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## Sesinoside, a New Iridoid Glucoside from Sesame (*Sesamum indicum*) Seedlings

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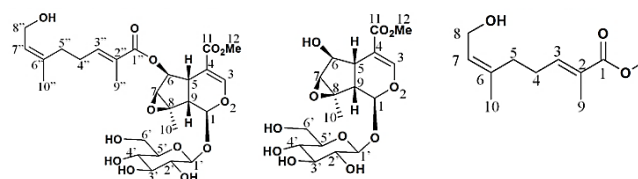
A new iridoid glucoside, sesinoside (**1**), was isolated from the seedlings of *Sesamum indicum*. The structure of **1** was elucidated by spectroscopic analyses and by methanolysis of **1**, which produced the known compounds, phlorigidosides C (**2**) and (6Z)-foliamenthic acid methyl ester (**3**). This is the first report of an iridoid glucoside with **3**.

**Keywords:** Sesinoside, Iridoid glucosides, *Sesamum indicum*, Seedling, Photostress.

Iridoids are secondary metabolites of terrestrial and marine flora and fauna and are found in a large number of plant families, usually as glucosides. Currently, a thousand or more iridoid compounds have been reported [1]. They have a great variety of bioactivity, for example, antibacterial [2], antiviral [3], antiprotozoal [4], anticancer [5], anti-inflammatory [6], and melanogenesis inhibitory [7]. In addition, there is a report that drought stress increases iridoid glucoside biosynthesis in the roots of *Scrophularia ningpoensis* seedlings [8]. In this paper, we report the new iridoid glucoside, sesinoside (**1**), isolated from the illuminated seedlings of sesame (*Sesamum indicum*).

Sesinoside (**1**) was obtained as an amorphous powder. The molecular formula of **1** was established as C<sub>27</sub>H<sub>38</sub>O<sub>13</sub> by high-resolution electrospray ionization mass spectrometry (HRESI-MS, *m/z* 593.2217 [M + Na]<sup>+</sup>, Δ+0.7 mmu). The IR spectrum exhibited absorption bands at 3398 cm<sup>-1</sup> for the hydroxyl group, and 1705 cm<sup>-1</sup> and 1635 cm<sup>-1</sup> for α,β-unsaturated ester groups. The <sup>13</sup>C NMR spectrum (Table 1) of **1** indicated the presence of 27 carbons, which were assigned to two ester carbonyl carbons at δ<sub>c</sub> 170.2 and 169.7; six olefinic carbons at δ<sub>c</sub> 154.4, 144.5, 139.5, 129.8, 127.4, and 108.6; nine oxygenated methine carbons at δ<sub>c</sub> 100.7, 96.9, 81.8, 79.6, 78.7, 75.8, 72.7, 63.8, and 63.5; two oxygenated methylene carbons at δ<sub>c</sub> 63.9 and 59.7; a methoxy carbon at δ<sub>c</sub> 52.7; two methine carbons at δ<sub>c</sub> 45.0 and 35.8; two methylene carbons at δ<sub>c</sub> 32.4 and 29.2; and three methyl carbons at δ<sub>c</sub> 24.3, 18.6, and 13.3. The <sup>1</sup>H NMR spectrum of **1** showed three olefinic protons at δ<sub>H</sub> 7.52, 6.89, and 5.46; eight oxygenated methine protons at δ<sub>H</sub> 5.48, 5.21, 4.85, 3.47, 3.45, 3.39, 3.30, and 3.26; two oxygenated methylene protons at δ<sub>H</sub> 4.13 and 3.98/3.65; a methoxy proton at δ<sub>H</sub> 3.62; two methine protons at δ<sub>H</sub> 3.02 and 2.42; two methylene protons at δ<sub>H</sub> 2.38 and 2.29; and three methyl protons at δ<sub>H</sub> 1.90, 1.82, and 1.61.

The <sup>1</sup>H-<sup>1</sup>H COSY data of **1** implied connectivities of H-1/H-9/H-5/H-6/H-7; H-1'/H-2'/H-3'/H-4'/H-5'/H-6'; H-3''/H-4''/H-5'' and H-7''/H-8'' (Figure 2). The HMBC spectrum (Figure 2) showed the correlations of H-1/C-1'; H-3/C-1, C-4 and C-11; H-5/C-3, C-4 and C-11; H-6/H-1''; H-7/C-10; H-9/C-10; H-10/C-8 and C-9; H-12/C-11; H-3''/C-1'', C-2'' and C-9''; H-7''/C-5'' and C-10''; H-9''/C-1'' and C-2''; and H-10''/C-5'' and C-6''. According to the molecular formula of **1**, there were nine degrees of unsaturation. Two carbonyl



Sesinoside (**1**) Phlorigidoside C (**2**) Foliamenthic acid methyl ester (**3**)

**Figure 1:** Structures of sesinoside (**1**), phlorigidoside C (**2**) and foliamenthic acid methyl ester (**3**)

**Table 1:** <sup>13</sup>C and <sup>1</sup>H NMR data of sesinoside (**1**) and phlorigidoside C (**2**) in CD<sub>3</sub>OD<sup>a</sup>.

<b>1</b>				<b>2</b>			
	<sup>13</sup> C, δ <sub>c</sub>		<sup>1</sup> H, δ <sub>H</sub> (mult, J in Hz)		<sup>13</sup> C, δ <sub>c</sub>		<sup>1</sup> H, δ <sub>H</sub> (mult, J in Hz)
1	96.9 <sup>a</sup>	CH	5.48 <sup>a</sup> d (9.7)	97.3 <sup>a</sup>	CH	5.31 <sup>a</sup>	d (9.7)
3	154.4	CH	7.52 br s	155.0	CH	7.59	br s
4	108.6	C		109.4	C		
5	35.8	CH	3.02 dd (8.3,7.4)	39.3	CH	2.71	td (7.9,1.2)
6	81.1	CH	5.21 dd (8.3,1.2)	80.3	CH	4.04	dd (7.9,1.2)
7	63.8	CH		65.7	CH		br s
8	63.5	C		63.9	C		
9	45.0	CH	2.42 dd (9.7,7.4)	46.0	CH	2.45	dd (9.7,7.6)
10	18.6	CH <sub>3</sub>	1.61 s	18.8	CH <sub>3</sub>	1.58	s
11	169.7	C		171.7	C		
12	52.7	CH <sub>3</sub>	3.62 s	53.1	CH <sub>3</sub>	3.78	s
1'	100.7	CH	4.85 dd (7.9)	100.7	CH	4.83	dd (7.9)
2'	75.8	CH	3.30 dd (9.3,7.9)	75.7	CH	3.30	dd (9.3,7.9)
3'	78.7	CH	3.45 dd (9.3,9.0)	78.7	CH	3.26	dd (9.3,9.0)
4'	72.7	CH	3.26 t (9.0)	72.6	CH	3.45	t (9.0)
5'	79.6	CH	3.39 m	79.6	CH	3.39	m
6'	63.9	CH <sub>2</sub>	3.98 dd (11.9,2.1)	63.9	CH <sub>2</sub>	3.97	dd (11.9,2.1) dd (11.9,7.0)
			3.65			3.65	
1''	170.2	C					
2''	129.8	C					
3''	144.5	CH	6.89 tq (7.4,1.5)				
4''	29.2	CH <sub>2</sub>	2.38 t (7.4)				
5''	32.4	CH <sub>2</sub>	2.29 t (7.4)				
6''	139.5	C					
7''	127.4	CH	5.46 t (6.8)				
8''	59.7	CH <sub>2</sub>	4.13 d (6.8)				
9''	13.3	CH <sub>3</sub>	1.90 br s				
10''	24.3	CH <sub>3</sub>	1.82 s				

<sup>a</sup>δ in ppm.

groups, three olefins, an iridoid skeleton, and one β-glucose unit accounted for eight of those. The remaining degree of unsaturation was assumed to be due to an epoxide ring formed between C-7 and C-8, as inferred from the <sup>13</sup>C NMR data (δ<sub>c</sub> 63.8 and 63.5). Therefore, the constitution of **1** was deduced. The relative structure of **1** was deduced from a nuclear Overhauser enhancement spectroscopy (NOESY) spectrum of **1**. The representative correlations are shown in Figure 2. In the NOESY spectrum, the

correlations of H-5''/H-8'' and H-7''/H-10'' were observed. Thus, the configuration of the C-6''/C-7'' double bond was denoted as *Z*. The correlations of H-1/H-10, H-6/H-7, and H-7/H-10 suggested that the relative structure of sesinoside (**1**) was as in Figure 1.

To determine the configuration of **1**, a methanolysis reaction was applied to **1** (Figure 3). Sodium methoxide solution was added to a solution of **1** in anhydrous methanol at room temperature under N<sub>2</sub> for 6 h. Then, phlorigidoside C (**2**) and foliamenthic acid methyl ester (**3**) were derived in 34% and 46% yield, respectively. The <sup>1</sup>H and <sup>13</sup>C NMR spectroscopic (Table) and ESI-MS data of **2** were identical with those of phlorigidoside C [9].

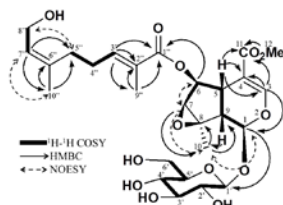


Figure 2: 2D NMR correlations of **1**.

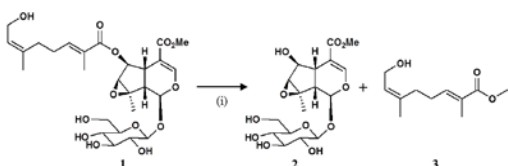


Figure 3: Methanolysis reaction of **1** [(i) NaOMe, MeOH, rt, 6 h, 34% (**2**), 46% (**3**)]

## Experimental

**General experimental procedure:** Optical rotations, JASCO DIP-370 spectrometer; UV, HITACHI U-2000A spectrometer; IR, JASCO FT/IR-300 spectrometer; NMR, BRUKER Avance 500 spectrometer; ESI-MS, WATERS SYNAPT G2 mass spectrometer.

**Plant materials:** Sesame seeds were purchased from Fukutane K. K. (Fukui, Japan). Seeds were spread evenly on moist vermiculite in trays and incubated at 25°C in the dark for 3-4 days. The seedlings (hypocotyls length, ca. 3~4 cm) were then illuminated by white light (30-50 μmol m<sup>-2</sup> s<sup>-1</sup>; FL 20SS/ W/ 18; Panasonic Electric Works Co., Osaka, Japan) for 7 days. After a week, they were harvested, collected, and frozen at -80°C until use.

**Extraction and isolation:** All parts of the illuminated seedlings (73 g FW) were homogenized in acetone (250 mL×2). The homogenate was filtered and allowed to dry *in vacuo* at 40°C. The residue (0.95 g) was subjected to ODS CC (φ 1.1 × 30 cm) with a MeOH/H<sub>2</sub>O (2:8/4:6/6:4/8:2/10:0) stepwise gradient and EtOAc, and separated into 5 fractions (SIA1-5). SIA4 (58.3 mg) was purified by reversed-

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phase HPLC (TSK-gel ODS-80Ts, TOSOH, φ 7.8 × 300 mm, flow rate 2.0 mL/min, 30% MeCN isocratic) to yield sesinoside (**1**, 5.6 mg).

**Methanolysis reaction of sesinoside:** Sodium methoxide solution (0.5 N, 0.1 mL) was added to a solution of sesinoside (**1**, 5.0 mg, 8.8 × 10<sup>-6</sup> mol) in anhydrous methanol (0.5 mL) and the mixture was stirred at room temperature under N<sub>2</sub> for 6 h. After 6 h, HCl (1 N, 0.12 mL) was added to stop the reaction. The reaction mixture was partition with EtOAc (10 mL) and H<sub>2</sub>O (10 mL). The EtOAc layer was dried with MgSO<sub>4</sub>, and both layers were evaporated. Water layer was purified by reversed-phase HPLC (TSK-gel ODS-80Ts, TOSOH, φ 7.8 × 300 mm, flow rate 2.0 mL/min, MeCN:H<sub>2</sub>O, 1:9 (0 min)→2:8 (30 min)) to afford phlorigidoside C (**2**, 1.2 mg) in 34% yield. The EtOAc layer was purified by reversed-phase HPLC [TSK-gel ODS-80Ts, TOSOH, φ 7.8 × 300 mm, flow rate 2.0 mL/min, MeCN:H<sub>2</sub>O, 1:9 (0 min)→5:5 (30 min)] to afford (6*Z*)-foliamenthic acid methyl ester (**3**, 0.8 mg) in 46% yield.

## Sesinoside (1)

Amorphous powder.

[α]<sub>D</sub><sup>25</sup>: -65.6 (c 1.00, CH<sub>3</sub>OH).

IR (KBr): 3398, 1705, 1635 cm<sup>-1</sup>.

UV λ<sub>max</sub> (MeOH) nm (log ε): 230 (4.10).

<sup>1</sup>H (500 MHz) and <sup>13</sup>C NMR (125 MHz): Table 1.

ESI-MS (positive ion): *m/z* 593 [M + Na<sup>+</sup>].

HRESI-MS: *m/z* 593.2217 [M + Na<sup>+</sup>] calcd for C<sub>27</sub>H<sub>38</sub>O<sub>13</sub>Na: 593.2210.

## Phlorigidoside C (2)

<sup>1</sup>H (500 MHz) and <sup>13</sup>C NMR (125 MHz): Table 1.

ESI-MS (positive ion): *m/z* 427 [M + Na<sup>+</sup>].

HRESI-MS: *m/z* 427.1226 [M + Na<sup>+</sup>] calcd for C<sub>17</sub>H<sub>24</sub>O<sub>11</sub>Na: 427.1216.

## (6Z)-Foliamenthic acid methyl ester (3)

<sup>1</sup>H NMR (500 MHz, CD<sub>3</sub>OD): δ<sub>H</sub> 6.79 (1H, tq, *J*=7.4 and 1.5 Hz, H-3), 5.45 (1H, t, *J*=6.5 Hz, H-7), 4.10, (2H, dd, *J*=6.5 and 1.0 Hz, H-8), 3.76, (3H, s, OMe), 2.37, (2H, td, *J*=7.5 and 7.4 Hz, H-4), 2.26, (2H, t, *J*=7.5 Hz, H-5), 1.87, (3H, br s, H-9), 1.80(3H, s, H-10)

ESI-MS (positive ion): *m/z* 221 [M + Na<sup>+</sup>].

HRESI-MS: *m/z* 221.1156 [M + Na<sup>+</sup>] calcd for C<sub>11</sub>H<sub>18</sub>O<sub>5</sub>Na: 221.1154.

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