SHORT REPORT

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Aromatic Compounds from the Marine-Derived Fungus *Aspergillus versicolor*

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Abstract: Chemical investigation of the EtOAc extract of a marine-derived fungus *Aspergillus versicolor* SZW-5 led to the isolation of one new compound, named aspeverether A (**1**), and seven known compounds. The structures were determined by extensive analyses of spectroscopic data (1D and 2D NMR, and HRESIMS). Compounds **1** and **3** possessed an unusual 1,3-dimethoxy-2-vinylbenzene moiety, which is rarely found in nature. Compound **6** showed strong inhibitory effect toward α-glucosidase with an IC_{50} value of 71 μM, being more active than the positive acarbose (210 μM).

Keywords: *Aspergillus versicolor*; aspeverether A; structure elucidation; marine.

1. Plant Source

Fungus SZW-5 was isolated from the sediments that were collected at a depth of -3.5 m from the Shenzhen River Estuary. The strain was identified as *Aspergillus versicolor* by analysis of the internal transcribed spacer (ITS) region of the rDNA sequence. The ITS sequence has been submitted to the GenBank data base (http://www.ncbi.nlm.nih.gov) with the accession number MG845247. The strain SZW-5 was deposited at the Marine Culture Collection of China.

2. Previous Studies

In recent years, marine-derived fungi have attracted much attention from natural medicinal chemists, and many secondary metabolites possessing intriguing structures and various activities have been reported. The fungus *A. versicolor* has been proved to be prolific. Previous chemical study of marine-derived *A. versicolor* led to the identification of many secondary metabolites, including alkaloids [1-3], cyclopeptides [4-6], polyketides [7, 8], and depsides [9, 10], some exhibited pronounced biological activities, such as cytotoxic [2], antimicrobial [1], lipid-lowering [6], and DPPH radical scavenging effects [10]. In our study of bioactive secondary metabolites of a marine-

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derived fungus *A. versicolor* SZW-5, eight aromatic compounds including a new one were obtained (Figure 1). Herein, the isolation, structural identification, and the inhibitory effects toward *α*-glucosidase of the metabolites were described.

3. Present Study

The solid-state fermentation was carried out in 15 erlenmeyer flasks (500 mL) with 70 g of rice and artificial sea-water (90 mL), and the contents were autoclaved at 15 psi for 30 min. Each flask was inoculated with 3.0 mL of the spore inoculum and incubated at room temperature for 35 days. The fermented materials were extracted with EtOAc (3 × 2000 mL) and to give an EtOAc extract (3.1g), which was subjected to ODS silica gel column chromatography (CC) eluted with MeOH/H_2O (20:80 to100:0) to afford five fractions (F1–F5). F3 was chromatographed over ODS silica gel CC (MeOH/H_2O: 20:80 to100:0) to give six fractions (F3a–F3f). F3a was purified by HPLC using CH_3CN/H_2O (28:72, 3 mL/min) as eluent to afford **4** (3.2 mg, t_R 28.1 min) and **5** (1.9 mg, t_R 33.2 min). F3c was separated by ODS silica gel CC eluting with MeOH/H_2O (20:80 to 100:0) to give six fractions (F3d1–F3d6). F3d2 was separated by HPLC (MeOH/H_2O = 50:50, 3 mL/min) to yield five fractions (F3d2a–F3d2e). F3d3c was purified by HPLC (CH_3CN/H_2O = 41:59, 3 mL/min) to afford **6** (6.5 mg, t_R 19.5 min). F5 was further chromatographed over ODS silica gel CC eluted with MeOH/H_2O (20:80→100:0) to afford four subfractions (F5a–F5d). Purification of F5a by HPLC (CH_3CN/H_2O = 54:46, 3 mL/min) gave **7** (5.3 mg, t_R 9.7 min) and **8** (3.7 mg, t_R 11.9 min). F5d was purified by HPLC (CH_3CN/H_2O=68:32, 3 mL/min) to give **2** (14 mg, t_R 24.5 min), **3** (8.8 mg, t_R 22.2 min), and **1** (24 mg, t_R 24.2 min).

Aspeverether A (1): light yellow oil; UV (MeOH) λ_{max} (log ε) 299 (3.81), 258 (4.22), 220 (4.39); ^1H and ^{13}C NMR data, see Table 1; positive ESIMS *m/z* 363.1561 $[M + Na]^+$ (calculated for $C_{21}H_{24}O_4Na$, 363.1567).

α-Glucosidase Assay: The *α*-glucosidase inhibitory effect was assessed as described in the literature [11].

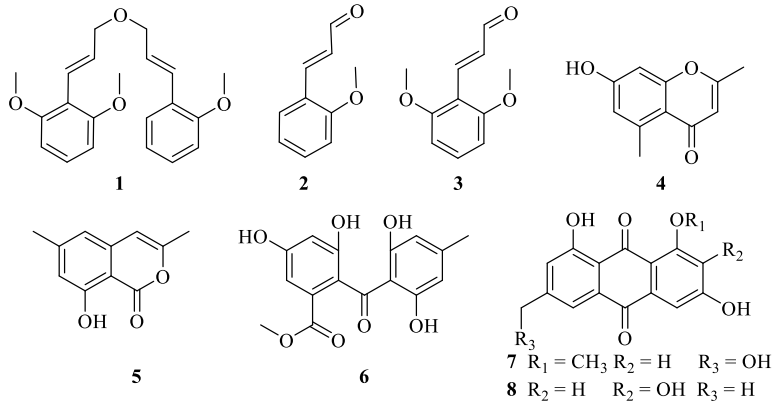

Figure 1. Structures of compounds **1**–**8** from *A. versicolor* SZW-5.

Compound **1**, a light yellow oil, had the molecular formula $C_{21}H_{24}O_4$ as established by the HRESIMS *m/z* 363.1561 $[M + Na]^+$ (calculated 363.1567) and NMR data (Table 1), requiring ten double bond equivalents. The ^1H NMR data exhibited the presences of three aromatic methoxys (δ_H 3.84, 9H), four olefinic protons [δ_H 6.96 (1H, d, *J* = 16.2 Hz), 6.76 (1H, dt, *J* = 16.2, 6.0 Hz), 6.38 (1H, dt, *J* = 16.1, 6.0 Hz), 6.98 (d, *J* = 16.1 Hz)], a symmetrically 1,2,3-trisubstituted benzene [δ_H 6.65 (2H, d, *J* = 8.4 Hz), 7.18 (1H, d, *J* = 8.4 Hz)] , and a 1,2-disubstituted benzene [6.98 (1H, d, *J* = 7.8 Hz), 6.99 (1H, t, *J* = 7.8, 7.6 Hz);7.24 (1H, td, *J* = 7.8, 1.5 Hz); 7.51 (1H, dd, *J* = 7.6, 1.5 Hz)] (Table 1). The ^{13}C NMR spectrum indicated the presences of twenty-one carbon resonances, including sixteen

aromatic carbons for two benzenes and two double bonds, together with three methoxys (δ 56.1, 56.1, 55.8), and two oxymethylenes (δ_C 73.0, 71.4) (Table 1).

Table 1. ^{1}H (400 Hz) and ^{13}C NMR (100 Hz) Data of **1** in Acetone-d_6 (δ in ppm)

1					
No.	δ_H (mult., *J* in Hz)	δ_C	No.	δ_H (mult., *J* in Hz	δ_C
1		114.7, C	1′		126.7, C
2		159.5, C	2′		157.7, C
3	6.65, d (8.4)	104.9, CH	3′	6.98, d (7.8)	111.9, CH
4	7.18, d (8.4)	129.1, CH	4′	7.24, td (7.8, 1.5)	129.5, CH
5	6.65, d (8.4)	104.9, CH	5′	6.99, t (7.8, 7.6)	127.3, CH
6		159.5, C	6′	7.51, dd (7.6, 1.5)	127.5, CH
7	6.96, d (16.2)	123.4, CH	7′	6.99, d (16.1)	123.4, CH
8	6.76, dt (16.2, 6.0)	131.0, CH	8′	6.38, dt (16.1, 6.0)	128.1, CH
9/9′	4.19, dt (6.0, 1.4)	73.0, CH_2	9′	4.19, dt (6.0, 1.4)	71.4, CH_2
2-OCH_3	3.84, s	56.1, CH_3	2″-OCH_3	3.84, s	55.8, CH_3
6-OCH_3	3.84, s	56.1, CH_3			

The HMBC correlations from the three aromatic methoxys (δ_H 3.84) to the oxygenated aromatic carbons (δ_C 159.5 × 2, 157.7) indicated the presences of a 1,3-dimethoxy-1,2,3-tri substituted and a 2-methoxy-1,2-disubstituted benzene rings (Figure 2). The COSY spectrum indicated the ^{1}H-^{1}H spin systems (H-7/H-8/H_2-9 and H-7′/H-8′/H_2-9′) for two propenyl moiety. Additional HMBC correlations from H-7 (δ_H 6.96) and H-7′ (δ_H 6.99) to C-1 and C-1′ assigned an 1,3-dimethoxy cinnamyl and a 2-methoxy cinnamyl moieties. And these two cinnamyl moieties were connected via a ether linkage by the HMBC correlations from H-9 to C-9′ and H-9′ to C-9. Thus, the structure of **1** was established as depicted and was named aspeverether A. Compound **1** possessed an unusual 1,3-dimethoxy-2-vinylbenzene moiety, which is rarely found in nature.

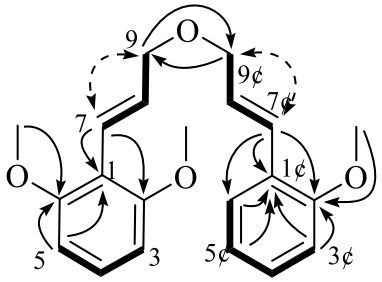

Figure 2. ^{1}H-^{1}H COSY (—), HMBC (→), and NOE (↖-↗) correlations of **1**.

Besides, the known compounds were established as O-methoxy cinnamaldehyde (**2**) [12], 2,6-dimethoxy cinnamaldehyde (**3**) [13], altechromone A (**4**) [14], saccharonol A (**5**) [15], sulochrin (**6**) [16], questinol (**7**) [17], 7-hydroxyemodin (**8**) [18] by comparing their ^{1}H and ^{13}C NMR data with reported data in the literature.

Compounds **1**–**8** were tested for their inhibitory activities against *α*-glucosidase. As results, compound **6** exhibited an IC_{50} value of 71 μM, which is more active than the positive control acarbose (210 *μ*M). And other compounds showed inhibitions less than 30% at the concentration of 200 μM.

Supporting Information

Supporting Information accompanies this paper on http://www.acgpubs.org/journal/records-of-natural-products

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