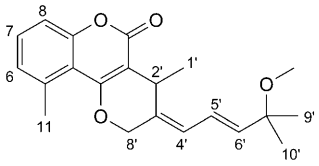
A New Monoterpene–Coumarin and a New Monoterpene–Chromone from *Gerbera delavayi*

by **Shuang-Zhu Liu**, **Jia-Quan Feng**, **Jian Wu**, and **Wei-Min Zhao***

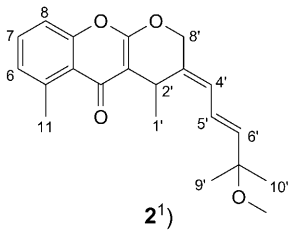
Shanghai Institute of Materia Medica, Shanghai Institutes for Biological Sciences, Chinese Academy of Sciences, Shanghai 201203, P. R. China
(phone/fax: +86-21-50806052; e-mail: wmzhao@mail.shcnc.ac.cn)

Phytochemical investigation of the whole plants of *Gerbera delavayi* (Compositae) led to the isolation and identification of 15 compounds, including the new monoterpene–coumarin **1** and the new monoterpene–chromone **2**. Their structures were determined on the basis of spectroscopic analyses including 1D- and 2D-NMR experiments and comparison with spectroscopic data of the literature.

Introduction. – The genus *Gerbera* (Compositae) consists of *ca*. 80 species all over the world, mainly distributed in Africa and Asia. There are 20 *Gerbera* species found in China, and several of them have long been used in folk medicines as detoxifying and diuretic agents, and for relieving cough, inner heats, and prostatitis [1][2]. Previous chemical studies on the genus *Gerbera* led to the isolation of acetylenes, *para*-hydroxyacetophenone derivatives [3–5], coumarins [3–11], sesquiterpenoids [5], triterpenoids [5], and cyanogenic glycosides [6][11]. As part of our ongoing search for bioactive compounds from Chinese herb medicines, *G. delavayi* was investigated and two new compounds, named gerdelavin A[1]) (**1**) and B[1]) (**2**), together with 13 known compounds, were isolated. Herein we report the isolation and structure elucidation of these compounds.



1[1])



2[1])

Results and Discussion. – The EtOH extract of the whole plants (3.5 kg) of *G. delavayi* was partitioned with petroleum ether, AcOEt, and BuOH. Each fraction was then subjected to a series of chromatographic steps to afford 15 compounds, including the new monoterpene–coumarin **1** and the new monoterpene–chromone **2**.

[1]) Trivial atom numbering; for systematic names, see *Exper. Part.*

Gerdelavin A (**1**) was obtained as yellow oil with the molecular formula $C_{21}H_{24}O_4$ as deduced from HR-ESI-MS and NMR analysis. The methyl signal at δ(H) 2.67 (Me(11)) and three aromatic-proton signals at δ(H) 7.01 (*d*, $J = 8.1$ Hz, H–C(6)), 7.33 (*t*, $J = 8.1$ Hz, H–C(7)), and 7.15 (*d*, $J = 8.1$ Hz, H–C(8)) in the ^{1}H-NMR spectrum (*Table*), together with the signals at δ(C) 162.7 (*s*), 104.6 (*s*), 162.4 (*s*), 136.7 (*s*), 127.4 (*d*), 130.8 (*d*), 114.9 (*d*), 153.4 (*s*), 114.4 (*s*), and 23.5 (*q*) in the ^{13}C-NMR spectrum (*Table*) suggested the structural similarity of **1** to the nassauvirevolutins A–C, 4-hydroxy-5-methylcoumarin derivatives [12]. The UV-absorption peaks at 231, 279, and 290 nm and IR-absorption bands at 1713, 1614, and 1566 cm^{-1} further confirmed the coumarin (=2*H*-1-benzopyran-2-one) skeleton of the structure of **1** [12][13]. In the ^{13}C-NMR spectrum, except for the ten signals belonging to the 5-methylcoumarin skeleton and a MeO signal at δ(C) 50.5 (*q*), ten other signals were also observed. Analyses of the ^{1}H,^{1}H-COSY (*Fig.*) and HSQC plots revealed the fragments Me(1′)–CH(2′), and CH(4′)–CH(5′)–C(6′). Analysis of ^{13}C,^{1}H long-range correlation signals in the HMBC spectrum led to the establishment of the planar structure of **1** as shown in the *Figure*. The NOE correlations H–C(4′)/CH$_2$(8′), H–C(4′)/H–C(6′), and H–C(5′)/H–C(2′) indicated the (*E*) configuration of the olefinic bonds at C(3′) and C(5′). To the best of our knowledge, gerdelavin A (**1**) is a new monoterpene–coumarin.

Gerdelavin B (**2**) possessed the same molecular formula $C_{21}H_{24}O_4$ as compound **1** according to HR-ESI-MS and NMR analyses. The ^{13}C-NMR spectrum of **2** (*Table*) was

Table. *^{1}H- and ^{13}C-NMR Data* ($CDCl_3$) *of* **1** *and* **2**[1]). δ in ppm, J in Hz.

	1		**2**	
	δ(H)	δ(C)	δ(H)	δ(C)
C(2)		162.7 (*s*)		162.3 (*s*)
C(3)		104.6 (*s*)		100.4 (*s*)
C(4)		162.4 (*s*)		179.8 (*s*)
C(5)		136.7 (*s*)		132.5 (*s*)
H–C(6)	7.01 (*d*, $J = 8.1$)	127.4 (*d*)	7.08 (*d*, $J = 7.8$)	127.8 (*d*)
H–C(7)	7.33 (*t*, $J = 8.1$)	130.8 (*d*)	7.37 (*t*, $J = 7.8$)	131.7 (*d*)
H–C(8)	7.15 (*d*, $J = 8.1$)	114.9 (*d*)	7.18 (*d*, $J = 7.8$)	115.2 (*d*)
C(9)		153.4 (*s*)		154.4 (*s*)
C(10)		114.4 (*s*)		120.7 (*s*)
Me(11)	2.67 (*s*)	23.5 (*q*)	2.86 (*s*)	22.6 (*q*)
CH$_3$(1′)	1.44 (*d*, $J = 7.2$)	20.9 (*q*)	1.40 (*d*, $J = 7.2$)	20.7 (*q*)
H–C(2′)	3.91 (*q*, $J = 7.2$)	28.5 (*d*)	4.06 (*q*, $J = 7.2$)	26.8 (*d*)
C(3′)		132.2 (*s*)		131.7 (*s*)
H–C(4′)	6.14 (*d*, $J = 11.2$)	126.6 (*d*)	6.12 (*d*, $J = 10.8$)	127.2 (*d*)
H–C(5′)	6.44 (*dd*, $J = 11.2, 15.3$)	123.6 (*d*)	6.42 (*dd*, $J = 10.8, 14.7$)	123.7 (*d*)
H–C(6′)	5.82 (*d*, $J = 15.3$)	142.6 (*d*)	5.82 (*d*, $J = 14.7$)	142.7 (*d*)
C(7′)		75.0 (*s*)		74.9 (*s*)
CH$_2$(8′)	4.67 (*d*, $J = 12.0$, H$_a$), 4.84 (*d*, $J = 12.0$, H$_b$)	69.0 (*t*)	4.62 (*d*, $J = 11.7$, H$_a$), 5.00 (*d*, $J = 11.7$, H$_b$)	70.9 (*t*)
Me(9′)	1.30 (*s*)	25.5 (*q*)	1.30 (*s*)	25.5 (*q*)
Me(10′)	1.30 (*s*)	25.8 (*q*)	1.30 (*s*)	25.7 (*q*)
MeO	3.16 (*s*)	50.5 (*q*)	3.15 (*s*)	50.5 (*q*)

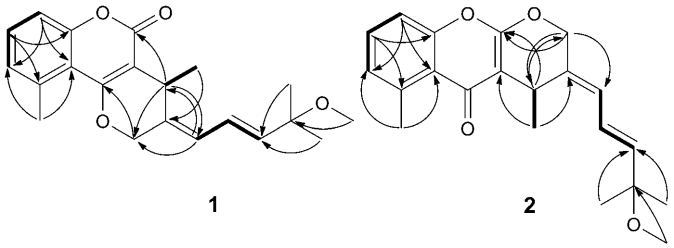


Figure. *$^1H,^1H$-COSY* (—) *and key HMBC* (H → C) *correlations of* **1** *and* **2**

similar to that of **1**, except that a carbonyl signal was observed at δ(C) 179.8 compared to δ(C) 162.7 in **1**. Its IR spectrum displayed absorption bands at 1622, 1568, 1416, 1259, and 1165 cm^{-1}. A chromone (=4*H*-1-benzopyran-4-one) skeleton possessing a conjugated ketone carbonyl group was proposed for the structure of **2** [14]. Analyses of its 2D-NMR spectra revealed the linkage of a monoterpene moiety identical to that of **1** to the chromone skeleton. The NOE correlations H–C(4′)/CH_2(8′), H–C(4′)/H–C(6′), and H–C(5′)/H–C(2′) indicated that the two olefinic bonds at C(3′) and C(5′) were both in (*E*) configuration. Gerdelavin B (**2**) was, therefore, identified as a new monoterpene–chromone.

Thirteen known compounds were also isolated and characterized by comparison with literature data as 3-geranyl-4-hydroxy-5-(hydroxylmethyl)coumarin [4], cyclobrachycoumarin [13], norbrachycoumarin [13], brachycoumarin [13], cycloisobrachycoumarin [13], 2′-epicycloisobrachycoumarin [13], brachychromone [13], xanthotoxin [14], cyclobrachycoumarin 3′-epimer [15], 4-(geranyloxy)-5-methylcoumarin [16], 4-(β-D-glucopyranosyloxy)-5-methylcoumarin [17], cnidioside B [18], and cnidioside B methyl ester [19].

The work was financially supported by the *National Science & Technology Major Project* 'Key New Drug Creation and Manufacturing Program', China (No. 2009ZX09301-001). The authors wish to thank Prof. *Hua Peng* of the Kunming Institute of Botany, Chinese Academy of Sciences, for identification of the plant material.

Experimental Part

General. Column chromatography (CC): *MCI* gel *CHP-20P* (75–150 μm; *Mitsubishi Chemical Industry Co., Ltd.*), silica gel *H60* (300–400 mesh), and *Sephadex LH-20* (*Pharmcia Biotech AB*, Uppsala, Sweden) as packing materials. Anal. TLC: *$HSGF_{254}$* silica gel plates (*Yantai Chemical Industrial Institute*, Yantai, China). Prep. HPLC: *Varian-SD-1* instrument with a *Merck-NW25-C_{18}* column (10 μm; 20 × 250 mm), and *Unimicro-Technologies* instrument with a *Waters-X-Bridge-C_{18}* column (5 μm; 19 × 100 mm). Optical rotations: *Perkin-Elmer-241MC* polarimeter. UV Spectra: *Beckman-DU-7* spectrometer; λ_{max} in nm. IR Spectra: *Perkin-Elmer-577* spectrometer; $\tilde{\nu}$ in cm^{-1}. NMR Spectra: *Bruker-AM-400* instrument; chemical shifts δ in ppm rel. to $SiMe_4$ as internal standard, *J* in Hz. MS: *Finnigan-LCQ-DECA* instrument (ESI) and *Mariner* spectrometer (HR-ESI-MS); in *m*/*z*.

Plant Material. The whole plants of *Gerbera delavayi* were collected from Guangxi Province, China, in October, 2008, and identified by Professor *Hua Peng* of the Kunming Institute of Botany, Chinese Academy of Sciences. A voucher specimen (No. SIMM20081008) was deposited with the Herbarium of the Shanghai Institute of Materia Medica, Chinese Academy of Sciences.

Extraction and Isolation. Powdered air-dried whole plants of *G. delavayi* (3.5 kg) were percolated at r.t. with 95% EtOH (3 × 10 l). After evaporation of EtOH *in vacuo*, the aq. residue (1.5 l) was extracted successively with petroleum ether, AcOEt, and BuOH (3 × 1.5 l each) yielding petroleum ether (30.0 g), AcOEt (45 g), and BuOH extracts (46 g), resp. The AcOEt extract was subjected to CC (silica gel, petroleum ether/acetone 20 : 1, 10 : 1, 5 : 1, 2 : 1, and 0 : 1, each 2 l): *Fractions B1 – B3*. *Fr. B1* was subjected to CC (*RP-18* silica gel, H_2O, 20%, 40%, 60%, 80%, 90%, and 100% MeOH): *Frs. B1.1 – B1.5*. *Fr. B1.3* was further purified by repeated CC (silica gel, *RP-18*) and prep. HPLC: **1** (7.2 mg) and **2** (10.5 mg).

Gerdelavin A (=*(3*E*)-3,4-Dihydro-3-[(2*E*)-4-methoxy-4-methylpent-2-en-1-ylidene]-4,10-dimethyl-2*H*,5*H*-pyrano[3,2-*c*][1]benzopyran-5-one*; **1**): Yellow oil. $[\alpha]_D^{22} = +5$ ($c = 0.06$, MeOH). UV (MeOH): 231, 279, 290. IR (film) 1713, 1614, 1566, 1464, 1346, 1171. ^{1}H- and ^{13}C-NMR: *Table*. ESI-MS (pos.): 363.1 ($[M+Na]^+$). HR-ESI-MS: 363.1571 ($[M+Na]^+$, $C_{21}H_{24}NaO_4^+$; calc. 363.1572).

Gerdelavin B (=*(3*E*)-3,4-Dihydro-3-[(2*E*)-4-methoxy-4-methylpent-2-en-1-ylidene]-4,6-dimethyl-2*H*,5*H*-pyrano[2,3-*b*][1]benzopyran-5-one*; **2**): Colorless oil. $[\alpha]_D^{22} = +26$ ($c = 0.11$, MeOH). UV (MeOH): 230, 274, 295. IR (film): 1622, 1568, 1416, 1259, 1165. ^{1}H- and ^{13}C-NMR: *Table*. ESI-MS (pos.): 363.2 ($[M+Na]^+$). HR-ESI-MS: 363.1562 ($[M+Na]^+$, $C_{21}H_{24}NaO_4^+$; calc. 363.1572).

REFERENCES

[1] Editorial Committee of Flora of China, 'Flora of China', 1st edn., Science Press, Beijing, 1996, Vol. 79, p. 73.
[2] Jiangsu College of New Medicine, 'Dictionary of Traditional Chinese Medicines', Shanghai Science and Technology Press, Shanghai, 1977, p. 446.
[3] F. Bohlmann, C. Zdero, H. Franke, *Chem. Ber.* **1973**, *10*, 382.
[4] F. Bohlmann, M. Grenz, *Chem. Ber.* **1975**, *108*, 26.
[5] Y.-J. Chen, Y. Li, J.-J. Chen, K. Gao, *Helv. Chim. Acta* **2007**, *90*, 176.
[6] S. Naguoma, K. Imamura, T. Inoue, M. Nagai, *Chem. Pharm. Bull.* **1985**, *33*, 4803.
[7] S. Naguoma, T. Toyonaga, T. Inoue, M. Nagai, *Chem. Pharm. Bull.* **1989**, *37*, 2621.
[8] Y. Xiao, Y. Ding, J.-B. Li, Y. Lu, T. Nohara, *Chem. Pharm. Bull.* **2004**, *52*, 1362.
[9] B. Wenkert, T. D. J. Hall, *J. Indian Chem. Soc.* **1985**, *62*, 916.
[10] A. Bhattacharya, S. K. Chakraborty, N. Adityachaudhury, *J. Indian Chem. Soc.* **2005**, *82*, 748.
[11] A. F. Halim, E. M. Marwan, F. Bohlmann, *Phytochemistry* **1980**, *19*, 2946.
[12] M. Bittner, J. Jakupovic, F. Bohlmann, *Phytochemistry* **1988**, *27*, 3845.
[13] C. Zdero, F. Bohlmann, R. M. King, H. Robinson, *Phytochemistry* **1986**, *25*, 509.
[14] M. H. A. Elgamal, N. H. Elewa, E. A. M Elkhrisy, H. Duddeck, *Phytochemistry* **1979**, *18*, 139.
[15] F. Bohlmann, A. Steinmeyer, *Tetrahedron Lett.* **1986**, *27*, 5359.
[16] C. Zdero, F. Bohlmann, J. Solomon, *Phytochemistry* **1988**, *27*, 891.
[17] Z. F. Mahmoud, T. M. Sarg, M. A. Amer, S. M. Khafagy, F. Bohlmann, *Phytochemistry* **1980**, *19*, 2029.
[18] S. Yahara, C. Sugimura, T. Nohara, Y. Niiho, Y. Nakajima, H. Ito, *Shoyakugaku Zasshi* **1993**, *47*, 74.
[19] M. Hani, A. Elgamal, M. M. S Nagwa, D. Helmut, *Nat. Prod. Lett.* **1993**, *3*, 209.

Received January 15, 2010