Molecules **2012**, *17*, 4474-4483; doi:10.3390/molecules17044474

OPEN ACCESS

molecules

ISSN 1420-3049

www.mdpi.com/journal/molecules

Article

Antiangiogenic Polyketides from *Peperomia dindygulensis* Miq.

Qi-Wei Wang [1,†], De-Hong Yu [2,†], Meng-Gan Lin [1,†], Mei Zhao [3,4], Wen-Jun Zhu [1], Qin Lu [2], Gui-Xiu Li [5], Chao Wang [2], Yi-Fang Yang [1], Xue-Mei Qin [5], Chao Fang [2,*], Hong-Zhuan Chen [2,*] and Guo-Hong Yang [1,*]

[1] Department of Traditional Chinese Medicine, Shanghai Institute of Pharmaceutical Industry, Shanghai 200040, China

[2] Department of Pharmacology, Institute of Medical Sciences, Shanghai Jiao Tong University School of Medicine, Shanghai 200025, China

[3] Department of Pharmacy, Shanghai Institute of Health Sciences, Shanghai 201318, China

[4] Department of Pharmacy, Health School Attached to Shanghai Jiao Tong University School of Medicine, Shanghai 201318, China

[5] Department of Pharmaceutical Sciences, School of Chemistry, Shanxi University, Taiyuan 030006, China

† These authors contributed equally to this work.

* Authors to whom correspondence should be addressed; E-Mails: fangchao100@hotmail.com (F.C.); hongzhuan_chen@hotmail.com (H.-Z.C.); ghyang@yahoo.cn (G.-H.Y.); Tel./Fax: +86-21-6467-4721 (F.C. and H.-Z.C.); Tel.: +86-21-6247-9808 (G.-H.Y.); Fax: +86-21-6247-3018 (G.-H.Y.).

Received: 17 February 2012; in revised form: 5 April 2012 / Accepted: 6 April 2012 / Published: 13 April 2012

Abstract: Two new polyketides: 2*Z*-(heptadec-12-enyl)-4-hydroxy-3,4,7,8-tetrahydro-*2H*-chromen-5(*6H*)-one (**1**) and 2-(heptadec-12-enyl)-5-hydroxy-5,6,7,8-tetrahydrochromen-4-one (**2**), together with eleven known compounds: 4-hydroxy-2-[(3,4-methylenedioxy-phenyl)tridecanoyl] cyclohexane-1,3-dione (**3**), oleiferinone (**4**), 4-hydroxy-2-[(3,4-methylenedioxyphenyl)undecanoyl]cyclohexane-1,3-dione (**5**), 4-hydroxy-2-[(11-phenyl-undecanoyl)cyclohexane-1,3-dione (**6**), proctorione C (**7**), surinone C (**8**), 5-hydroxy-7,8,4'-trimethoxyflavone (**9**), 5-hydroxy-7,8,3',4'-tetramethoxyflavone (**10**), 5-hydroxy-7,3',4'-trimethoxyflavone (**11**), 5,8-dihydroxy-7,3',4'-trimethoxyflavone (**12**) and cepharanone B (**13**) were isolated from the whole plant of *Peperomia dindygulensis* Miq. Their structures were elucidated by spectroscopic methods, including 2D-NMR techniques.

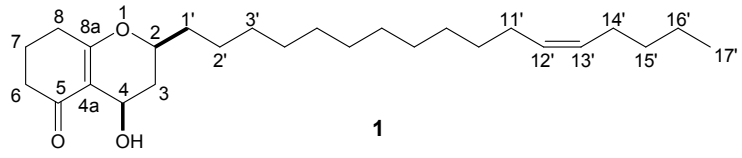
Compounds **2**, **3**, **5** and **8** inhibited human umbilical vein endothelial cell (HUVEC) proliferation and compounds **5** and **8** sharply suppressed HUVEC tube formation.

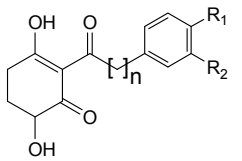
Keywords: *Peperomia dindygulensis* Miq.; polyketides; antiangiogenic activity

1. Introduction

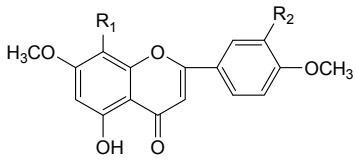
Peperomia dindygulensis Miq. (Piperaceae), a widespread herb in the south of China, is used in the folk medicine to treat cough, asthma, phthisis, and stomach, lung, mammary and liver cancers [1]. The common constituents of *Peperomia* genus include secolignans, tetrahydrofuran lignans, chromones and acylcyclohexane-1,3-diones [2–7], which possess various bioactivities, such as antitumor and anti-HIV activities [8]. We found that the chloroform extract prepared from *P. dindygulensis* showed significant suppression acitivity against the proliferation of primary human umbilical vein endothelial cells (HUVEC). In our previous research, we isolated some antiangiogenic secolignans including two new secolignans from *P. dindygulensis* [9]. Further fractionation and purification of the $CHCl_3$ extract led to the isolation and characterization of two new polyketides: 2-(heptadec-12-enyl)-4-hydroxy-3,4,7,8-tetrahydro-*2H*-chromen-5(*6H*)-one (**1**) and 2-(heptadec-12-enyl)-5-hydroxy-5,6,7,8-tetrahydrochromen-4-one (**2**), together with eleven known compounds: 4-hydroxy-2-[(3,4-methylenedioxyphenyl)tridecanoyl] cyclohexane-1,3-dione (**3**) [10], oleiferinone (**4**) [11], 4-hydroxy-2-[(3,4-methylenedioxyphenyl) undecanoyl]cyclohexane-1,3-dione (**5**) [10], 4-hydroxy-2-[(11-phenylundecanoyl)cyclohexane-1,3-dione (**6**) [12], proctorione C (**7**) [13], surinone C (**8**) [14], 5-hydroxy-7,8,4'-trimethoxyflavone (**9**) [15], 5-hydroxy-7,8,3',4'-tetramethoxyflavone (**10**) [16], 5-hydroxy-7,3',4'-trimethoxyflavone (**11**) [17], 5,8-dihydroxy-7,3',4'-trimethoxyflavone (**12**) [15] and cepharanone B (**13**) [18] (Figure 1).

Figure 1. Structures of compounds **1**–**13**.



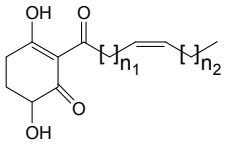


3 R_1,R_2= OCH_2O, n= 12
4 R_1=R_2= H, n= 12
5 R_1,R_2= OCH_2O, n= 10
6 R_1=R_2= H, n= 10

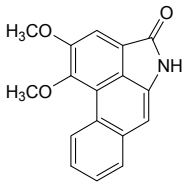


9 R_1= OCH_3, R_2= H
10 R_1= R_2= OCH_3
11 R_1= H R_2= OCH_3
12 R_1= OH, R_2= OCH_3

Figure 1. *Cont.*



7 n_1= 9, n_2= 5
8 n_1= 12, n_2= 4



13

2. Results and Discussion

Compound **1** was assigned the molecular formula $C_{26}H_{44}O_3$ from the HRESI-MS *m/z* 427.3185 $[M+Na]^+$ peak (calcd for $C_{26}H_{44}O_3Na$, 427.3188). The IR spectrum exhibited a hydroxyl absorption at 3,466 cm^{-1}. A long alkyl chain was indicated from the multiple-proton signal in the range δ_H 1.26–1.37 in the ^{1}H-NMR spectrum (Table 1). Two olefinic signals at δ_C 129.8 and 129.9 in the ^{13}C-NMR spectrum (Table 1) suggested the presence of a double bond, and its position at C-12' was further confirmed by EI-MS (Figure 2), HMBC and ^{1}H-^{1}H COSY spectra (Figure 3). The *cis*-geometry of a double bond could be deduced from chemical shifts of C-11' (δ_C 27.2) and C-14' (δ_C 26.9) [19]. Two oxymethine [δ_H 4.00 (1H, *dddd*, 1.7, 5.4, 7.3,11.2, H-2) and δ_H 4.75 (1H, *dd*, 7.0, 9.3, H-4)] and five methylenes [δ_H 2.22 (1H, *ddd*, 2.0, 6.7, 13.5, H-3a) and 1.70 (1H, *m*, H-3b), δ_H 2.33 (1H, *dd*, 9.6, 16.8, H-6a) and 2.39 (1H, *m*, H-6b), δ_H 1.97 (1H, *dd*, *J* = 6.3, 12.9, H-7a) and 1.96 (1H, *dd*, *J* = 6.1, 12.9, H-7b), δ_H 2.40 (2H, *m*, H-8), δ_H 1.62 (1H, *m*, H-1'a) and 1.73 (1H, *m*, H-1'b)] were found to be connected to two moieties, $^6CH_2$–$^7CH_2$–$^8CH_2$ and O–^{4}CH–$^3CH_2$–^{2}CH(O)–$^{1'}CH_2$ using the ^{1}H–^{1}H COSY spectrum. The above two moieties were linked by the two quaternary olefinic carbons δ_C 173.4 (C-8a) and 114.7 (C-4a) which showed HMBC cross-peaks with H-4, H-7, H-8, and with H-3, H-8, respectively. The location of carbonyl carbon δ_C 200.6 (C-5) could be confirmed by the HMBC correlations with H-6 and H-7. Thus, the moiety were determined as O=^{5}C–$^6CH_2$–$^7CH_2$–$^8CH_2$–^{8a}C=^{4a}C–^{4}CH(O)–$^3CH_2$–^{2}CH(O)–$^{1'}CH_2$ and further confirmed by the homoallylic coupling between H-4 and H-8 in the ^{1}H-^{1}H COSY spectrum. The downfield chemical shift of C-8a and the remaining two degrees of unsaturation suggested that the oxygen at C-2 connected to C-8a, and C-5 to C-4a. The 5-hydroxytetrahydrochromen moiety was also confirmed by the mass spectrum which showed a fragment at *m/z* 167 (Figure 2). Thus, the structure of **1** was elucidated as 2Z-(heptadec-12-enyl)-4-hydroxy-3,4,7,8-tetrahydro-*2H*-chromen-5(*6H*)-one. The NOE correlation between H-2 and H-4 indicated their *cis*-configuration.

Table 1. ^{1}H- (400 MHz) and ^{13}C-NMR (100 MHz) data of compound **1** (in $CDCl_3$; δ in ppm, *J* in Hz).

Position	δ_C	δ_H
2	77.1	4.00 (1H, *dddd*, 1.7, 5.4, 7.3,11.2)
3	35.2	2.22 (1H, *ddd*, 2.0, 6.7, 13.5); 1.70 (1H, *m*)
4	62.1	4.75 (1H, *dd*, 7.0, 9.3)
4a	114.7	
5	200.6	

Table 1. *Cont.*

Position	δ_C	δ_H
6	36.7	2.33 (1H, *dd*, 9.6, 16.8); 2.39 (1H, *m*)
7	20.5	1.97 (1H, *dd*, 6.3, 12.9); 1.96 (1H, *dd*, 6.1, 12.9)
8	28.4	2.40 (2H, *m*)
8a	173.4	
1'	34.7	1.62 (1H, *m*); 1.73 (1H, *m*)
2'	25.0	1.46 (2H, *m*)
3'-10'	29.3–29.8	1.26–1.37 (16H, *m*)
11'	27.2	2.00 (2H, *m*)
12', 13'	129.8, 129.9	5.35 (2H, *m*)
14'	26.9	2.01 (2H, *m*)
15'	32.0	1.30 (2H, *m*)
16'	22.4	1.31 (2H, *m*)
17'	14.0	0.88 (3H, *t*, 7.0)
OH-4		4.63 (*brs*)

Figure 2. MS fragmentation of **1**.

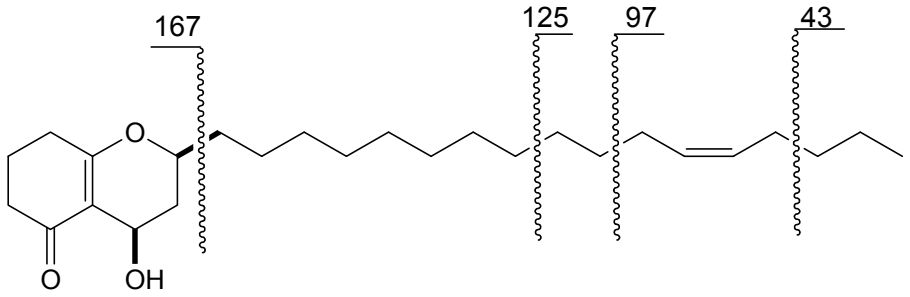
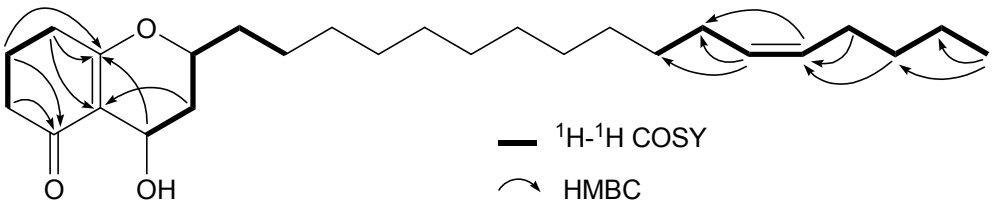


Figure 3. Key ^{1}H-^{1}H COSY and HMBC correlations of **1**.



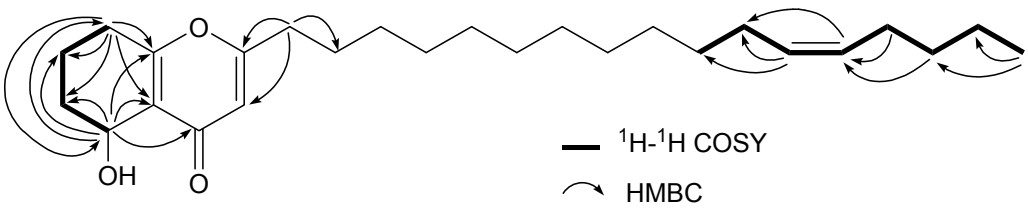
Compound **2** had the molecular formula $C_{26}H_{42}O_3$ as deduced from the HRESI-MS peak at *m/z* 425.3029 $[M+Na]^+$ (calcd for $C_{26}H_{42}O_3Na$, 425.3032). The UV maxima at 249 nm, and the IR absorptions at 1,661, 1,605 cm^{-1} suggested the presence of a γ-pyrone ring, which was 2,3,5-trisubstituted according to the olefinic signals at δ_C 112.7 (C-3) and δ_H 6.10 (1H, s, H-3) in the NMR spectra (Table 2) [20]. Similar to compound **1**, it showed evidence for one moiety, ^{5}CH(O)–^{6}CH$_2$–^{7}CH$_2$–^{8}CH$_2$, and a alkyl chain from the ^{1}H-NMR, ^{13}C-NMR, and ^{1}H-^{1}H COSY and HMBC spectra (Figure 4). In the HMBC spectrum, the proton of the oxymethylene δ_H 4.91 (1H, *br t*, J = 3.8 Hz, H-5) showed correlation with the carbonyl carbon (δ_C 180.7), C-4a (δ_C 123.2), C-6 (δ_C 29.5), C-7 (δ_C 18.1) and C-8 (δ_C 27.6), indicating that C-5 is connected with C-4a. The protons of

the methylene [δ_H 2.46 (1H, *m*, H-8a) and 1.98 (1H, *m*, H-8b)] gave cross peaks with the carbons at C-5, C-6, C-7, C-4a and C-8a, but not with C-4, suggesting that C-8 is attached to C-8a. Surprisingly, the weak four bond reciprocal H-5/C-8 and H-8/C-5 HMBC correlations signals were observed. Although these may be considered unusual, such long-range correlations have been reported, especially in constrained ring systems [21–23]. The HMBC spectrum also suggested the linkage of C-2 and the alkyl chain. Thus, the structure of **2** was determined to be 2-(heptadec-12-enyl)-5-hydroxy-5,6,7,8- tetrahydrochromen-4-one.

Table 2. ^{1}H- (400 MHz) and ^{13}C-NMR (100 MHz) data of compound **2** (in $CDCl_3$; δ in ppm, *J* in Hz).

Position	δ_C	δ_H
2	169.3	
3	112.7	6.10 (1H, *s*)
4	180.7	
4a	123.2	
5	63.8	4.91 (1H, *br t*, 3.8)
6	29.5	1.76 (1H, *m*); 1.96 (1H, *m*)
7	18.1	1.74 (1H, *m*); 1.97 (1H, *m*)
8	27.6	2.49 (1H, *m*); 2.57 (1H, *m*)
8a	165.0	
1'	33.5	2.48 (2H, *t*, 7.6)
2'	26.8	1.61 (2H, *m*)
3'–10'	28.9–29.7	1.26–1.37 (16H, *m*)
11'	27.1	2.00 (2H, *m*)
12', 13'	129.8	5.35 (2H, *m*)
14'	26.9	2.01 (2H, *m*)
15'	31.9	1.30 (2H, *m*)
16'	22.3	1.31 (2H, *m*)
17'	14.0	0.89 (3H, *t*, 6.4)
5-OH		4.43 (*br*s)

Figure 4. Key ^{1}H-^{1}H COSY and HMBC correlations of **2**.



The structures of known compounds **3**~**13** were confirmed by detailed NMR and MS data comparison with those in the literature [10–18]. In addition, some similar compounds have been reported from *Trichoderma* [24,25].

In vitro cytotoxicity of all the isolated compounds to HUVEC was examined after 48 h incubation. It was found that compounds **2**, **3**, **5**, **8** could dose dependently induced significant toxicity to HUVEC at different concentrations (Figure 5). The growth of HUVEC was almost completely inhibited by

compound **3** at 24 μM. Compounds **5** and **8** also exhibited significant tube formation-inhibiting activity at 3, 6, 12 and 24 μM, respectively (Figure 6).

Figure 5. Effect of compounds **2** (**A**), **3** (**B**), **5** (**C**), **8** (**D**) on the viability of HUVEC after 48 h incubation. For blank control, the DMSO concentration was adjusted to below 0.1%. Values are expressed as mean ± SD, n = 4–6. * $p < 0.05$, ** $p < 0.01$ as compared with control.

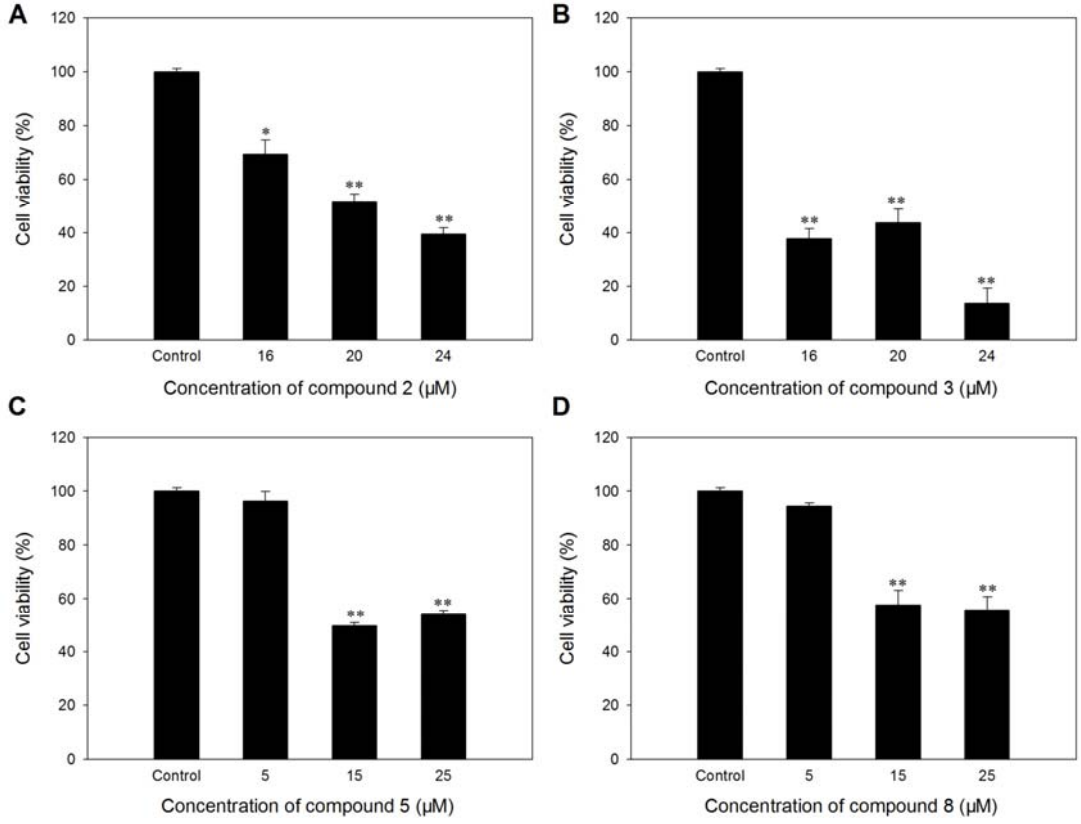


Figure 6. Effect of compounds **5**, compound **8**, and ursolic acid on HUVEC tube formation. **A**, **B**, and **C**: Tube length (% of control) after treatment with compound **5**, compound **8**, and ursolic acid (positive control), respectively. Values are expressed as mean ± SD, n = 4. * $p < 0.05$, ** $p < 0.01$ as compared with control. (**D**): The representative photographs of tube networks after treatment with ursolic acid (10 μM) and compounds **5** and **8** at various concentrations. Bar = 200 μm.

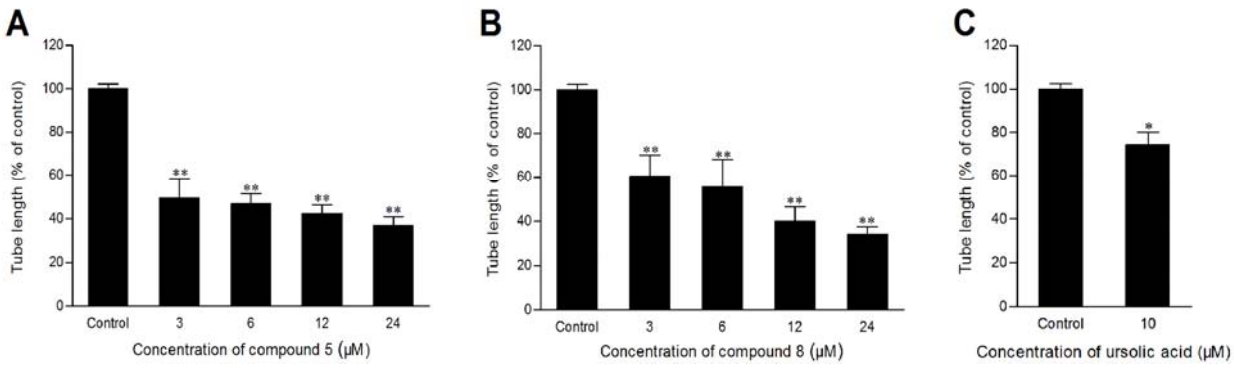
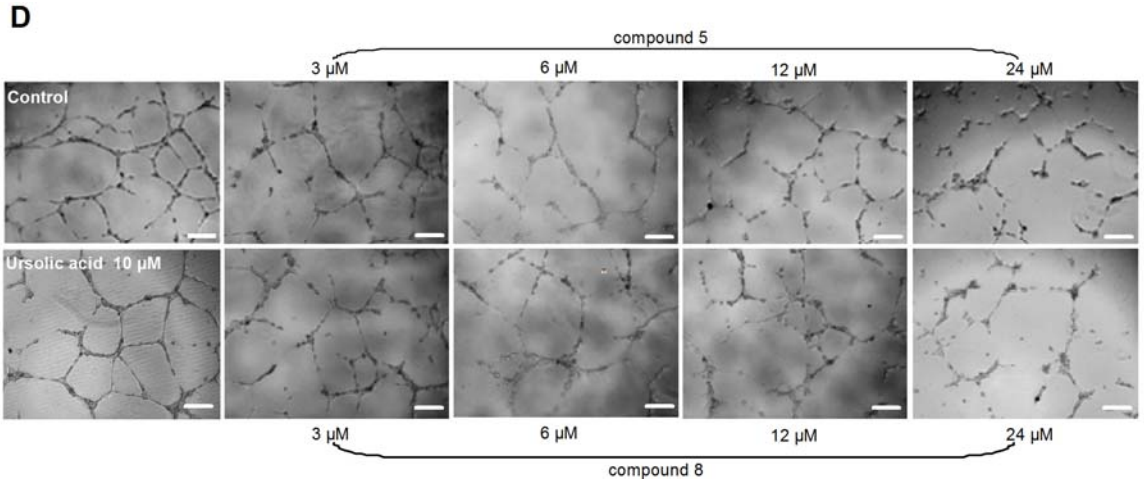


Figure 6. *Cont.*



3. Experimental

3.1. General

Optical rotations were measured on a Perkin-Elmer 341 polarimeter. UV spectra were recorded on a Shimadzu UV-2500 PC spectrophotometer. IR spectra were recorded on a Nexus 670 spectrometer. NMR spectra were measured on a Bruker DRX 400 spectrometer and Bruker AV 500 spectrometer. EI-MS (70 eV) was carried out on an Autospec Premier P708 mass spectrometer. ESI-MS was carried out on a Waters Q-Tof micro YA019 mass spectrometer. Silica gel (200–300 mesh) was used for column chromatography, and pre-coated silica gel GF254 plates (Qingdao Marin Chemical Plant, Qingdao, China) were used for TLC.

3.2. Plant Material

Peperomia dindygulensis Miq., collected in Simao Region Yunnan Province of China in June 2008, was identified by Associate Professor Guo-Hong Yang. A voucher specimen (GHY-PDM20080728) has been deposited in the Herbarium of the Laboratory of Department of Traditional Chinese Medicine, Shanghai Institute of Pharmaceutical Industry, China.

3.3. Extraction and Isolation

The air-dried whole plant (10 kg) of *P. dindygulensis* was extracted exhaustively with 95% EtOH at r.t. (250 L, 7 days). The EtOH extract was evaporated *in vacuo* to yield a semisolid (1,300 g), of which 1,290 g was suspended in H_2O (2,000 mL) and partitioned with $CHCl_3$ (2,000 mL × 5) to yield 756 g of extract after concentration. Part of the $CHCl_3$ extract (300 g) was subjected to column chromatography on Si gel (200~300 mesh, 3 kg) eluted with petroleum ether/EtOAc (100:0, 99:1, 49:1, 19:1, 9:1, 4:1, 7:3, 3:2, 1:1) and EtOAc to yield ten fractions (Frs. **1**–**10**). Fraction **6** (13.9 g) was separated repeatedly on silica gel columns (5 × 50 cm) using *n*-hexane/acetone (5:1) as eluent to obtain six fractions (**6A**–**F**). Fraction **6B** (227 mg) was further purified by Sephadex LH-20 and eluted with $CHCl_3$/MeOH (1:1) to give **1** (10 mg). Fraction **6D** (139 mg) was purified repeatedly by Sephadex

LH-20 using $CHCl_3$/MeOH (1:1) as eluent to give **3** (20 mg). Fraction **7** (21.8 g) was separated repeatedly on silica gel columns (5 × 50 cm) using *n*-hexane/acetone (4:1) as eluent to obtain five fractions (**7A**–**E**). Fraction **7B** (1.6 g) was further purified by Sephadex LH-20 [eluted with $CHCl_3$/MeOH (1:1)] to give four fractions, and the second fraction (700 mg) was applied to preparative silica gel TLC using *n*-hexane/acetone/acetic acid (5:1:0.1) as eluent to afford **4** (40 mg), **5** (100 mg) and **6** (12 mg). Fraction **7C** (7.6 g) was chromatographed over silica gel columns (3 × 50 cm) and eluted with *n*-hexane/EtOAc (3:1) to obtain five fractions, the second fraction (154 mg) was applied to preparative silica gel TLC using toluene/EtOAc (9:1) as eluent to give **11** (4 mg). Fraction **8** (4.5 g) was chromatographed over silica gel columns (3 × 50 cm) eluted with $CHCl_3$/MeOH (50:1) to obtain four fractions (**8A**–**D**). Fraction **8B** (205 mg) was recrystallized from $CHCl_3$/MeOH (1:1) to afford **9** (51 mg). Fraction **8C** (600 mg) was recrystallized from $CHCl_3$/MeOH (1:1) to afford **10** (246 mg). Fraction **8D** (1.4 g) was chromatographed over silica gel columns (3 × 50 cm) and eluted with *n*-hexane/acetone/acetic acid (100:10:1) to give **2** (277 mg) and **6** (36 mg). Fraction **9** (18.9 g) was separated repeatedly on silica gel columns (5 × 50 cm) using n-hexane/acetone (4:1) as eluent to obtain eight fractions (**9A**–**H**). Fraction **9B** (1.5 g) was further separated repeatedly on silica columns (3 × 50 cm) and eluted with $CHCl_3$/acetone (200:1) to give three fractions, and the second fraction was subjected to preparative silica gel TLC using *n*-hexane/acetone/acetic acid (100:10:1) as eluent to give **8** (20 mg). Fraction **9D** (1.8 g) was chromatographed on silica gel columns (3 × 50 cm) using *n*-hexane/acetone (5:1) as eluent to obtain three fractions, and the last fraction (222 mg) was further purified by Sephadex LH-20 and eluted with $CHCl_3$/MeOH (1:1) to give **13** (5 mg). Fraction **9E** (12.2 g) was separated repeatedly on silica gel columns (5 × 50 cm) using $CHCl_3$ as eluent to obtain six fractions, and the last fraction was separated repeatedly by Sephadex LH-20 and eluted with $CHCl_3$/MeOH (1:1) to give **12** (12 mg).

2Z-(Heptadec-12-enyl)-4-hydroxy-3,4,7,8-tetrahydro-2H-chromen-5(6H)-one (**1**). Yellowish oil; $[\alpha]_D^{13}$ 126° (c = 0.368, $CHCl_3$); UV λ_{max} (MeOH) nm (log ε): 258 (4.44); IR (NaCl) ν_{max}: 3466, 2925, 2854, 1613, 1427, 1370, 1249, 1188, 1083, 1054 cm^{-1}; EI-MS *m/z* 404 $[M]^+$ (9.1), 386 (100.0), 167 (24.1), 139 (50.7), 125 (43.1), 111(41.9), 97 (5.2), 43 (21.5); ^{1}H- and ^{13}C-NMR data: see Table 1; HRESI-MS *m/z* 427.3185([*M*+Na]$^+$, calcd for $C_{26}H_{44}O_3Na$ 427.3188).

2-(Heptadec-12-enyl)-5-hydroxy-5,6,7,8-tetrahydrochromen-4-one (**2**). Yellowish oil; $[\alpha]_D^{13}$ 34° (c = 0.435, $CHCl_3$); UV λ_{max} (MeOH) nm (log ε): 216 (3.66), 249 (3.68); IR(NaCl) ν_{max}: 3431, 3003, 2926, 2854, 1716, 1661, 1605, 1436, 1176, 1086, 950, 859, 722 cm^{-1}; ^{1}H- and ^{13}C-NMR data: see Table 2; HRESI-MS *m/z* 425.3029 ([*M*+Na]$^+$, calcd for $C_{26}H_{42}O_3Na$ 425.3032).

3.4. Antiangiogenic Activity Assays

The effect of isolated compounds on the proliferation of HUVEC was evaluated by CCK-8. HUVEC tube formation was conducted for the assay of *in vitro* angiogenesis using the Chemicon *in vitro* angiogenesis assay kit (ECM625). Details of the assays were provided in a previous report [9].

4. Conclusions

Two new polyketides: 2*Z*-(heptadec-12-enyl)-4-hydroxy-3,4,7,8-tetrahydro-*2H*-chromen-5(*6H*)-one (**1**), and 2-(heptadec-12-enyl)-5-hydroxy-5,6,7,8-tetrahydrochromen-4-one (**2**), were isolated from *Peperomia dindygulensis*, together with eleven known compounds **3**–**13**. Compounds **2**, **3**, **5** and **8** inhibited human umbilical vein endothelial cells (HUVEC) proliferation and compounds **5** and **8** sharply suppressed HUVEC tube formation.

Acknowledgments

This work was financially supported by State Innovative Drugs Science and Technology Major Projects of China (No. 2009ZX09301-007), National Natural Science Foundation of China (No. 30600788, 30873179, 30901852), Shanghai Rising-Star Program (No. 09QA1403500, 10QB1404000), Innovation Program of Shanghai Municipal Education Commission (No. 12zz200), and "Chen Guang" project supported by Shanghai Municipal Education Commission and Shanghai Education Development Foundation (No. 107GB03).

References and Notes

1. Editorial Board of China Herbal, State Administration of Traditional Chinese Medicine, China. *China Herbal*; Shanghai Scientific and Technical Publishers: Shanghai, China, 1999; p. 421.
2. Govindachari, T.R.; Kumari, K.G.N.; Partho, P.D. Two secolignans from *Peperomia dindigulensis*. *Phytochemistry* **1998**, *49*, 2129–2131.
3. Wu, J.L.; Li, N.; Hasegawa, T.; Sakai, J.; Kakuta, S.; Tang, W.; Oka, S.; Kiuchi, M.; Ogura, H.; Kataoka, T.; *et al*. Bioactive tetrahydrofuran lignans from *Peperomia dindygulensis*. *J. Nat. Prod.* **2005**, *68*, 1656–1660.
4. Wu, J.L.; Li, N.; Hasegawa, T.; Sakai, J.; Mitsui, T.; Ogura, H.; Kataoka, T.; Oka, S.; Kiuchi, M.; Tomida, A.; *et al*. Bioactive dibenzylbutyrolactone and dibenzylbutanediol lignans from *Peperomia duclouxii*. *J. Nat. Prod.* **2006**, *69*, 790–794.
5. Xu, S.; Li, N.; Ning, M.M.; Zhou, C.H.; Yang, Q.R.; Wang, M.W. Bioactive compounds from *Peperomia pellucida*. *J. Nat. Prod.* **2006**, *69*, 247–250.
6. Monache, F.D.; Compagnone, R.S. A secolignan from *Peperomia glabella*. *Phytochemistry* **1996**, *43*, 1097–1098.
7. Mbah, J.A.; Tchuendem, M.H.K.; Tane, P.; Sterner, O. Two chromones from *Peperomia vulcanica*. *Phytochemistry* **2002**, *60*, 799–801.
8. Zhang, G.L.; Li, N.; Wang, Y.H.; Zheng, Y.T.; Zhang, Z.; Wang, M.W. Bioactive lignans from *Peperomia heyneana*. *J. Nat. Prod*. **2007**, *70*, 662–664.
9. Lin, M.G.; Yu, D.H.; Wang, Q.W.; Lu, Q.; Zhu, W.J.; Bai, F.; Li, G.X.; Wang, X.W.; Yang, Y.F; Qin, X.M.; *et al*. Secolignans with antiangiogenic activities from *Peperomia dindygulensis*. *Chem. Biodiv.* **2011**, *8*, 862–871.
10. Li, N.; Wu, J.L.; Hasegawa, T.; Sakai, J.; Bai, L.M.; Wang, L.Y.; Kakuta, S.; Furuya, Y.; Ogura, H.; Kataoka, T.; *et al*. Bioactive polyketides from *Peperomia duclouxii*. *J. Nat. Prod.* **2007**, *70*, 998–1001.

11. Azevedo, N.R.; Santos, S.C.; De Miranda, E.G.; Ferri, P.H. A 2-Acylcyclohexane-1,3-dione from *virola oleifera*. *Phytochemistry* **1997**, *46*, 1375–1377.
12. Kato, M.J.; Lopes, X.L.M.; Paulino Fo, H.F.; Yoshida, M.; Gottlieb, O.R. Acylresorcinols from *Virola sebifera* and *Virola elongate*. *Phytochemistry* **1985**, *24*, 533–536.
13. Seeram, N.P.; Lewis, A.; Jacobs, H.; Nair, M.G.; McLean, S.; Reynolds, W.F. Proctoriones A–C: 2-Acylcyclohexane-1,3-dione derivatives from *Peperomia proctorii*. *J. Nat. Prod.* **2000**, *63*, 399–402.
14. Cheng, M.J.; Lee, S.J.; Chang, Y.Y.; Wu, S.H.; Tsai, I.L.; Jayaprakasam, B.; Chen, I.S. Chemical and cytotoxic constituents from *Peperomia sui*. *Phytochemistry* **2003**, *63*, 603–608.
15. Chu, H.W.; Wu, H.T.; Lee, Y.J. Regioselective hydroxylation of 2-hydroxychalcones by dimethyldioxirane towards polymethoxylated flavonoids. *Tetrahedron* **2004**, *60*, 2647–2655.
16. Shaw, S.C.; Azad, R.; Mandal, S.P.; Gandhi, R.S. Synthesis of 6-hydroxyluteolin and sinensetin by wessely-Moser rearrangement. *J. Indian Chem. Soc.* **1988**, *LXV*, 107–109.
17. Tang, J.; Li, H.L.; Li, Y.L.; Zhang, W.D. Flavonoids from rhizomes of *Veratum dahuricum*. *Chem. Nat. Compd.* **2007**, *43*, 696–697.
18. Araújo, J.X.; Chaves, M.C.O.; Da Cunha, E.V.L.; Gray, A.I. Cepharanone B from *Piper tuberculatum*. *Biochem. Syst. Ecol.* **1999**, *27*, 325–327.
19. Mizutani, K.; Fuknaga, Y.; Tanaka, O.; Takasugi, N.; Saruwatari, Y.I.; Fuwa T.; Yamauchi T.; Wang, J.; Jia, M.R.; Li, F.Y.; *et al*. Amides from Huajiao, Pericarps of *Zanthoxylum bungeanum* maxim. *Chem. Pharm. Bull.* **1988**, *36*, 2362–2365.
20. Yoshii, E.; Koizumi, T.; Oribe, T. The structure of agarotetrol, a novel highly oxygenated chromone from agarwood (*jinko*). *Tetrahedron Lett.* **1978**, *41*, 3921–3924.
21. El-Elimat, T.; Li, C.; Qandil, A.; Alkofahi, A.; Tawaha, K.; Burgess, J.P.; Nakanishi, Y.; Kroll, D.J.; Navarro, H.A. New colchicinoids from a native Jordanian meadow saffron, *Colchicum brachyphyllum*: Isolation of the first naturally occurring dextrorotatory colchicinoid. *J. Nat. Prod.* **2005**, *68*, 173–178.
22. Isaka, M.; Palasarn, S.; Auncharoen, P.; Kornmijit, S.; Jones, E.B.G. Acremoxanthones A and B, novel antibiotic polyketides from the fungus *Acremonium* sp. BCC 31806. *Tetrahedron Lett.* **2009**, *50*, 284–287.
23. Liu, Y.B.; Mulabagal, V.; Bowen-Forbes, C.S.; Aviayan, R.; Nair, M.G. Inhibition of lipid peroxidation, cyclooxygenase enzyme and human tumor cell proliferation by compounds in herbal water. *Mol. Nutr. Food Res.* **2009**, *53*, 1177–1186
24. Dunlop, R.W.; Simon, A.; Sivasithamparam, K.; Ghisalberti E.L. An antibiotic from *Trichoderma koningii* active against soilborne plant pathogens. *J. Nat. Prod.* **1989**, *52*, 67–74.
25. Cutler, H.G.; Himmelsbach, D.S.; Yagen, B.; Arrendale, R.F.; Jacyno, J.M.; Cole, P.D.; Cox, R.H. Koninginin B: A biologically active congener of koninginin A from *Trichoderma koningii*. *J. Agric. Food Chem.* **1991**, *39*, 977–980.

Sample Availability: Not available.