SHORT REPORT

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Polyacetylenes from the Roots of *Aralia dumetorum*

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Abstract: A new polyacetylene, heptadeca-8,16-dien-4,6-diyn-3,l0-diol (**1**) along with four known polyacetylenes, 1,2-dihydrodendroarboreol B (**2**), heptadeca-1,8-dien-4,6-diyn-3,l0-diol (**3**), 3*R*, 8*S*-falcarindiol (**4**) and 3*R*,8*R*-dehydrofalcarindiol (**5**) were isolated from the ethanol extract of *Aralia dumetorum*. The structures of the isolates were elucidated on the basis of 1D and 2D NMR spectrums and by comparison of the spectroscopic data with those reported for structurally related compounds. The α-glucosidase inhibitory activity of compounds **1**-**5** was evaluated using α-glucosidase inhibitory assay, in which all compounds displayed good inhibitory activity with IC_{50} values ranging from 4.2 ~ 36.2 μM.

Keywords: Araliaceae; *Aralia dumetorum*; polyacetylenic compound; *α*-glucosidase inhibitor. © 2019 ACG Publications. All rights reserved.

1. Plant Source

The plant of *A. dumetorum* was collected in Kunming, Yunnan Province, P.R. China, September 2012, and identified by Associate Prof. Qingsong Yang from Yunnan Minzu University. A voucher specimen (YNMZ-20120901) was deposited in the Key Laboratory of Chemistry in Ethnic Medicinal Resources, State Ethnic Affairs Commission & Ministry of Education, Yunnan Minzu University.

2. Previous Studies

Previous phytochemical studies have reported several diterpenes with cytotoxic activities from *A. dumetorum* [1,2].

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3. Present Study

The air-dried roots of *A. dumetorum* (9.5 kg) were extracted with 95% EtOH (50 L) at room temperature for three times. After being concentrated *in vacuo*, the extract (1 kg) was suspended in water and fractionated by successive partitioning with petroleum ether and EtOAc to provide a PE fraction (480 g) and EtOAc (110 g) fraction. The EtOAc fraction was subjected to a silica gel CC in a step gradient manner with petroleum ether-acetone (1:0 to 0:1) to afford fractions A-G. Fraction C (18 g) was subjected to a silica gel CC and eluted with petroleum ether-EtOAc (50:1, 1:1) to afford five fractions C1 – C5. The fraction C3 (90 mg) was purified by a Sephadex LH-20 CC ($CHCl_3$/MeOH 1:1) to obtain compound **5** (7.0 mg). The fraction C5 (670 mg) was further purified by HPLC (MeOH/H_2O 80:20) give compound **3** (5.6 mg). Fraction D4 (8.7 g) was performed on a silica gel CC (petroleum ether- EtOAc, 30:1 to 0:1) to offer six fractions D1-D6. The fraction D1 (120 mg) was purified by a Sephadex LH-20 CC ($CHCl_3$/MeOH 1:1) to obtain compound **2** (2.6 mg). Compound **4** (8.9 mg) was obtained from fraction D3 (320 mg) by HPLC (MeOH/H_2O 85:15). Fraction D4 (289 mg) was subjected to a silica gel CC (petroleum ether-EtOAc, 30:1 to 0:1) and further purified by HPLC (MeOH/H_2O 75:25) to yield compound **1** (2.1 mg).

Heptadeca-8,16-dien-4,6-diyn-3,l0-diol (1): light yellow oil. $[\alpha]_D^{23.6}$ = -7.7 (c = 0.078, $CHCl_3$); UV ($CHCl_3$): λ_{max} (log ε): 242 (3.72), 270 (3.46) ; IR ν_{max} ($CHCl_3$): = 3433, 2925, 2854, 1662, 1633, 1383, 131 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 1.03 (3H, *t*, *J* = 7.2 Hz, H-1), 1.77 (2H, *m*, H-2), 1.30 (2H, *m*, H-12), 1.31 (2H, *m*, H-13), 1.35 (2H, *m*, H-14), 1.50 (2H, *m*, H-11), 2.05 (2H, *m*, H-15), 4.44 (1H, *t*, *J* = 6.0 Hz, H-3), 4.65 (1H, *m*, H-10), 4.94 (1H, *brd*, *J* = 10.2 Hz, H-17b), 5.00 (1H, *brd*, *J* = 17.2 Hz, H-17a), 5.59 (1H, *d*, *J* = 10.8 Hz, H-8), 6.06 (1H, *dd*, *J* = 10.8, 8.3 Hz, H-9), 5.81 (1H, *m*, H-16), ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = 9.3 (CH_3, C-1), 30.6 (CH_2, C-2), 64.2 (CH, C-3), 84.2 (C, C-4), 69.1 (C, C-5), 74.5 (C, C-6), 78.3 (C, C-7), 108.6 (CH, C-8), 149.6 (CH, C-9), 69.3 (CH, C-10), 36.5 (CH_2, C-11), 24.8 (CH_2, C-12), 28.9 (CH_2, C-13), 28.8 (CH_2, C-14), 33.7 (CH_2, C-15), 139.0 (CH, C-16), 114.3 (CH_2, C-17); HRESIMS: *m/z* 261.1867 (calcd. 261.1855 for $C_{17}H_{25}O_2$).

Bioactivity Test- Alpha-glucosidase inhibitory assay: Alpha-glucosidase is a carbohydrate-hydrolase that releases alpha-glucose and hydrolyzes terminal non-reducing (1→4)-linked alpha-glucose residues to release a single alpha-glucose molecule. Less glucose is absorbed because the carbohydrates are not broken down into glucose molecules. [3] The alpha-glucosidase inhibitory assay was employed to detect the α-glucosidase inhibitory activity of the isolates and acarbose was used as the positive control [4]. 50 µL of 100 mM phosphate buffer (pH 6.8), 10 µL of 1.0 mg/mL reduced glutathione and 10 µL of the sample were mixed together. The mixture was added to a 96-well plate, and the 20 µL of 0.5 U/mL *α*-glucosidase solution was added. After incubating at 37 ºC for 5 min, 20 µL of *p*-Nitrophenyl *α*-D-glucopyranoside substrate was added to the mixture to start the reaction. The reaction mixture was incubated at 37 °C for 15 min, and then 50 µL of 0.1 M Na_2CO_3 solution was added to the mixture to terminate the reaction. The absorbance (A) was immediately recorded with a microplate spectrophotometer at 400 nm to estimate the enzymatic activity.

The dried and powdered roots of *A. dumetorum* (9.5 kg) were extracted with 95% EtOH (50 L) at room temperature for three times. After being concentrated *in vacuo*, the extract (1 kg) was suspended in water and fractionated by successive partitioning with petroleum ether and EtOAc to provide a PE fraction (480 g) and EtOAc (110 g) fraction. The EtOAc fraction was subjected to conventional purification procedures and resulting in the isolation one new polyacetylene named heptadeca-8,16-dien-4,6-diyn-3,l0-diol (**1**), as well as four known polyacetylenes (**2 - 5)** (Figure 1).

Figure 1. The structures of compounds **1-5**

Compound **1** was obtained as light yellow oil. The molecular formula, $C_{17}H_{24}O_2$, was established by ^{13}C NMR and HRESIMS data (261.1867 [M + H]$^+$, calcd 261.1855), suggesting 6 indices of hydrogen deficiency. IR absorptions at 3433 and 1662 cm^{-1} indicated the presence of hydroxyl and double bond functional groups. Analysis of the ^{13}C NMR data and the HMQC spectrum showed that the 17 carbons comprised seven methylenes (including one terminal olefin), five methines (three olefinic carbons and two oxygenated carbon), four quaternary carbons and a methyl group. ^{1}H NMR (Table 1) exhibited a terminal olefin signals (δ_H 5.81, m; δ_H 5.00, brd, J = 17.2 Hz; δ_H 4.94, brd, J = 10.2 Hz), two oxymethine signals (δ_H 4.44, t, J = 6.0 Hz and δ_H 4.65, m), and a methyl (δ_H 1.03, t, J = 7.2 Hz) as well as six methylenes (δ_H 1.30-2.06). ^{1}H NMR spectrum also exhibited a pair of doublets at δ_H 5.59 (1H, H-8) and δ_H 6.06 (1H, H-9). The ^{1}H-^{1}H COSY spectrum provided two sequences of correlated protons: CH_3–CH_2–CH(OH)– and –CH=CH–CH(OH)–$(CH_2)_5$–CH=CH_2. Detailed analysis of the HMBC spectrum established the connectivity of the two partial structures was separated by four quaternary carbons. Selected ^{1}H-^{1}H COSY and HMBC (H→C) correlations for **1** were presented in Figure 2. All data of compound **1** were highly similar to those of 1,2-dihydrodendroarboreol B (**2**), a polyacetylenic natural product found in *Tridax procumbens* [5]. Two compounds differed only in the coupling constant of H-8 and H-9. The C-8–C-9 double-bond configuration was identified as *cis* on the basis of the $J_{8,9}$ coupling constant of 10.8 Hz. The relative configuration of C-3 was deduced the same as compound **2** for the optical rotation of **1** [$[\alpha]_D^{23.6}$ = -7.7 (c = 0.078, $CHCl_3$)] is very close to that of **2** [[α] = -10 (*c* 0.2, $CHCl_3$)]. The NMR data and the coupling constants at C-1 to C-3 of the two compounds are very consistent. The configuration at C-3 can not be determined by NOE for there is no correlation signal in its ROESY spectrum. The absolute configuration of **1** was unable to define for the paucity of its. Thus, compound **1** was elucidated as heptadeca-8,16-dien-4,6-diyn-3,l0-diol. Compounds **2**-**5** were identified on the basis of the NMR data as well as comparison with values from the literature [5-8].

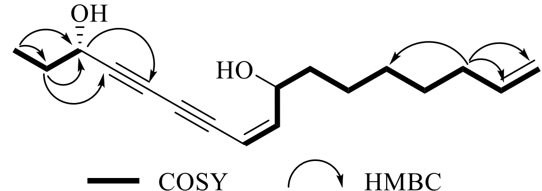

Figure 2.^{1}H-^{1}H COSY correlations and the selected HMBC correlations of compound **1**

Compounds (**1-5**) were tested for their *α*-glucosidase inhibitory activity. Acarbose was used as the positive control. Compounds **1 - 3** showed significant activity with IC_{50} values of 12.23, 9.38, and 4.15 μM, respectively. (Table 1)

Table 1. Inhibitory effects of compounds **1-5** on α-glucosidase

Compounds	IC_{50}, μM
1	12.23
2	9.38
3	4.15
4	36.23
5	35.62
Acarbose	162.64

Briefly, we reported five polyacetylene secondary metabolites from *A. dumetorum* to and their *α*-glucosidase inhibition activity. They could be the main bioactive components in the crude 95% EtOH extract of *A. dumetorum*. The plant may be a potential source for *α*-glucosidase inhibitors. The results supplied additional data for future utilization of *A. dumetorum*.

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Supporting Information

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

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