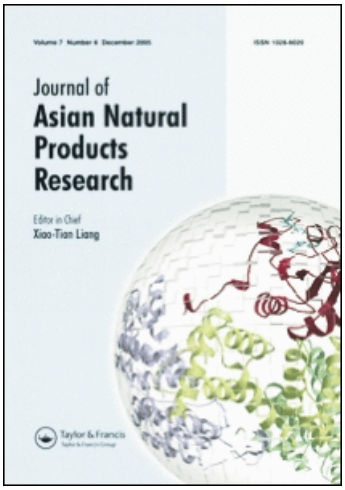

Journal of Asian Natural Products Research
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713454007

Two new anthraquinone glycosides from the roots of *Rheum palmatum*

Cun Zhang[a]; Li Li[a]; Yong-Qing Xiao[a]; Guo-Fang Tian[a]; Dong-Dong Chen[a]; Yun Wang[a]; Yu-Tian Li[a]; Wen-Qian Huang[a]
[a] Institute of Chinese Materia Medica, China Academy of Chinese Medical Sciences, Beijing, China

Online publication date: 01 December 2010

To cite this Article Zhang, Cun , Li, Li , Xiao, Yong-Qing , Tian, Guo-Fang , Chen, Dong-Dong , Wang, Yun , Li, Yu-Tian and Huang, Wen-Qian(2010) 'Two new anthraquinone glycosides from the roots of *Rheum palmatum*', Journal of Asian Natural Products Research, 12: 12, 1026 — 1032
To link to this Article: DOI: 10.1080/10286020.2010.529612
URL: http://dx.doi.org/10.1080/10286020.2010.529612

Journal of Asian Natural Products Research
Vol. 12, No. 12, December 2010, 1026–1032

Taylor & Francis
Taylor & Francis Group

Two new anthraquinone glycosides from the roots of *Rheum palmatum*

Cun Zhang, Li Li, Yong-Qing Xiao*, Guo-Fang Tian, Dong-Dong Chen, Yun Wang, Yu-Tian Li and Wen-Qian Huang

Institute of Chinese Materia Medica, China Academy of Chinese Medical Sciences, Beijing 100700, China

(*Received 28 June 2010; final version received 3 October 2010*)

Two new anthraquinone glycosides, named 1-methyl-8-hydroxyl-9,10-anthraquinone-3-*O*-β-D-(6′-*O*-cinnamoyl)glucopyranoside (**1**) and rhein-8-*O*-β-D-[6′-*O*-(3″-methoxyl malonyl)]glucopyranoside (**2**), have been isolated from the roots of *Rheum palmatum*, together with seven known compounds, rhein-8-*O*-β-D-glucopyranoside (**3**), physcion-8-*O*-β-D-glucopyranoside (**4**), chrysophanol-8-*O*-β-D-glucopyranoside (**5**), aleo-emodin-8-*O*-β-D-glucopyranoside (**6**), emodin-8-*O*-β-D-glucopyranoside (**7**), aleo-emodin-ω-*O*-β-D-glucopyranoside (**8**), and emodin-1-*O*-β-D-glucopyranoside (**9**). Their structures were elucidated on the basis of chemical and spectral analysis.

Keywords: *Rheum palmatum*; anthraquinone glycoside; 1-methyl-8-hydroxyl-9,10-anthraquinone-3-*O*-β-D-(6′-*O*-cinnamoyl)glucopyranoside; rhein-8-*O*-β-D-(6′-*O*-methoxyl malonyl)glucopyranoside

1. Introduction

Radix et Rhizoma Rhei (Dahuang in Chinese), the dried rhizomes and roots of *Rheum palmatum* L., *R. tanguticum* Maxim. ex Balf., and *R. officinale* Baill. in Pharmacopoeia of the People's Republic of China, is one of the most important and frequently used herbal drugs in traditional Chinese medicine for purging fire, dispelling heat, detoxification, removing blood stasis, and so on. For their various pharmacological effects such as antibacterial, antitumor, improving renal disorders, and promoting blood circulation [1–6], a lot of bioactive components including anthraquinones, phenylbutanones, stilbenes, tannins, and chromones have been isolated and identified from this plant. As a continual investigation of the chemical constituents of *R. palmatum*, two new compounds named 1-methyl-8-hydroxyl-9,10-anthraquinone-3-*O*-β-D-(6′-*O*-cinnamoyl)glucopyranoside (**1**) and rhein-8-*O*-β-D-[6′-*O*-(3″-methoxyl malonyl)]glucopyranoside (**2**), along with the seven known anthraquinone glycosides: rhein-8-*O*-β-D-glucopyranoside (**3**), physcion-8-*O*-β-D-glucopyranoside (**4**), chrysophanol-8-*O*-β-D-glucopyranoside (**5**), aleo-emodin-8-*O*-β-D-glucopyranoside (**6**), emodin-8-*O*-β-D-glucopyranoside (**7**), aleo-emodin-ω-*O*-β-D-glucopyranoside (**8**), and emodin-1-*O*-β-D-glucopyranoside (**9**) were isolated. Among them, the isolation and structural elucidation of compounds **1** and **2** are briefly described in this paper.

2. Results and discussion

Compound **1** was obtained as a pale yellow powder (MeOH). It was positive to the Borntrager reaction, revealing that it was a hydroxyl anthraquinone compound. The UV spectrum gave the absorption maxima

*Corresponding author. Email: x.heqi@163.com

ISSN 1028-6020 print/ISSN 1477-2213 online

DOI: 10.1080/10286020.2010.529612
http://www.informaworld.com

at 218, 269, and 411 nm. Its molecular formula was established as $C_{31}H_{26}O_{12}$ by positive HR-ESI-MS at *m/z* 608.1760 $[M + NH_4]^+$ and negative ESI-MS at *m/z* 589 $[M - H]^-$ experiments.

The ^{1}H NMR spectrum of **1** showed the presence of one hydroxyl proton at δ_H 12.65 (1H, s), a three-proton singlet at δ_H 2.68 (3H, s), nine aromatic protons ascribed to one singlet aromatic proton at δ_H 7.88 (1H, s), three *ortho*-coupled protons at δ_H 7.36 (1H, d, $J = 8.0$ Hz), 7.73 (1H, t, $J = 8.0$ Hz), 7.58 (1H, m), and five correlated protons at δ_H 7.58 (2H, m), 7.28 (2H, t, $J = 7.6$ Hz), and 7.35 (1H, m), two *trans* olefinic protons at δ_H 7.57 (1H, d, $J = 16.0$ Hz) and 6.70 (1H, d, $J = 16.0$ Hz), as well as one sugar moiety at δ_H 3.18–5.41 including one anomeric proton signal at δ_H 5.26 (1H, d, $J = 4.8$ Hz). These functional groups were also identified by ^{13}C NMR and HSQC spectra which revealed the presence of 31 carbon signals, including two typical carbonyl signals of anthraquinone (δ_C 189.5, 181.6), one methyl (δ_C 19.7), one carboxyl carbon (δ_C 167.4), a cinnamoyl moiety containing two olefinic carbons (δ_C 144.5, 117.9), six aromatic carbons (δ_C 134.0, 128.2, 128.8, 130.4, 128.8, 128.2), and one carbonyl carbon (δ_C 166.2). Besides this, the other 12 aromatic carbons and one β-D-glucose moiety at δ_C 100.3, 73.1, 76.4, 70.0, 74.4, 63.9 were also observed. According to the above spectroscopic and chemical information, compound **1** was deduced to be an anthraquinone glucoside with a cinnamoyl group.

The ^{1}H and ^{13}C NMR signals of **1** were assigned by HSQC, HMBC, and NOESY experiments. From the HMBC spectrum, the signals at δ_H 7.88, 7.58 simultaneously had correlations with the carbon at δ_C 181.6 indicating that they were located at H-4 and H-5, respectively. So, the other two *ortho*-coupled protons at δ_H 7.73, 7.36 were assigned to H-6 and H-7, respectively. The hydroxyl group at δ_H 12.65 (1H, s) was attributed to C-8 due to its HMBC correlations with C-8 and C-7. Several other long-distance correlations also confirmed their linkage positions (Figure 1).

In another aromatic ring, the key HMBC correlations from H-4 at δ_H 7.88 and 1-CH_3 at δ_H 2.68 to C-2 at δ_C 125.4 confirmed that the methyl group was attached to C-1. Meanwhile, the NOESY correlation between H-4 and H-1′ at δ_H 5.26 was observed, proving the linkage of sugar unit at C-3. In addition, the signals at δ_H 4.54 (1H, br d, $J = 11.2$ Hz, H-6′), 4.13 (1H, dd, $J = 11.2$, 8.8 Hz, H-6′) showed cross-peaks with C-1″ at δ_C 166.2,

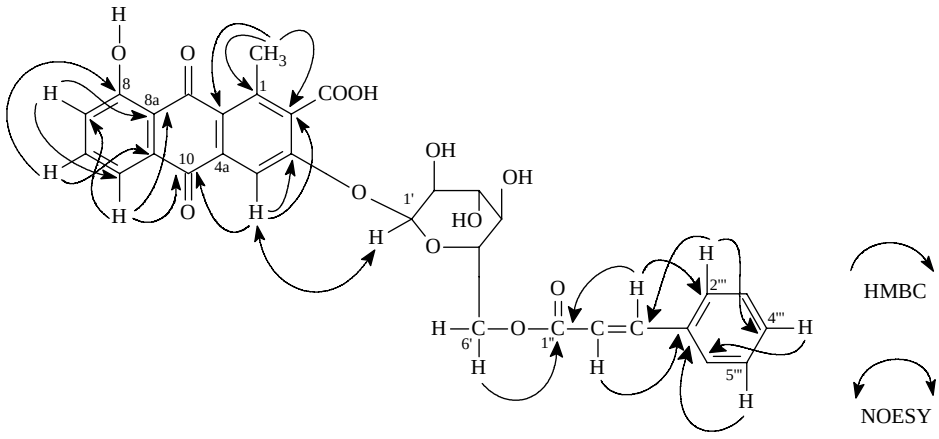

Figure 1. Key HMBC and NOESY correlations of compound **1**.

confirming that the cinnamoyl group was connected to C-6′. The HMBC correlations between H-3″ (δ_H 7.57) and C-1″, H-2″ (δ_H 6.70), H-3‴, 5‴ (δ_H 7.58) and C-1‴ (δ_C 134.0), H-4‴ (δ_H 7.35) and C-2‴, C-6‴ (δ_C 128.2) further confirmed the cinnamoyl existence.

Apart from the above description, only one carboxyl carbon signal (δ_C 167.4) remained and it was linked to C-2 by carefully analyzing the ^{1}H, ^{13}C NMR, HMQC, HMBC, ESI-MS spectra, and all the NMR signals were assigned as shown in Table 1.

On the basis of these data, the structure of **1** was unambiguously elucidated as 1-methyl-8-hydroxyl-9,10-anthraquinone-3-*O*-β-D-(6′-*O*-cinnamoyl)glucopyranoside.

Compound **2** was isolated as a pale yellow powder (MeOH), which also gave the characteristic hydroxyl anthraquinone color reaction and turned red with 5% NaOH solution (Borntrager reaction). The UV spectrum exhibited the absorption maxima at 410, 260, and 230 nm. Its molecular formula was deduced to be $C_{25}H_{22}O_{14}$ by positive HR-ESI-MS at *m/z* 1110.2325 $[2M + NH_4]^+$ and negative ESI-MS at *m/z* 545 $[M - H]^-$ and 1091 $[2M - H]^-$.

The ^{1}H NMR spectrum of **2** showed the presence of one carboxyl proton peak at δ_H 13.76 (1H, s), one hydroxyl group at δ_H 12.72 (1H, s), five aromatic protons ascribed to a pair of *meta*-coupled protons at δ_H 8.11 (1H, d, $J = 2.0$ Hz), 7.75 (1H, d, $J = 2.0$ Hz), and three *ortho*-coupled protons at δ_H 7.90 (1H, d, $J = 7.6$ Hz), 7.88 (1H, t, $J = 7.6$ Hz), 7.68 (1H, dd, $J = 7.6$, 2.5 Hz), one methoxyl at δ_H 3.61 (3H, s), one methylene at δ_H 3.51 (2H, d, $J = 4.0$ Hz), and one sugar moiety at δ_H 3.20–5.36 including one anomeric proton at δ_H 5.22 (1H, d, $J = 7.6$ Hz). The ^{13}C NMR spectrum of **2** displayed the presence of 25 carbon signals, including two typical carbonyl signals of anthraquinone at δ_C 187.4, 181.6, and three other carbonyl carbons at δ_C 166.9, 166.4, 165.6, one methylene (δ_C 40.9), one methoxyl (δ_C 52.1), and 12 aromatic carbons except for one monosaccharide unit. All the above data indicated that compound **2** was an anthraquinone glucoside.

A detailed comparison of ^{1}H and ^{13}C NMR spectral data of **2** with those of **3** [7] implied that they had the similar signals except that **2** had four additional carbon signals at δ_C 166.4, 166.9, 52.1, and 40.9. They were assigned as methoxyl malonyl group ($ROOC—CH_2—COOCH_3$) according to the HMBC correlations between 3″-OCH_3, H-2″ and C-3″ at δ_C 166.9, H-2″ and C-1″. The HMBC correlations from H-6′ to C-1″ confirmed that the methoxyl malonyl group was connected to C-6′ (Figure 2). All the NMR signals were assigned by carefully analyzing the ^{1}H, ^{13}C NMR, HMQC, and HMBC spectra as shown in Table 1. Therefore, the structure of **2** was determined as rhein-8-*O*-β-D-[6′-*O*-(3″-methoxyl malonyl)]glucopyranoside (Figure 2).

The other seven known compounds (**3**–**9**) were identified as rhein-8-*O*-β-D-glucopyranoside (**3**) [7], physcion-8-*O*-β-D-glucopyranoside (**4**) [8], chrysophanol-8-*O*-β-D-glucopyranoside (**5**) [9,10], aleoemodin-8-*O*-β-D-glucopyranoside (**6**) [8], emodin-8-*O*-β-D-glucopyranoside (**7**) [11], aleo-emodin-ω-*O*-β-D-glucopyranoside (**8**) [12], and emodin-1-*O*-β-D-glucopyranoside (**9**) [13], respectively, by comparison of their physical and spectroscopic data with those reported in the literature.

3. Experimental

3.1 General experimental procedures

Melting points were determined on an X-4 apparatus and are uncorrected. Optical rotations were measured on a PE Model 343. The IR spectra were recorded on a Nicolet 5700 spectrophotometer with Centaurus FT-IR Microscope. The UV spectra were recorded on a Shimadzu UV-1650PC spectrophotometer. The ^{1}H and

Table 1. The NMR spectroscopic data of compounds **1**–**3** (400 MHz, DMSO-d_6).

	1				**2**			**3**	
No.	δ_H (J in Hz)	HMBC	δ_C	No.	δ_H (J in Hz)	HMBC	δ_C	δ_H (J in Hz)	δ_C
1			139.4	1			161.1		161.1
2			125.4	2	7.75 (1H, d, $J = 2.0$)	C-4, 3-COOH	123.9	7.75 (1H, br s)	123.9
3			156.5	3			137.3		137.2
4	7.88 (1H, s)	C-2, C-3, C-10	111.1	4	8.11 (1H, d, $J = 2.0$)	C-2, 3-COOH, C-9a, C-10	118.1	8.11 (1H, br s)	118.0
5	7.58 (1H, m)	C-7, C-10, C-8a	118.5	5	7.90 (1H, d, $J = 7.6$)	C-7, C-10, C-8a	120.8	7.88 (1H, dd, $J = 7.2, 2.8$)	120.6
6	7.73 (1H, t, $J = 8.0$)	C-8, C-10a	136.3	6	7.88 (1H, t, $J = 7.6$)	C-8, C-10a	136.3	7.88 (1H, d, $J = 7.2$)	136.3
7	7.36 (1H, d, $J = 8.0$)	C-5, C-8a	124.5	7	7.68 (1H, dd, $J = 2.5, 7.6$)	C-5, C-8a	122.4	7.72 (1H, dd, $J = 7.2, 2.8$)	122.5
8			161.4	8			158.0		158.3
9			189.5	9			187.4		187.4
10			181.6	10			181.6		181.6
4a			136.0	4a			133.0		133.0
8a			116.9	8a			120.8		120.7
9a			134.0	9a			119.6		119.5
10a			132.4	10a			134.8		134.7
1-CH_3	2.68 (3H, s)	C-2, C-9a	19.7	1-OH	12.72 (1H, s)	C-1, C-2, C-9a		12.73 (1H, s)	
2-COOH			167.4	3-COOH	13.76 (1H, s)		165.6	13.76 (1H, s)	165.5
8-OH	12.65 (1H, s)	C-8							
1′	5.26 (1H, d, $J = 4.8$)		100.3	1′	5.22 (1H, d, $J = 7.6$)	C-8	100.1	5.18 (1H, d, $J = 7.6$)	100.4
2′			73.1	2′			73.2		73.3
3′			76.4	3′			76.2		77.3
4′			70.0	4′			69.5		69.5
5′			74.4	5′			73.8		76.5
6′	4.54 (1H, br d, $J = 11.2$), 4.13 (1H, dd, $J = 11.2, 8.8$)	C-1″	63.9	6′	4.40 (1H, br d, $J = 10.0$), 4.14 (1H, dd, $J = 10.0, 6.4$)	C-1″	64.2		60.6
1″-CO—			166.2	1″-CO—			166.4		

Table 1 – *continued*

	1				2		3	
No.	δ_H (*J* in Hz)	HMBC	δ_C	No.	δ_H (*J* in Hz)	HMBC	δ_C	δ_H (*J* in Hz)	δ_C
2″-CH=	6.70 (1H, d, *J* = 16.0)	C-1‴	117.9	2″-CH_2–	3.51 (2H, d, *J* = 4.0)	C-1″, C-3″	40.9		
3″-CH=	7.57 (1H, d, *J* = 16.0)	C-2‴, 1″-CO–	144.5	3″-CO–			166.9		
1‴			134.0	3″-OCH_3	3.61 (3H, s)	C-3″	52.1		
2‴, 6‴	7.58 (2H, m)	C-3″, C-4‴	128.2						
3‴, 5‴	7.28 (2H, t, *J* = 7.60)	C-1‴	128.8						
4‴	7.35 (1H, m)		130.4						

^{13}C NMR, along with the 2D NMR spectra were obtained on a Mercury-400 spectrometer in DMSO-d_6 with TMS as internal standard. ESI-MS data were recorded on a Q-Trap LC/MS/MS with turbo ion spray source. HR-MS data were recorded on a Bruker APEX IV FT-MS (7.0 T) spectrum. Separation and purification were performed by column chromatography on silica gel (100–200, 200–300 mesh, Qingdao Marine Chemical, Inc., Qingdao, China), Sephadex LH-20 (Fuji Silysia Chemical Ltd, Aichi, Japan), and polyamide (100–200 mesh, Taizhou Luqiao Sijia Biological and Chemical Plastics Factory, Taizhou, China). TLC was carried out with precoated silica gel 60 F254 plates (0.25 mm, Merck, Darmstadt, Germany) and polyamides thin-layer chromatography membrane (Taizhou Luqiao Sijia Biological and Chemical Plastics Factory). Detection of spots was done by UV light (254 and 365 nm).

3.2 Plant material

The roots of *R. palmatum* were collected from Yushu County, Qinghai Province, China, in November 2007, and were identified by Prof. Shilin Hu (Institute of Chinese Materia Medica, Chinese Academy of Chinese Medical Sciences, Beijing, China). The voucher specimens (No. DH-200711) have been deposited in our laboratory.

3.3 Extraction and isolation

The dried, powdered roots (10 kg) of *R. palmatum* were percolated with 70% EtOH. The extract was concentrated under reduced pressure to yield 1480 g of residue, which was chromatographed over a silica gel (100–200 mesh) column eluted with $CHCl_3$–MeOH (20:1, 10:1, 6:1, 3:1) to afford five fractions (A–E), respectively. Each fraction was combined on the basis of TLC.

The fraction A (110 g) was subjected to silica gel column eluted with petroleum

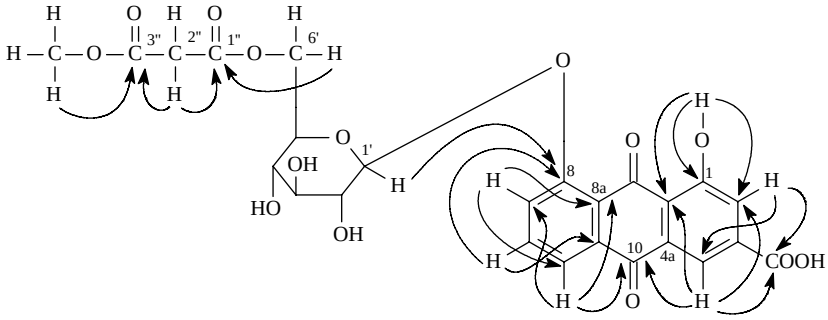

Figure 2. Key HMBC correlations of compound **2**.

ether–EtOAc (10:1–3:1) and 95% ethanol to yield six combined fractions (A1–A6). Fraction A2 (32 g) was repeatedly separated through silica gel column chromatography ($CHCl_3$–MeOH (20:1–1:1)) and then purified by polyamide column with EtOH–H_2O (0:1–1:0) to give compound **1** (10 mg). The fraction of 95% EtOH (A6, 35 g) was repeatedly isolated on silica gel chromatographic columns, eluting with $CHCl_3$–MeOH (20:1–1:1) to afford compound **7** (50 mg).

The fraction B (350 g) was chromatographed over a silica gel column eluted with $CHCl_3$–MeOH (20:1–3:1) to afford fractions B1–B5. Fraction B3 (135 g) was further subjected to silica gel columns eluted with $CHCl_3$–MeOH (10:1–3:1) and purified by Sephadex LH-20 to give **4** (200 mg) and **5** (160 mg). The separation of fraction B5 (95 g) was carried out on the silica gel columns eluted with $CHCl_3$–MeOH (10:1–3:1) to give compound **9** (30 mg).

The fraction C (240 g) was subjected to silica gel column eluted with $CHCl_3$–MeOH (10:1–1:1) to yield five combined fractions (C1–C5). Fraction C2 (26 g) was separated by silica gel column chromatography eluted with $CHCl_3$–MeOH (10:1) to afford compounds **2** (8 mg) and **8** (60 mg). Fraction C3 (85 g) was charged on the silica gel column eluted with $CHCl_3$–MeOH (10:1–1:1) and then purified by silica gel column with EtOAc–MeOH–H_2O (20:3:2) to give compound **3** (650 mg) and compound **6** (360 mg).

*3.3.1 1-Methyl-8-hydroxyl-9,10-anthraquinone-3-O-β-D-(6′-O-cinnamoyl)glucopyranoside (**1**)*

Pale yellow powder, mp 282–284°C, $[\alpha]_D^{20}$ + 2.5 (c = 0.084, MeOH), UV λ_{max} (MeOH) (nm): 218, 269, 411. IR ν_{max} (cm^{-1}): 3350, 2961, 1702, 1633, 1582, 1351, 1313, 1260, 1078, 801. ^1H and ^{13}C NMR spectral data are listed in Table 1. ESI-MS (negative): *m/z* 589 $[M - H]^-$. HR-ESI-MS (positive): *m/z* 608.1760 $[M + NH_4]^+$ (calcd for $C_{31}H_{30}NO_{12}$, 608.1763).

*3.3.2 Rhein-8-O-β-D-[6′-O-(3″-methoxyl malonyl)]glucopyranoside (**2**)*

Pale yellow powder, mp 247–249°C, $[\alpha]_D^{20}$ + 12.5 (c = 0.0112, MeOH), UV λ_{max} (MeOH) (nm): 230, 260, 410. IR ν_{max} (cm^{-1}): 3432, 3295, 1761, 1731, 1631, 1443, 1270, 1070, 1053, 750. ^1H and ^{13}C NMR spectral data are listed in Table 1. ESI-MS (negative): *m/z* 545 $[M - H]^-$, 1091 $[2M - H]^-$. HR-ESI-MS (positive): *m/z* 1110.2325 $[2M + NH_4]^+$ (calcd for $C_{50}H_{48}NO_{28}$, 1110.2357) (Figure 2).

Acknowledgement

This study was financially supported by the National Natural Science Foundation of China (No. 30730111).

References

[1] H. Oshio, Y. Naruse, and M. Tsukui, *Chem. Pharm. Bull.* **26**, 2458 (1978).
[2] T. Matumoto, H. Kiyohara, H. Yamada, K. Arakawa, J. Cyong, and Y. Otsuka, *J. Med. Pharm. Soc. Wakan-Yaku* **2**, 248 (1985).
[3] H. Ito, E. Kobayashi, Y. Takamatsu, S.H. Li, T. Hatano, H. Sakagami, K. Kusama, K. Satoh, D. Sugita, S. Shimura, Y. Itoh, and T. Yoshida, *Chem. Pharm. Bull.* **48**, 687 (2000).
[4] S. Shibutani, T. Nagasawa, T. Yokozawa, and H. Oura, *Jpn J. Pharmacol.* **100**, 434 (1980).
[5] S. Shibutani, T. Nagasawa, H. Oura, G. Nonaka, and I. Nishioka, *Chem. Pharm. Bull.* **31**, 2378 (1983).
[6] K. Komatsu, Y. Nagayama, K. Tanaka, Y. Ling, P. Basnet, and M.R. Meselhy, *Chem. Pharm. Bull.* **54**, 941 (2006).
[7] X.W. Yang, J. Zhao, Y. Zhang, J.X. Li, and C.M. Ma, *Chin. Tradit. Herb. Drugs* **29**, 289 (1998).
[8] J.L. Li, A.Q. Wang, J.S. Li, W.Y. He, and M. Kong, *Chin. Tradit. Herb. Drugs* **31**, 321 (2000).
[9] Y.H. Wei, X.A. Wu, C.Z. Zhang, and C. Li, *J. Chin. Med. Mater* **28**, 658 (2005).
[10] H. Kang, L. Xiang, G.Q. Fan, Q.S. Li, X.Z. Wang, Y.P. Duan, C. Qin, J.H. Zhen, and D.A. Guo, *Chin. Tradit. Herb. Drugs* **33**, 394 (2002).
[11] L. Xiang, J.H. Zheng, D.A. Guo, J.P. Kou, G.Q. Fan, Y.P. Duan, and C. Qin, *Chin. Tradit. Herb. Drugs* **32**, 395 (2001).
[12] Y.H. Wei, X.A. Wu, C.Z. Zhang, C. Li, and L. Song, *Chin. Pharm. J.* **41**, 253 (2006).
[13] J. Zhao, J.M. Chang, and N.S. Du, *Chin. J. Chin. Mater. Med.* **27**, 361 (2002).