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\(^8\). Their structures were established by spectroscopic techniques (\(^1\)D- and \(^2\)D-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 IC\(_{50}\) 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 10\(^5\)/ml, 100 μl/well, incubated at 37 °C with 5 % CO\(_2\) 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 $^1$H NMR spectroscopic data (100/400 MHz, CDCl3) for compounds 1-2

| Position | $\delta$ C | $\delta$ H | $\delta$ C | $\delta$ H |
|----------|------------|------------|------------|------------|
| 1        | 168.4      |            |            |            |
| 2        | 117.0      |            |            | 104.9      |
| 3        | 157.6      |            |            | 165.3      |
| 4        | 96.6       | 6.24 (1H, s) | 101.4      | 6.29 (1H, br s) |
| 5        | 157.0      |            |            | 160.6      |
| 6        | 108.1      | 6.22 (1H, s) | 110.9      | 6.24 (1H, br s) |
| 7        | 143.1      |            |            | 148.5      |
| 8        | 31.2       | 2.56 – 2.45 (1H, overlap m) | 36.6       | 2.84 (2H, $t$, $J = 7.9$ Hz) |
|          |            | 2.40 – 2.31 (1H, m) |           |            |
| 9        | 30.2       | 1.52 (2H, overlap m) | 31.5       | 1.63 – 1.48 (2H, overlap m) |
|          |            |            |            |            |
| 10       | 25.4       | 1.52 (2H, overlap m) | 29.1       | 1.36 – 1.24 (2H, overlap m) |
|          |            |            |            |            |
| 11       | 30.5       | 2.28 – 2.17 (1H, overlap m) | 29.3       | 1.36 – 1.24 (2H, overlap m) |
|          |            | 2.14 – 2.02 (1H, m) |           |            |
| 12       | 132.3      | 5.32 (1H, $t$, $J = 12.6$ Hz) | 29.0       | 1.36 – 1.24 (2H, overlap m) |
| 13       | 127.7      | 5.56 – 5.46 (1H, overlap m) | 23.7       | 1.63 – 1.48 (2H, overlap m) |
| 14       | 40.9       | 2.56 – 2.45 (1H, overlap m) | 43.7       | 2.44 (2H, $t$, $J = 7.3$ Hz) |
|          |            | 2.28 – 2.17 (1H, overlap m) |            |            |
| Position | 3          | 4          |
|----------|------------|------------|
|          | $\delta_C$ | $\delta_H$ | $\delta_C$ | $\delta_H$ |
| 1        | 171.8      |            | 171.5      |            |
| 2        | 105.3      |            | 105.0      |            |
| 3        | 165.6      |            | 165.3      |            |
| 4        | 101.4      | 6.29 (1H, $d$, $J = 2.6$ Hz) | 101.3      | 6.28 (1H, $d$, $J = 1.6$ Hz) |
| 5        | 160.2      |            | 160.3      |            |
| 6        | 110.6      | 6.23 (1H, $d$, $J = 2.4$ Hz) | 110.7      | 6.23 (1H, $d$, $J = 2.0$ Hz) |
| 7        | 149.2      |            | 148.9      |            |
|          |            | 3.27 (1H, $td$, $J = 12.3$ 4.1 Hz) |            |            |
| 8        | 37.2       | 2.43 (1H, $td$, $J = 12.5$ 4.8 Hz) | 37.0       | 2.85 (2H, $t$, $J = 7.8$ Hz) |
| 9        | 31.3       | 1.91 – 1.73 (1H, overlap $m$) | 32.0       | 1.59 – 1.47 (2H, m) |
| 10       | 26.9-26.7  | 1.64 – 1.38 (2H, overlap $m$) | 29.3-29.9  | 1.34-1.23 (2H, overlap $m$) |

Table S2. $^{13}$C and $^1$H NMR spectroscopic data (100/400 MHz, CDCl$_3$) for compounds 3-4.
| No. | 1H (ppm) | 1H-1H COSY (ppm) | 1H-1H COSY (ppm) |
|-----|-----------|------------------|------------------|
| 11  | 22.4-22.7 | 1.64 – 1.38 (2H, overlap m) | 29.3-29.9 |
| 12  | 26.9-26.7 | 1.64 – 1.38 (2H, overlap m) | 29.3-29.9 |
| 13  | 22.4-22.7 | 1.64 – 1.38 (2H, overlap m) | 29.3-29.9 |
| 14  | 22.4-22.7 | 1.64 – 1.38 (2H, overlap m) | 31.8 |
| 15  | 26.9-26.7 | 1.64 – 1.38 (2H, overlap m) | 22.6 |
| 16  | 34.7      | 1.4-1.56 (1H, m)           | 14.1 |
|     |           | 1.91 – 1.73 (1H, overlap m) | 0.88 (3H, t, J = 6.7 Hz) |
| 17  | 73.7      | 5.24 – 5.15 (1H, m)         | 61.3 |
| 18  | 21.3      | 1.36 (3H, d, J = 6.2 Hz)    | 14.1 |
|     | 3-OH      | 12.20 (1H, s)               | 11.87 (1H, s) |

Figure S1  Key $^1$H–$^1$H 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 IC\textsubscript{50} values (\( \mu \)M). MMQ: The rat pituitary adenoma cell line. GH3: The rat pituitary adenoma cell lines. RPC: rat normal pituitary cells. 

\( b \) 100 \( \mu \)M stand for compound's IC\textsubscript{50} values\( \geq 100 \mu \)M.

\( c \) 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 (CDCl3)

Figure S6 The 13C-NMR spectrum of compound 1 (CDCl3)

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 13C-NMR spectrum of compound 2 (CDCl3)
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