A NOVEL COMPOUND FROM *Penicillium* sp. (M207142)

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Marine fungi have proved to be rich sources of bioactive secondary metabolites [1–4]. During our systematic screening for bioactive compounds from marine-derived fungi, the strain of *Penicillium* sp. (M207142) was regarded as having one of the highest potentials among 174 strains isolated from sea sediment. The main active components of the strain are in the ethyl acetate extracts [5]. The extracts were subjected to a succession of chromatographic procedures to afford six pure components, the structures of which were established by spectral methods (IR, ESI-MS, and 1D and 2D NMR).

Compound **1** ((2*E*,4*E*)-1-(2,6-dihydroxy-3,5-dimethyl-phenyl)hexa-2,4-dien-1-one)), yellow needle-like crystal, easily soluble in methanol. IR (KBr, ν_{max}, cm^{-1}): 3343.23, 2925.66, 1642.35, 1626.30, 1482.66, 1383.38, 1364.54, 1282.22, 1180.34, 1154.15, 1027.66, 992.72, 860.37, 806.45, 755.68. The ESI-MS spectrum showed a molecular ion peak at *m*/*z* 231.4 $[M–1]^-$ consistent with the molecular formula $C_{14}H_{16}O_3$.

The $^1H–^1H$ COSY correlations revealed a spin system for protons of H-2 (7.12) with H-3 (7.42); H-3 (7.42) with H-2 (7.12) and H-4 (6.46); H-4 (6.46) with H-3 (7.42) and H-5 (6.32); H-5 (6.32) with H-4 (6.46) and H-6 (1.90); H-6 (1.90) with H-5 (6.32) (Table 1).

The $^1H–^{13}C$ HMBC spectrum contained cross-peaks H-2/C-1′, C-1, C-3, C-4; H-3/C-1, C-4, C-5; H-4/C-2, C-3, C-5, C-6; H-5/C-3, C-4, C-6; H-6/C-4, C-5; H-4′/C-2′, C-6′, C-7′, C-8′; H-7′/C-2′, C-4′, C-3′; H-8′/C-5′, C-4′, C-6′ for the main correlation between the protons and carbons shown in Fig. 1.

Compound **2**, colorless solid, easily soluble in chloroform. IR (KBr, ν_{max}, cm^{-1}): 3440.72, 2925.81, 2855.30, 1722.32, 1598.51, 1383.93, 1025.13. The ESI-MS spectrum showed a molecular ion peak at *m*/*z* 251.2 [M+1] corresponding to the molecular formula $C_{14}H_{18}O_4$, with molecular weight 250.2. Furthermore, the structure of compound **2** was confirmed by PMR, ^{13}C NMR, DEPT, COSY, HSQC, and HMBC experiments (Table 2), which is consistent with the structure of penicillone A [6].

Compound **3**, colorless solid, IR (KBr, ν_{max}, cm^{-1}): 3355.81, 2926.10, 1625.97, 1383.45, 1158.12, 1026.36. ESI-MS spectrum of compound **3** showed a molecular ion peak at *m*/*z* 235.3 $[M+1]^+$, with molecular weight 234.3 corresponding to the molecular formula $C_{14}H_{18}O_3$. 1D and 2D NMR spectrum showed that the structure of compound **3** was consistent with the known compound dihydrosorbicillin [7].

Compounds **4** to **6** were identified as 4-methoxybenzoic acid (**4**), 4-hydroxyphenylacetic acid (**5**), and methyl-4-hydroxybenzoate (**6**). All of them are important chemical products used widely in industry.

Compounds **1** and **3** exhibited potent cytotoxicity (IC_{50} 11.2 μM and 104.2 μM) against Hela cell line. Compounds **1** and **2** also showed potent cytotoxity against SW620 cell line, with inhibition 74 and 44% and tested concentration 10 μg/mL.

The cytotoxic values demonstrate the strong potential of compound **1** as a promising lead compound and the strain of *Penicillium* sp. (M207142) as a promising fungi source of new agents for cancer chemotherapy.

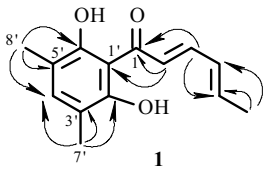

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Fig. 1. $^1H–^{13}C$ HMBC interactions of atoms in compound **1**.

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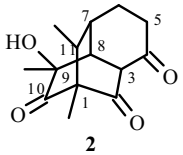
TABLE 1. NMR Data for Compound **1** (500 MHz, CD_3OD, ppm, J/Hz)

C atom	δ_H	δ_C	HMBC (H→C)	^1H–^1H COSY
1		193.9 s		
2	7.12 (d, J = 14.7)	123.5 d	C-1′, C-1, C-3, C-4	H-3
3	7.42 (dd, J = 11.1/14.7)	145.3 d	C-1, C-4, C-5	H-2, H-4
4	6.46 (dd, J = 11.1/14.7)	132.0 d	C-2, C-3, C-5, C-6	H-3, H-5
5	6.32 m	141.7 d	C-3, C-4, C-6	H-4, H-6
6	1.90 (d, J =6.7)	18.9 q	C-4, C-5	H-5
1′		114.0 s		
2′		162.2 s		
3′		117.2 s		
4′	7.56 s	130.1 d	C-2′, C-6′, C-7′, C-8′	
5′		112.0 s		
6′		163.7 s		
7′	2.17 s	16.4 q	C-2′, C-3′, C-4′	
8′	2.06 s	8.0 q	C-4′, C-5′, C-6′	

TABLE 2. NMR Data for Compound **2** (500 MHz, CD_3OD, ppm, J/Hz)

C atom	δ_H	δ_C	HMBC (H→C)	^1H–^1H COSY
1		67.3 s		
2		201.3 s		
3	3.50 m	62.6 d	C-2, C-4, C-8	H-8
4		201.7 s		
5	2.47 m	34.8 t	C-4, C-6, C-7	H-6
	2.47 m			
6	2.00 m	28.1 t	C-5	H-5, H-7
	2.06 m			
7	2.58 m	33.5 d		H-6, H-8, H-11
8	2.52 m	46.6 d	C-3, C-9, C-10, C-11	H-3, H-7
9		73.9 s		
10		209.4 s		
11	1.95 m	41.1 d	C-1, C-2, C-6, C-7, C-10, CH_3-11	H-8, H-(CH_3-11)
CH_3-1	1.18 s	9.9 q	C-1, C-2, C-10, C-11	
CH_3-9	1.25 s	22.6 q	C-8, C-9, C-10	
CH_3-11	1.09 (d, J = 7.0)	17.9 q	C-1, C-7, C-10	H-11



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Penicillium sp. (M207142) was isolated from sea sediment; the specimen was stored in CCTCC, No. M207142. The strain grown on agar slants (7 days) was used to inoculate full seawater potato culture medium and incubated at 28°C for 14 days. The fermentation product was mixed with 85% ethyl acetate–15% methanol–5% acetic acid, and about 4.8 g crude extracts was obtained. The extracts were applied to a middle-pressure silica gel column (methanol–water), an RP-18 column (acetone–water), and a silica gel column (petroleum–ethyl acetate), with gradient elution. The pure components **1** (6 mg), **2** (12 mg), and **3** (9 mg) were obtained and subjected to spectroscopic ^1H NMR, ^{13}C NMR, DEPT, ^1H–^1H COSY, HSQC, HMBC, and IR and ESI-MS analysis.

In the cytotoxic bioassay, the MTT method of Scudiero [8] was used.

REFERENCES

1. A. Tamil Selvi, G. S. Joseph, and G. K. Jayaprakasha, *Food Microbiol*., **20**, 455 (2003).
2. H. Shih-Jeng and M. Jeng-Leun, *LWT*, **39**, 707 (2006).
3. W. Jingxue, J. Xiaolu, M. Haijin, and G. Huashi, *J. Appl. Phycol.*, **16**, 333 (2004).
4. L. Rui, G. QianQuan, Z. WeiMing, C. Chengbin, F. Guotao, Z. Tianjio, and L. Hongbing, *J. Nat. Prod.*, **69**, 871 (2006).
5. Y. Xuefen, H. Danhong, D. Yubo, and Z. Lianru, *J. Xiamen Univ.*, **2**, 56 (2007).
6. W. Liu, Q. Gu, W. Zhu, C. Cui, G. Fan, T. Zhu, H. Liu, and Y. Fang, *Tetrahedron Lett*., **46**, 4993 (2005).
7. P. Maskey, I. Grun-Wollny, and H. Laatsch, *J. Nat. Prod.*, **68**, 865 (2005).
8. D. A. Scudiero, R. H. Shoemaker, K. D. Paull, A. Monks, S. Tiemey, T. H. Nofziger, M. J. Currens, D. Seniff, and M. R. Boyd, *Cancer Res*., **48**, 4827 (1988).