Flavonoids from *Daphne aurantiaca* and Their Inhibitory Activities against Nitric Oxide Production

Shuang LIANG,[a,b] Jun-Mian TIAN,[c] Yi FENG,[b] Xiao-Hua LIU,[c] Zhi XIONG,[b] and Wei-Dong ZHANG*,[a,c]

[a] *School of Pharmacy, Shanghai Jiaotong University; Shanghai 200240, P.R. China:* [b] *Shanghai University of Traditional Chinese Medicine Engineering Research Center of Modern Preparation Technology of TCM, Ministry of Education; Shanghai 201203, P.R. China: and* [c] *Department of Natural Product Chemistry, School of Pharmacy, Second Military Medical University; Shanghai 200433, P.R. China.*

Received October 11, 2010; accepted January 17, 2011; published online February 22, 2011

Chemical examination of the methanolic extract from the stem bark of *Daphne aurantiaca* led to the isolation of three new flavonoids (1—3), and 29 known flavonoids. All 32 compounds were isolated for the first time from *Daphne aurantiaca*. The isolates were tested for inhibitory activities against lipopolysaccharide (LPS)-induced nitric oxide (NO) production in RAW 264.7 macrophages. Compounds 21 and 24 showed potent inhibitory activities against the production of NO with IC_{50} values of 0.006 and 0.076 μM, respectively.

Key words *Daphne aurantiaca*; flavonoid; RAW 264.7 macrophage; nitric oxide

Daphne aurantiaca DIELS is a common evergreen shrub native to Yunnan, and Sichuan provinces in China. Its stem bark is used for the treatment of injuries from falls and bruises in folk medicine.[1)] A literature search revealed no previous phytochemical studies on this plant. In the course of our study on the constituents of thymelaeaceous plants,[2—5)] three new flavonoids, compounds **1**—**3**, together with 29 known flavonoids, were isolated from the titled plant. This paper concerned with the structural elucidation of compounds **1**—**3** and inhibitory activities of 32 compounds against lipopolysaccharide (LPS)-induced nitric oxide (NO) production in macrophages.

The EtOAc-soluble fraction of the methanolic extract from the stem bark of *D. aurantiaca* was subjected to column chromatography over silica gel, RP-18, and Sephadex LH-20 in various solvent systems to afford three new flavonoids (Fig. 1) and 29 known flavonoids. By comparing physical and spectroscopic data with reported data, the 29 known compounds were identified as chamaechromone (**4**),[6)] neochamaejasmin B (**5**),[7)] neochamaejasmin A (**6**),[7)] 7-methoxy neochamaejasmin A (**7**),[8)] daphnodorin A (**8**),[9,10)] daphnodorin B (**9**),[9,10)] daphnodorin C (**10**),[10,11)] dihydrodaphnodorin B (**11**),[12)] daphnodorin I (**12**),[13)] daphnodorin J (**13**),[12)] afzelechin (**14**),[14)] epiafzelechin (**15**),[15,16)] farrerol (**16**),[17)] naringenin (**17**),[18)] sakuranetin (**18**),[19)] sakuranin (**19**),[20)] genkwanin (**20**),[21)] apigenin (**21**),[22)] kaempferol (**22**),[23)] luteolin (**23**),[24)] Chrysoeriol (**24**),[25)] 7,4′-dimethyl-ether-luteolin (**25**),[21)] luteolin-5-*O*-β-glucoside (**26**),[26)] 5,7,4′-trihydroxy-3′-methoxyflavone (**27**),[27)] diosmetin (**28**),[28)] 5,3′,4′-trihydroxy-7-methoxyflavone (**29**),[29)] genk wanin-5-*O*-β-glucopyranoside (**30**),[29)] luteolin-7-methyl-ether-5-*O*-β-D-glucoside (**31**),[30)] and yuankanin (**32**).[31)] The structures of the new compounds were determined by spectroscopic methods.

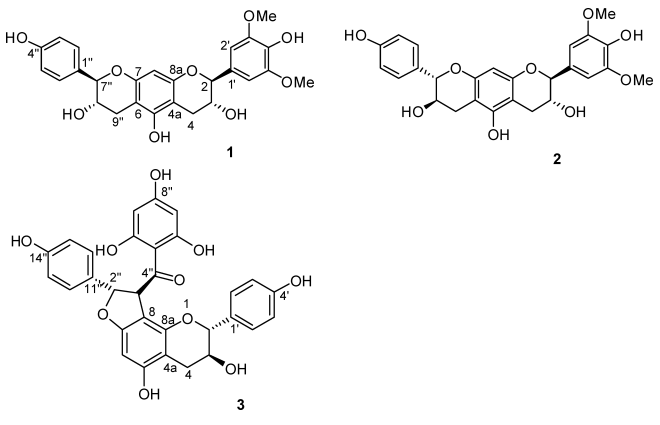

Fig. 1. The Structures of Compounds **1**—**3**

Daphnotin A (**1**) was assigned the molecular formula $C_{26}H_{26}O_9$ by high resolution-electrospray ionization-mass spectra (HR-ESI-MS) ($[M-H]^-$ at *m/z* 481.1518). In the ^{1}H-NMR spectrum, four protons at δ_H 4.58 (1H, d, J=7.2 Hz, H-2), δ_H 4.01 (1H, m, H-3), δ_H 2.51 (1H, dd, J=7.6, 16.0 Hz, H-4α), and δ_H 2.87 (1H, dd, J=5.2, 16.0 Hz, H-4β) indicated a typical flavan-3-ol moiety. Four additional protons at δ_H 4.71 (1H, d, J=7.2 Hz, H-7″), 4.01 (1H, m, H-8″), 2.55 (1H, dd, J=7.6, 16.0 Hz, H-9″α) and 2.84 (1H, dd, J=5.2, 16.0 Hz, H-9″β) exhibited the presence of a second flavan-3-ol moiety. Two singlets at δ_H 6.68 (2H, s) and two *O*-methyl groups [δ_H 3.82 (6H, s)] indicated the existence of a 4-hydroxy-3,5-dimethoxyphenyl ring. A pair of A_2X_2 aromatic protons at δ_H 7.19 (2H, d, J=8.8 Hz) and δ_H 6.77 (2H, d, J=8.8 Hz) indicated the existence of a 4-hydroxyphenyl ring. The ^{1}H-NMR spectrum also showed another aromatic proton at δ_H 5.99 (1H, s, H-8). The NMR spectra of **1** (Table 1) were very similar to those of 5-methoxy-2,8-bis-(3,4-dimethoxyphenyl)-2,3-*cis*-7,8-*trans*-3,4,6,7-tetrahydro-2*H*,8*H*-pyrano[2,3-*f*]-chromene, which was obtained in 1999 by chemical synthesis,[32)] except for the signals of *O*-methyl groups. The relative configuration of **1** was obtained through an analysis of coupling constants and the nuclear Overhauser effect spectroscopy (NOESY) spectrum. H-2, H-3, H-7″, and H-8″ were determined to be β-, α-, α-, and β-oriented, respectively, based on the coupling constant ($^3J_{H\text{-}2,\,H\text{-}3}$=7.2 Hz, $^3J_{H\text{-}7'',\,H\text{-}8''}$=7.2 Hz), and the NOE correlation of MeO(3′)/H(3″) (Fig. 2). Thus, compound **1** was deduced, and named daphnotin A.

Daphnotin B (**2**) had the molecular formula $C_{26}H_{26}O_9$ as deduced by HR-ESI-MS ($[M-H]^-$ at *m/z* 481.1518). The NMR data of **2** (Table 1) were very similar to those of daph-

* To whom correspondence should be addressed. e-mail: wdzhangy@hotmail.com

© 2011 Pharmaceutical Society of Japan

notin A (**1**), and the same planar structure as that of **1** was deduced from the heteronuclear single quantum coherence (HSQC), heteronuclear multiple bond connectivity (HMBC), and ^{1}H, ^{1}H–correlation spectroscopy (COSY) data of **2**, which suggested that **2** would be a diastereoisomer of **1**. The relative configuration of **2** was obtained through analysis of coupling constants ($^{3}J_{\text{H-2, H-3}}$=7.2 Hz, $^{3}J_{\text{H-7}'', \text{H-8}''}$=7.2 Hz). Thus, compound **2** was deduced, and named daphnotin B.

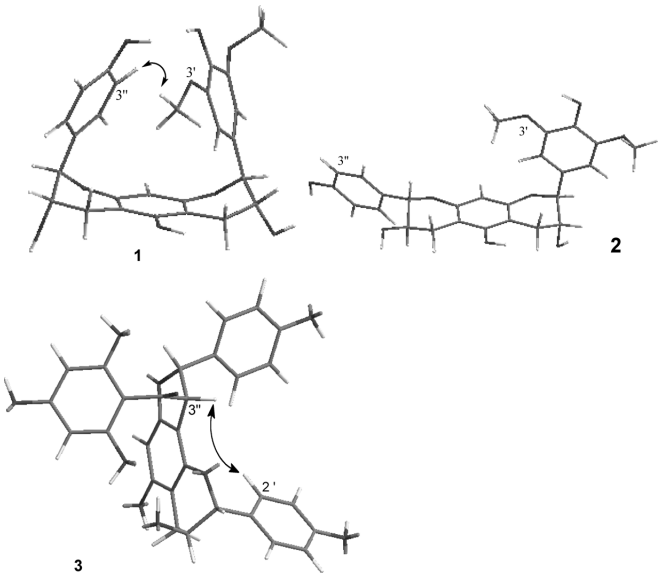

Fig. 2. Minimize Energy Calculation for Compounds **1**—**3** by Chembio 3D Ultra (Version 11.0), and Key NOESY Correlations

3″-epi Dihydrodaphnodrin B (**3**) had the molecular formula $C_{30}H_{24}O_{10}$ as deduced by HR-ESI-MS ($[M+Na]^{+}$ at *m/z* 567.1239). In the ^{1}H-NMR spectrum, two pairs of aromatic protons with A_2B_2 patterns (δ_H 7.11 (2H, d, *J*=8.4 Hz), and δ_H 6.69 (2H, d, *J*=8.4 Hz); δ_H 7.17 (2H, d, *J*=8.4 Hz), and δ_H 6.74 (2H, d, *J*=8.4 Hz)) indicated the presence of two 1,4-disubstituted aromatic rings, and two AX coupling aromatic protons (δ_H 5.82 (1H, br s), and δ_H 5.78 (1H, br s)) indicated established a 1,2,3,5-tetrasubstituted aromatic ring. In addition, the NMR data of **3** (Table 1) showed signals assignable to a carbonyl (δ_C 205.8 (C-4″)), three oxygenated CH groups (δ_C 82.4 (C-2), δ_C 68.7 (C-3) and δ_C 90.8 (C-2″)), a CH group (δ_C 58.9 (C-3″)), and a CH_2 group (δ_C 29.2 (C-4)). The NMR spectra were very closely related to those of known dihydrodaphnodrin B (**11**),[12] and had the same planar structure as that of dihydrodaphnodrin B due to analysis of the ^{1}H-detected heteronuclear multiple quantum coherence (HMQC), HMBC, and ^{1}H, ^{1}H–COSY data, which suggested that **3** may be a diastereoisomer of dihydrodaphnodrin B. The relative configuration of **3** was obtained through analysis of

Table 1. ^{1}H- and ^{13}C-NMR Spectral Data for **1**—**3** (δ in ppm, *J* in Hz, in CD_3OD)

Carbon	**1**		**2**		**3**	
	δ_C	δ_H	δ_C	δ_H	δ_C	δ_H
2	82.7	4.58 d (7.2)	82.5	4.72 d (7.2)	82.4	4.54 d (7.8)
3	68.9	4.01 m	68.7	4.03 m	68.7	3.98 m
4	29.0	2.51 dd (7.6, 16.0)	28.6	2.53 dd (7.6, 6.0)	29.2	2.90 dd (15.6, 5.4)
		2.87 dd (5.2, 16.0)		2.87 dd (7.6, 2.0)		2.56 dd (15.6, 7.8)
4a	102.0		102.0		101.8	
5	155.6		155.7		165.6	
6	100.9		100.7		91.1	5.99 s
7	154.0		153.9		166.5	
8	96.0	5.99 s	96.1	5.99 s	106.9	
8a	154.6		154.6		161.4	
1′	131.3		131.4		131.1	
2′	105.8	6.68 s	105.3	6.65 s	129.3	7.11 d (8.4)
3′	149.2		149.2		116.1	6.69 d (8.4)
4′	136.5		136.3		158.3	
5′	149.2		149.2		116.1	6.69 d (8.4)
6′	105.8	6.68 s	105.3	6.65 s	129.3	7.11 d (8.4)
1″	158.4		158.5			
2″	116.1	7.19 d (8.8)	116.2	7.19 d (8.8)	90.8	5.66 d (5.4)
3″	129.3	6.77 d (8.8)	129.4	6.76 d (8.8)	58.9	5.90 d (5.4)
4″	131.6		131.5		205.8	
5″	116.1	6.77 d (8.8)	116.2	6.76 d (8.8)	105.9	
6″	129.3	7.19 d (8.8)	129.4	7.19 d (8.8)	158.4	
7″	83.2	4.71 d (7.2)	82.9	4.65 d (7.2)	97.1	5.82 br s
8″	68.7	4.01 m	68.7	4.03 m	157.9	
9″	28.6	2.55 dd (7.6, 16.0)	28.4	2.55 dd (7.6, 6.0)	96.0	5.78 br s
		2.84 dd (5.2, 16.0)		2.84 dd (7.6, 2.0)		
10″					157.9	
11″					134.1	
12″					128.5	7.17 d (8.4)
13″					115.9	6.74 d (8.4)
14″					152.4	
15″					115.9	6.74 d (8.4)
16″					128.5	7.17 d (8.4)
2′-OCH_3	56.8	3.82 s	56.8	3.78 s		
6′-OCH_3	56.8	3.82 s	56.8	3.78 s		

coupling constants and the NOESY spectrum. H-2, H-3, H-2″, and H-3″ were determined to be β, α, α, β-oriented, respctively, on the basis of the coupling constants of H-2 and H-3 (J=7.8 Hz), and of H-2″ and H-3″ (J=5.4 Hz), and the NOE correlation of H-2′/H-3″. Consequently, compound **3** was named 3″-epi dihydrodaphnodrin B.

Twenty five isolates were tested for inhibitory activities against LPS-induced NO production in RAW 264.7 macrophages, expert for compounds **8**—**13** and **5**, which had been reported in the our previous paper about *Daphne feddei* level.[5] Compounds **21** and **24** showed potent inhibitory activities against the production of NO with IC_{50} values of 0.006 and 0.076 μM, respectively.

Nitric oxide (NO) plays an important role in inflammatory process,[33] therefore, the inhibition of NO release may be considered as a therapeutic agent in the inflammatory diseases.[34] Our investigation showed that compounds **21** and **24** strongly inhibited nitric oxide release, and possibly become the potential nitric oxide synthase inhibitors.

Experimental

Optical rotations were acquired with a Perkin-Elmer 341 polarimeter, whereas UV spectra were obtained by using a Shimadzu UV-2550 UV–vis spectrophotometer. IR spectra were recorded on a Bruker Vector 22 spectrometer with KBr pellets. NMR spectra were recorded on a Bruker Avance 400 NMR spectrometer with TMS as interal standard. HR-ESI-MS were measured using a Q-TOF micro mass spectrometer (Waters, Millford, MA, U.S.A.). Materials for column chromatography were silica gel (100—200 mesh; Huiyou Silica Gel Development Co., Ltd., Yantai, People's Republic of China), silica gel H (10—40 μm; Yantai), Sephadex LH-20 (40—70 μm; Amersham Pharmacia Biotech AB, Uppsala, Sweden), and YMC-gel ODS-A (50 μm; YMC, Allentown, PA, U.S.A.). Preparative TLC (0.4—0.5 mm) was conducted with glass precoated silica gel GF_{254} plates (Yantai).

Plant Material The plant material was collected in July 2006 in Lijiang City, Yunnan province, People's Republic of China, and identified as *Daphne aurantiaca* by Prof. Li-Shan Xie of Kunming Institute of Botany. A voucher specimen has been deposited in the Herbarium of the School of Pharmacy, Second Military Medical University, Shanghai (No. 200607-11).

Extraction and Isolation The air-dried and powdered stem bark of *D. aurantiaca* (6.5 kg) was extracted with methanol for 3×2 h. The solvent was evaporated under vacuum. Then the extract was suspended in water and partitioned with petroleum ether (10 l×3), EtOAc (10 l×3) and *n*-butanol (10 l×3) successively. EtOAc extract (400 g) was subjected to CC on silica gel (200—300 mesh, 1000 g) eluted successively with gradient $CHCl_3$–MeOH mixtures of increasing polarity and separated into six fractions (F_1—F_6). Fraction F_2 was rechromatographed on silica gel with $CHCl_3$–MeOH (1—2%) and separated into nine fractions ($F_{2\text{-}1}$—$F_{2\text{-}9}$). $F_{2\text{-}4}$ was rechromatographed on octadecylsilan (ODS) (CH_3OH–H_2O, 10 : 100—100 : 0) followed by Sephadex LH-20 with $CHCl_3$–MeOH (1 : 1) to give compounds **1** (25 mg), **2** (30 mg), **22** (380 mg) and **23** (30 mg). By the same procedures, compound **4** (200 mg) were obtained from $F_{2\text{-}6}$; compound **24** (18 mg) was obtained from $F_{2\text{-}7}$. Fraction F_4 was rechromatographed on silica gel with $CHCl_3$–MeOH (4—10%) and separated into seven fractions ($F_{4\text{-}1}$—$F_{4\text{-}7}$). $F_{4\text{-}2}$ was rechromatographed on ODS (CH_3OH–H_2O, 10 : 100—100 : 0) followed by Sephadex LH-20 with MeOH to give compounds **3** (250 mg), **5** (140 mg), **6** (110 mg), **7** (80 mg) and **30** (140 mg). By the same procedures, compounds **8** (70 mg), **9** (100 mg), **10** (300 mg), **27** (100 mg) and **29** (120 mg) were obtained from $F_{4\text{-}3}$; compound **11** (110 mg) were obtained from $F_{4\text{-}4}$; compounds **15** (10 mg) and **25** (20 mg) were obtained from $F_{4\text{-}6}$. Fraction F_5 was rechromatographed on ODS (CH_3OH–H_2O, 10 : 100—100 : 0) and separated into four fractions ($F_{5\text{-}1}$—$F_{5\text{-}4}$). $F_{5\text{-}1}$ was rechromatographed on silica gel with $CHCl_3$–MeOH (10—25%) followed by Sephadex LH-20 with MeOH to give compounds **12** (2 g), **14** (150 mg), **16** (8 mg) and **18** (50 mg), **19** (17 mg). By the same procedures, compounds **20** (15 mg), **21** (30 mg), **26** (18 mg), **28** (80 mg) and **31** (130 mg) were obtained from $F_{5\text{-}2}$; compounds **13** (15 mg), **17** (120 mg) and **32** (20 mg) were obtained from $F_{5\text{-}3}$.

Compound **1**: Pale yellow viscous oil (MeOH), $[\alpha]_D^{18}$ −25 (c=0.11, MeOH); UV (MeOH): 275 (2.11); IR (KBr) cm^{-1}: 3028, 2969, 2944, 1738, 1612, 1450, 1366, 1217, 1115, 528; ^{1}H- and ^{13}C-NMR spectroscopic data, see Table 1; negative HR-ESI-MS Found 481.1518, Calcd 481.1499 for $C_{26}H_{25}O_9$ $[M-H]^-$.

Compound **2**: Pale yellow viscous oil (MeOH), $[\alpha]_D^{18}$ −13 (c=0.13, MeOH); UV (MeOH): 275 (1.97); IR (KBr) cm^{-1}: 3015, 2967, 2923, 1739, 1619, 1456, 1382, 1217, 1115, 522; ^{1}H- and ^{13}C-NMR spectroscopic data, see Table 1; negative HR-ESI-MS Found 481.1518, Calcd 481.1499 for $C_{26}H_{25}O_9$ $[M-H]^-$.

Compound **3**: Brown oil (MeOH), $[\alpha]_D^{19}$ −32 (c=0.28, MeOH); UV (MeOH): 289 (3.73); IR (KBr) cm^{-1}: 3333, 2922, 1699, 1615, 1517, 1454, 1231, 1089, 832, 654, 527; ^{1}H- and ^{13}C-NMR spectroscopic data, see Table 1; positive HR-ESI-MS Found 567.1239, Calcd 567.1267 for $C_{30}H_{24}O_{10}Na$ $[M+Na]^+$.

Assay for Inhibitory Ability against LPS-Induced NO Increase in RAW 264.7 Macrophages RAW 264.7 macrophages were seeded in 24-well plates (10^5 cells/well). The cells were co-incubated with drugs and LPS (1 μg/ml) for 24 h. The amount of NO was assessed by determining the nitrite concentration in the cultured RAW 264.7 macrophage supernatants with Griess reagent. Aliquots of supernatants (100 μl) were incubated, in sequence, with 50 μl 1% sulphanilamide and 50 μl 0.1% naphthyl ethylene diamine in 2.5% phosphoric acid solution. The absorbance at 570 nm was read using a microtiter plate reader. Results are expressed as means±S.D. Statistical analysis was performed using Student's t-test, and $p<0.05$ was considered significant. Inhibition (%) was calculated using the following equation and IC_{50} values were determined graphically (n=4).[35,36]

$$\text{inhibition (\%)} = [(A-B)/(A-C)] \times 100$$

[A: LPS (+), sample (−); B: LPS (+), sample (+); C: LPS (−), sample (−)]

Acknowledgment The work was supported by program NCET Foundation, NSFC (30725045), the Special Program for New Drug Innovation of the Ministry of Science and Technology, China (2009ZX09311-001, 2008ZX09308-005), Shanghai Leading Academic Discipline Project (B906) and in part by the Scientific Foundation of Shanghai China (09DZ1975700, 09DZ1971500).

References

1) Gu C. Z., "Flora Reipubicae Popularis Sinicae," Vol. 52, Science Press, Beijing, 1999, pp. 361—364.
2) Liang S., Shen Y. H., Feng Y., Tian J. M., Liu X. H., Xiong Z., Zhang W. D., *J. Nat. Prod.*, **73**, 532—535 (2010).
3) Liang S., Shen Y. H., Tian J. M., Wu Z. J., Jin H. Z., Zhang W. D., Yan S. K., *J. Nat. Prod.*, **71**, 1902—1905 (2008).
4) Liang S., Shen Y, H., Tian J. M., Wu Z. J., Jin H. Z., Zhang W. D., Yan S. K., *Helv. Chim. Acta*, **92**, 133—138 (2009).
5) Liang S., Tang J., Shen Y. H., Jin H. Z., Tian J. M., Wu Z. J., Zhang W. D., Yan S. K., *Chem. Pharm. Bull.*, **56**, 1729—1731 (2008).
6) Niwa M., Liu G. Q., Tatematsu H., Hirata Y., *Tetrahedron Lett.*, **25**, 3735—3738 (1984).
7) Niwa M., Tatematsu H., Liu G. Q., Hirata Y., *Chem. Lett.*, **13**, 539—542 (1984).
8) Baomin F., Yuehu P., Huiming H., *J. Asian Nat. Prod. Res.*, **4**, 259—263 (2002).
9) Baba K., Takeuchi K., Doi M., Masatoshi T., Inoue M., Kozawa M., *Chem. Pharm. Bull.*, **34**, 1540—1545 (1986).
10) Baba K., Takeuchi K., Hamasaki F., Kozawa M., *Chem. Pharm. Bull.*, **33**, 416—419 (1985).
11) Baba K., Takeuchi K., Doi M., Kozawa M., *Chem. Pharm. Bull.*, **34**, 2680—2683 (1986).
12) Taniguchi M., Fujiwara A., Baba K., *Phytochemistry*, **45**, 183—188 (1997).
13) Taniguchi M., Baba K., *Phytochemistry*, **42**, 1447—1453 (1996).
14) Hong C., Mingkui W., *Chin. J. Appl. Environ. Biol.*, **5**, 103—105 (1999).
15) Waterman P. G., Faulkner D. F., *Planta Med.*, **37**, 178—179 (1979).
16) Xinan W., Yimin Z., *China J. Chin. Mater. Med.*, **30**, 443—444 (2005).
17) Yuanyuan Z., Dong W., Feng G., *Med. Mater. Med. Res.*, **18**, 2641—2642 (2007).
18) Heba H. B., Ahmed M. S., Sahar A. H. Ola A. I., Mahmoud A. N., *Phytochemistry*, **51**, 139—142 (1999).
19) Kodama O., Miyakawa J., Akatsuka T., Kiyosawa S., *Phytochemistry*, **31**, 3807—3809 (1992).
20) Martin G., Walter F., *Phytochemistry*, **30**, 1519—1521 (1991).
21) Honggang W., Minhua Z., Jingjing L., Boyang Y., *Chem. Ind. Forest*

Prod., **28**, 1—5 (2008).
22) Sinha N. K., Seth K. K., Pandey V. B., Dasgupta B., Shah A. H., *Planta Med.*, **42**, 296—298 (1981).
23) Jianguang L., Lingyi K., *China J. Chin. Mater. Med.*, **30**, 516—518 (2005).
24) Guido F., Elena A., Ivano M., *Phytochemistry*, **57**, 559—564 (2001).
25) Neeraj K., Bikram S., Pamita B. Ajai P. G., Sanjay K. U., Vijay K. K., *Phytochemistry*, **66**, 2740—2744 (2005).
26) Haiyong C., Changxin Z., Yijia L., Zhihong D., Yu Z., *China J. Chin. Mater. Med.*, **30**, 1589—1591 (2005).
27) Guangtong C., Huiyuan G., Jian Z., Bin W., Xiaoke Y., Lijun W., *China J. Chin. Mater. Med.*, **31**, 560—562 (2006).
28) Timmermann B. N., Mues R., Mabry T. J., Powell A. M., *Phytochemistry*, **18**, 1855—1858 (1979).
29) Markus V., Hans G., Franz C., Kenneth R. M., *Phytochemistry*, **29**, 2555—2559 (1990).
30) Ayhan U., Roland B. R., Tom J. M., *Phytochemistry*, **21**, 801—803 (1982).
31) Sloan A., Deborah L. Z., Kenneth M., Joanne S. P., Christine M. B., Terry M., Robert B., Seef P., Dennis S., Donald T., Sheo B., *Phytochemistry*, **69**, 541—545 (2008).
32) Hongxiang L., Yoshimitsu Y., Tsutomu S., Masaru U., Hideoki T., Syuichi O., *Phytochemistry*, **51**, 297—308 (1999).
33) Moncada S., Palmer R. M., Higgss E. A., *Pharmacol. Rev.*, **43**,109—142 (1991).
34) Anggard E., *Lancet*, **343**,1199—1206 (1994).
35) Su-Mei L., Xian-Wen Y., Yun-Heng S., Lin F., Yue-Hu W., Hua-Wu Z., Xiao-Hua L., Jun-Mian T., Ya-Na S., Chun-Lin L., Wei-Dong Z., *Phytochemistry*, **69**, 2200—2204 (2008).
36) Xian-Wen Y., Su-Mei L., Lin F. C., Yun-Heng S., Jun-Mian T., Xiao-Hua L., Hua-Wu Z., Chuan Z., Wei-Dong Z., *Tetrahedron*, **64**, 4354—4362 (2008).