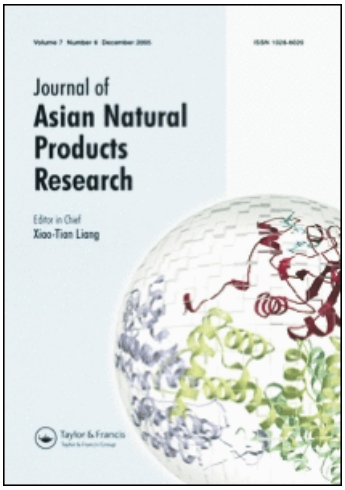

Journal of Asian Natural Products Research
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713454007

Two novel phloroglucinol derivatives from *Euphorbia ebracteolata* hayata

Guang-Miao Fu[a]; Bo-Yang Yu[a]; Dan-Ni Zhu[a]
[a] School of Chinese Pharmacy, China Pharmaceutical University, Nanjing, China

To cite this Article Fu, Guang-Miao , Yu, Bo-Yang and Zhu, Dan-Ni(2006) 'Two novel phloroglucinol derivatives from *Euphorbia ebracteolata* hayata', Journal of Asian Natural Products Research, 8: 1, 149 — 153
To link to this Article: DOI: 10.1080/1028602042000325663
URL: http://dx.doi.org/10.1080/1028602042000325663

Journal of Asian Natural Products Research,
Vol. 8, No. 1–2, January–March 2006, 149–153

Taylor & Francis
Taylor & Francis Group

Two novel phloroglucinol derivatives from *Euphorbia ebracteolata* hayata

GUANG-MIAO FU, BO-YANG YU* and DAN-NI ZHU

School of Chinese Pharmacy, China Pharmaceutical University, Nanjing 210009, China

(Received 13 May 2004; revised 17 June 2004; in final form 20 July 2004)

Two new phloroglucinol derivatives, named ebracteolatain A and ebracteolatain B, along with three known phloroglucinol derivatives were isolated from *Euphorbia ebracteolata* Hayata., and their structures were elucidated as 3,3′-diacetyl-2,4′-dimethoxy-2′,4,6,6′-tetrahydroxy-5′-methyl diphenylmethane (**1**) and 1-[3,5-bis-(3-acetyl-2,6-dihydroxy-4-methoxy-benzyl)-2,4,6-trihydroxy-phenyl]-ethanone (**2**) on the basis of spectroscopic techniques and chemical methods.

Keywords: *Euphorbia ebracteolata* Hayata; Euphorbi aceae; Phloroglucinol derivatives; Ebracteolatain A; Ebracteolatain B

1. Introduction

Euphorbia ebracteolata Hayata. (Euphorbiaceae) is a perennial herbaceous plant, sporadical distributed in China, Korea and Japan. It has been used as an antitumor drug in traditional chinese medicine for more than two thousand years. The roots of the plant, named "LangDu" and classified as a 'toxic drug' in traditional Chinese medicine for its high potency and relatively violent pharmacological effects, are used with great care for the treatment of edema, indigestion, cough, asthma and chronic bronchitis [1]. Earlier investigations on the constituents of this plant resulted in the isolation of steroids [2], diterpenes [3,4], triterpenes [5], flavonol glycosides [6], tannins [7] and phloroglucinol derivatives [8,9]. Further study on constituents of *Euphorbia ebracteolata* is reported in this paper. Two new phloroglucinol derivatives, named ebracteolatain A (**1**) and ebracteolatain B (**2**), along with three known phloroglucinol derivatives were isolated from the roots of the plant. Structures of the five compounds were elucidated as 3,3′-diacetyl-2,4′-dimethoxy-2′,4,6,6′- tetrahydroxy-5′-methyl diphenylmethane (**1**), 1-[3,5-bis-(3-acetyl-2,6-dihydroxy-4-methoxy-benzyl)-2,4,6-trihydroxy-phenyl]-ethanone (**2**), 3,3′-diacetyl-4,4′-dimethoxy-2,2′,6,6′-tetrahydroxy diphenylmethane (**3**) [10], 2,4-dihydroxy-6-methoxy-3-methyl-acetophenone [9], and 2,4-dihydroxy-3-formyl-6-methoxy acetophenone [11] (figure 1). This paper deals with the

*Corresponding author. E-mail: boyangyu@cpu.edu.cn

Journal of Asian Natural Products Research
ISSN 1028-6020 print/ISSN 1477-2213 online © 2006 Taylor & Francis
http://www.tandf.co.uk/journals
DOI: 10.1080/1028602042000325663

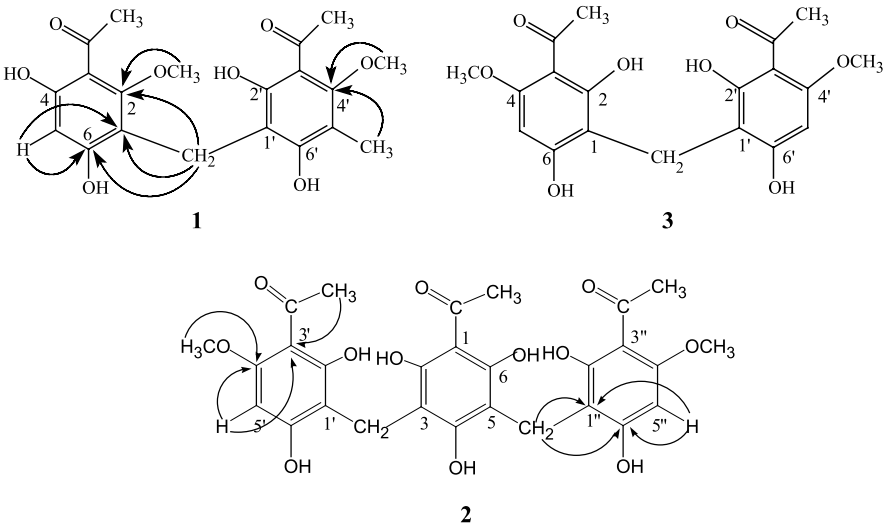

Figure 1. Structures of compounds **1**–**3** and selected HMBC correlations of **1**, **2**.

structural elucidation of the new compounds on the basis of spectroscopic analysis, including 2D NMR spectroscopic data and MS data. Compound **2** was isolated as a trimer phloroglucinol derivative from *Euphorbia ebracteolata* Hayata for the first time.

2. Results and discussion

Ebracteolatain A (**1**) was obtained as light yellow needles. The molecular formula, $C_{20}H_{22}O_8$, consistent with ten degrees of unsaturation, was determined by HRFABMS, which gave a molecular ion peak at *m/z* 413.1222 $[M + Na]^+$. ^{1}H NMR spectrum of **1** showed seven singlets for the two acetyls at δ 2.63 (3H) and 2.69 (3H), two methoxyls at δ 3.99 (3H) and 3.96 (3H), a methylene proton at δ 3.74 (2H), a aromatic proton at δ 6.02 (1H), a methyl proton at δ 2.06 (3H) as well as four phenolic hydroxyls at δ 16.15(1H), 13.21(1H), 9.17(1H), 8.84(1H), respectively. The ^{13}C NMR spectrum indicated the presence of only one nonsubstituted and eleven substituted aromatic carbons, along with two groups of acetyl carbons, three methyl carbons and one methylene carbon. The ^{13}C NMR spectrum was similar to that of **4** [2], except for another phloroglucinol unit, indicating that the structure of **1** was composed of two phloroglucinol units. Detailed assignment of the protons and carbons was accomplished by means of the HMQC, HMBC experiments (figure 1). On the basis of above evidence, the structure of **1** was established as 3,3′-diacetyl-2,4′-dimethoxy-2′,4,6,6′-tetrahydroxy-5′-methyl diphenyl-methane.

Ebracteolatain B (**2**) was obtained as light yellow needles. The molecular formula, $C_{28}H_{28}O_{12}$, consistent with fifteen degrees of unsaturation, was determined by HRFABMS, which gave a molecular ion peak at *m/z* 579.1479 $[M + Na]^+$. ^{1}H NMR spectrum of **2** showed nine singlets for the three acetyls at δ 2.55 (3H) and 2.33 (6H), two methoxyls δ 3.35 (6H), two methylene protons at δ 4.10 (4H) and two aromatic protons at δ 5.90(2H). The ^{13}C NMR spectrum was very similar to that of **1**. From ^{1}H NMR, ^{13}C NMR and MS spectral data, we concluded the structure of **2** was composed of three phloroglucinol units, which indicated **2** has a symmetrical structure. Detailed assignment of the protons and carbons was

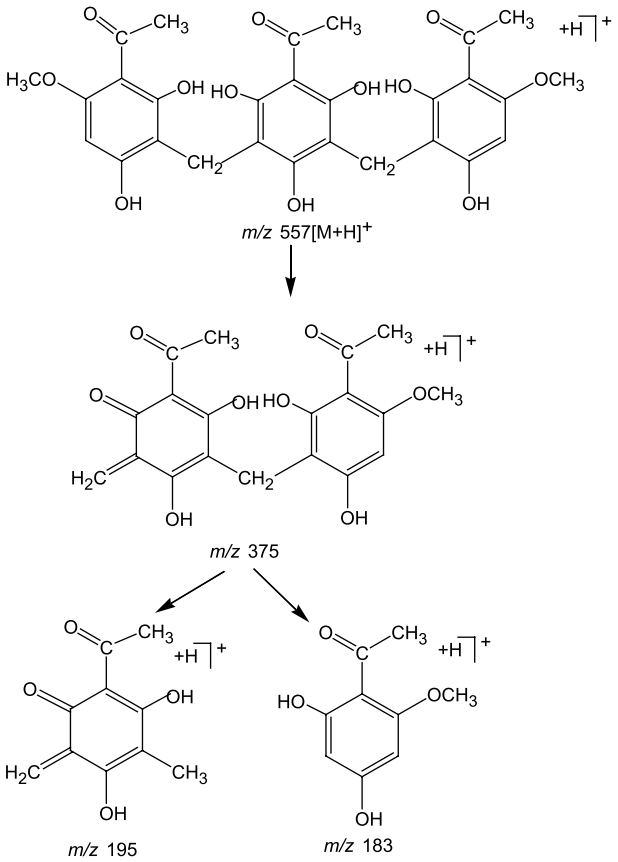

Figure 2. Significant ESI mass fragmentations patterns of compound **2**.

accomplished by means of the HMQC, HMBC experiments (figure 1). From mass fragmentation analysis the above conclusions were further confirmed (figure 2). On the basis of above evidence, the structure of **2** was established as 1-[3,5-bis-(3-acetyl-2,6-dihydroxy-4-methoxy-benzyl)-2,4,6-trihydroxy-phenyl]-ethanone.

3. Experimental

3.1 General experimental procedures

Melting points were obtained on an X4 micro-melting point apparatus and are uncorrected. IR spectra were recorded on a Nicolet Impact-410 spectrometer; UV spectra were recorded on a Varian cary 300 Bio spectrophotometer; Optical rotations were measured at 25°C on a JASCO DIP-370 polarimeter in $CHCl_3$ or C_5H_5N. ^1H NMR and ^{13}C NMR spectra were measured with a Bruker DRX-400 (400 MHz for ^1H and 100 MHz for ^{13}C) spectrometer. Chemical shifts (δ) are in ppm relative to TMS as internal standard, and coupling constants (*J*) are in Hz. The ESIMS were obtained on a HP5989A mass spectrometer in the position ion mode. HRFABMS were obtained on a MAT-90 instrument (Finnigan-MAT, Bermen, Germang) equipped with Microvip date system. Commercial Si gel plates (Qing Dao Hai Yang Chemical Group Co.) were used for TLC.

3.2 Plant material

Dried roots of *Euphorbia ebracteolata* were purchased from Beijing Chinese Medicinal Herbs Corporation in October 2000 and identified by Dr. Bo-yang YU. A voucher specimen (Herbarium No. 20004003) of the plant is deposited at the herbarium of China Pharmaceutical University, Nanjing, Jiangsu, China.

3.3 Extraction and isolation

The air-dried roots (4.75 Kg) of *Euphorbia ebracteolata* were ground and refluxed three times with 95% EtOH (40 L). The 95% EtOH solution was combined and evaporated *in vacuo* to yield 320 g of residue. The residue was suspended in water and extracted successively with petroleum, $CHCl_3$ and n-BuOH. Parts of the $CHCl_3$ extract (86 g) were chromatographed on silica gel, eluting with $CHCl_3$–MeOH in a gradient manner, by which five fractions (I–V) were obtained. Fraction II (8.6 g) was subjected to Sephadex LH-20 column chromatography eluted with $CHCl_3$–MeOH (1:1) to yield compound **1** (56 mg) and compound **3** (286 mg). Fraction III (12.6 g) was subjected to silica gel column chromatography to yield compound **4** (96 mg) and compound **5** (38 mg). Fraction IV (4.2 g) was resubmitted to silica gel column chromatography to yield compound **2** (18 mg).

3.3.1 Ebracteolatain A. 3,3′-diacetyl-2,4′-dimethoxy-2′,4,6,6′-tetrahydroxy-5′-methyl diphenylmethane (**1**), light yellow needles, $C_{20}H_{22}O_8$; mp 191–192°C; $[\alpha]_D^{20}$ + 1.2 (c 0.50 $CHCl_3$); UV (MeOH)λ_{max} (log ϵ) 297 (0.15) nm; IR (KBr) ν_{max} cm^{-1}: 3251, 1630, 1609, 1596, 1471, 1437, 1364, 1200, 1146, 1114, 673, 609; ESI-MS: *m/z* 391 $[M + H]^+$, 389 $[M - H]^-$; HRFABMS *m/z*: 413.1222 $[M + Na]^+$ (calcd for $C_{20}H_{22}O_8Na$, 413.1212); ^1H and ^{13}C NMR($CDCL_3$, 400/100 MHz) spectral data are shown in table 1.

Table 1. NMR spectral data for compound **1** (in $CDCL_3$) and **2** (in pyridine-d_5)

Compound 1				*Compound 2*			
Position	*^{13}C NMR*	*^1H NMR*	*DEPT*	*Position*	*^{13}C NMR*	*^1H NMR*	*DEPT*
1	105.7		C	1	103.7		C
2	156.2		C	2	161.0		C
3	105.6		C	3	108.1		C
4	163.0		C	4	170.1		C
5	92.8	6.02, 1H,s	CH	5	108.1		C
6	163.5		C	6	161.0		C
2-OMe	56.1	3.99, 3H, s	CH_3	1-Ac	32.8	2.55, 3H, s	CH_3
3-Ac	33.0	2.63, 3H, s	CH_3	1-Ac	201.8		C
3-Ac	204.3		C	1′, 1″	109.1		C
1′	111.3		C	2′, 2″	165.0		C
2′	162.9		C	3′, 3″	105.1		C
3′	108.1		C	4′ 4″	162.0		C
4′	163.1		C	5′, 5″	93.1	5.90, 2H, s	CH
5′	111.2		C	6′, 6″	166.9		C
6′	161.0		C	4′, 4″-OMe	55.2	3.35, 6H, s	CH_3
3′-Ac	31.0	2.69, 3H, s	CH_3	3′, 3″-Ac	32.4	2.33, 6H, s	CH_3
3′-Ac	202.7		C	3′, 3″-Ac	204.4		C
4′-OMe	65.1	3.96, 3H, s	CH_3	Ar-CH2-Ar	17.8	4.10, 4H, s	CH_2
5′- CH_3	8.5	2.06, 3H, s	CH_3				
Ar–CH2–Ar	16.7	3.74, 2H, s	CH_2				

3.3.2 Ebracteolatain B. 1-[3,5-bis-(3-acetyl-2,6-dihydroxy-4-methoxy-benzyl)-2,4,6-trihydroxy-phenyl]−ethanone (**2**), light yellow needles, $C_{28}H_{28}O_{12}$; mp 274−276°C; $[\alpha]_D^{20}$ + 8.9 (c 0.60 C_5H_5N); UV (MeOH) λ_{max} (log ϵ) 298 (0.99) nm; IR (KBr) ν_{max} cm^{-1}; 3400, 3251, 1629, 1610, 1595, 1473, 1438, 1365, 1201, 1157, 1114; ESI-MS: *m/z* 557 $[M + H]^+$, 556 $[M - H]^-$, 375 $[557-C_9H_{10}O_4]^+$, 357 $[375 - H_2O]^+$ (**5**), 195 $[375 - C_9H_{10}O_4]^+$(95)和 183 $[375 - C_{10}H_9O_4]^+$ (100); HRFABMS *m/z*: 579.1479 $[M + Na]^+$ (calcd for $C_{28}H_{28}O_{12}Na$, 579.1478); ^1H and ^{13}C NMR(pyridine-d_5, 400/100 MHz) spectral data are shown in table 1.

Acknowledgements

We are grateful to Dr. Qiu Shengxiang, Professor of Washington University for the measurement of part of NMR spectrum, and the members of MS measurement center of the school of China Matreia Madica, China Pharmaceutical University, Nanjing, China. This work was supported by both a grant from the State Ministry of Education (No. 02118), and a grant for outstanding scholar from Jangsu Province Government, awarded to Dr Bo-yang YU.

References

[1] Jiangsu College of New Medicine, *Dictionary of Chinese Materia Madica,* Vol. 2, pp. 1898−1900, Shanghai Science and Technology Press, Shanghai (1986).
[2] H.Q. Zhang, Y.M. Ding, G.M. Chen, Y.F. Dong, Y.L. Zhu. *Acta Bot. Sin.*, **29**, 429−431 (1987).
[3] Z.H. Xu, J. Sun, R.S. Xu, G.W. Qin. *Phytochemistry*, **49**, 149−151 (1998).
[4] Z.H. Xu, G.W. Qin, R.S. Xu. *J. Asian Nat. Prod. Res.*, **2**, 257−261 (2000).
[5] X.F. Sun, S.P. Wang, Z.R. Zheng. *China J. Chin. Mater. Med.*, **24**, 226−227 (1999).
[6] Byung Tae Ahn, Kap Jin Oh, Jai Seup Ro, Kyong Soon Lee. *Planta Med.*, **62**, 383−384 (1996).
[7] B.T. Ahn, S.C. Lee, W.Y. Park, S.H. Lee, J.S. Ro, K.S. Lee, E.G. Ryu. *Kor. J. Phamacogn.*, **23**, 211−217 (1992).
[8] Y.F. Dong, Y.M. Ding. *J. Plant Res. Environ.*, **1**, 1−3 (1992).
[9] H.Q. Zhang, Y.M. Ding. *J. Plant Res. Environ.*, **1**, 6−9 (1992).
[10] W.X. Wang, X.B. Ding. *Acta Pharm. Sin.*, **34**, 514−517 (1999).
[11] Y.L. Ding, Z.J. Jia. *Photychemistry*, **31**, 1435−1436 (1992).