Available online at www.sciencedirect.com
SCIENCE DIRECT®
Bioorganic & Medicinal Chemistry 12 (2004) 4387–4392
Bioorganic & Medicinal Chemistry

Antibacterial prenylflavone derivatives from *Psoralea corylifolia*, and their structure–activity relationship study

Sheng Yin, Cheng-Qi Fan, Ying Wang, Lei Dong and Jian-Min Yue*

State Key Laboratory of Drug Research, Institute of Materia Medica, Shanghai Institutes for Biological Sciences, Chinese Academy of Sciences, 555 Zu Chong Zhi Road, Zhangjiang Hi-Tech Park, Shanghai 201203, PR China

Received 21 May 2004; revised 10 June 2004; accepted 10 June 2004
Available online 2 July 2004

Abstract—Three new prenylflavonoids, namely corylifols A–C (**1**–**3**), together with 13 known ones, were isolated from the seeds of *Psoralea corylifolia*. Their structures were elucidated by spectral methods including 1D and 2D NMR techniques. All the isolates were tested on antibacterial assays, and nine of them showed significant antibacterial activities against two pathogenic bacteria *Staphylococcus aureus* and *S. epidermidis*. The antibacterial structure–activity relationship of these prenylflavonoids (**1**–**16**) was also briefly discussed.

1. Introduction

The seeds of *Psoralea corylifolia* L. (Fabaceae), a well-known traditional Chinese medicine, are widely applied for the cure of gynaecological bleeding, vitiligo and psoriasis. A number of chemical constituents including coumarins, flavonoids and meroterpene phenols were isolated from this plant, and some of which exhibited antibacterial, antitumour, broadening coronary artery and estrogen-like activities.[1] There were also several reports on antioxidative,[2] antiplatelet,[3] DNA polymerase and topoisomerase II inhibition[4] and osteoblastic proliferation stimulating[5] activities of the plant extracts or its constituents in later years. Quite recently, a simple flavonoid, 4′-methoxy flavone, from this plant was reported to display antifungal activities,[6] and a few coumarins of this plant were showed antibacterial activities.[7] During our antibacterial screening programme, the ethanol extract of the seeds of *P. corylifolia* showed remarkable growth inhibitory effects against two major hospital pathogenic bacteria, *Staphylococcus aureus* and *S. epidermidis*. This extract, when examined by TLC, proved to contain bakuchiol, a meroterpene phenol, which was initially isolated from this plant and reported as an antibacterial agent.[8] After removal of bakuchiol and some fatty acids by column chromatography in a small scale sample, the remained part of this extract showed more strong antibacterial activity, inferring that the antibacterial components of this plant are more than bakuchiol. The ethanolic extract was then partitioned with petroleum ether and ethyl acetate successively to yield two major antibacterial fractions PE and EA, respectively. The fraction PE contained mainly bakuchiol, while the fraction EA mainly contained prenylflavone derivatives (also a small amount of bakuchiol). An antibacterial bioassay-guided fractionation and purification of the EA fraction were then carried out. In addition to the isolation of a series of potent antibacterial prenylflavone derivatives, some other inactive analogous were also collected and tested for the antibacterial SAR discussion. Herein, we present the isolation and structural elucidation of three new flavonoids corylifols A–C (**1**–**3**), along with thirteen known compounds **4**–**16** isolated from the seeds of *P. corylifolia*. This paper also dealt with the antibacterial evaluation of all the isolates against *S. aureus* ATCC 25923 and *S. epidermidis* ATCC 12228 in vitro, and a brief antibacterial SAR discussion. Among the tested compounds, nine of them **2**, **4**–**10** and **16** showed significant antibacterial activities against the tested microbes at the level of MICs 0.009–0.073 mM.

Keywords: *Psoralea corylifolia*; Fabaceae; Corylifols A–C; Antibacterial activity; Structure–activity relationship.
* Corresponding author. Tel./fax: +86-21-50806718; e-mail: jmyue@mail.shcnc.ac.cn

0968-0896/$ - see front matter © 2004 Elsevier Ltd. All rights reserved.
doi:10.1016/j.bmc.2004.06.014

2. Results and discussion

2.1. Structural elucidation of three new compounds

Compound **1**, obtained as a light yellow amorphous powder, showed the molecular formula as $C_{25}H_{26}O_4$ determined by HREIMS at m/z 390.1833 $[M]^+$ (calculated 390.1831). Its ^1H NMR spectrum indicated the signals of two 1,3,4-trisubstituted benzene rings and a typical proton signal at δ 8.08 (s) assignable for the H-2 of isoflavonoid. Comparison of its ^1H and ^{13}C NMR spectral data (Table 1) with those of a known compound neobavaisoflavone (**4**),[9] which also isolated from this plant showed a characteristic 3′-alkyl-4′,7-dihydroxyisoflavone features. A typical geranyl moiety of 3″,7″-dimethyl-octa-2″,6″-dienyl was also inferred by its ^1H and ^{13}C NMR spectral data. In the NOESY spectrum of **1** (Fig. 2), an aromatic proton signal at δ 7.32 (d, $J = 1.8$ Hz) correlated with H-2 was assigned to H-2′, which was correlated with the proton signals at δ 3.34 (2H, d, $J = 7.0$ Hz) attributable to the H_2-1″ of the geranyl moiety, suggesting that the geranyl moiety was attached to C-3′. In the HMBC spectrum (Table 1), the strong correlation between H_2-1″ and the carbon signal at δ 128.30 assignable to C-3′ confirmed the linkage of the geranyl moiety. On the basis of above evidences, compound **1** was elucidated to be 4′,7-dihydroxy-3′-geranylisoflavone, namely corylifol A as showed in Figure 1. The ^1H and ^{13}C NMR spectral data were completely assigned (Table 1) by extensive analysis of its 1D and 2D NMR (^1H, ^{13}C NMR, NOESY, HMQC and HMBC) spectra.

Compound **2** was obtained as a brown amorphous powder. The molecular formula of **2** was arranged to be $C_{20}H_{20}O_5$ by HREIMS at m/z 340.1315 $[M]^+$ (calculated 340.1311). Analysis of its ^1H and ^{13}C NMR spectral data (Table 2) revealed a typical feature of chalcone analogues comprising of one 1,3,4-trisubstituted benzene ring, one 1,2,3, 4-tetrasubstituted benzene ring and a prenyl moiety. Comparison of its ^1H and ^{13}C NMR spectral data with those of a known compound isobavachalcone (**5**) also obtained in the current research, showed that the only difference was presence of one more hydroxyl at C-3′ in compound **2**. The prenyl moiety was linked to the C-3 by the correlation between the H_2-1″ (δ 3.37, 2H, d, $J = 7.1$ Hz) and C-3 at δ 115.28 in the HMBC spectrum. Two hydroxyls at C-3′,4′ were confirmed by the coupling patterns of the 1,3,4-trisubstituted benzene ring and the correlations of H-c at δ 7.77 (d, $J = 15.4$ Hz) with H-2′ (δ 7.35, d, $J = 1.9$ Hz) and H-6′ (δ 7.22, dd, $J = 1.9$, 8.2 Hz) in its NOESY spectrum (Fig. 2). Compound **2** was therefore determined to be 3′-hydroxyisobavachalcone, namely corylifol B, as shown in Figure 1.

Compound **3** was obtained as a yellow amorphous powder. The molecular formula of **3** was determined as $C_{20}H_{18}O_5$ by HREIMS at m/z 338.1161 $[M]^+$ (calculated 338.1154). In the ^1H NMR spectrum (Table 2), the coupling patterns and the chemical shifts of the most protons were quite similar to those of compound **2**, except for the presence of a singlet proton signal at δ 6.64 (H-3) in **3** instead of the two *trans*-olefinic proton signals (H-b and H-c) of **2**, indicating that **3** was a flavone, which probably derived from compound **2** by the formation of an ether bond between the C-8a and C-2 in **3**. Comparison of the molecular formulae of compounds **2** and **3**, compound **3** showed two mass units less than that of compound **2**, supporting the assumption made above. Two hydroxyl groups at C-3′ and C-4′ were deduced by NOESY correlations of H-3 with H-2′ (δ 7.60, d, $J = 2.0$ Hz) and H-6′ (δ 7.42, dd, $J = 2.0$, 8.3 Hz) in its NOESY spectrum (Fig. 2). The location of the prenyl group at C-8 was validated by the correlation between two protons signal of H_2-1″ (δ 3.56, 2H, d, $J = 7.4$ Hz) and the carbon signal of C-8 at δ 114.02 in the HMBC spectrum. The structure of compound **3** was thus elucidated as 8-prenyl-3′,4′,7-trihydroxyflavone, namely corylifol C (Fig. 1).

2.2. Structural identification of known compounds

Among the known compounds, isobavachalcone (**5**), bavachin (**9**) and bavachinin (**10**) were identified by direct comparison with authentic samples (co-TLC, ^1H NMR, MS); bavachalcone (**8**), whose structure was determined previously in the literature[11] by chemical correlation, but no spectral data are available up to now, was identified by spectroscopic method in the current research and the spectral data was thus reported

Table 1. ^1H, ^{13}C NMR data and key HMBC correlations of corylifol A (**1**)[a]

	^{13}C	^1H	HMBC		^{13}C	^1H	HMBC
2	153.05	8.08, s		5′	115.29	6.88, d, 8.3	
3	125.46		H-2, 2′, 6′	6′	128.30	7.25, dd, 1.8, 8.3	H-2′, 5′
4	176.01		H-2, 5	1″	28.81	3.34, d, 7.0	H-2′, 2″
4a	118.17		H-6, 8	2″	123.57	5.40, t-like, 7.0	H-1″, 4″, 10″
5	128.30	8.03, d, 8.7		3″	136.24		H-1″, 10″
6	115.71	6.96, dd, 2.1, 8.7	H-8	4″	40.41	2.02, m	H-2″, 6″
7	163.56		H-5, 6, 8	5″	27.30	2.09, m	H-4″, 6″
8	102.93	6.85, d, 2.2	H-6	6″	125.04	5.08, t-like, 6.9	H-5″, 8″, 9″
8a	158.81		H-5, 8	7″	131.66		H-5″, 8″, 9″
1′	124.15		H-2, 5′	8″	17.64	1.55, s	H-6″, 9″
2′	130.96	7.32, d, 1.8	H-6′	9″	25.69	1.57, s	H-6″, 8″
3′	128.30		H-2′, 5′, 1″	10″	16.14	1.72, s	H-2″, 4″
4′	155.74		H-2′, 5′, 6′, 1″				

[a] Measured in acetone-d_6, δ in parts per million, J in hertz.

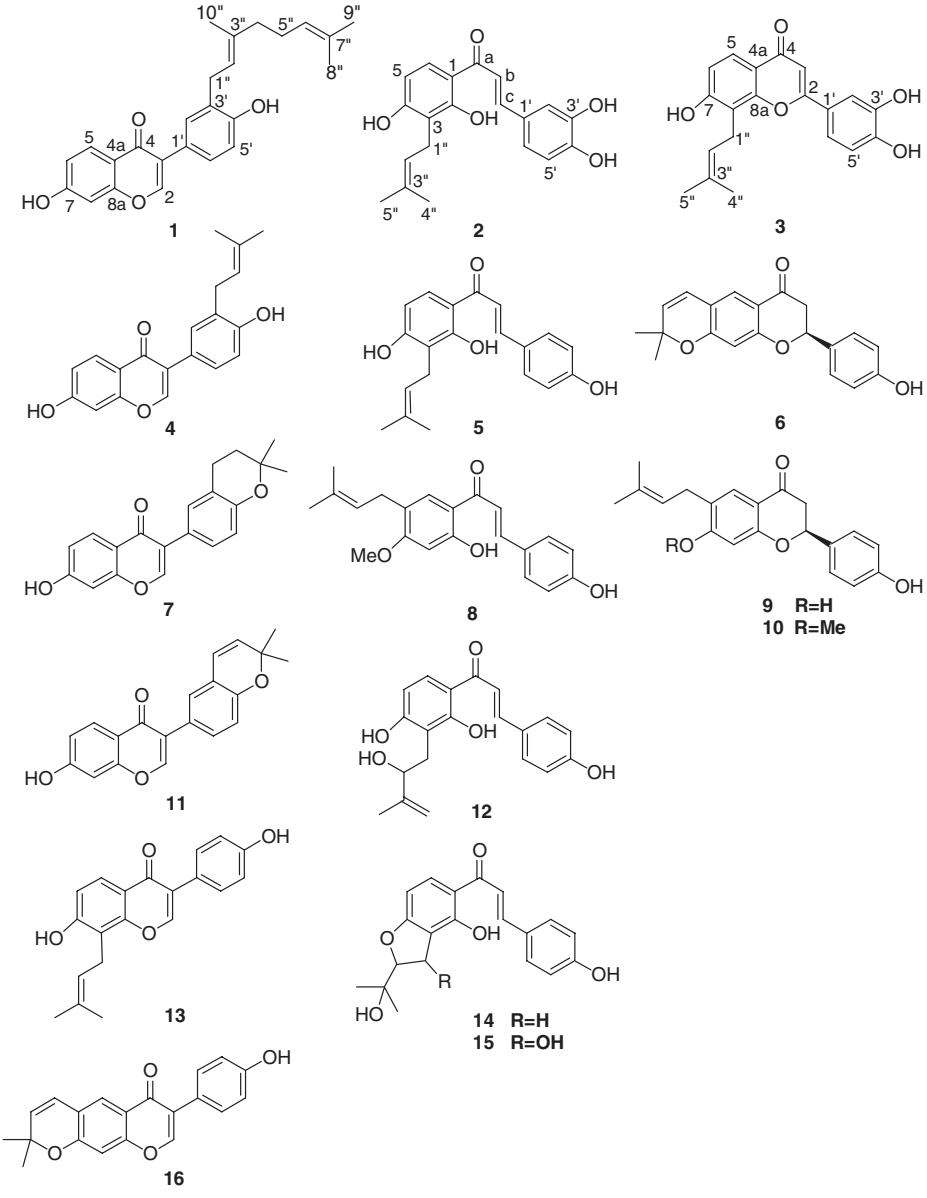

Figure 1. Structures of compounds **1**–**16**.

in the experimental part; neobavaisoflavone (**4**),[9] 7, 8-dihydro-8-(4-hydroxyphenyl)-2,2-dimethyl-2H,6H-benzo[1,2-*b*:5,4-*b*′]dipyran-6-one (**6**),[10] isoneobavaisoflavone (**7**),[9] corylin (**11**),[12] 1-[2, 4-dihydroxy-3-(2-hydroxy-3-methyl-3-butenyl)phenyl]-3-(4-hydroxyphenyl)-2-propen-1-one (**12**),[13] 8-prenyldaidzein (**13**),[14] bakuchalcone (**14**),[15] brosimacutin G (**15**)[16] and erythrinin A (**16**)[17] were identified by comparison of their spectral data (^{1}H, ^{13}C NMR, MS, $[\alpha]_D$) with those reported. Four of these compounds, **12**, **13**, **15** and **16** were isolated from this plant for the first time.

2.3. Antibacterial evaluation of all the isolates and their antibacterial SAR discussion

All isolates were assayed for the antibacterial activities against two hospital pathogenic Gram-positive bacteria *S. aureus* ATCC 25923 and *S. epidermidis* ATCC 12228 in vitro. Two most potential natural antibacterial agents, bakuchiol[8] and magnolol,[18] were used as positive controls in this tests. Among the tested compounds, nine of them **2**, **4**–**10** and **16** showed significant antimicrobial activities against *S. aureus* and *S. epidermidis* at the level of MICs 0.009–0.073 mM (Table 3). Compounds **2**, **4**, **6**, **8** and **9** showed comparable antibacterial activities as that of the positive controls, bakuchiol and magnolol. Compounds **5**, **10** and **16** were even stronger than that of two well-known natural antimicrobial agents, bakuchiol and magnolol (their MICs are twofold lower than that of positive controls).

Observation of antibacterial results of compounds **1**–**16** and their structural features has inferred some regular patterns of structure–activity relationship, which are: (1) For the chalcone derivatives **2**, **5**, **8**, **12**, **14** and **15**, the compounds, such as **2**, **5** and **8**, with a prenyl group at the A-ring are more active; if the prenyl group at A-ring

Table 2. ^{1}H and ^{13}C NMR data of corylifols B (**2**) and C (**3**)

	2[a]			**3**[a]	
	^{13}C	^{1}H		^{13}C	^{1}H
a	192.11		2	146.70	
b	117.77	7.70, d, 15.4	3	112.26	6.64, s
c	144.62	7.77, d, 15.4	4	182.48	
1	113.57		4a	114.02	
2	162.18		5	118.30	7.46, d, 8.4
3	115.28		6	122.86	6.82, d, 8.4
4	163.86		7	163.39	
5	107.40	6.53, d, 8.8	8	112.26	
6	129.58	7.98, d, 8.8	8a	165.99	
1′	127.35		1′	124.78	
2′	115.08	7.35, d, 1.9	2′	115.83	7.60, d, 2.0
3′	145.68		3′	145.56	
4′	148.54		4′	147.58	
5′	115.69	6.91, d, 8.2	5′	111.83	6.95, d, 8.3
6′	122.68	7.22, dd, 1.9, 8.2	6′	124.66	7.42, dd, 2.0, 8.3
1″	21.91	3.37, d, 7.1	1″	22.19	3.56, d, 7.4
2″	122.68	5.28, t-like, 7.1	2″	121.55	5.41, t-like, 7.4
3″	130.76		3″	132.11	
4″	17.56	1.78, s	4″	17.74	1.88, s
5″	25.50	1.64, s	5″	25.48	1.68, s
2-OH		14.0, s			

[a] Measured in acetone-d_6, δ in parts per million, J in hertz.

Table 3. Antibacterial activities of compounds **1**–**16**

Compounds and controls	MICs (mM)[a]	
	S. aureus ATCC 25923	*S. epidermidis* ATCC 12228
1	0.147	0.147
2	0.037	0.037
3	>0.147	>0.147
4	0.037	0.037
5	0.018	0.009
6	0.037	0.037
7	0.073	0.037
8	0.037	0.018
9	0.037	0.037
10	0.018	0.018
11	>0.147	>0.147
12	>0.147	>0.147
13	>0.147	>0.147
14	>0.147	>0.147
15	>0.147	>0.147
16	0.018	0.018
Bakuchiol	0.037	0.018
Magnolol	0.037	0.018

[a] MIC was defined as the lowest concentration that inhibited visible growth.

is oxygenated/and further cyclized, the compounds, such as **12**, **14** and **15**, become inactive; the compound **2** with an additional hydroxyl group at C-3′ showed remarkable attenuation of the antibacterial activities (2–4-folds lower) compared with compound **5** with only C-4′ hydroxyl group. (2) For the prenylflavone derivatives **3**, **6**, **9** and **10**, three dihydro flavone derivatives **6**, **9** and **10** displayed strong antibacterial activities; Compound **10** with a 7-methoxy group showed more stronger activities than that of **9** with a 7-hydroxy group. (3) For the prenylisoflavone derivatives **1**, **4**, **7**, **11**, **13** and **16**, because their structures are so diversified, the patterns of structure–activity relationship are difficult to sum up.

2.4. Conclusion

In conclusion, three new prenylflavonoids corylifols A–C (**1**–**3**) and thirteen known prenylflavone derivatives were isolated from the seeds of *P. corylifolia*. All the isolates were tested on antibacterial assays, and some of the prenylflavone derivatives described in this work are markedly potent in vitro test against two pathogenic bacteria *S. aureus* and *S. epidermidis*. The antimicrobial activities of compounds **5**, **10** and **16** were even stronger than that of two well-known natural antimicrobial agents, bakuchiol and magnolol. The prenylflavone derivatives are one major class of constituents of *P. corylifolia*, especially compounds **1**, **5** and **8**–**10** with high contents in the seeds. Antibacterial test results of compounds **1**–**16** and their structural features have inferred some regular patterns of structure–activity relationship.

3. Experimental section

3.1. General

Optical rotations were recorded on a Perkin–Elmer polarimeter 341. UV spectra were measured on a Varian Cary 300 BIO spectrometer. IR spectra were made on a Nicolet Magna 750 spectrometer with KBr discus. NMR spectra were obtained on a Brucker AM-400 MHz spectrometer. General ^{1}H NMR data were run at 400 MHz, and ^{13}C NMR data were measured at

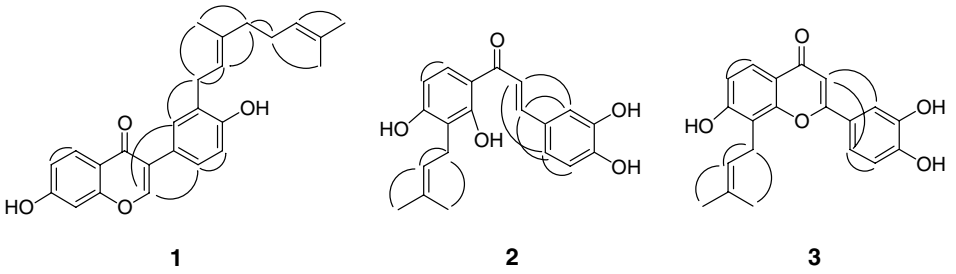

Figure 2. Key NOE correlations of compounds **1**–**3**.

100.6 MHz. Chemical shifts are expressed in parts per million relative to TMS. EIMS and ESIMS were recorded with a Finnigan MAT 95 and Finnigan LCQ^{DECA} Mass spectrometers, respectively.

3.2. Plant material

The seeds of *P. corylifolia* were collected in September 1999 from farm cultivation in Anhui Province of China, which was authenticated by Professor Zeng-Tao Wang of Shanghai Traditional Chinese Medical University. A voucher specimen has been deposited in the Herbarium of Shanghai Institute of Materia Medica (Accession number Pc-1999-1Y), Shanghai Institutes for Biological Sciences, Chinese Academy of Sciences, PR China.

3.3. Extraction and isolation

The powder of dried seeds of *P. corylifolia* (2.0 kg) was extracted with 95% EtOH for three times to give 592 g crude extract. 392 g of the extract was suspended in 2.5 L water and then partitioned with petroleum ether and ethyl acetate successively to give fractions PE (143 g), EA (120 g) and W (81.5 g), respectively.

EA fraction (100 g) was subjected to column chromatography (CC) on silica gel eluted with a gradient of acetone in petroleum ether to yield fractions **1**–**9** monitored by TLC tests. Fractions **1**–**4** (total 46 g) contained three major constituents, including bakuchiol and two coumarins, psoralen and isopsoralen, identified by co-TLC with authentic samples. Fraction **5** (4.5 g) was re-chromatographed on silica gel eluted with $CHCl_3$ and $CHCl_3$–MeOH (60:1) to give fractions **5a**–**e** and a pure compound **10** (670 mg). Fraction **5e** (0.12 g) was passed through Sephadex LH-20 eluted with EtOH, and then purified to yield **11** (67 mg) by CC on a silica gel column eluted with $CHCl_3$–MeOH (40:1). Fraction **6** (11 g) was subjected to CC of silica gel eluted with petroleum ether–EtOAc (6:1 → 1:1) to obtain six fractions **6a**–**f**. Compound **5** (1.6 g) was obtained from fraction **6d** (2.4 g) by recrystallization in MeOH, and it was found to be major compound in other three fractions **6b** (1.1 g), **6c** (2.2 g) and **6e** (1.4 g) by TLC tests. Compounds **16** (53 mg), **6** (18 mg), **10** (136 mg) and **8** (235 mg) were isolated from fraction **6a** (0.82 g) by CC on silica gel eluted with petroleum ether–$CHCl_3$ (1:2 → 1:8), $CHCl_3$ and $CHCl_3$–MeOH (40:1), successively. Fraction **6f** (1.2 g) was chromatographed on a column of MCI GEL CHP 20P eluted with MeOH/H_2O (60% → 100%) to yield a crude compound **1** (0.65 g) and a mixture (0.22 g). Compound **1** (460 mg) was further purified by CC of silica gel eluted with petroleum ether–acetone (2:1), and the mixture was subjected to CC of silica gel eluted with petroleum ether–isopropanol (15:1 and 10:1) to give three compounds **7** (37 mg), **4** (82 mg) and **14** (42 mg). Fraction **7** (4.3 g) was separated over a column of MCI GEL CHP 20P eluted with MeOH/H_2O (60% → 100%) to give a crude product of compound **5** (1.2 g) and four fractions **7a**–**d**. Fraction **7a** (0.92 g) was purified by a column of Sephadex LH-20 eluted with EtOH to obtain the major part, which was then purified to yield **9** (340 mg) by CC of silica gel eluted with $CHCl_3$–MeOH (40:1). Fraction **7b** (0.51 g) was separated by a column of Sephadex LH-20 eluted with EtOH to give a pure compound **2** (32 mg) and a mixture, which was further purified to yield compound **13** (43 mg) by CC of a silica gel eluted with $CHCl_3$–MeOH (20:1). Compound **12** (87 mg), compounds **3** (39 mg) and **15** (12 mg) were obtained from fraction **7c** (0.32 g) by CC of Sephadex LH-20 eluted with EtOH to collect the major fraction, which was then purified on a column of silica gel eluted with $CHCl_3$–MeOH (30:1 → 15:1).

3.3.1. Corylifol A (1). Light yellow amorphous powder. UV (MeOH) λ_{max} (lg ε) 249 (4.44) nm; IR (KBr disc) ν_{max} 3346, 2914, 1624, 1590, 1580, 1508, 1456, 1379, 1269, 1240, 1200, 1097 cm^{-1}; HREIMS m/z 390.1833 $[M]^+$ (calcd for $C_{25}H_{26}O_4$, 390.1831); EIMS m/z (rel int.) 390 ($[M]^+$, 28), 375 (2), 347 (10), 321 (36), 268 (100), 137 (24); ^1H and ^{13}C NMR data: see Table 1.

3.3.2. Corylifol B (2). Brown amorphous powder. UV (MeOH) λ_{max} (lg ε) 377 (4.47) nm; IR (KBr disc) ν_{max} 3365, 3168, 2921, 1693, 1627, 1606, 1544, 1506, 1446, 1373, 1259, 1234, 1111, 1043 cm^{-1}; HREIMS m/z 340.1315 $[M]^+$ (calcd for $C_{20}H_{20}O_5$, 340.1311); EIMS m/z (rel int.) 340 ($[M]^+$, 100), 325 (9), 297 (76), 149 (88); ^1H and ^{13}C NMR data: see Table 2.

3.3.3. Corylifol C (3). Yellow amorphous powder. UV (MeOH) λ_{max} (lg ε) 271 (4.22) nm; IR (KBr disc) ν_{max} 3384, 2920, 1668, 1641, 1602, 1583, 1525, 1433, 1317, 1267, 1139, 1039 cm^{-1}; HREIMS m/z 338.1161 $[M]^+$ (calcd for $C_{20}H_{18}O_5$, 338.1154); EIMS m/z (rel int.) 338 ($[M]^+$, 61), 301 (36), 283 (40), 149 (100); ^1H and ^{13}C NMR data: see Table 2.

3.3.4. Bavachalcone (8). Orange amorphous powder. ESIMS m/z positive mode 339.2 $[M+H]^+$, negative mode 337.2 $[M-H]^+$; ^1H NMR ($CDCl_3$): δ 1.74 (3H, s, H-5″), 1.78 (3H, s, H-4″), 3.26 (2H, d, J = 7.0 Hz, H-1″), 5.28 (1H, br t, J = 7.1 Hz, H-2″), 6.44 (1H, s, H-3), 6.90 (2H, d, J = 8.5 Hz, H-3′, 5′), 7.43 (1H, d, J = 15.4 Hz), 7.55 (2H, d, J = 8.5 Hz, H-2′, 6′), 7.59 (1H, s, H-6), 7.83 (1H, d, J = 15.4 Hz), 5.92 (OH, br s), 13.58 (OH, s); ^{13}C NMR ($CDCl_3$) δ 18.0 (C-4″), 25.9 (C-5″), 28.2 (C-1″), 55.8 (4-OMe), 99.2 (C-3), 113.2 (C-1), 116.0 (C-3′, 5′), 117.6 (C-b), 121.6 (C-5), 122.0 (C-2″), 127.2 (C-1′), 129.6 (C-6), 130.4 (C-2′, 6′), 132.8 (C-3″), 144.0 (C-c), 158.4 (C-4′), 163.9 (C-2), 164.9 (C-4), 191.7 (C-a).

3.4. Antibacterial tests

Bioassay on antibacterial activities against *S. aureus* and *S. epidermidis* in vitro was carried out according to the protocols described in the literature.[19] The microbial cells were suspended in Mueller Hinton broth to form a final density of 5×10^{-5}–10^{-6} CFU/mL and incubated at

37 °C for 18 h under aerobic conditions with the respective compounds, which have been dissolved in DMSO. The blank controls of microbial culture were incubated with limited DMSO under the same condition. DMSO was determined not to be toxic at a limited amount under the experimental conditions.

Acknowledgements

Financial support of the National Natural Science Foundation (30025044), the Shanghai Municipal Scientific Foundation (03DZ19529) and the foundation from the Ministry of Science and Technology (2002CB512807) are gratefully acknowledged. We thank Professor Zeng-Tao Wang of Shanghai Traditional Chinese Medical University for the identification of the plant material.

References and notes

1. Ji, L.; Xu, Z. L. *Zhongguozhongyaozhazhi* **1995**, *20*, 120.
2. Haraguchi, H.; Inoue, J.; Tamura, Y.; Mizutani, K. *Phytother. Res.* **2002**, *16*, 539.
3. Tsai, W.; Hsin, W. C.; Chen, C. C. *J. Nat. Prod.* **1996**, *59*, 671.
4. Sun, N. J.; Woo, S. H.; Cassady, J. M.; Snapka, R. M. *J. Nat. Prod.* **1998**, *61*, 362.
5. Wang, D. W.; Li, F. M.; Jiang, Z. M. *Planta Med.* **2001**, *67*, 748.
6. Rajendra, P. N.; Anandi, C.; Balasubramanian, S.; Pugalendi, K. V. *J. Ethnopharm.* **2004**, *91*, 21.
7. Khatune, N. A.; Islam, M. E.; Haque, M. E.; Khondkar, P.; Rahman, M. M. *Fitoterapia* **2004**, *75*, 228.
8. Mehta, G.; Nayak, U. R.; Sukh, D. *Tetrahedron* **1973**, *29*, 1119.
9. Bajwa, B. S.; Khanna, P. L.; Seshadri, T. R. *Indian J. Chem.* **1974**, *12*, 15.
10. Krishnamurti, M.; Parthasarathi, J. *Indian J. Chem.* **1981**, *20B*, 247.
11. Bhalla, V. K.; Nayak, U. R.; Dev, S. *Tetrahedron Lett.* **1968**, *9*, 2401.
12. Jain, A. C.; Gupta, G. K.; Rao, P. R. *Indian J. Chem.* **1974**, *12*, 659.
13. Elsohly, H. N.; Joshi, A. S.; Nimrod, A. C.; Walker, L. A.; Clark, A. M. *Planta Med.* **2001**, *67*, 87.
14. Hakamatsuka, T.; Ebizuka, Y.; Sankawa, U. *Phytochemistry* **1991**, *30*, 1481.
15. Gupta, G. K.; Suri, J. L.; Gupta, B. K.; Dhar, K. L. *Phytochemistry* **1982**, *21*, 2149.
16. Takashima, J.; Ohsaki, A. *J. Nat. Prod.* **2002**, *65*, 1843.
17. Jain, A. C.; Gupta, S.; Bambah, P. *Indian J. Chem.* **1985**, *24B*, 609.
18. Ho, K.; Tsai, C.; Chen, C.; Huang, J.; Lin, C. *Phytotherapy Res.* **2001**, *15*, 139.
19. Yang, S. P.; Yue, J. M. *Bioorg. Med. Chem. Lett.* **2001**, *11*, 3119.