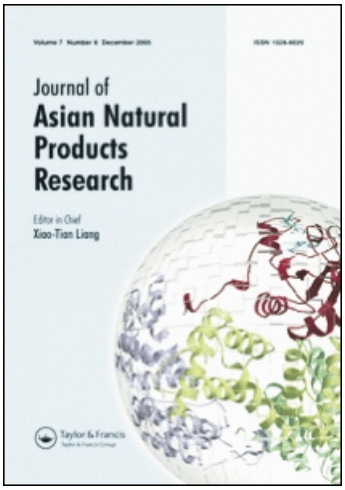

Journal of Asian Natural Products Research
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713454007

Three novel compounds from the leaves of *Smallanthus sonchifolius*

Ying-Kun Qiu[ab]; Ting-Guo Kang[a]; De-Qiang Dou[a]; Li Liang[a]; Feng Dong[c]
[a] School of Pharmacy, Liaoning University of Traditional Chinese Medicine, Dalian, China [b] Medical College, Xiamen University, Xiamen, China [c] Zhenao Group Co, Dalian, China

To cite this Article Qiu, Ying-Kun , Kang, Ting-Guo , Dou, De-Qiang , Liang, Li and Dong, Feng(2008) 'Three novel compounds from the leaves of *Smallanthus sonchifolius*', Journal of Asian Natural Products Research, 10: 12, 1109 — 1115
To link to this Article: DOI: 10.1080/10286020802361230
URL: http://dx.doi.org/10.1080/10286020802361230

Journal of Asian Natural Products Research
Vol. 10, No. 12, December 2008, 1109–1115

Taylor & Francis
Taylor & Francis Group

Three novel compounds from the leaves of *Smallanthus sonchifolius*

Ying-Kun Qiu[ab], Ting-Guo Kang[a], De-Qiang Dou[a]*, Li Liang[a] and Feng Dong[c]

[a]*School of Pharmacy, Liaoning University of Traditional Chinese Medicine, Dalian 116600, China;* [b]*Medical College, Xiamen University, Xiamen 361005, China;* [c]*Zhenao Group Co., Dalian 116600, China*

(*Received 12 December 2007; final version received 23 June 2008*)

Three novel compounds, together with five known ingredients, octacosanol, 3′,4′,5-trihydroxy-3,7-dimethoxyflavone, 3,4-dihydroxybenzaldehyde, isorhamnetin, and *ent*-kaurane-3β,16β,17-triol, were obtained from the leaves of *Smallanthus sonchifolius* (yacon), and their structures were elucidated as *ent*-kaurane-3β,16β,17,18-tertol (**1**), 3*R*,7*E*-9-butoxyl-megastigma-3-ol-3-*O*-β-D-glucopyranoside (**2**), and 3*S*,5*R*,6*Z*-megastigma-6-en-3,5,8,9-tertol (**3**) on the basis of spectroscopic and chemical methods.

Keywords: *Smallanthus sonchifolius*; yacon; *ent*-kaurane-3β,16β,17,18-tertol; 3*R*,7*E*; 7*E*-9-butoxyl-megastigma-3-ol-; 3-*O*-β-D-glucopyranoside; 3*S*,5*R*,6*Z*-megastigma-6-en-3,5,8,9-tertol

1. Introduction

Yacon [*Smallanthus sonchifolius* (Poepp. and Endl.) H. Robinson], which was originally cultivated in the Andean highlands, was introduced into China via Japan in the 1990s. It has been reported that the tubers of yacon contained a high content of oligofructans [1] and polyphenols [2], and its leaf extract showed potent antidiabetic effects [3]. Therefore, the yacon has recently become popular as a healthy functional food in Japan and other countries. Chemical investigations of yacon have revealed that its leaves contain monoterpenes, sesquiterpenes, and diterpenes, responsible for the pest-resistant and antimicrobial activities of this plant [4,5]. In addition, a considerable number of cadinene-related, homogeranyl nerol-related, and many other types of compounds have been reported as constituents of yacon essential oil [6]. In this paper, we report the isolation and structural elucidation of three novel compounds, *ent*-kaurane-3β,16β,17,18-tertol (**1**), 3*R*,7*E*-9-butoxyl-megastigma-3-ol-3-*O*-β-D-glucopyranoside (**2**), and 3*S*,5*R*,6*Z*-megastigma-6-en-3,5,8,9-tertol (**3**), together with five known ingredients. β-Ionol-related compounds (**2**, **3**) were isolated from the genus *Smallanthus* for the first time.

2. Results and discussion

Compound **1** was isolated as white powder. ESI-MS gave its quasi-molecular ion at *m/z* 339 $[M + H]^+$, corresponding to the molecular formula $C_{20}H_{34}O_4$ in agreement with the HR-ESI-MS measurement. The absence of absorption in UV spectrum indicated that there are no double bonds in its molecule. Two methyl signals could be observed at δ 1.05 (3H, s, H-20) and 0.99 (3H, s, H-19) in the ^{1}H NMR spectrum. The ^{13}C NMR and DEPT spectra showed the presence of 20 carbons, including two methyls mentioned above, 10 secondary carbons, four tertiary carbons, and four quaternary carbons. Compound **1** comprises

*Corresponding author. Email: doudeqiang2003@yahoo.com.cn

ISSN 1028-6020 print/ISSN 1477-2213 online

DOI: 10.1080/10286020802361230
http://www.informaworld.com

four carbons bearing oxygen, conducted by the presence of four signals in the low field of its ^{13}C NMR spectrum at δ 73.3 (CH), 67.8 (CH_2), 81.5 (C), and 66.3 (CH_2). By comparing its ^{13}C NMR spectral data with those of compound **8** [15], **1** was considered as an *ent*-kaurane-type compound, whose structure was almost identical to that of **8**, except for the introduction of a hydroxyl to C-18. The hydroxyl at C-18 leads to the hydroxylation shifts in the resonances of C-18 (+38.9 ppm), C-4 (+3.4 ppm), C-3 (−4.9 ppm), C-5 (7.2 ppm), and C-19 (5.4 ppm). The linkage of 18-hydroxyl was also supported by the HMBC cross-peaks between CH_2-18 (δ 4.12 and 3.62) and C-3, C-4, and C-19 (δ 73.3, 42.7, and 12.7), as shown in Figure 1. The relative configurations of chiral carbons were revealed by the experiments of NOESY. The key correlations between H-3 (δ 4.15) and H-5 (δ 1.42), H-5 (δ 1.42) and H-9 (δ 1.02), and 18-CH_2OH (δ 4.12 and 3.62), indicated that H-3, H-5, H-9, and 18-CH_2OH are on the same side. The cross-peaks between CH_3-19 (δ 0.99) and CH_3-20 (δ 1.05), protons on the other side, can be observed as well. All of the relative configurations in **1** are in concordance with those in **8**. Therefore, the structure of **1** was determined as *ent*-kaurane-3β,16β,17,18-tertol.

Compound **2** was isolated as a white amorphous powder. ESI-MS gave its quasi-molecular ion peak at *m/z* 429 $[M + H]^+$, corresponding to the molecular formula $C_{23}H_{40}O_7$ in agreement with the HR-ESI-MS measurement. The IR spectrum showed the absorption bands at 3365 and 1642 cm^{-1}, attributed to the existence of hydroxyl and C=C double bond. The UV absorption maximum at 231 nm indicated the presence of a conjugated diene system. The ^{1}H NMR spectrum of **2** showed the presence of a pair of *trans*-alkene protons at δ 6.04 (1H, d, J = 16.0 Hz) and 5.40 (1H, m), an anomeric proton at δ 5.09 (1H, d, J = 7.7 Hz), a methyl at δ 0.85 (3H, t, J = 7.4 Hz) linked with a methylene, and another methyl at δ 1.33 (3H, d, J = 6.3 Hz), neighbor to a methenyl. The ^{13}C NMR spectrum showed the presence of a butyl (δ 68.0, 32.4, 19.7, and 14.0) and a terminal β-glucopyranose (δ 102.5, 75.3, 78.6, 71.8, 78.4, and 62.8) moieties, together with the remaining 13 carbon signals including di- and tetra-substituted double bonds (δ 125.9, 137.1, 128.3, and 137.5), and two secondary carbinols (δ 71.4 and 76.9), two methylenes (δ 46.5 and 39.4), four methyls (δ 21.4, 30.2, 28.2, and 22.2), and one quaternary carbon atom (δ 36.6). The above data suggested the structure of **2** was almost identical to that of platanionoside B, isolated from the leaves of *Alangium platanifolium* [7], except for the presence of the butyl in **2** instead of the glucopyranosyl moiety in platanionoside B. The HMBC correlations between H-1′ (δ 5.09) of glucose and C-3 (δ 71.1) and between H-1″ [δ 3.57 (1H, m) and 3.35 (1H, m)] of butyl and C-9 (δ 76.9) indicated that the glucose unit was linked at C-3 and the butyl at C-9. The D-glucose moiety was further confirmed by acid hydrolysis of **2**, and its β-anomeric configuration was determined

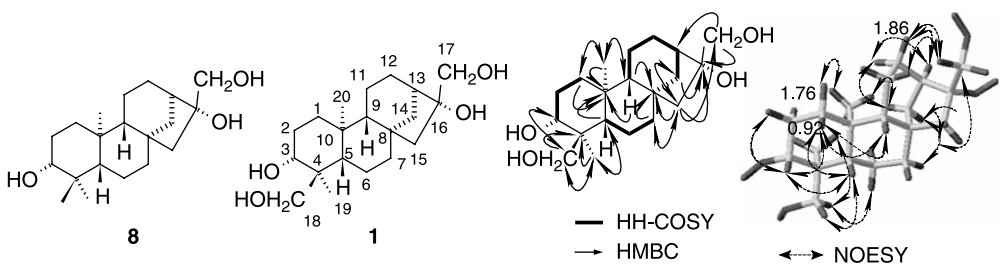

Figure 1. Structure, key ^{1}H–^{1}H COSY, HMBC, and NOESY correlations of **1**, and structure of **8**.

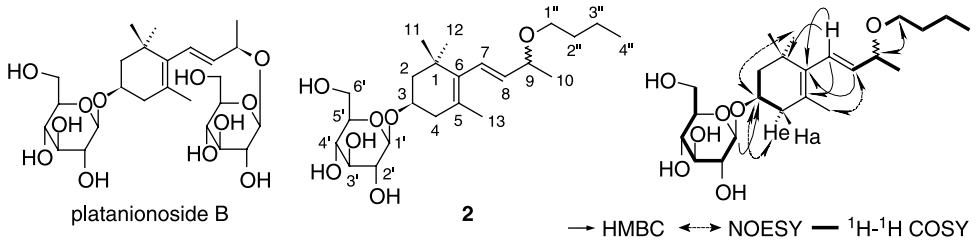

Figure 2. Structure, key ^{1}H–^{1}H COSY, HMBC, and NOESY correlations of **2**, and structure of platanionoside B.

from the coupling constant 7.7 Hz. The relative configuration of **2** was determined from the NOESY cross-peaks. The key correlations between H-4a and H-3 (assigned for 3*R*) and H-3 and CH_3-12 were observed (Figure 2). The absolute stereochemistry of C-3 was assigned as *R* by comparison of the ^{13}C NMR spectral data of **2** with those of platanionoside B and linarionoside C, similar compounds isolated from *Linaria japonica* [8]. The evidence that some signals emerged in couples, whose chemical shifts and peak intensities were in close approximation, in both the ^{1}H and ^{13}C NMR spectra, revealed that the configuration of C-9 should be a mixture of *R* and *S* at a ratio of about 1:1. Therefore, the structure of **2** was determined as 3*R*,7*E*-9-butoxyl-megastigma-3-ol-3-*O*-β-D-glucopyranoside, which should be an artificial new compound generated in the process of extraction and separation, based on the fact that compound **2** could not be detected in the ethanolic extract while appeared in the *n*-BuOH-soluble extract.

Compound **3** was isolated as colorless oil. The HR-ESI-MS spectrum showed an $[M + H]^+$ ion peak at *m/z* 245.1744, corresponding to the molecular formula of $C_{13}H_{24}O_4$. The IR spectrum showed the absorption bands at 3350 and 1670 cm^{-1}, attributed to the existence of hydroxyl and C=C double bond. All the 13 carbon signals in its ^{13}C NMR spectrum were expected to present a β-ionol-related skeleton. These signals were assigned to one tri-substituted double bond, three methines bearing a hydroxyl function (δ 63.9, 72.3, and 71.0), two methylenes, four methyl groups, and two quaternary carbons. Most of the carbons at the ring (δ 37.2, 47.0, 49.5, and 73.4) and methyls linked to them (δ 33.8, 32.4, and 33.0) were almost identical to those of cannabiside D, which has been isolated from *Senecio cannabifolius* [9], expect for the chemical shift of C-3 at δ 63.9 with a little upfield, due to the absence of the glucosyl. But the carbon signals of the side chain were quite different from those of cannabiside D,

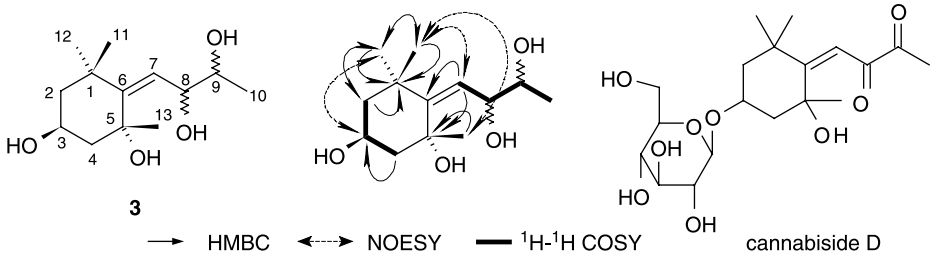

Figure 3. Structure, key ^{1}H–^{1}H COSY, HMBC, and NOESY correlations of **3**, and structure of cannabiside D.

because of the hydroxyls in **3**, instead of carbonyls in cannabiside D, on C-8 and C-9 positions (δ 72.3 and 71.0). The linkage of the side chain was established by proton couplings from the methyl at δ 1.55 to H-9 (δ 4.38), H-8 (δ 5.43), and H-7 (δ 6.23) in the $^1H-^1H$ COSY spectrum. The HMBC cross-peaks between H-7 (δ 6.23) and C-1, C-5, and C-6 (δ 37.2, 73.4, and 154.8) on the ring indicated the linkage of the side chain at C-6. The relative configurations and the configuration of the double bond were elucidated on the aid of the NOESY spectrum as 3*S* [H-3 (δ 4.57) and CH_3-12 (δ 1.23)], 5*R* [CH_3-13 (δ 1.98) and CH_3-11 (δ 1.33)], and 6*Z* [H-7 (δ 6.23) and CH_3-11 (δ 1.33)] (Figure 3). Therefore, the structure of **3** was determined as 3*S*,5*R*,6*Z*-megastigma-6-en-3,5,8,9-tertol.

By comparing the physical and spectral data with those of authentic sample or literature value, four known compounds were identified as 3′,4′,5-trihydroxy-3,7-dimethoxyflavone (**4**) [11], 3,4-dihydroxybenzaldehyde (**5**) [12], isorhamnetin (**6**) [13], octacosanol (**7**) [10], and *ent*-kaurane-3β,16β,17-triol (**8**) [15].

3. Experimental

3.1 General experimental procedures

Melting points were determined on an XT-4 micro-melting point apparatus and are uncorrected. Optical rotations were measured on a Perkin-Elmer digital polarimeter. UV spectra were recorded on a Shimadzu UV-260 spectrometer. IR spectra were determined on a Perkin-Elmer 683 infrared spectrometer with KBr pellets. NMR spectra were taken with TMS as internal standard on a Bruker Avance 400 FT-NMR spectrometer. HR-ESI-MS were measured on a Bruker FT-MS Apex III spectrometer and ESI-MS on a Finnigan LCQ Advantage spectrometer. Column chromatography was performed on silica gel (Marine Chemical Factory, Qingdao, China), Sephadex LH-20 (Amersham–Pharmacia Biotech AB, Uppsala, Sweden), COSMOSIL 75 C_{18}-OPN (75 μm, Nakalai Tesque Co. Ltd., Kyoto, Japan). TLC was conducted on silica gel GF254 (Marine Chemical Factory, Qingdao, China) and RP-18 F254 (Merck, Darmstadt, Germany) plates. Detection was done by spraying 1% $Ce(SO_4)_2$–10% aqueous H_2SO_4, followed by heating. HPLC was performed with a Shimadzu LC-10AS chromatograph apparatus using an ODS column (Phenomenex Luna C18, 20 × 250 mm, USA).

3.2 Plant material

The leaves of *Smallanthus sonchifolius* were collected in Liaoning province, China, in April 2005, and identified by Prof. Tingguo Kang, School of Pharmacy, Liaoning University of Traditional Chinese Medicine. A voucher specimen (yacon20050927) has been deposited at the Pharmacognosy Laboratory, College of Pharmacy, Liaoning University of TCM.

3.3 Extraction and isolation

The leaves of *S. sonchifolius* (5.0 kg) were extracted with 60% EtOH under reflux. Evaporation of the solvent under reduced pressure gave the aqueous EtOH extract (100 g). The EtOH extract was partitioned in a $CHCl_3$–H_2O mixture, and then extracted with *n*-BuOH. Removal of the solvent under reduced pressure from the $CHCl_3$-, *n*-BuOH-, and H_2O-soluble fractions yielded 20, 40, and 55 g of residues, respectively. The *n*-BuOH-soluble fraction was subjected to normal phase silica gel column [1.2 kg, $CHCl_3$–MeOH (100:0 → 0:100, v/v)] to give 12 fractions. Fraction 2 was further separated by normal phase silica gel column chromatography [30 g, *n*-hexane–AcOEt (10: 1 → 5:1, v/v)] to give octacosanol (**7**, 56 mg). Fraction 3 was separated by silica gel column chromatography [120 g, $CHCl_3$–MeOH (100:0 → 0:100, v/v)] and by repeated HPLC [Phenomenex Luna C18, 20 × 250 mm, MeOH–H_2O (63:37, v/v)] to give *ent*-kaurane-3β,16β,17,18-tertol (**1**, 90 mg), *ent*-kaurane-3β,16β,17-triol (**8**, 20 mg). Fraction 6 was separated by reversed-phase silica gel column [120 g, MeOH–H_2O

(30:70 → 40:60 → 60:40 → 80:20, v/v) → MeOH] and Sephadex LH-20 (20 g, MeOH) column chromatography to give 3′,4′,5-trihydroxy-3,7-dimethoxyflavone (**4**, 8 mg), 3,4-dihydroxybenzaldehyde (**5**, 10 mg), and isorhamnetin (**6**, 6 mg). Fraction 7 was separated by repeated HPLC [Phenomenex Luna C18, 20 × 250 mm, MeOH–H_2O (70:30, v/v)] to give 3*R*,7*E*-9-butoxyl-megastigma-3-ol-3-*O*-β-D-glucopyranoside (**2**, 19 mg) and 3*S**,5*R**,6*Z*-megastigma-6-en-3,5,8,9-tertol (**3**, 10 mg).

3.3.1 ent-*Kaurane-7β,26β,21,29-tertol* (***1***)

White powder, m.p. 203–207°C. $[\alpha]_D^{25}$ 41.0 (*c* 1.0, MeOH). ^{1}H NMR (400 MHz, C_5D_5N) and ^{13}C NMR (100 MHz, C_5D_5N) spectral data are shown in Table 1. Positive ion ESI-MS *m/z*: 339 $[M + H]^+$, 361 $[M + Na]^+$. HR-ESI-MS *m/z*: 339.2538 $[M + H]^+$ (calcd for $C_{20}H_{35}O_4$, 339.2535).

3.3.2 3R,7E-*9-Butoxyl-megastigma-3-ol-3-O-β-D-glucopyranoside* ***(2).***

White amorphous powder, m.p. 122–125 °C. $[\alpha]_D^{25}$ −30.1 (*c* 0.43, MeOH). IR (KBr) (ν_{max}, cm^{-1}): 3365, 2927, 1642, 1386, 1075, 1042. UV λ_{max} (nm) (MeOH) 231; log ε, 3.71. ^{1}H NMR (400 MHz, C_5D_5N) and ^{13}C NMR (100 MHz, C_5D_5N) spectral data are given in Table 2. Positive ion ESI-MS *m/z*: 429 $[M + H]^+$. HR-ESI-MS *m/z*: 429.2849 $[M + H]^+$ (calcd for $C_{23}H_{41}O_7$, 429.2847). Acid hydrolysis of **2** was performed as described in the literature [14] to give β-D-glucopyranose, which was identified by HPLC.

3.3.3 7S,5R-*Megastigma-6-en-7,5,8,9-tertol* ***(3).***

Colorless oil, amorphous powder. $[\alpha]_D^{25}$ −13.2 (*c* 0.23, MeOH). IR (KBr) (ν_{max} cm^1): 3350, 3019, 2926, 1670, 1385. ^{1}H NMR (400 MHz, C_5D_5N) and ^{13}C NMR (100 MHz,

Table 1. ^{13}C NMR (100 MHz, C_5D_5N) spectral data of compounds **1** and **8** and ^{1}H NMR (400 MHz, C_5D_5N) spectral data of compound **1**.

	δ_C		
No.	**1**	**8**	δ_H of **1**
1	38.7	39.1	0.92 (1H, dt, *J* = 3.3, 12.6 Hz) and 1.75 (1H, overlapped)
2	27.5	28.2	1.90 (2H, overlapped)
3	73.3	78.2	4.15 (1H, t, *J* = 5.2 Hz)
4	42.7	39.3	
5	48.2	55.4	1.42 (1H, t, *J* = 11.9 Hz)
6	20.3	20.7	1.61 (1H, m) and 1.38 (1H, m)
7	42.1	42.6	1.66 (2H, m)
8	44.5	44.7	
9	56.8	57.0	1.02 (1H, m)
10	39.0	39.4	
11	18.7	18.8	1.58 (2H, m)
12	26.7	26.8	1.86 (1H, m) and 1.56 (1H, m)
13	45.8	46.1	2.43 (1H, br s)
14	37.6	37.7	1.98 (2H, br s)
15	53.7	53.9	1.78 (1H, d, *J* = 13.9 Hz) and 1.68 (1H, overlapped)
16	81.5	81.6	
17	66.3	66.5	4.09 (1H, d, *J* = 10.8 Hz) and 4.00 (1H, d, *J* = 10.8 Hz)
18	67.8	28.9	4.12 (1H, d, *J* = 10.4 Hz) and 3.62 (1H, d, *J* = 10.4 Hz)
19	12.7	18.1	0.99 (3H, s)
20	18.3	16.3	1.05 (3H, s)

Table 2. ^{13}C (100 MHz) and ^{1}H NMR (400 MHz) spectral data of compounds **2** and **3** (C_5D_5N).

	δ_C		δ_H	
No.	**2**	**3**	**2**	**3**
1	36.63 (36.60)	37.2		
2	46.5	47.0	2.15 (1H, dd, overlapped) and 1.72 (1H, dd, overlapped)	2.09 (1H, dd, $J = 13.4$, 7.0 Hz) and 1.96 (1H, dd, $J = 13.4$, 8.6 Hz)
3	71.4	63.9	4.43 (1H, m)	4.57 (1H, m)
4	39.4	49.5	2.61 (1H, dd, $J = 16.7$, 4.6 Hz) and 2.31 (1H, dd, overlapped)	2.62 (1H, dd, $J = 13.8$, 5.7 Hz) and 2.39 (1H, dd, $J = 13.8$, 6.1 Hz)
5	125.97 (125.94)	73.4		
6	137.1	154.8		
7	128.36 (128.28)	126.3	6.04 (1H, br d, $J = 16.0$ Hz)	6.23 (1H, d, $J = 8.2$ Hz)
8	137.5	72.3	5.40 (1H total, dd × 2, $J = 16.0$, 6.4 Hz)	5.43 (1H, dd, $J = 8.2$, 4.6 Hz)
9	76.91 (76.87)	71.0	3.89 (1H, quintuplicate like, 6.4 Hz)	4.38 (1H, m)
10	21.43 (21.36)	19.7	1.68 and 1.70 (3H total, s × 2)	1.55 (3H, d, $J = 6.4$ Hz)
11	30.20 (30.08)	33.8	1.00 (3H, s)	1.33 (3H, s)
12	28.25 (28.19)	32.4	0.98 (3H, s)	1.23 (3H, s)
13	22.24 (22.17)	33.0	1.33 and 1.32 (3H total, s × 2)	1.98 (3H, s)
1′	102.5		5.09 (1H, d, $J = 7.7$ Hz)	
2′	75.3		4.06 (1H, m)	
3′	78.6		4.29 (1H, m)	
4′	71.8		4.26 (1H, m)	
5′	78.4		4.01 (1H, m)	
6′	62.8		4.56 (1H, m) and 4.39 (1H, m)	
1″	68.03 (67.98)		3.57 (1H, dd, $J = 15.8$, 6.7 Hz) and 3.35 (1H, dd, $J = 15.8$, 6.3 Hz)	
2″	32.4		1.58 (2H, m)	
3″	19.7		1.38 (2H, m)	
4″	14.0		0.85 (3H, t, $J = 7.4$ Hz)	

C_5D_5N) spectral data are given in Table 2. Positive ion ESI-MS *m/z*: 245 $[M + H]^+$. HR-ESI-MS *m/z*: 245.1744 $[M + H]^+$ (calcd for $C_{23}H_{25}O_4$, 245.1747).

Acknowledgements

The authors are grateful to Li Shen, Centre of Analysis and Test, School of Pharmacy, Yaitai University, for her kind help in the determination of our samples.

References

[1] T. Ohyama, O. Ito, S. Yasuyoshi, T. Ikarashie, K. Minamisawa, M. Kubota, T. Tsukihashi, and T. Asami, *Soil Sci. Plant Nutr.* **36**, 167 (1990).
[2] M. Hondo, A. Nakano, Y. Okumura, and T. Yamaki, *J. Jpn. Soc. Food. Sci.* **47**, 148 (2000).
[3] M.J. Aybar, A.N. Sanchez Riera, A. Grau, and S.S. Sanchez, *J. Ethnopharmacol.* **74**, 125 (2001).
[4] H. Kakuta, T. Seki, and Y. Hashidoko, *J. Mizutani. Biosci. Biotechnol. Biochem.* **56**, 1562 (1992).
[5] F.Q. Lin, M. Hasegawa, and O. Kodama, *Biosci. Biotechnol. Biochem.* **67**, 2154 (2003).
[6] X.A. Dominguez, S. Hafez, and H.V. Sanchez, *J. Slim. Phytochemistry* **27**, 1863 (1988).
[7] A. Tamaki, H. Otsuka, and T. Ide, *J. Nat. Prod.* **62**, 1074 (1999).
[8] H. Otsuka, *Phytochemistry* **37**, 461 (1994).
[9] B. Wu, W.H. Lin, H.Y. Gao, L. Zheng, L.J. Wu, and C.S. Kim, *Indian J. Pharm. Sci.* **68**, 332 (2006).
[10] X.R. Shen and D.Z. Zhang, *Acad. J. Guangdong Coll. Pharm.* **22**, 594 (2006).
[11] Y. Wang, M. Hamburger, J. Gueho, and K. Hostettmann, *Phytochemistry* **28**, 2323 (1989).
[12] M. Fujita, M. Nagai, and T. Inoue, *Chem. Pharm. Bull.* **30**, 1151 (1982).
[13] A.G. Valesi, E. Rodriguez, V.G. Vander, and T.J. Mabry, *Phytochemistry* **11**, 2812 (1972).
[14] Y.K. Qiu, Y.J. Chen, Y.P. Pei, H. Matsuda, and M. Yoshikawa, *Chem. Pharm. Bull.* **50**, 1507 (2002).
[15] X. Li, D.Z. Zhang, and M. Onda, *J. Nat. Prod.* **53**, 657 (1990).