SUPPLEMENTARY MATERIAL

New Lasiodiplodins From Mangrove Endophytic Fungus *Lasiodiplodia* sp. 318[#]

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Abstract: Two new lasiodiplodins (1-2) together with three known analogues, were isolated from a mangrove endophytic fungus, *Lasiodiplodia* sp.318[#]. Their structures were established by spectroscopic techniques (¹D- and ²D-NMR, HR-ESI-MS, etc), and electronic circular dichroism (ECD). Cytotoxic activities of compounds 1–5 were evaluated *in vitro*. Compound 4 was the most potent, with IC₅₀ values of 5.29 μM against MMQ, 13.05 μM against GH3. Preliminary structural-activity analysis indicated that the functional group (resorcinol-3-OH) contribute great to the binding of Lasiodiplodins to the cytotoxic activities.

Keywords: Mangrove endophytic fungus; *Lasiodiplodia*; lasiodiplodins

1. Cytotoxic assay

Following the previous procedures(Wang et al. 2015), Cell Counting Kit-8 assay (CCK-8) (Dojindo, Japan) was used to assess cell proliferation. Briefly, the GH3, MMQ, RPC, REF were seeded on 96-well plates (Nest, China) at a density of 10⁵/ml ,100 μl/well, incubated at 37 °C with 5 % CO₂ for 24 h, According to the manufacturer's protocol, the CCK8 reagent was added to each well and cells were incubated at 37°C for 1-4 h. The absorbance was measured at 450 nm using a microplate reader and cell proliferation rate relative to the control was calculated.

Table S1. ^{13}C and ^1H NMR spectroscopic data (100/400 MHz, CDCl_3) for compounds 1-2

Position	1		2	
	δ_{C}	δ_{H}	δ_{C}	δ_{H}
1	168.4		171.5	
2	117.0		104.9	
3	157.6		165.3	
4	96.6	6.24 (1H, <i>s</i>)	101.4	6.29 (1H, br <i>s</i>)
5	157.0		160.6	
6	108.1	6.22 (1H, <i>s</i>)	110.9	6.24 (1H, br <i>s</i>)
7	143.1		148.5	
8	31.2	2.56 – 2.45 (1H, overlap <i>m</i>) 2.40 – 2.31 (1H, <i>m</i>)	36.6	2.84 (2H, <i>t</i> , $J = 7.9$ Hz)
9	30.2	1.52 (2H, overlap <i>m</i>)	31.5	1.63 – 1.48 (2H, overlap <i>m</i>)
10	25.4	1.52 (2H, overlap <i>m</i>)	29.1	1.36 – 1.24 (2H, overlap <i>m</i>)
11	30.5	2.28 – 2.17 (1H, overlap <i>m</i>) 2.14 – 2.02 (1H, <i>m</i>)	29.3	1.36 – 1.24 (2H, overlap <i>m</i>)
12	132.3	5.32 (1H, <i>t</i> , $J = 12.6$ Hz)	29.0	1.36 – 1.24 (2H, overlap <i>m</i>)
13	127.7	5.56 – 5.46 (1H, overlap <i>m</i>)	23.7	1.63 – 1.48 (2H, overlap <i>m</i>)
14	40.9	2.56 – 2.45 (1H, overlap <i>m</i>) 2.28 – 2.17 (1H, overlap <i>m</i>)	43.7	2.44 (2H, <i>t</i> , $J = 7.3$ Hz)

15	70.1	5.56 – 5.46 (1H, overlap <i>m</i>)	210.6	
16	20.5	1.35 (3H, <i>d</i> , <i>J</i> = 6.4 Hz)	29.9	2.15 (3H, <i>s</i>)
17	55.8	3.76 (3H, <i>s</i>)	61.3	4.39 (2H, <i>q</i> , <i>J</i> = 7.1 Hz)
18				1.40 (3H, <i>t</i> , <i>J</i> = 7.1 Hz)
			14.1	
3-OH				11.82 (1H, <i>s</i>)

Table S2. ^{13}C and ^1H NMR spectroscopic data (100/400 MHz, CDCl_3) for compounds 3-4

Position	3		4	
	δ_{C}	δ_{H}	δ_{C}	δ_{H}
1	171.8		171.5	
2	105.3		105.0	
3	165.6		165.3	
4	101.4	6.29 (1H, <i>d</i> , <i>J</i> = 2.6 Hz)	101.3	6.28 (1H, <i>d</i> , <i>J</i> = 1.6 Hz)
5	160.2		160.3	
6	110.6	6.23 (1H, <i>d</i> , <i>J</i> = 2.4 Hz)	110.7	6.23 (1H, <i>d</i> , <i>J</i> = 2.0 Hz)
7	149.2		148.9	
		3.27 (1H, <i>td</i> , <i>J</i> = 12.3 4.1 Hz)		
8	37.2	2.43 (1H, <i>td</i> , <i>J</i> = 12.5 4.8 Hz)	37.0	2.85 (2H, <i>t</i> , <i>J</i> = 7.8 Hz)
9	31.3	1.91 – 1.73 (1H, overlap <i>m</i>) 1.32 – 1.19 (1H, overlap <i>m</i>)	32.0	1.59 – 1.47 (2H, <i>m</i>)
10	26.9-26.7	1.64 – 1.38 (2H, overlap <i>m</i>)	29.3-29.9	1.34-1.23 (2H, overlap <i>m</i>)

11	22.4-22.7	1.64 – 1.38 (2H, overlap <i>m</i>)	29.3-29.9	1.34-1.23 (2H, overlap <i>m</i>)
12	26.9-26.7	1.64 – 1.38 (2H, overlap <i>m</i>)	29.3-29.9	1.36-1.38 (2H, overlap <i>m</i>)
13	22.4-22.7	1.64 – 1.38 (2H, overlap <i>m</i>)	29.3-29.9	1.34-1.23 (2H, overlap <i>m</i>)
14	22.4-22.7	1.64 – 1.38 (2H, overlap <i>m</i>)	31.8	1.34-1.23 (2H, overlap <i>m</i>)
15	26.9-26.7	1.64 – 1.38 (2H, overlap <i>m</i>)	22.6	1.34-1.23 (2H, overlap <i>m</i>)
16	34.7	1.91 – 1.73 (1H, overlap <i>m</i>) 1.4-1.56 (1H, <i>m</i>)	14.1	0.88 (3H, <i>t</i> , <i>J</i> = 6.7 Hz)
17	73.7	5.24 – 5.15 (1H, <i>m</i>)	61.3	4.40(2H, <i>t</i> , <i>J</i> = 7.1 Hz)
18	21.3	1.36 (3H, <i>d</i> , <i>J</i> = 6.2 Hz)	14.1	1.41 (3H, <i>t</i> , <i>J</i> = 7.2 Hz)
3-OH		12.20 (1H, <i>s</i>)		11.87 (1H, <i>s</i>)

Figure S1 Key ^1H - ^1H COSY (**bold**), HMBC (**arrow**) correlations of compounds **1-4**

Figure S2 Experimental ECD spectra of 1 and 6 (in MeOH).

^a compound 6: (*R*)-lasiodiplodin

Figure S3 *In vitro* cytotoxic activities of compounds 1-5

^a Data are expressed in IC₅₀ values (μM). MMQ: The rat pituitary adenoma cell line. GH3: The rat pituitary adenoma cell lines. RPC: rat normal pituitary cells.

^b 100 μM stand for compound's IC₅₀ values ≥ 100 μM.

^c RPC use as positive control.

^d RPC cells (ScienCell, Logan, UT, USA, NO: R1200), MMQ and GH3, were purchased from Xie-he Bank (Beijing, China). REF were isolated from rat embryonic

Figure S4 The HRESIMS spectrum of compound 1

Figure S5 The ^1H -NMR spectrum of compound 1(CDCl_3)

Figure S6 The ^{13}C -NMR spectrum of compound 1 (CDCl_3)

Figure S7 The HMBC spectrum of compound 1

Figure S8 The ^1H - ^1H COSY spectrum of compound 1

Figure S9 The HSQC spectrum of compound 1

Figure S10 The DEPT spectrum of compound 1

Figure S11 The HRESIMS spectrum of compound **2**

Figure S12 The ¹H-NMR spectrum of compound **2** (CDCl₃)

Figure S13 The ^{13}C -NMR spectrum of compound **2** (CDCl_3)

Figure S14 The DEPT spectrum of compound 2

Figure S15 The HMBC spectrum of compound **2**

Figure S16 The ¹H-¹H COSY spectrum of compound 2

Figure S17 The HSQC spectrum of compound 2