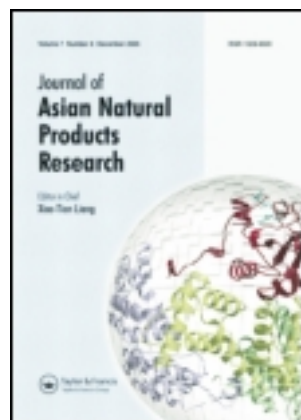


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## NOTE

### A novel 1,10-*seco* withanolide from *Physalis peruviana*

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A novel 1,10-*seco* withanolide, 1,10-*seco* withaperuvin C (**1**), together with four known withanolides, 4 $\beta$ -hydroxywithanolide E (**2**), visconolide (**3**), withanolide F (**4**), and withaphysanolide (**5**), was isolated from the aerial parts of *Physalis peruviana*. The structures of compounds **1–5** were determined on the basis of spectroscopic methods including extensive 1D and 2D NMR analysis. In addition, the possible biogenetic relationships among these five withanolides are discussed.

**Keywords:** *Physalis peruviana*; 1,10-*seco* withaperuvin C; withanolide; steroid

#### 1. Introduction

The genus *Physalis* (Solanaceae) includes about 120 species mainly distributed in South and North America. Five species of this genus are found in China [1]. *Physalis peruviana* is a common plant in China, and its fruit is edible, called ‘cape gooseberry’. It is also a medicinal plant widely used in folk medicine for treating diseases such as malaria, asthma, hepatitis, dermatitis, diuretics, and rheumatism [2,3]. In previous studies, a series of withanolides had been isolated from this plant [4–12]. In this paper, we report the isolation and elucidation of a new 1,10-*seco* withanolide, 1,10-*seco* withaperuvin C (**1**), together with four known withanolides: 4 $\beta$ -hydroxywithanolide E (**2**) [13,14], visconolide (**3**) [15], withanolide F (**4**) [16], and withaphysanolide (**5**) [14] from the aerial parts of *P. peruviana* (Figure 1). Compound 1,10-*seco* withaperuvin C (**1**) is the first example of steroids with a unique 1,10-*seco* withanolide skeleton isolated from the genus *Physalis*.

#### 2. Results and discussion

Compound **1** was isolated as a white amorphous solid, and showed a quasi-molecular ion peak  $[M+Na]^+$  at  $m/z$  509 in its positive ESI-MS. Its molecular formula was established as  $C_{28}H_{38}O_7$  by HR-ESI-MS at  $m/z$  509.2520. The IR spectrum showed strong absorptions at 3424 and 1708  $cm^{-1}$ , indicating the presence of hydroxyl and ester groups. The  $^1H$  NMR and  $^{13}C$  NMR spectra of **1** showed the presence of 28 carbons consisting of two carbonyls, three carbon–carbon double bonds including two four-substituted and one-disubstituted, four quaternary carbons including three oxygen-bearing functional groups, four  $sp^3$  methines including two oxygen-bearing functional groups, seven methylenes, and five methyls. Comparison of the NMR spectral data of **1** with those of the known withaperuvin C [17] indicated that compound **1** is also a withanolide derivative, and they have the same substituent patterns and relative configurations in

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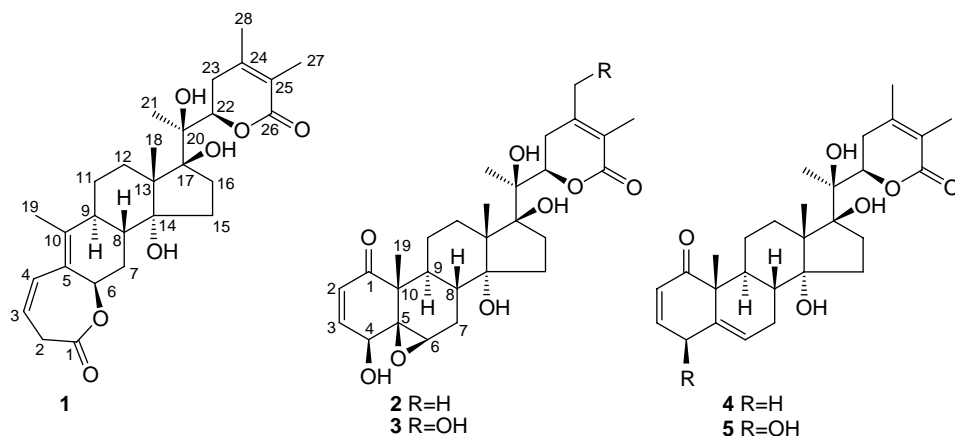


Figure 1. Structures of compounds 1–5.

rings C, D and in their respective lactone ring, except for the major differences in the A/B rings. In the  $^1\text{H}$  NMR spectrum, the signals at  $\delta_{\text{H}}$  3.84 (br d,  $J = 17.3$  Hz), 3.18 (dd,  $J = 17.3, 8.7$  Hz), 5.45 (br dd,  $J = 11.4, 8.7$  Hz), and 6.55 (dd,  $J = 11.4, 3.2$  Hz) were assigned to H-2 $\alpha$ , H-2 $\beta$ , H-3, and H-4, respectively, on the basis of an analysis of the  $^1\text{H}$ - $^1\text{H}$  COSY spectrum, and the downfield chemical shift at  $\delta_{\text{H}}$  1.79 (3H, s) implied that Me-19 was a vinylic methyl. In addition, a signal at  $\delta_{\text{H}}$  5.15 (1H, br s, H-6) together with the signal at  $\delta_{\text{C}}$  173.0 (C-1) in the  $^{13}\text{C}$  NMR spectrum indicated that **1** possesses a 1,10-*seco* withanolide skeleton [19]. This was

confirmed by the analysis of the HMBC spectrum, in which long-range correlations were observed between C-1 and H-2 $\beta$ , H-3 and H-6, between H-4 and C-5, C-6, and C-10, and between C-5 and Me-19, as shown in Figure 2. Therefore, a seven-membered  $\beta, \gamma$ -unsaturated lactone moiety was considered in ring A.

The  $\beta$ -configuration of the lactone bond at C-6 was established by a ROESY experiment (Figure 2). The ROESY spectrum showed the correlation between H-6 ( $\delta$  5.15, br s) and H-2 $\alpha$ , H-7 $\alpha$  and H-7 $\beta$ , indicating that H-6 has the same configuration as H-2 $\alpha$ . Since a small coupling between H-2 $\alpha$  and H-3 in the

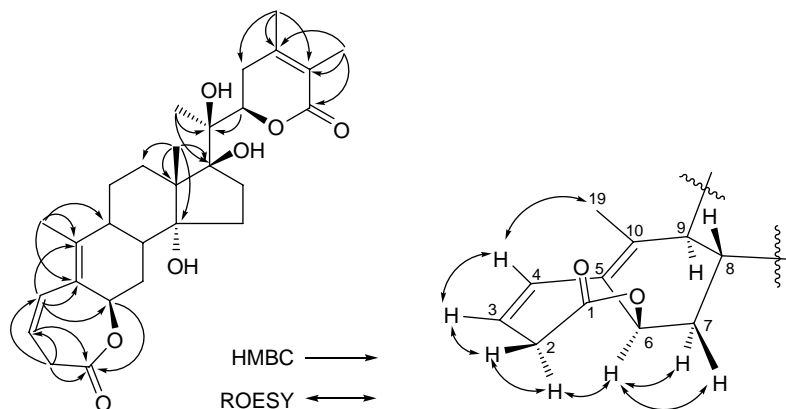


Figure 2. The key HMBC and ROESY correlations of compound 1.

$^1\text{H}$  NMR spectrum was observed due to an approximate  $90^\circ$  dihedral angle between them, a  $\beta$ -configuration of the lactone bond at C-6 was inferred, which is in agreement with those of stolonilide I [18] and 1,10-*seco* withametelin B [19]. Therefore, the structure of **1** was deduced as shown in Figure 1, which was named 1,10-*seco* withaperuvic C.

In addition to the new 1,10-*seco* withanolide **1**, four known withanolides **2–5** were isolated from the aerial parts of *P. peruviana*. The possible biogenetic relationships among these five compounds are discussed in Scheme 1.

were measured on a Bio-Rad FTS-135 spectrometer. 1D and 2D NMR spectra were recorded on a Bruker AM-400 and DRX-500 instruments with TMS as an internal standard. ESI-MS and HR-ESI-MS were measured on VG AutoSpec-3000 and API Qstar-Pulsar LC/TOF mass spectrometers. Column chromatography (CC) was performed over silica gel (200–300 mesh; Qingdao Marine Chemical Inc., Qingdao, China). TLC was performed on precoated silica gel G plates (Qingdao Marine Chemical Inc.), and spots were visualized by spraying with 10%  $\text{H}_2\text{SO}_4$  in EtOH, followed by heating.

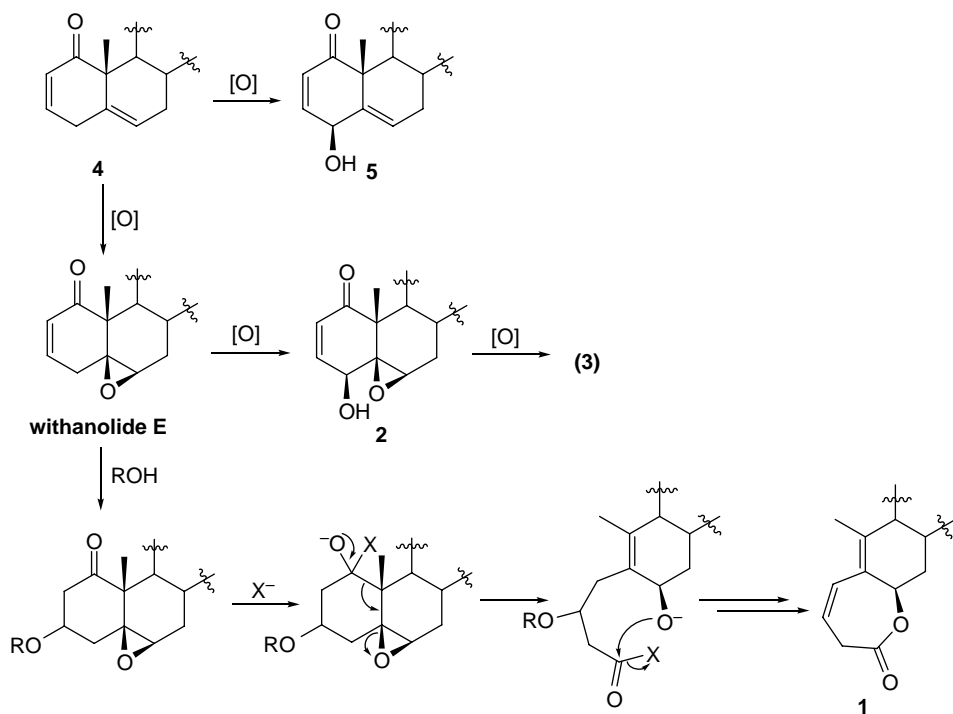
### 3. Experimental

#### 3.1 General experimental procedures

Optical rotations were determined on a Horiba SEPA-300 spectropolarimeter. UV spectra were recorded on a Shimadzu UV-2401PC spectrophotometer. IR spectra

#### 3.2 Plant material

The aerial parts of *P. peruviana* were collected from Kunming, Yunnan Province, China, in September 2005, and were identified by Prof. Chengmin Zhang, Kunming Institute of Botany. A voucher



Scheme 1. Possible biogenetic relationships of compounds 1–5.

Table 1.  $^1\text{H}$  NMR (400 MHz) and  $^{13}\text{C}$  NMR (100 MHz) spectral data for compound **1** in  $\text{CDCl}_3$  ( $\delta$  in ppm,  $J$  in Hz).

Position	$\delta_{\text{H}}$	$\delta_{\text{C}}$
1		173.0
2	3.84 (br d, $J = 17.3$ ) $\alpha$ -H, 3.18 (dd, $J = 17.3, 8.7$ ) $\beta$ -H	35.6
3	5.45 (br dd, $J = 11.4, 8.7$ )	116.7
4	6.55 (dd, $J = 11.4, 3.2$ )	129.3
5		124.1
6	5.15 (br s)	73.8
7	2.04 (m), 1.81 (m)	29.5
8	2.05 (m)	36.9
9	2.57 (m)	39.5
10		143.4
11	2.00 (m), 1.43 (m)	25.5
12	2.39 (m), 1.43 (m)	31.1
13		55.0
14		82.0
15	1.79 (m), 1.67 (m)	37.1
16	2.77 (m), 1.50 (m)	37.9
17		87.5
18	1.13 (s)	21.2
19	1.79 (s)	15.7
20		78.9
21	1.43 (s)	19.6
22	4.86 (dd, $J = 12.2, 4.0$ )	79.7
23	2.54 (m)	34.3
24		151.0
25		121.2
26		166.1
27	1.87 (s)	12.3
28	1.94 (s)	20.6

specimen (No. 20050911) is deposited in the State Key Laboratory of Phytochemistry and Plant Resources in West China, Kunming Institute of Botany, Chinese Academy of Sciences.

### 3.3 Extraction and isolation

The air-dried aerial parts (6.0 kg) of *P. peruviana* were extracted with MeOH at room temperature ( $4 \times 40$  liters). The extracts were combined and concentrated, and the residue was suspended in  $\text{H}_2\text{O}$ , and then successively partitioned with petroleum ether,  $\text{CHCl}_3$ , and *n*-BuOH, respectively. The  $\text{CHCl}_3$ -soluble extract (33 g) was subjected to CC (silica gel;  $\text{CHCl}_3$ -MeOH 100:0-80:20) to afford 11

fractions (1-11). Fraction 8 was separated by repeated CC on silica gel, eluting with  $\text{CHCl}_3$ -MeOH (30:1-15:1) and petroleum ether-Me<sub>2</sub>CO (4:1-2:1) to afford **1** (10 mg) and **4** (234 mg). Fraction 6 provided **2** (425 mg) and **5** (34 mg) after being chromatographed over silica gel, eluting with petroleum ether-Me<sub>2</sub>CO (3:1-2:1). Fraction 10 was subjected to a silica gel column with gradient elution (petroleum ether-Me<sub>2</sub>CO 10:1-1:1), followed by repeated CC to obtain **3** (16 mg).

#### 3.3.1 1,10-seco withaperuvin C (I)

A white amorphous solid;  $[\alpha]_{\text{D}}^{22.8} + 76.1$  ( $c = 0.18, \text{CHCl}_3$ ); UV ( $\text{CHCl}_3$ )  $\lambda_{\text{max}}$  ( $\log \epsilon$ ) nm: 242 (3.93); IR (KBr)  $\nu_{\text{max}}$  ( $\text{cm}^{-1}$ ): 3424, 2923, 1708, 1388, 1288, 1137, 1088, 995;  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectral data: see Table 1; ESI-MS:  $m/z$  509  $[\text{M}+\text{Na}]^+$ ; HR-ESI-MS:  $m/z$  509.2520  $[\text{M}+\text{Na}]^+$  (calcd for  $\text{C}_{28}\text{H}_{38}\text{O}_7\text{Na}$ , 509.2515).

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