14	1.55 (3H, s)	15.3	0.96 (3H, d, *J* = 6.7 Hz)	22.6
15	1.35 (3H, s)	15.2	1.98 (3H, s)	28.4

Compound **1** was isolated as colorless granular crystal, The molecular formula was determined as $C_{15}H_{18}O_4$ by the HR-ESI-MS (*m/z* 285.1099 $[M+Na]^+$, calcd. 285.1084) with seven degrees of unsaturation. The ^{1}H-NMR spectrum showed three methyl groups at δ_H 2.12 (3H, d, *J* = 1.3 Hz, H-13), 1.55 (3H, s, H-14) and 1.35 (3H, s, H-15), two olefinicprotons at δ_H 6.04 (1H, m, H-1) and 7.19 (1H, t, *J* = 1.2 Hz, H-12), two methylene at δ_H 2.59 (1H, m, H-2a), 2.30 (1H, m, H-2b) and 2.32 (1H, m, H-3a), 1.33 (1H, m, H-3b). The combination of ^{13}C-NMR and HSQC data indicated 15 carbon resonances, including three methyl δ_C 10.3 (C-13), 15.3 (C-14), and 15.2 (C-15), two methylene δ_C 23.9 (C-2), 38.1 (C-3), one oxygen-substituted δ_C 71.2 (C-9), two dioxycarbons δ_C 64.2 (C-4), 66.4 (C-5). This deduction was supported by the HMBC correlations from Me-13 to C-11 and 12, and from H-12 to C-7, 8, 11 and 13 indicated **1** contains one methyl located in C-11. Respectively, other correlations from Me-15 to C-3, 4 and 5, Me-14 to C-1, 10 and 9 , H-9 to C-1 , 7 and 10, H-1 to C-2 , 9, 15 and 10, H-5 to C-4 and 6 observed in HMBC, together with the six indices of hydrogen deficiency, structurally similar with zederone [11] , however, the chemical shift of δ_C 71.2 for C-9 in **1** was different from its shift of δ_C 71.2 in zederone. Analysis of the indices of hydrogen deficiency and the chemical shifts indicated that C-9 carried a hydroxy substituent in **1**. The planar structure of **1** was thus identified as a germacrane sesquiterpenoid. Meanwhile, according to the X-ray crystallography (Figure 3) of the compound **1**. Thus, the absolute configuration of the compound is determined as (4*S*, 5*R*, 9*R*).

Compound **2** was isolated as colorless granular crystal. The molecular formula was determined as $C_{15}H_{22}O_5$ by the HR-ESI-MS (*m/z* 281.1394 $[M-H]^-$, calcd. 281.1390) with five degrees of unsaturation. The ^{1}H-NMR spectrum exhibited three methyl groups δ_H 2.05 (3H, s, H-13), 0.96 (3H, d, *J* = 6.7 Hz, H-14) and 1.98 (3H, s, H-15), two methine δ_H 1.38 (1H, dd, *J* = 12.3, 3.7 Hz, H-1) and 1.96 (1H, m, H-4). The ^{13}C NMR spectrum of **2** showed signals of three methyl, four methylene, two methine, and six quaternary carbons include three -OH signals at δ_C (75.0 , 105.8 , 73.0). In HMBC spectrum, cross-peaks from H-5 to C-3, 4 and 6, from H-9 to C-7, 8 and 10, Me-14 to C-3, 4 and 5, and from Me-15 to C-9 and 10, and Me-13 to C-11 and 12. The three -OH groups were connected to C-6, C-8, and C-10 by the HMBC cross-peaks from H-9 to C-8 and 10, and from H-1 and H-5 to C-6. Meanwhile, the absolute configuration of the compound **2** was determined to be (1*S*, 4*S*, 6*R*, 8*R*, 10*R*) by the X-ray crystallography (Figure 3).



H^1-H^1 COSY: — HMBC (H → C): ⌒

Figure 2. Key H^1-H^1 COSY and HMBC correlations of compounds **1** and **2** Q2

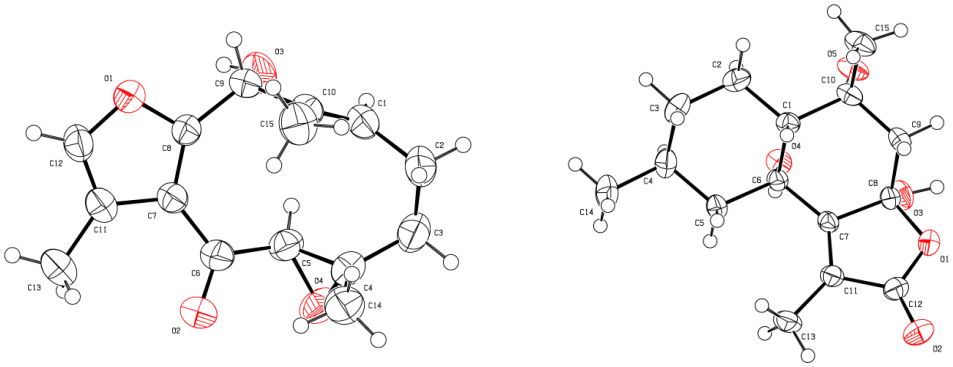


Figure 3. ORTEP drawing of compounds **1** and **2**

The fourteen known sesquiterpenes were identified as chlorajapolide I (**3**) [12], chloraniolide A (**4**) [13], 8*β*-Hydroxy-isogermafurenolide (**5**) [14], neolitacumone C (**6**) [15], 4(*R*),15-epoxy-atractylenolide II (**7**) [16], japonicone A (**8**) [17], spicachlorantin C (**9**) [18], shizukaol F (**10**) [19], 7'-hydroxyisoasperphenamate (**11**) [20], 2*α*,3*β*-dihydroxy-urs-12-en- 28-oic acid (**12**) [21], euscaphic acid (**13**) [22], hemisesmin-1 (**14**) [23], mycophenolic methyl ester (**15**) [24], 4-hydroxy-2,3-dimethyl-2-nonen-4-olide (**16**) [25] by comparing their NMR and MS date with those reported in the literature. All of them were found in this plant for the first time.

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Supporting Information

Supporting Information accompanies this paper on http://www.acgpubs.org/journal/records-of-natural-products

ORCID
Yuting Bian:0000-0002-8500-0418
Fangyou Chen:0000-0002-4650-3987
Weiming Huang:0000-0003-2707-7246
Zhichao Chen:0000-0002-4779-6240
Pengcheng Shuang:0000-0002-4612-9913
Yongming Luo:0000-0001-9688-9956

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