Bioorganic & Medicinal Chemistry Letters 21 (2011) 3261–3267

Contents lists available at ScienceDirect

Bioorganic & Medicinal Chemistry Letters

journal homepage: www.elsevier.com/locate/bmcl

Phenolic compounds with NF-κB inhibitory effects from the fungus *Phellinus baumii*

Chang-Sheng Wu [a], Zhao-Min Lin [a], Li-Ning Wang [a], Dong-Xiao Guo [a], Shu-Qi Wang [a], Yong-Qing Liu [a], Hui-Qing Yuan [b], Hong-Xiang Lou [a,*]

[a] Department of Natural Products Chemistry, School of Pharmaceutical Sciences, Shandong University, 44 West Wenhua Road, Jinan 250012, People's Republic of China
[b] Department of Biochemistry and Molecular Biology, School of Medicine, Shandong University, 44 West Wenhua Road, Jinan 250012, People's Republic of China

ARTICLE INFO

Article history:
Received 24 January 2011
Revised 18 March 2011
Accepted 8 April 2011
Available online 13 April 2011

Keywords:
Fungus
Phellinus baumii
NF-κB
Hispidin
Benzyl dihydroflavones
HPLC–CD

ABSTRACT

Chemical investigation of the fungus *Phellinus baumii* has resulted in characterization of five previously undescribed hispidin derivatives, phellibaumins A–E (**1**–**5**), as well as two pairs of new non-equivalent epimeric benzyl dihydroflavones, methylphelligrin A (**9**), *epi*-methylphelligrin A (**10**), methylphelligrin B (**11**), and *epi*-methylphelligrin B (**12**), together with five known compounds, interfungin B (**6**), phelligridin H (**7**), phelligridimer A (**8**), phelligrin A (**13**), and *epi*-phelligrin A (**14**). Phellibaumin A (**1**) was a novel hispidin derivative with a unique 3,4-dihydroxybenzofuran unit. These compounds exhibited NF-κB inhibitory activity with IC_{50} values of 52.96 μM (**1**), 41.40 μM (**2**), 52.92 μM (**5**), 36.44 μM (**9** and **10**), and 22.46 μM (**11** and **12**), respectively.

Phellinus baumii Pilát, a fungus belonging to the family Hymenochaetaceae, known as 'Forest Gold', preferably hosts on the stems of genus *Prunus*, *Syringa*, *Crataegus*, and other hardwood trees.[1] Its fruiting body has been traditionally used for treatment of gastrointestinal cancer, liver or heart diseases, and stomach ailments in China.[2] Previous chemical investigation of *Phellinus* fungi indicated that they produce a variety of yellowish polyphenols with a styrylpyrone skeleton (hispidin),[3–10] which exhibit antioxidative and free radical scavenging activities.[11–19]

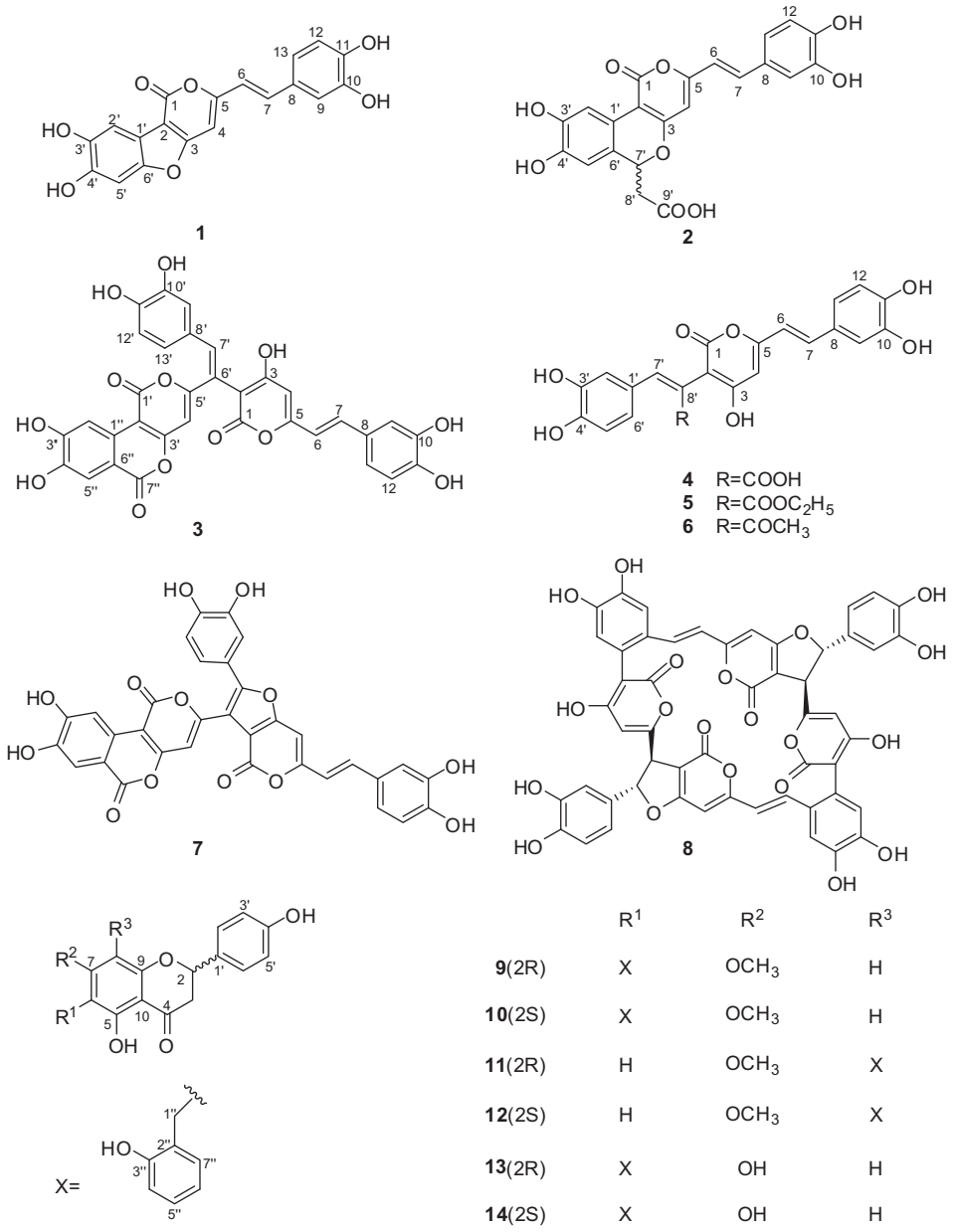
In our ongoing research of natural phenolic compounds,[20,22] chemical investigation on the fruit body of *P. baumii* has led to the characterization of nine new compounds, including five hispidin-derived polyphenols phellibaumins A–E (**1**–**5**) and two pairs of epimeric benzyl dihydroflavones (**9**–**12**), along with five known phenolic compounds (**6**–**8**, **13**, and **14**). The absolute structures of the epimeric benzyl dihydroflavones were determined by HPLC–CD analysis,[21–24] we found these epimeric pairs were non-equivalently present in nature. Inhibitory activities of **1**–**14** against NF-κB have also been tested.

The EtOH extract of the fruit body of the fungus *P. baumii* was evaporated to dryness and then suspended in water followed by partitioned with EtOAc and *n*-butanol, The EtOAc-soluble extract was subjected to column chromatography and semi-preparative HPLC in the reversed phase mode to yield compounds **1**–**14** (Fig. 1).

Compound **1** was obtained as a yellowish amorphous powder. Its molecular formula, $C_{19}H_{12}O_7$, was established by the HRESIMS ion peak at *m/z* 351.1895 $[M-H]^-$ (calcd for $C_{19}H_{11}O_7$, 351.1899). The ^1H NMR spectrum of **1** (Table 1) exhibited signals including a 1,3,4-trisubstituted phenyl moiety at δ_H 7.18 (d, 1H, J = 1.8 Hz, H-9), 7.02 (dd, 1H, J = 8.4, 1.8 Hz, H-13), and 6.86 (d, 1H, J = 8.4 Hz, H-12), a *trans*-disubstituted double bond at δ_H 6.85 and 7.34 (1H each, d, J = 15.6 Hz, H-6 and H-7), three singlet aromatic protons at δ_H 6.91, 7.35, and 7.13 (1H each, s, H-4, H-2′, and H-5′). Its ^{13}C NMR spectrum (Table 1) revealed the presence of 19 sp^2 carbons. The long-range correlations between H-4/C-2 (δ_C 104.4), C-3 (δ_C 163.5), C-5 (δ_C 158.6), and C-6 (δ_C 116.6), H-6/C-4 (δ_C 95.7), C-5, and C-8 (δ_C 127.7), H-7/C-5, C-9 (δ_C 113.6), and C-13 (δ_C 120.6), H-9/C-7 (δ_C 134.6), C-10 (δ_C 145.9), C-11 (δ_C 147.2), and C-13, H-12/C-8 and C-10, H-13/C-7, C-9, and C-11 observed in HMBC determined the hispidin moiety (Fig. 2). Besides the 13 carbons of hispidin, a tetrasubstituted benzene moiety was revealed by the splitting pattern of two methine singlets at δ_H 7.35 (s, H-2′) and 7.13 (s, H-5′). To satisfy the molecular formula $C_{19}H_{12}O_7$ and 14 degrees of unsaturation, a furan ring should exist in **1**, which was further confirmed by the HMBC correlations between H-2′/C-2, C-4′ (δ_C 144.3), and C-6′ (δ_C 149.7), H-5′/ C-1′ (δ_C 114.4), C-3′ (δ_C 145.6). Consequently, the structure of **1** was finally determined as shown and named as phellibaumin A.

* Corresponding author. Tel.: +86 531 88382012; fax: +86 531 88382019.
E-mail address: louhongxiang@sdu.edu.cn (H.-X. Lou).

0960-894X/$ - see front matter © 2011 Elsevier Ltd. All rights reserved.
doi:10.1016/j.bmcl.2011.04.025



	R^1	R^2	R^3
9(2R)	X	OCH_3	H
10(2S)	X	OCH_3	H
11(2R)	H	OCH_3	X
12(2S)	H	OCH_3	X
13(2R)	X	OH	H
14(2S)	X	OH	H

Figure 1. Structures of isolated phenolic compounds (**1**–**14**) from *P. baumii*.

Compound **2**, a yellowish amorphous powder, has a molecular formula $C_{22}H_{16}O_9$ as determined for the *m/z* 423.0704 $[M-H]^-$ in HRESIMS (calcd for $C_{22}H_{15}O_9$, 423.0709). Besides the characteristic signals of a hispidin moiety, the ^1H NMR spectrum of **2** (Table 1) showed two additional aromatic singlets at δ_H 7.90 and 6.61 (1H each, s, H-2′ and H-5′), a methine multiplet at δ_H 5.66 (dd, 1H, J = 4.8, 9.0 Hz, H-7′), two protons at δ_H 2.74 (dd, 1H, J = 9.0, 15.6 Hz, H-8′a) and 2.70 (dd, 1H, J = 4.8, 15.6 Hz, H-8′b) attributable to one methylene group. The ^{13}C NMR (Table 1) and HSQC spectra revealed the presence of 20 sp^2 and 2 sp^3 carbons. The HMBC correlations of the hispidin moiety were consistent with those of **1**. Meanwhile, long-range correlations between H-2′/C-6′ (δ_C 121.3), C-4′ (δ_C 145.2), and C-2 (δ_C 99.5), H-5′/C-1′ (δ_C 116.3), C-3′ (δ_C 145.0), and C-7′ (δ_C 75.1) revealed the presence of a 1,2,4,5-tetrasubstituted phenyl moiety. The oxygen-bearing sp^3 carbon of C-7′ was adjacent to C-6′ and C-8′ (δ_C 40.5), which was assigned by the HMBC correlations between H-7′/C-6′, C-5′ (δ_C 111.8), C-1′, C-8′, and C-3 (δ_C 162.0), H-8′/C-6′ and C-7′, together with COSY correlation between H-7′ and H-8′. A remaining –COOH (δ_C 170.7, C-9′) was unequivocally connected to C-8′, which was further confirmed by the HMBC correlations between H-7′/C-9′ (δ_C 170.7) and H-8′/C-9′. Accordingly, the structure of **2** (phellibaumin B) was finally determined. It is a new hispidin derivative with an undetermined configuration at C-7′.

Compound **3** was an orange, amorphous powder with a molecular $C_{33}H_{20}O_{13}$ as determined by HRESIMS at *m/z* 623.1753 $[M-H]^-$ (calcd for $C_{33}H_{19}O_{13}$, 623.1759). By comparison of its NMR spectra (Table 2) with the known compound **7** (phelligridin H) which was previously isolated from the fungus *Phellinus igniarius*,[15] the main difference was that the furan ring of **7** was opened in **3** as revealed by the presence of an additional methine and absence of an unsaturation in **3**. The final structure of **3** was established by the interpretation of relevant 2D NMR spectra. In the HMBC spectrum, the correlations of the hispidin moiety were consistent with those of **1**. The pyranobenzopyran moiety was assigned by the HMBC correlations between H-4′/C-2′ (δ_C 98.6), C-3′ (δ_C 161.2),

Table 1
^{1}H and ^{13}C NMR Data for **1**, **2**, and **4**

No.	**1**[a]		**2**[b]		**4**[c]	
	δ_C	δ_H (J in Hz)	δ_C	δ_H (J in Hz)	δ_C	δ_H (J in Hz)
1	158.5		159.8		165.0	
2	104.4		99.5		99.5	
3	163.5		162.0		170.2	
4	95.7	6.91 s	100.4	6.34 s	101.9	6.17 s
5	158.6		157.9		159.0	
6	116.6	6.85 d (15.6)	115.7	6.72 d (15.6)	115.8	6.65 d (15.6)
7	134.6	7.34 d (15.6)	134.4	7.19 d (15.6)	135.2	7.35 d (15.6)
8	127.7		126.7		127.4	
9	113.6	7.18 d (1.8)	113.8	7.04 d (1.8)	113.4	7.06 d (1.8)
10	145.9		145.5		144.8	
11	147.2		147.4		147.0	
12	115.5	6.86 d (8.4)	115.7	6.77 d (7.8)	114.7	6.72 d (8.4)
13	120.6	7.02 dd (8.4, 1.8)	120.5	6.97 dd (7.8, 1.8)	120.4	6.96 dd (8.4, 1.8)
1′	114.4		116.3		127.7	
2′	104.8	7.35 s	111.2	7.90 s	115.8	6.98 d (1.8)
3′	145.6		145.0		145.4	
4′	144.3		145.2		147.1	
5′	98.3	7.13 s	111.8	6.61 s	115.2	6.79 d (8.4)
6′	149.7		121.3		123.1	6.85 dd (8.4, 1.8)
7′			75.1	5.66 dd (4.8, 9)	143.3	7.76 s
8′			40.5	2.74 dd (9, 15.6)	120.2	
				2.70 dd (4.8, 15.6)		
9′			170.7		170.8	

[a] Recorded in acetone-d_6.
[b] Recorded in DMSO-d_6.
[c] Recorded in CD_3OD. Proton coupling constants (J) in Hertz are given in parentheses. ^{1}H and ^{13}C NMR were recorded at 600 and 150 MHz, respectively. All chemical shift assignments were done on the basis of 1D and 2D NMR techniques.

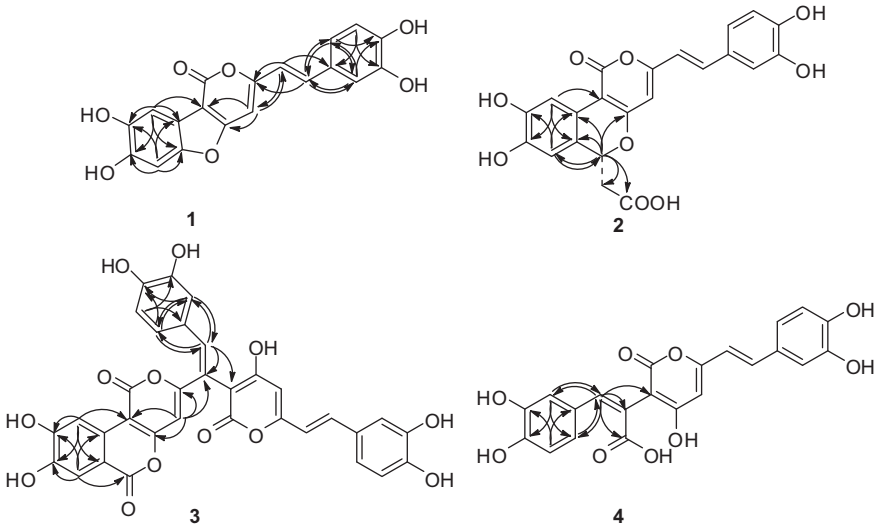


Figure 2. Key HMBC correlations of **1**–**4**.

and C-5′ (δ_C 160.9), H-5″/C-3″ (δ_C 153.6), C-1″ (δ_C 127.8), C-4″ (δ_C 146.7), and C-7″ (δ_C 159.9), H-2″/C-2′ (δ_C 98.6), C-3″, C-4″, and C-6″ (δ_C 111.8) (Fig. 2). The 3,4-dihydroxybenzylidene moiety was unequivocally established by the correlations of H-7′/C-9′ (δ_C 116.1) and C-13′ (δ_C 123.2), H-9′/C-7′ (δ_C 136.8), C-13′, and C-11′ (δ_C 147.0), H-13′/C-9′, C-11′, and C-7′, H-12′/C-8′ (δ_C 127.8), and C-10′ (δ_C 145.3). The linkage of the above three moieties through a quaternary carbon C-6′ at δ_C 120.5 was determined on the basis of the HMBC correlations between H-7′/C-6′, C-5′, and C-2 (δ_C 96.5), and H-4′/C-6′. Although the geometry of the $\Delta^{6',7'}$ double bond has not been established, the proposed biosynthesis of phelligridin H (**7**) suggested the stereochemistry to be *cis*.[15,19] In addition, compared with other protons, the chemical shift of H-7′ (δ_H 7.70) located in comparatively lower magnetic field, partly because of the potential deshielding effect originating from the carbonyl of C-3. Accordingly, the structure of **3** (phellibaumin C) was determined as an analogue of phelligridin H.

The molecular formula of compound **4** was determined to be $C_{22}H_{16}O_9$ by HRESIMS at m/z 423.0714 $[M-H]^-$ (calcd for $C_{22}H_{15}O_9$, 423.0711). ^{1}H and ^{13}C NMR spectra of **4** (Table 1) showed the presence of a hispidin moiety and a caffeic acid moiety. The above-mentioned partial structures were unambiguously connected to each other on the basis of the HMBC correlation between H-7′/C-2 (δ_C 99.5). Therefore, the structure of **4** was assigned as depicted and named phellibaumin D.

The molecular formula of **5** was determined as $C_{24}H_{20}O_9$ by HRESIMS at m/z 451.1019 $[M-H]^-$ (calcd for $C_{24}H_{19}O_9$, 451.1024). It was an ethyl ester of **4** as determined by the addi-

Table 2
^{1}H and ^{13}C NMR data for **3** and **5**[a]

No.	**3**		**5**	
	δ_C	δ_H (J in Hz)	δ_C	δ_H (J in Hz)
1	165.6		165.5	
2	96.5		98.7	
3	171.2		170.2	
4	104.4	6.15 s	103.6	6.10 s
5	159.1		158.5	
6	116.2	6.67 d (15.6)	116.2	6.63 d (15.6)
7	135.0	7.36 d (15.6)	134.7	7.33 d (15.6)
8	128.1		127.8	
9	113.3	7.08 br s	113.2	7.06 d (1.8)
10	144.8		145.3	
11	146.8		146.9	
12	114.8	6.73 d (8.4)	115.1	6.79 d (8.4)
13	120.4	6.98 br d (8.4)	120.3	6.98 dd (8.4, 1.8)
1′	162.0		127.5	
2′	98.6		116.0	7.02 d (1.8)
3′	161.2		144.7	
4′	96.5	6.30 s	147.0	
5′	160.9		114.6	6.70 d (8.4)
6′	120.5		123.3	6.90 dd (8.4, 1.8)
7′	136.8	7.70 s	143.1	7.75 s
8′	127.8		120.2	
9′	116.1	7.07 br s	168.7	
10′	145.3		60.5	4.24 q (7.2)
11′	147.0		13.2	1.31 t (7.2)
12′	115.1	6.80 d (8.4)		
13′	123.2	6.95 br d (8.4)		
1″	127.8			
2″	110.3	8.44 s		
3″	153.6			
4″	146.7			
5″	114.1	7.59 s		
6″	111.8			
7″	159.9			

[a] Recorded in CD_3OD. Proton coupling constants (J) in Hertz are given in parentheses.^{1}H and ^{13}C NMR were recorded at 600 and 150 MHz, respectively. All chemical shift assignments were done on the basis of 1D and 2D NMR techniques.

tional signals at δ_H 4.24 (q, 1H, J = 7.2 Hz, H-10′) and 1.31 (t, J = 7.2 Hz, H-11′) in ^{1}H NMR, along with δ_C 60.5 (C-10′) and 13.2 (C-11′) in the ^{13}C NMR spectrum (Table 2). The long-range HMBC correlation between H-10′/C-9′ (δ_C 168.7) confirmed the ethoxyl linkage at C-9′. It was also a new compound and named as phellibaumin E.

Methylphelligrin A (**9**–**10**) was obtained as a white amorphous powder. Its molecular formula was determined as $C_{23}H_{20}O_6$ by the negative mode HRESIMS $[M-H]^-$ found at m/z 391.2640 (calcd 391.2645). It was a methylated derivative of phelligrin A (**13**–**14**)[10] as determined by comparison of their ^{1}H and ^{13}C NMR spectra (Table 3). A long-range correlation of the methoxyl protons at δ_H 3.88 to C-7 (δ_C 165.8) in the HMBC spectrum also confirmed the conclusion. To investigate the absolute configuration of methylphelligrin A, an on-line chiral HPLC–CD coupling technique was developed. Although the peaks (**9** and **10**) were not well separated with the chiral HPLC–CD at the given condition, one positive signal (**9**) and a negative signal (**10**) in the CD trace were well differentiated (Fig. 3A). The opposite Cotton Effects (CE) as revealed by the CD curves indicated methylphelligrin A was a mixture of a pair of enantiomers with the first peak (**10**) about thirty times larger than the second peak (**9**). In the CD spectrum of **9**, an obvious negative cotton effect (CE) at 340 nm for $n\rightarrow\pi^*$ absorption band and a positive CE at 290 nm for $\pi\rightarrow\pi^*$ absorption band established a *R*-configuration at C-2.[25–27] Meanwhile, compound **10**, the enantiomer of **9**, was 2*S*-configuration, for the positive CE at 340 nm and negative CE at 290 nm (Fig. 3B). Compounds **9** and **10** were named as methylphelligrin A (+) and *epi*-methylphelligrin A (−), respectively.

Methylphelligrin B (**11** and **12**), a white amorphous powder, possessed the same molecular formula as methylphelligrin A for the ion $[M-H]^-$ at m/z 391.2635 (calcd 391.2641) found in HRESIMS. The ^{1}H and ^{13}C NMR spectrometric data (Table 3) resembled those of methylphelligrin A as well. However, in the HMBC spectrum, the long-range correlations between H-1″/C-7 (δ_C 166.7), C-8 (δ_C 107.7), and C-9 (δ_C 160.5) determined the linkage of *ortho*-

Table 3
^{1}H and ^{13}C NMR data of compounds **9**–**12**[a]

No.	**9** and **10**			**11** and **12**	
	δ_C	δ_H (J in Hz)	HMBC	δ_C	δ_H (J in Hz)
2	79.4	5.52 dd (13.2, 3.0)	1′, 2′, 6′	79.7	5.48 dd (12.0, 3.0)
3	42.5	3.26 dd (16.8, 13.2)	4, 10	43.4	3.19 dd (17.4, 12.0)
		2.78 dd (16.8, 3.0)	2, 4, 1′		2.84 dd (17.4, 3.0)
4	197.1			198.1	
5	160.2			164.1	
6	107.5			93.2	6.22 s
7	165.8			166.7	
8	91.3	6.24 s	6, 7, 9, 10	107.7	
9	162.4			160.5	
10	102.6			103.7	
1′	129.8			130.7	
2′	128.2	7.43 br d (8.4)	2, 4′, 6′	128.8	7.30 br d (8.4)
3′	115.3	6.92 br d (8.4)	1′, 4′, 5′	116.1	6.83 br d (8.4)
4′	157.9			158.6	
5′	116.2	6.94 br d (8.4)	1′, 3′, 4′	116.1	6.85 br d (8.4)
6′	129.1	7.45 br d (8.4)	2, 2′, 4′	128.8	7.32 br d (7.8)
1″	21.4	3.87 s	5,6,7,2″,3″,7″	22.8	3.88 s
2″	126.5			127.5	
3″	155.0			155.8	
4″	114.9	6.81 br d (7.8)	2″,6″	115.6	6.78 br d (8.4)
5″	126.7	6.98 m	3″,7″	127.4	6.97 m
6″	119.2	6.67 m	2″,4″	120.1	6.66 m
7″	128.9	6.87 br d (7.8)	3″,5″	129.7	6.81 br d (7.2)
7-OCH_3	55.7	3.88 s	7	56.6	3.87 s

[a] Recorded in acetone-d_6. Proton coupling constants (J) in Hertz are given in parentheses. ^{1}H and ^{13}C NMR were recorded at 600 and 150 MHz, respectively. All chemical shift assignments were done on the basis of 1D and 2D NMR techniques.

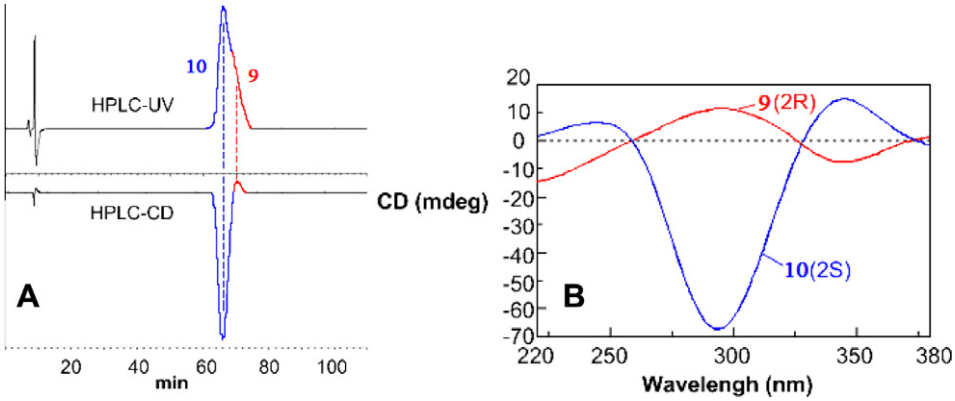


Figure 3. HPLC–UV and HPLC–CD analysis of methylphelligrin A using a chiral phase and assignment of the absolute configurations of methylphelligrin A by CD spectrum.

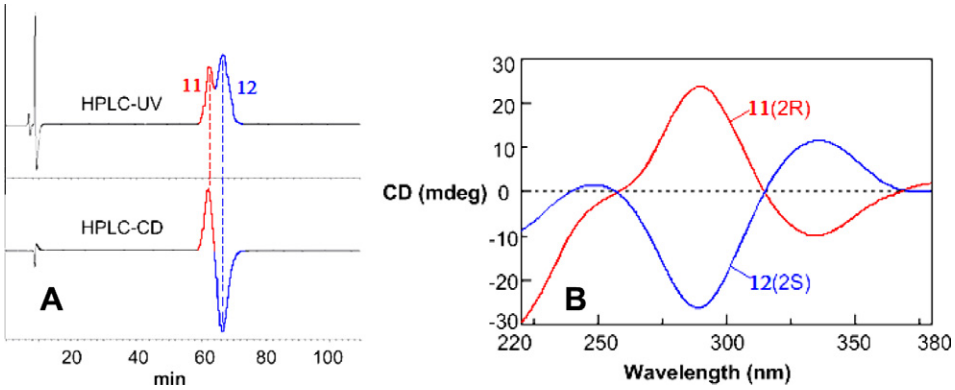


Figure 4. HPLC–UV and HPLC–CD analysis of methylphelligrin B using a chiral phase and assignment of the absolute configurations of methylphelligrin B by CD spectrum.

disubstituted phenyl moiety at C-8 through a methylene other than C-6 (δ_C 93.2). Again, separation of methylphelligrin B with the chiral HPLC–CD coupling technique provided one positive peak (**11**) and a negative peak (**12**) in the CD trace with two opposite CD curves. The ratio of quantity of **11** and **12** was nearly 5:6 according to the area of respective peak (Fig. 4A). A negative CE at 340 nm and a positive CE at 290 nm in the on-line measured CD determined a 2*R*-configuration for methylphelligrin B (**11**) while the opposite CD determined a 2*S*-configuration for *epi*-methylphelligrin B (**12**) (Fig. 4B).

Phelligrin A (**13** and **14**) was a known compound, however, its C-2 absolute configuration had not been determined.[10] The chiral HPLC–CD separated two peaks, a positive one (**13**) and a negative one (**14**) in the CD trace, corresponding to two enantiomers with the ratio of **13**:**14** nearly 1:2 (Fig. 5A). The negative CE at 340 nm and a positive CE at 290 nm in the CD spectrum determined **13** was 2*R*-configuration and named phelligrin A while the opposite CD data determined **14** (*epi*-phelligrin A) to be 2*S*-configuration (Fig. 5B).

The mushrooms belonging to *Phellinus* and *Inonotus* produce a wide variety of hispidin derivatives possessing unprecedented carbon skeletons. These compounds were proposed to be biogenerated by the oxidative coupling of the precursor hispidin with phenolic compounds or additional hispidins catalyzed by peroxidase.[8–18] Based on the previous postulated biogenetic pathway of hispidin class compounds,[8–13,15–18] we proposed the plausible

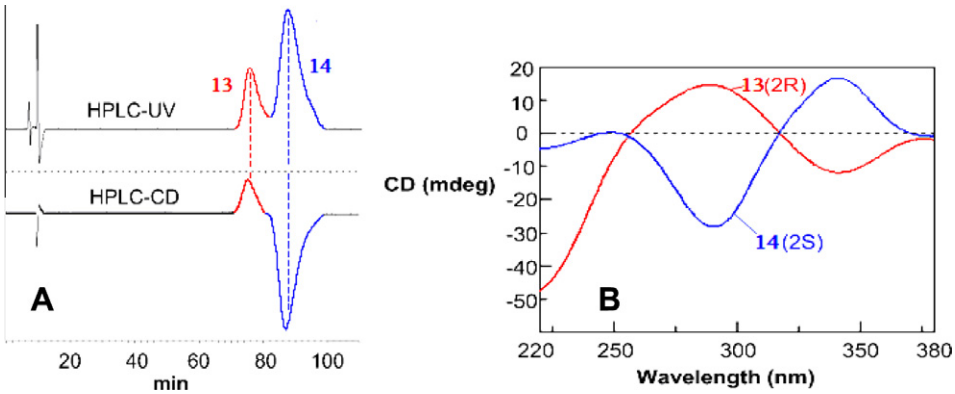
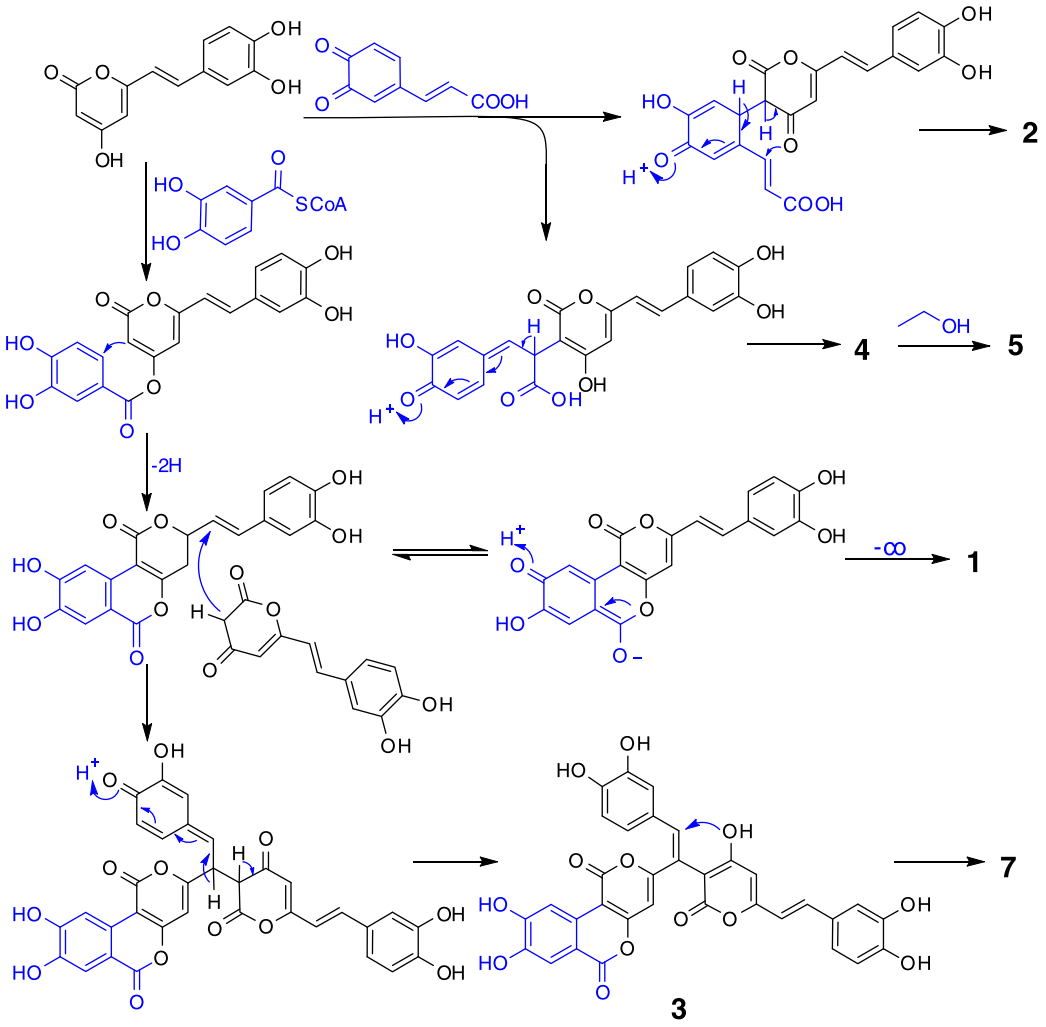


Figure 5. HPLC–UV and HPLC–CD analysis of phelligrin A using a chiral phase and assignment of the absolute configurations of phelligrin A by CD spectrum.



Scheme 1. Proposed biogenesis of phellibaumins A–E.

biogenesis of phellibaumins A–E (**1**–**5**) (Scheme 1). Phellibaumins B and D may be both formed by coupling between a molecule of hispidin and a molecule of activated caffeic acid, but different oxidative styles result in two disparate compounds. Further coupling of phellibaumin D with ethanol generates phellibaumin E. Phellibaumin C is supposed to be just the precursor of phelligridin H,[15] which has actually been deduced by a previous review.[19] Phellibaumin A may be derived from the decarboxylation of phelligridin D.[11]

The transcriptional activator, nuclear factor kappa-B (NF-κB) has gained much attention as an inhibitor of apoptosis because NF-κB regulated genes are involved in tumor cell proliferation and metastasis. Therefore, intercepting NF-κB signaling might be an attractive antitumor approach.[28] NF-κB has been shown to be constitutively activated in human androgen independent prostate cancer cell lines and contribute to the progression of prostate cancer.[29] Effects of dihydroflavones and hispidin derivatives from *P. baumii* on NF-κB activation in prostate cancer cells were examined in a luciferase gene reporter assay. PC-3 cells, an androgen-insensitive cell line, are IKKs (inhibitor of NF-κB kinases) aberrant with high basal activities of NF-κB.[30] Treatment of PC-3 cells with desired compounds (**1**–**14**) decreased the basal NF-κB activity in a dose-dependent manner except that of phelligridimer A (**8**) (Table 4). In addition, we treated androgen-sensitive LNCaP cells with phelligrin A, methylphelligrins A and B, resulting in the inhibition of NF-κB activity in response to LPS stimulation, an activator for NF-κB activation. The result indicated that pretreatment of cells with phelligrin A, methylphelligrins A and B substantially inhibited LPS-induced NF-κB activation. Phelligrin A displayed a dose-dependent reduction in reporter activity by 18.4%, 29.4%, and 81.5% at the desired concentrations, methylphelligrin A by 35.0%, 84.2%, and 85.8%, and methylphelligrin B by 62.5%, 63.5%, and 70.8%, respectively. These preliminary bioassay data indicated that the phenolics in *P. baumii* play an important role in blocking both LPS-induced and constitutive NF-κB activity in human prostate cancer cells.

Table 4
Inhibitory effects of compounds **1**–**14** on NF-κB activation in PC-3 cells

Compound	IC_{50} (μM)
1	52.96 ± 2.26
2	41.40 ± 1.46
3	62.28 ± 4.31
4	74.62 ± 2.38
5	52.92 ± 0.21
6	71.19 ± 1.99
7	84.90 ± 1.11
8	—*
9, **10**	36.44 ± 2.11
11, **12**	22.46 ± 2.04
13, **14**	54.50 ± 1.02

* No inhibition.

Acknowledgments

Financial support from the Shandong Provincial Funds (Nos. JQ 200806, Y2006C38, and 06GG1102023) is gratefully acknowledged.

Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.bmcl.2011.04.025.

References and notes

1. Zhang, X. Q.; Dai, Y. C. In *Flora Fungorum Sinicorum (Zhongguo Zhenjun Zhi)*; Science Press: Beijing, 2005; Vol. 29,
2. Zeng, N. K.; Wang, Q. Y.; Su, M. S. *Edible Fungi of China* **2008**, *27*, 56.
3. Chang, Z. Q.; Oh, B. C.; Rhee, M. H.; Kim, J. C.; Lee, S. P.; Park, S. C. *World J. Microbiol. Biotechnol.* **2007**, *23*, 723.
4. Ge, Q.; Zhang, A.; Sun, P. *Food Chem.* **2009**, *114*, 391.
5. Jang, B. S.; Kim, J. C.; Bae, J. S.; Rhee, M. H.; Jang, K. H.; Song, J. C. *Biotechnol. Lett.* **2004**, *26*, 31.
6. Shon, M. Y.; Kim, T. H.; Sung, N. J. *Food Chem.* **2003**, *82*, 593.
7. Nagatsu, A.; Tanaka, R. *Tetrahedron Lett.* **2004**, *45*, 5931.
8. Min, B. S.; Yun, B. S.; Lee, H. K. *Bioorg. Med. Chem. Lett.* **2006**, *16*, 3255.
9. Mo, S. Y.; Yang, Y. C.; He, W. Y.; Shi, J. G. *Chin. Chem. Lett.* **2003**, *14*, 704.
10. Mo, S. Y.; He, W. Y.; Yang, Y. C.; Shi, J. G. *Chin. Chem. Lett.* **2003**, *14*, 810.
11. Mo, S. Y.; Wang, S. J.; Yang, Y. C.; Chen, X. G.; Shi, J. G. *J. Nat. Prod.* **2004**, *67*, 823.
12. Wang, Y.; Mo, S. Y.; Wang, S. J.; Li, S.; Yang, Y. C.; Shi, J. G. *Org. Lett.* **2005**, *7*, 1675.
13. Wang, Y.; Wang, S. J.; Mo, S. Y.; Li, S.; Yang, Y. C.; Shi, J. G. *Org. Lett.* **2005**, *7*, 4733.
14. Wang, Y.; Wang, S. J.; Mo, S. Y.; Li, S.; Yang, Y. C.; Shi, J. G. *Chin. Chem. Lett.* **2006**, *17*, 481.
15. Wang, Y.; Shang, X. Y.; Wang, S. J.; Mo, S. Y.; Li, S.; Yang, Y. C.; Ye, F.; Shi, J. G. *J. Nat. Prod.* **2007**, *70*, 296.
16. Lee, I. K.; Han, M. S.; Lee, M. S.; Kim, Y. S.; Yun, B. S. *Bioorg. Med. Chem. Lett.* **2010**, *20*, 5459.
17. Lee, I. K.; Jung, J. Y.; Seok, S. J.; Kim, W. G.; Yun, B. S. *Bioorg. Med. Chem. Lett.* **2006**, *16*, 5621.
18. Lee, I. K.; Yun, B. S. *Bioorg. Med. Chem.* **2007**, *15*, 3309.
19. Zhou, Z. Y.; Liu, J. K. *Nat. Prod. Rep.* **2003**, *20*, 615.
20. Yu, B. B.; Han, X. Z.; Lou, H. X. *J. Agric. Food Chem.* **2007**, *55*, 7753.
21. Bringmann, G.; Muhlbacher, J.; Reichert, M.; Dreyer, M.; Kolz, J.; Speicher, A. *J. Am. Chem. Soc.* **2004**, *126*, 9283.
22. Ren, D. M.; Guo, H. F.; Wang, S. Q.; Lou, H. X. *J. Chromatogr., A* **2007**, *1161*, 334.
23. Bringmann, G.; Messer, K.; Saeb, W.; Peters, E. M.; Peters, K. *Phytochemistry* **2001**, *56*, 387.
24. Zhu, J. J.; Zhang, C. F.; Zhang, M.; Annie Bligh, S. W.; Yang, L.; Wang, Z. M.; Wang, Z. T. *J. Chromatogr., A* **2010**, *1217*, 5384.
25. Caccamese, S.; Caruso, C.; Parrinello, N.; Savarino, A. *J. Chromatogr., A* **2005**, *1076*, 155.
26. Slade, D.; Ferreira, D.; Marais, J. P. J. *Phytochemistry* **2005**, *66*, 2177.
27. Ren, D. M.; Guo, H. F.; Yu, W. T.; Wang, S. Q.; Ji, M.; Lou, H. X. *Phytochemistry* **2008**, *69*, 1425.
28. Karin, M.; Yamamoto, Y.; Wang, Q. M. *Nat. Rev. Drug Discovery* **2004**, *3*, 17.
29. Luo, J. L.; Tan, W.; Ricono, J. M.; Korchynskyi, O.; Zhang, M.; Gonias, S. L.; David, A.; Cheresh, D. A.; Michael Karin, M. *Nature* **2007**, *446*, 690.
30. Gasparian, A. V.; Yao, Y. J.; Kowalczyk, D.; Lyakh, L. A.; Karseladze, A.; Slaga, T. J.; Budunova, I. V. *J. Cell Sci.* **2002**, *115*, 141.