Two Flavonoid Dimers from *Sarcandra hainanensis* (Pei) Swamy *et* Bailey

Cong-Mei Cao,[a,b] Yong Peng,[a,b] Li-Jia Xu,[a,b] Ya-Jun Wang,[a] Jun-Shan Yang,[a] and Pei-Gen Xiao*,[a,b]

[a] *Institute of Medicinal Plant Development, Chinese Academy of Medical Science, Peking Union Medical College; Beijing 100193, P. R. China: and* [b] *Key Laboratory of Bioactive Substances and Resources Utilization of Chinese Herbal Medicine (Peking Union Medical College), Ministry of Education; 100193 Beijing, P. R. China.*

Received February 9, 2009; accepted March 30, 2009; published online April 7, 2009

Two new flavonoid dimers (1, 2) consisting of flavan-chalcone together with three known compounds (3—5) were isolated from the ethanol extract of the whole plants of *Sarcandra hainanensis*. Their structures were determined by extensive spectroscopic analysis. Human immunodeficiency virus-1 integrase inhibition activities of compounds 1 and 2 were evaluated and they showed weak activities with IC_{50} at 18.05 and 25.27 μM, respectively.

Key words flavonoid dimer; flavan-chalcone; *Sarcandra hainanensis*; Chloranthaceae; human immunodeficiency virus-1 integrase inhibition

Sarcandra belongs to Chloranthaceae family of 3 species, *S. glabra* (Thunb.) Nakai, *S. hainanensis* (Pei) Swamy *et* Bailey and *S. chloranthoides* Gardner.[1] *S. glabra* and *S. hainanensis* are widely used to invigorate blood circulation and eliminate blood-stasis as traditional Chinese medicine.[2] Many phytochemical and biological studies on *S. glabra* have been carried out, however, to the best of our knowledge, there is no phytochemical report about *S. hainanensis* and *S. chloranthoides*, which are endemic plants to China and India, respectively.[3] *S. hainanensis* is a shrub distributing only in the south of China. In order to better understand the chemotaxonomic relationship between *S. hainanensis* and *S. glabra*, we initiated an investigation on the chemical constituents of *S. hainanensis*.

Our chemical study on the ethanol extracts of the whole plant of *S. hainanensis* had led to the isolation of chalcones.[4] Continuous studies achieved the isolation of two new flavonoid dimers comprised of flavan-chalcone (**1**, **2**). Some flavonoid dimers including a 3,4-de-*H*-flavanol-chalcone dimer with linkage of C-3(C)–C-4(E),[5] a flavan-flavonol with linkage of C4(C)–C5(D)[6] and a flavan-flavonol with linkage of C4(C)–C8(D)[7] were isolated from *Lophira alata*, *Acacia nigrescens* and *Xanthorrhoea resinosa*, respectively. However, novel dimers consisting of flavan-chalcone with linking position of C-4(C)–C-3′(D) as compounds **1** and **2** were detected for the first time. Structures and absolute configurations of these two compounds were established through detailed analysis of their spectroscopic data. No bioactivity about flavan-chalcone dimers were reported before. In the present study, human immunodeficiency virus (HIV)-1 integrase inhibition activity of compounds **1** and **2** indicated the two new compounds exhibited weak activities with IC_{50} at 18.05 and 25.27 μM, respectively.

In addition to two new compounds, 3 known compounds (**3**—**5**) were also isolated from the title plant for the first time. Structures of those compounds were identified as isofraxidin (**3**), 7-hydroxy-5,8-dimethoxyflavanone (**4**) and pinostrobin (**5**) by comparison of their spectroscopic data with those reported in literature.[8—10]

Results and Discussion

Compound **1** was obtained as a yellow amorphous solid and its molecular of $C_{33}H_{30}O_8$ was established by HR-electro spray ionization (ESI)-MS at *m/z* 553.1850 ([M−H]$^-$), indicating 19 degrees of unsaturation.

Thirty-three carbon signals in the ^{13}C-NMR spectrum of **1** were categorized by distortionless enhancement by polarization transfer (DEPT) experiments as one carbonyl, fourteen sp^2 methines, twelve sp^2 quaternary, three methoxyls, one sp^3 methylenes and two sp^3 methines carbons. The number of sp^2 carbons suggested that four benzene rings existed in the structure of **1**. Their substitutions might be elucidated as two mono-substituted and two penta-substituted benzene rings or two mono-substituted, one tetra-substituted (1,2,4,5-tetrasubstituted) and one hexa-substituted benzene rings by the singlets at δ_H 5.85 (1H), 6.22 (1H) and two A_5 proton spin system together with three methoxyl proton signals in the ^{1}H-NMR of **1**.

The ^{1}H-NMR spectrum showed obvious signals of 2′-hydroxy-chalcone including a coupling signal of two doublets at δ_H 7.95 (1H, d, J=15.5 Hz), 7.80 (1H, d, J=15.5 Hz) and a broad singlet at δ_H 14.95.[11] Its carbon skeleton of chalcones was confirmed by long range correlations of δ_H 7.95 (H-α)

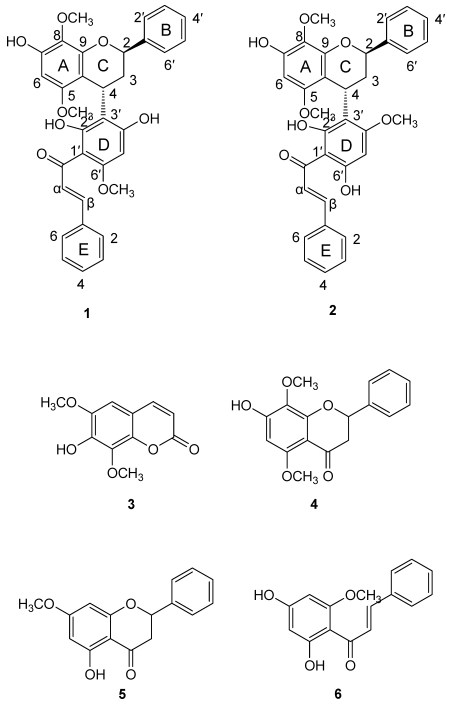

Fig. 1. Structures of Compounds **1**—**6**

* To whom correspondence should be addressed. e-mail: xiaopg@public.bta.net.cn

to δ_C 135.7 (C-1, E), 192.8 (ketone carbonyl) as well as δ_H 7.80 (H-β) to δ_C 192.8 (ketone carbonyl), 135.7 (C-1, E), 128.3 (C-2, 6, E), 128.9 (C-3, 5, E) in the heteronuclear multiple bond coherence (HMBC) spectrum of **1**. A carbonyl, a double bond and four benzene rings accounted for 18 degrees of unsaturation. The residual one double bond equivalent revealed the presence of a ring. The AB_2C proton spin system of δ_H 5.05 (1H, br d, J=11.5 Hz), 4.70 (1H, br d, J=2.0 Hz), 2.39 (1H, br d, J=14.0 Hz) and 2.07 (1H, m) indicated that compound **1** might have a flavan part. The presence of the flavan part of compound **1** was further confirmed by correlations of δ_H 5.05 (H-2, C) to δ_C 36.7 (H-3, C), 126.1 (C-2′,6′, B) and 140.8 (C-1′, B); δ_H 4.70 (H-4, C) to δ_C 76.1 (C-2, C), 36.7 (C-3, C), 149.0 (C-9, A/C), 101.0 (C-10, A/C) and 154.9 (C-5, A) in the HMBC experiment (Fig. 2).

HMBC correlation peaks of the signal at δ_H 4.70 (H-4, C) with δ_C 165.5 (C-2′, D), 109.2 (C-3′, D), 162.7 (C-4′, D) and δ_H 2.39 (H-3a, C) with δ_C 109.2 (C-3′, D) suggested a C-4 (C) to C-3′ (D) linkage between the units of flavan-chalcone of **1** (Fig. 2). The special chemical shift of C-4 (C) and H-4 (C) at δ_C 27.3 and δ_H 4.70 in the ^{13}C- and ^{1}H-NMR spectra confirmed a phenyl substituent. In according with the postulated linkage, comparison spectra of compound **1** and cardamonin (**6**)[4] indicated the absence of δ_H 6.03 (H-3′) of **6** and little difference between chemical shifts of H-5′ (D) of the two compounds (δ_H 5.85 for **1** and δ_H 5.96 for **6**).

The HMBC correlations of signals at δ_H 5.85 (1H, s) with the signals at δ_C 106.2 (C-1′, D), 109.2 (C-3′, D), 162.7 (C-4′, D), 160.9 (C-6′, D) and δ_H 6.22 (1H, s) with δ_C 154.9 (C-5, A), 149.8 (C-7, A), 129.3 (C-8, A), 101.0 (C-10, A/C) illustrated that the position of the two protons was at C-5′ (D) and C-6 (A), respectively (Fig. 2). Additionally, the ^{1}H-NMR spectrum exhibited the resonances of three methoxyl singlets at δ_H 3.92, 3.91 and 3.69. The HMBC correlations between these three singlets and C-6′ (D), C-8 (A) and C-5 (A), respectively, confirmed the location of the methoxyl groups.

The coupling constants of the spin systems in the ^{1}H-NMR spectrum of **1** [$J_{2,3b(C)}$=11.5 Hz; $J_{3b,4(C)}$=2.0 Hz] indicated 2,3b-*trans*-3b,4-*cis*-relative stereochemistry with sofa form.[12] An *R* absolute configuration of compound **1** at C-4 (ring C) was realized by a positive Cotton effect of $[\theta]_{209.5}=1.798\times10^6$ and a negative Cotton effect of $[\theta]_{205.0}=-8.153\times10^6$.[13] Therefore, it was presumed that compound **1** processed a 2*R*,4*R* (C-ring) absolute configuration. Herein, the structure of compound **1** was established as (2*R*,4*R*)-7-hydroxy-5,8-dimethoxyflavan(4$\beta\rightarrow$3′)-2′,4′-dihydroxy-6′-methoxychalcone and it was named as sarcandrone A.

The stereochemistry of compound **1** was defined on the basis of its nuclear Overhauser effect spectroscopy (NOESY) spectrum and MM2 calculation (Fig. 3). Both H-2 (C) and H-4 (C) showed connectivity to H-3a (br dd, C) and H-3b (m, C) in ^{1}H–^{1}H correlation spectroscopy (COSY) spectrum of compound **1** (Fig. 3). However, no NOE was observed between H-2 (C) and H-3b (C) while H-4 (C) exhibited NOEs to both H-3a and H-3b. These results were in agreement with their relative stereochemistry, which was further confirmed by their coupling constant and split pattern. The relative stereochemistry between rings C and B, between rings C and D, between rings D and E could be determined from the

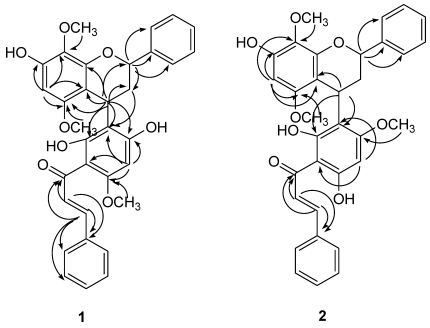

Fig. 2. Key HMBC Correlations (H→C) of Compounds **1** and **2**

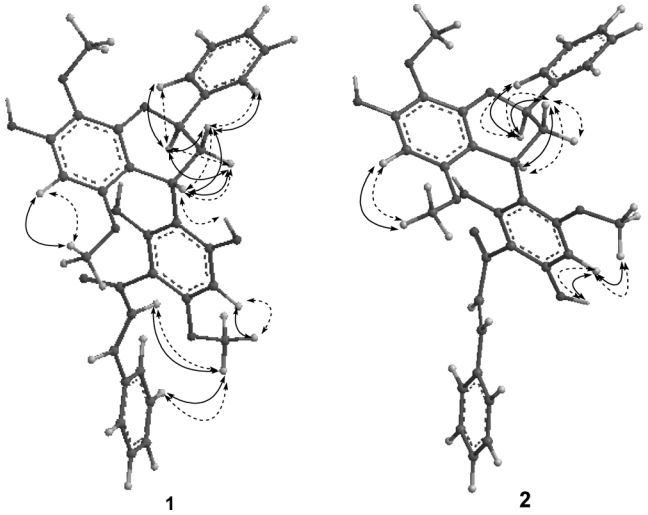

Fig. 3. Calculated Conformation by MM2 for Compounds **1** and **2**

NOEs of H-2′, 6′ (B), 4′-OH (D), 5′-OCH_3 (D) and 5′-OCH_3 (A) as it was showed in Fig. 3.

Compound **2**, a dark yellow powder, had a molecular formula of $C_{33}H_{30}O_8$ determined by HR-ESI-MS at *m/z* 553.1850 ($[M-H]^-$). Comparison of both ^{1}H- and ^{13}C-NMR data between compounds **2** and **1** suggested that their spectroscopic data were quite similar and indicated that compound **2** was also a flavan-chalcone dimer. The main differences in the ^{13}C-NMR spectrum between **1** and **2** were the chemical shifts of carbon signals at rings A, C and D. The long-range correlations between δ_H 4.95 (H-4, C) and δ_C 103.3 (C-10, A/C), 110.6 (C-3′, D), 160.8 (C-2′, D) revealed the two carbons connected the two parts of the dimers were at C4 (C) and C-3′ (D).

The long-range correlations between δ_H 6.18 (H-6, A) and δ_C 103.3 (C-10, A/C), 129.9 (C-8, A), 149.2 (C-7, A) and 155.2 (C-5, A) in HMBC spectrum of **2** suggested the substitution positions of ring A, which was exactly the same as that of **1** (Fig. 2). The HMBC correlations of δ_H 5.84 (H-5′, D) to δ_C 106.0 (C-1′, D) and 110.6 (C-3′, D) gave the possible substitutions of ring D. Considering the chemical shifts of the remaining five aliphatic carbon atoms, the structure of compound **2** was elucidated as 7-hydroxy-5,8-dimethoxyflavan-(4$\beta\rightarrow$3′)-2′,6′-dihydroxy-4′-methoxychalcone.

The coupling constant of the spin systems in the ^{1}H-NMR spectrum [$J_{2,3b(C)}$=11.0 Hz], the broad singlet of H-4 and Cotton effects ($[\theta]_{207.0}=1.125\times10^6$, $[\theta]_{202.5}=-5.317\times10^6$) of **2** were similar to the data of **1**. It could be deduced **2** also

Table 1. ^{1}H- and ^{13}C-NMR Data of Compounds **1** and **2** in $CDCl_3$ (500 MHz for ^{1}H and 125 MHz for ^{13}C)

Position ring	Carbon	**1**		**2**	
		δ_C	δ_H (J in Hz)	δ_C	δ_H (J in Hz)
A/C	2	76.1	5.05, br d (11.5)	78.9	5.09, d (11.0)
	3	36.7	2.39, br d (14.0), 2.07, m	36.8	2.59, br s 2.07, br dd (12.5, 11.0)
	4	27.3	4.70, br d (2.0)	28.1	4.95, br s
	5	154.9		155.2	
	6	91.3	6.22, s	92.5	6.18, s
	7	149.8		149.2	
	8	129.3		129.9	
	9	149.0		150.1	
	10	101.0		103.3	
B	1′	140.8		140.5	
	2′, 6′	126.1	7.41, d (7.0)	125.9	7.48, d (7.5)
	3′, 5′	128.4	7.36, t (7.0)	128.5	7.38, m
	4′	128.0	7.30, t (7.0)	128.0	7.32, d (7.5)
	C=O	192.8		192.9	
	α	127.8	7.95, d (15.5)	128.0	7.93, d (15.5)
	β	142.1	7.80, d (15.5)	142.0	7.79, d (15.5)
D	1′	106.2		106.0	
	2′	165.5		160.8	
	3′	109.2		110.6	
	4′	162.7		160.9	
	5′	92.0	5.85 (s)	91.7	5.84, s
	6′	160.9		164.9	
E	1	135.7		135.7	
	2, 6	128.3	7.62, d (6.5)	128.3	7.61, d (6.5)
	3, 5	128.9	7.40, t (6.5)	128.9	7.41, m
	4	130.0	7.39, t (6.5)	130.0	7.39, m
OMe	5(A)-OCH_3	56.0	3.69, s	56.1	3.53, s
	8(A)-OCH_3	55.7	3.91, s	61.5	3.91, s
	6′(D)-OCH_3	61.4	3.92, s		
	4′(D)-OCH_3			55.7	3.88, s
OH	2′(D)-OH		14.95, s		14.82, s
	4′(D)-OH		6.48, s		
	6′(D)-OH				5.88, s
	7(A)-OH		5.92, s		5.63, br s

had a 2*R*,4*R* (ring C) absolute configuration.[12,13] Herein, the structure of **2** could be concluded as (2*R*,4*R*)-7-hydroxy-5,8-dimethoxyflavan-(4β→3′)-2′,6′-dihydroxy-4′-methoxychalcone which we named as sarcandrone B.

The stereochemistry of compound **2** was revealed as it showed in Fig. 3 based on its NOESY spectrum and MM_2 calculation. Different stereochemistry of **2** from **1** mainly reflected on the NOEs of H-2 (C), H-4 (C) and 4′-OCH_3 (D). H-2 (C) and H-4 (C) displayed weak NOEs to H-3b (m, C) and no NOEs to H-3a (br dd, C). It might be caused by the weakness of the signals or a smaller angle of the dihedral angle between H-2 (C) and H-3b (C). The stereochemistry of the chalcone part of **2** might be deduced from the NOEs of 4′-OCH_3 (D) (Fig. 3).

Compounds **1** and **2** were assayed for their HIV-1 integrase (IN) inhibition activities with a microplate screening method using magnetic beads.[14] Baicalein was used as the standard medicine with an IC_{50} value as 1.06 μM in the test. Compounds **1** and **2** showed weak activities for the integrase strand transfer reaction. The *in vitro* IC_{50} values of compounds **1** and **2** were 18.05 and 25.27 μM, respectively.

Experimental

General Experimental Procedures UV spectra were measured on a Shimadzu UV-2550 UV–visible spectrophotometer. Optical rotations were made on a Perkin-Elmer 341 polarimeter at room temperature. Circular dichroism (CD) spectra were measured on a JASCO J-725 spectropolarimeter in MeOH. IR spectra were measured on a NEXUS-470 FTIR spectrophotometer. ^{1}H- (500 MHz) and ^{13}C- (125 MHz) NMR spectra were measured on a Bruker Avance DRX-500 spectrometer. Chemical shifts were referenced to the residual solvent signal ($CDCl_3$: δ_H 7.26, δ_C 77.0). HR-ESI-MS spectra were performed on APEX Q-FT-MS/MS spectrometer. ESI-MS spectra were performed on ABI Qtrap spectrometer. All solvents used were of analytical grade (Beijing Chemical Plant, Beijing, People's Republic of China). Silica gel (300—400 mesh, Qingdao Marine Chemical Plant, Qingdao, People's Republic of China), C_{18} reversed-phase silica gel (150–200 mesh, Merck), Sephadex LH-20 gel (pharmacia), and MCI gel (CHP20P, 75–150 μM, Mitsubishi Chemical Industries Ltd.) were used for column chromatography, and precoated silica gel GF_{254} plates (Qingdao Marine Chemical Plant) were used for TLC.

Plant Material The whole plants of *Sarcandra hainanensis* were collected in Baishan county, Hainan province, China, in April 2007 and were authenticated by Professor Pei-Gen Xiao of Institute of Medicinal Plant Development, Chinese Academy of Medicinal Science. A voucher specimen (SH070706) has been deposited in the Herbarium of Institute of Medicinal Plant Development, Chinese Academy of Medical Science and Peking Union Medical College.

Extraction and Isolation The air dried, chipped whole plants of *S. hainanensis* (29 kg) were exhaustively extracted with 95% ethanol under reflux for twice (210 l×2). The extracts were evaporated to yield 2928.0 g of green residue. The EtOH extract was suspended in water saturated with NaCl and then extracted with petroleum ether, CH_2Cl_2, EtOAc and *n*-BuOH sequencely.

The CH_2Cl_2-soluble portion was evaporated to leave a residue (720.3 g). A portion (611.0 g) of it was subjected to CC (column chromatography) of silica gel (200—300 mesh, 3000 g). Five fractions (C1 to C5) were collected

according to TLC. Fraction C3 was further chromatographed on silica gel column with a gradient of CH_2Cl_2–EtOAc with increasing polarity to give 15 subfractions (C3-1 to C3-15).

Fraction C3-3 (6.5 g) was submitted to CC on a silica gel column eluting with petroleum ether–acetone (20 : 1—6 : 1) to give C3-3-1 to C3-3-7. C3-3-7 was purified by CC of Sephadex LH-20 using $CHCl_3$–MeOH (2 : 3) as elutent to afford **1** (50.4 mg). Fraction C3-4 (3.4 g) was absorbed onto 5.6 g of silica gel and applied to a silica gel (200—300 mesh, 133 g) column chromatography eluted with a gradient of petroleum ether–EtOAc (6 : 1—1 : 1) with increasing polarity to give C3-4-1 to C3-4-8. C3-4-7 was subjected to a column of Sephadex LH 20 eluted with $CHCl_3$–MeOH (0 : 1—2 : 3) to give **2** (21.7 mg). Fraction C3-6 (6.4 g) was submitted to CC on a silica gel column eluting with petroleum ether–EtOAc (5 : 2) to give **3** (1026.1 mg). Fraction C3-7 (2.4 g) was absorbed onto 2.7 g of silica gel and packed on a dry CC (silica gel 200—300 mesh, 110 g). Successive elution with petroleum ether–EtOAc (6 : 1—1 : 1) yielded 8 subfractions (C3-7-1 to C3-7-8). Further purification of C3-7-4 by CC of Sephadex LH-20 using MeOH furnished **4** (158.8 mg). Repeated purification of C3-10 on a Sephadex LH 20 column ($CHCl_3$–MeOH 2 : 3) gave **5** (10.3 mg).

Sarcandrone A (**1**): Yellow powder ($CHCl_3$); $[\alpha]_D^{20}$ −103 (c=4.85×10^{-2}, $CHCl_3$); UV (MeOH) λ_{max} (log ε) 349 (3.29), 232 (3.22) nm; CD $[\theta]_{209.5}$=1.798×10^6; $[\theta]_{205.0}$=−8.153×10^6; IR (KBr) ν_{max} (cm^{-1}) 3398, 2942, 2852, 1627, 1585, 1491, 1453, 1435, 1342, 1272, 1200, 1171, 1113, 1024, 976; ^{1}H- and ^{13}C-NMR data see Table 1; ESI-MS *m*/*z*: 553.16 [M−H]$^-$, 383.13 (100); HR-ESI-MS *m*/*z*: 553.1850 (Calcd for $C_{33}H_{30}O_8$ 553.1868, [M−H]$^-$).

Sarcandrone B (**2**): Dark yellow powder ($CHCl_3$); $[\alpha]_D^{20}$ −468 (c=4.70×10^{-2}, $CHCl_3$); UV (MeOH) λ_{max} (log ε) 350 (3.14), 235 (3.02) nm; CD $[\theta]_{207.0}$=1.125×10^6; $[\theta]_{202.5}$=−5.317×10^6; IR (KBr) ν_{max} (cm^{-1}) 3423, 2934, 2854, 1613, 1563, 1495, 1433, 1332, 1287, 1226, 1140, 1103, 1018, 973; ^{1}H- and ^{13}C-NMR data see Table 1; ESI-MS *m*/*z*: 553.16 [M−H]$^-$ (32), 383.13 (100); HR-ESI-MS *m*/*z*: 553.1850 (Calcd for $C_{33}H_{30}O_8$ 553.1868, [M−H]$^-$).

HIV-1 Integrase Strand Transfer Inhibition Assays HIV-1 integrase strand transfer (ST) assays were performed in a 96-well microplate (Corning, New York, NY, U.S.A.) in a final volume of 50 μl. The wells were washed once with the reaction buffer (25 mmol/l PIPES, pH 7.0, 10 mmol/l β-mercaptoethanol, 5% (w/v) glycerol, 0.1 g/l bovin serum albumin (BSA), and 10 mmol/l $MnCl_2$). The compounds were diluted with dimethyl sulfoxide (DMSO) to a final concentration of 10% DMSO into the reaction volume (v/v) and pre-incubated with 15 pmol integrase (IN) at 37 °C in the reaction buffer in the absence of $MnCl_2$ (10 mmol/l) for 10 min. Subsequently, 1.5 pmol donor DNA and 15 pmol target DNA were added and the reaction was initiated. After incubation for 1 h at 37 °C, 1.5 ml magnetic particles (6.7×10^8 beads/ml) and 51.5 μl binding buffer (10 mmol/l Tris–HCl, pH 7.6, 2 mol/l NaCl, 20 mmol/l ethylenediaminetetraacetic acid (EDTA), and 0.1% [w/v] Tween 20) were added and incubated at 20 °C for 15 min. Then the wells holding the mixture were placed in a magnetic concentrator, the supernatant was discarded, and the wells were washed 3 times with phosphate-buffered saline (PBS) containing 0.1% Tween 20 (PBST). Subsequently, 100 μl of 1 : 5000 diluted alkaline phosphatase (AP) conjugate anti-DIG antibody was added and incubated for 30 min at 37 °C. Finally, the wells were washed 3 times with PBST and the magnetic beads were transferred into fresh wells; 100 μl P-nitrophenyl phosphate (P-NPP) substrate (0.1 mol/l Na_2CO_3, pH 9.5, 6.7 mmol/l P-NPP, and 2 mmol/l $MgCl_2$) was added. The plates were read at 405 nm with a Model 680 microplate reader (Bio-Rad, U.S.A.). The inhibition percentage and IC_{50} values were calculated based on the assay results after curve fitting according to a non-linear regression.

Acknowledgments This project was financially supported by the National Natural Science Foundation of China, Grant (No. 30530860). We are grateful to Kui Chen, Hainan Branch Institute of Medicinal Plant, Chinese Academy of Medical Science, for the collection of plant materials. The authors also expressed thanks to Prof. Shishan Yu, Institute of Materia Medica, Chinese Academy of Medical Science, Dr. Jingchun Gao, Neptunus Group Corporation Limited, and Prof. Qingwen Shi, Laboratory of Medicinal Natural Product Chemistry, School of Pharmaceutical Sciences, Hebei Medicinal University, for their suggestions.

References

1) Cheng Y. Q., Chen D. Z., Wu G. F., Cheng P. S., Zhu P. Z., "Flora of China," Vol. 20, Science Press, Beijing, 1982, p. 77.
2) Xiao P. G., "Modern Chinese Materia Medica," Vol. 3, Chemical Industry Press, Beijing, 2002, pp. 195—199.
3) Cao C. M., Peng Y., Shi Q. W., Xiao P. G., *Chemistry & Biodiversity*, **5**, 219—238 (2008).
4) Cao C. M., Xu L. J., Chen K., Peng Y., Xiao P. G., *China J. Chin. Mater. Med.*, **34**, 1009—1010 (2008).
5) Tih A. E., Tih R. G., Sondengam B. L., Martin M. T., Bodo B., *J. Nat. Prod.*, **53**, 964—967 (1990).
6) Howell H., Malan E., Steenkamp J. A., Brandt E. V., Brand J., *J. Nat. Prod.*, **65**, 769—771 (2002).
7) Birch A. J., Dahl C. J., Pelter A., *Tetrahedron Lett.*, **8**, 481—487 (1967).
8) Ceng A. H., Luo Y. M., *J. Chin. Med. Mater.*, **28**, 292—293 (2005).
9) Kamperdick C., Van N. H., Sung T. V., *Phytochemistry*, **61**, 991—994 (2002).
10) Luo Y. M., Liu A. H., Yu B. W., Kang L. J., Huang L. Q., *Chin. Pharmaceut. J.*, **40**, 1296—1298 (2005).
11) Xu R. S., Ye Y., Zhao W. M., "Chemistry of Natural Products," Science Press, Beijing, 2004, p. 546.
12) Botha J. J., Young D. A., Ferreira D., Roux D. G., *J. Chem. Soc., Perkin Trans. 1*, **1981**, 1213—1219 (1981).
13) Barrett M. W., Klyne W., Scopes P. M., Fletcher A. C., Porter L. J., Haslam E., *J. Chem. Soc., Perkin Trans. 1*, **1979**, 2375—2377 (1979).
14) He H. Q., Ma X. H., Liu B., Chen W. Z., Wang C. X., Cheng S. H., *Acta Pharmacol. Sin.*, **29**, 397—404 (2008).