ORIGINAL ARTICLE

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Rec. Nat. Prod. 11:2 (2017) 166-170

records of natural products

A New Phenolic Compound Isolated from *Semen Celosia cristata* L.

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(Received May 31, 2016; Revised November 7, 2016; Accepted November 8, 2016)

Abstract: A new phenolic compound, named 3-geranyl-2,5-dihydroxy-benzaldehyde (**1**), together with seven known chalone derivatives (**2**–**8**) has been isolated from the seeds of *Celosia cristata* L. Their chemical structures have been elucidated by spectroscopic analysis. All these compounds (**1**–**8**) were isolated from *C. cristata* for the first time.

Keywords: *Celosia cristata* L.; phenolic compound; chalone derivatives.

1. Introduction

The plant genus *Celosia* consisting of about 60 species in *Amaranthaceae* family, is native in subtropical and temperature zones of Africa, South America and South East Asia. *Celosia cristata* L. is a traditional medicinal herb used for the treatment of fatigue, atherosclerosis, leucorrhoea and osteoporosis [1]. Semen *C. cristata* is the seeds of *C. cristata*, commonly known as "Ji Guan Hua Zi" in Chinese, and has been utilized as a folk medicine for removing liver-heat, improving eyesight and clearing wind-heat. Phytochemical investigations of *C. cristata* have led to the isolation of several kinds of chemical constituents such as flavonoids, phenolic glycosides and saponins [2-4]. As part of our systematic phytochemical study on the genus *Celosia* of China plants, we have investigated the chemical constituents of Semen *C. cristata.*

A new phenolic compound, together with seven known chalcone derivatives, was obtained from the EtOAc and *n*-butanol extracts. In this work, we report the process of isolation and elucidation of one new compound (**1**) and seven known chalone derivatives (**2**–**8**).

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The article was published by Academy of Chemistry of Globe Publications
www.acgpubs.org/RNP © Published 12/24/2016 EISSN:1307-6167

2. Materials and Methods

2.1 General

1D and 2D NMR spectra (^{1}H-NMR, ^{13}C-NMR, DEPT, HMBC, HMQC and ^{1}H-^{1}H COSY) were obtained on a Bruker DRX-500 (^{1}H: 500 MHz and ^{13}C 125 MHz; Karlsrhe, Germany). Chemical shifts were given as δ values related to TMS as internal standard. Mass spectra were measured on a ThermoFinnigan MS spectrometer (Thermo-Finngan, Austin, TX USA). HPLC spectra were recorded on Agilent 1100 series (Santa Clara, CA, USA). Silica gel (200–300 mesh) for column chromatography, and GF 254 for TLC was obtained from Qingdao Haiyang Chemical Co. Ltd. (Qingdao, China).

2.2 Plant material

The seeds of *C. cristata* L. were purchased from Chengdu city, Sichuan Province, China, in September 2012, and identified by Prof. Mei-Li Guo from the Second Military Medical University School of Pharmacy (Shanghai, China). A voucher specimen (20120912A) was originally deposited in the State Key Laboratory of New Drugs, Shanghai Institute of Pharmaceutical Industry (Shanghai, China).

2.3 Extraction and isolation

The air-dried seeds of *C. cristata* (5 kg) were extracted with ethanol (60% v/v) twice, 3 h for each time. The ethanol extract was concentrated under reduced pressure to yield a crude residue, which was then suspended in 4 liters of water and partitioned sequentially with ethyl acetate (EtOAc) and *n*-BuOH to give three portions. The EtOAc extract (71.5 g) was subjected to silica gel column chromatography (300–400 mesh) eluting with stepwise gradient of petroleum ether/EtOAc to afford five fractions (Fr.1 to Fr.5). Fr.3 (2.9 g) was subjected to silica gel column eluting with CH_2Cl_2/MeOH (25:1 to 10:1) to give three sub-fractions (Fr.3.3.1 to Fr.3.3.3). The sub-fraction Fr.3.3.1 was purified by Sephadex LH-20 eluting with MeOH to yield compounds **1** (5.5 mg) , **2** (3.8 mg) and **3** (4.5 mg). Fr.4 (3.0 g) was subjected to silica gel column eluting with $CHCl_2$/MeOH (20:1 to 5:1) to obtain two sub-fractions (Fr.4.1 and Fr.4.2). Compounds **4** (5.5 mg) and **5** (5.0 mg) were isolated after eluting the Fr.4.1 with MeOH using Sephadex LH-20 column.

The *n*-BuOH extract (40.0 g) was decolorized on a MCI gel (CHP 20P) column chromatography eluted with MeOH/H_2O (0:100 to 100:0), yielding seven sub-fractions (Fr. A–Fr. G). The sub-fraction (Fr. D, 3.5 g) was subjected to reversed phase silica gel column employing MeCN/H_2O (23:77), yielding three portions (Fr. D1–Fr. D3). Further purification of Fr. D3 by Sephadex LH-20 (MeOH) gave birth to compound **6** (6.0 mg). The sub-fraction (Fr. E, 5.0 g) was chromatographed over reversed phase silica gel column. Successful elution of the column with MeOH/H_2O (32: 68) yielded three portions (Fr. E1–Fr. E3) after removing the solvent. Fr. E1 was further separated by Sephadex LH-20 column chromatography eluting with MeOH to give compounds **7** (18.0 mg) and **8** (20.0 mg).

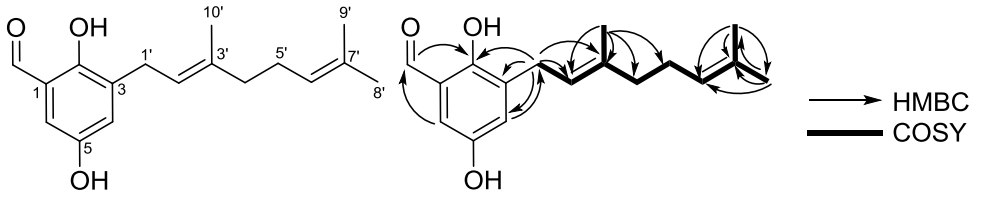

Figure 1. Chemical structure and key ^{1}H-^{1}H COSY and HMBC correlations of compound **1**

3. Results and Discussion

Compound **1** was obtained as yellow amorphous powder, UV (MeOH): λ_{max} (log ε), 228 (4.97), 265 (4.55), 365 (4.26), whose molecular formula was determined as $C_{17}H_{22}O_3$ by HR-ESI-MS (*m/z*, 275.1496 $[M+H]^+$; calc. 275.1647), and its value of unsaturation was 7 (Figure 1). The IR spectrum displayed absorptions for hydroxyl (3350 cm^{-1}), double bonds (1630 cm^{-1}) and aldehyde group (2700 and 1700 cm^{-1}). The ^{1}H NMR spectrum exhibited three methyl signals at δ ppm 1.69 (3H, s), 1.68 (3H, s) and 1.60 (3H, s), and also showed three methylene proton signals at δ 3.35 (2H, t, J = 7.5 Hz), 2.12 (2H, t, J = 7.2 Hz) and 2.07 (2H, t, J = 6.7 Hz). Two aromatic proton signals at δ 6.96 (1H, s) and 6.83 (1H, s) suggested the presence of a 1,2,3,5-substituted benzene ring. Two olefinic proton signals at δ 5.30 (1H, t, J = 7.3 Hz) and 5.10 (1H, t, J = 7.2 Hz) were observed in ^{1}H NMR spectrum. The appearance of a methine proton signal at δ 9.80 (1H, s) indicated the presence of an aldehyde group. The ^{13}C NMR and DEPT spectrum of compound **1** displayed 17 distinct signals, including three methyls, three methylenes, five methines and six quaternary carbons. With the aid of HMQC, HMBC and ^{1}H-^{1}H COSY experiments, all the ^{1}H and ^{13}C NMR were assigned as shown in Table 1. The 1D NMR spectroscopic data of compound **1** showed a quite similar pattern with those of 3-farnesyl-2,5-dihydroxy-benzaldehyde [5]. The difference between them was lack of an isoprene group. In the HMBC spectrum of compound **1**, cross-peaks of δ_H 6.83 (H-6) with δ_C 196.1 (C-7) and δ_H 9.80 (H-7) with δ_C 154.1 (C-2) suggested that the aldehyde group is directly connected to C-1. In the ^{1}H-^{1}H COSY spectrum, cross signals between δ_H 3.35 (H-1') and δ_H 5.30 (H-2'), δ_H 2.12 (H-5') with δ_H 2.07 (H-4') and δ_H 5.10 (H-6'), along with the long correlations of δ_H 2.07 (H-4') to δ_H 1.69 (H-10') and δ_H 5.10 (H-6') to δ_H 1.60 (H-8') and δ_H 1.68 (H-9') indicated the presence of $–CH_2CH=C(CH_3)-(CH_2)_2CHC(CH_3)_2$. From HMBC spectral data, the correlations between δ_H 3.35 (H-1') and δ_C 125.2 (C-2'), 125.2 (C-4), 132.2 (C-3), 137.7 (C-3'), 154.1 (C-2) indicated that the $–CH_2CH=C(CH_3)-(CH_2)_2CHC(CH_3)_2$ group was located at C-3,which was also supported by the HMBC correlations of δ_H 6.96 (H-4) to δ_C 27.0 (C-1'). On the basis of the above evidence, compound **1** was identified as 3-geranyl-2,5-dihydroxy-benzaldehyde.

Seven known compounds were identified by comparing their spectral data with those reported in the previous literature as follows, cardamonin (**2**) [6], 2-hydroxy-4,6-dimethoxylchalcone (**3**) [7], 2',4'-dihydroxy-3',6'-dimethoxychalone (**4**) [8], 3-hydroxy-phloridzin (**5**) [9], sieboldin (**6**) [10], 3-hydroxyphloretin 4'-O-[4'',6''-O-(s)-HHDP]-ß-D-glucoside (**7**) [11] and 3-hydroxyphloretin 4'-O-[3''-O-galloyl-4'',6''-O-(s)-HHDP]-ß-D-glucoside (**8**) [11] (Figure 2).

Table 1. ^{1}H NMR (500 MHz) and ^{13}C NMR (125 MHz) spectral data of compound **1** in $CDCl_3$ (δ in ppm and J in Hz)

Position	δ_H	δ_C
1		119.7 (s)
2		154.1 (s)
3		132.1 (t)
4	6.96 (1H, s)	125.2 (d)
5		148.1 (s)
6	6.83 (1H, s)	115.2 (d)
7	9.80 (1H, s)	196.1 (d)
1'	3.35 (2H, t, J = 7.5 Hz)	27.0 (t)
2'	5.30 (1H, t, J = 7.3 Hz)	120.8 (d)
3'		137.7 (s)
4'	2.07 (2H, q, J = 6.7 Hz)	39.7 (t)
5'	2.12(2H, q, J = 7.2 Hz)	26.6 (t)
6'	5.10 (2H, t, J = 7.2 Hz)	124.2 (d)
7'		131.6 (s)
8'	1.60 (3H, s)	25.7 (q)
9'	1.68 (3H, s)	17.7 (q)
10'	1.69 (3H, s)	16.1 (q)

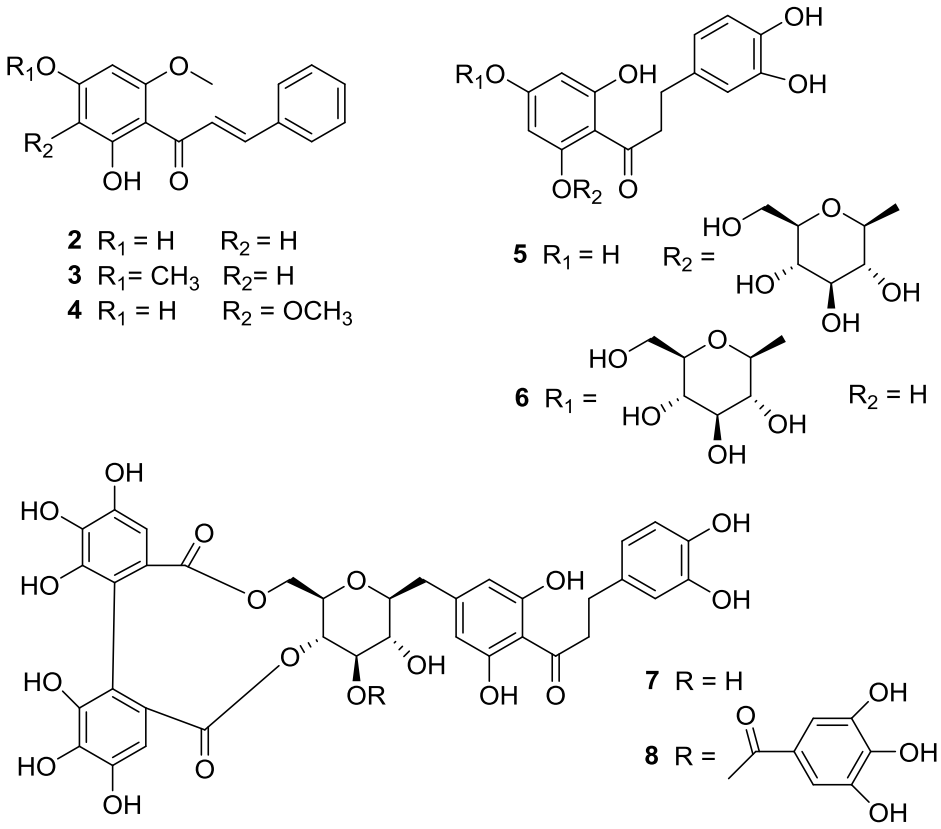

Figure 2. Structures of compounds **2**–**8**

Acknowledgments

This work is funded by Research Project of Shanghai Municipal Commission of Health and Family Planning (No. 201540027), and partly supported by Shanghai Fengxian District Science and Technology Project (20141001), Shanghai Fengxian District Science and Technology Project (20151205) and Shanghai No.6 People's Medical Group Project.

Supporting Information

Supporting Information accompanies this paper on http://www.acgpubs.org/RNP

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