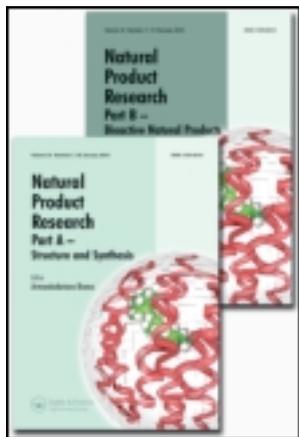


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Plantagiolide F, a minor withanolide from *Tacca plantaginea*

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A minor new withanolide, named plantagiolide F, was isolated from the whole plant of *Tacca plantaginea* (Hance). The structure of plantagiolide F was elucidated on the basis of spectroscopic methods including extensive 1- and 2-D NMR experiments.

Keywords: *Tacca plantaginea*; Taccaceae; plantagiolide F

1. Introduction

Tacca plantaginea (Taccaceae) is distributed in the southern part of China, and its rhizome has long been used in folk medicine as an analgesic, antipyretic, anti-inflammatory and for incised wounds (Jiangsu New Medical College, 1977). Recent chemical and pharmaceutical investigations on this species have demonstrated that taccalonolides A and E were the first natural steroids to show microtubule-stabilising activity (Tinley et al., 2003). Besides taccalonolides A and E, 11 other highly oxygenated taccalonolides have been isolated from this species (Z. Chen, Wang, & M. Chen, 1987; Chen, Wang, & Shen, 1988; Shen, Chen, & Gao, 1991, 1996; Shen, Chen, Gao, & Wichtl, 1997). Our previous chemical investigation of this plant led to the isolation of four new steroidal saponins; five new withanolides, plantagiolides A–E and three new taccalonolides (Liu & Chen, 2002; Liu, Ni, Hao, & Chen, 2006; Liu et al., 2006; Yang et al., 2008). As a part of our continuing search for novel structures, one new minor withanolide, named plantagiolide F, was isolated from the species. The structure was identified by extensive NMR spectroscopic means including HMQC, HMBC and ROESY techniques. In this article, we report the isolation and structural elucidation of this new withanolide.

2. Results and discussion

Plantagiolide F (**1**) was obtained as colourless powder. The molecular formula of **1** was deduced to be C₃₀H₄₂O₁₀ from HRESI-MS at *m/z* 585.2648 [M + Na]⁺

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(Calcd 585.2675), requiring 10 degrees of unsaturation. The UV spectrum of **1** showed absorption maxima at 240 nm, indicating the presence of conjugated systems. The IR spectrum, showing absorptions at 3446, 1735, 1698 and 1648 cm^{-1} implied the existence of hydroxyl, acyl and double bonds, respectively. Preliminary inspection of the ^1H - and ^{13}C -NMR spectra of **1** suggested that compound **1** was a C_{28} steroid with a six-membered α,β -unsaturated lactone ring in the side chain, and thus a withanolide. Under careful comparison, the ^1H - and ^{13}C -NMR spectral data (Table 1) of plantagiolide F (**1**) appear quite similar to those of plantagiolide B ($\text{C}_{32}\text{H}_{44}\text{O}_{11}$) (Liu et al., 2006), except for the reduction of an acetyl group, which was confirmed by the mass difference of $m/z=42$. Therefore, it was presumed that a hydroxyl group in **1** substituted the acetoxy group at C-1 or C-12 of plantagiolide B.

Table 1. ^1H - and ^{13}C -NMR and spectra data, HMBC correlations for **1** (400 MHz for ^1H and 100 MHz for ^{13}C in CDCl_3 , δ in ppm, J in Hz).

Position	δ_{H}	δ_{C}	HMBC
1	3.62 (d, 4.8)	69.4 (d)	C-2, 5, 10, Me-19
2	3.46 (brs)	52.7 (d)	C-1, 4, 5, 10
3	3.31 (brs)	57.1 (d)	C-1, 4, 5, 10
4 α	2.40 (d, 15.7)	33.2 (t)	C-2, 5, 10
4 β	2.00 (m)		C-2, 6
5		70.9 (s)	
6	2.91 (d, 3.5)	57.5 (d)	C-4, 5
7	3.46 (brs)	53.2 (d)	C-5
8	1.87 (m)	35.1 (d)	C-9, 15, 14
9	1.80 (m)	28.3 (d)	C-8, 12
10		39.3 (s)	
11 α	2.05 (m)	24.5 (t)	C-9, 13, 8
11 β	1.53 (m)		C-8, 9, 13
12	5.12 (brs)	74.7 (d)	C-9, 14, Ac
13		46.1 (s)	
14	1.86 (m)	43.1 (d)	C-8, 9, 15, Me-18
15 α	2.16 (m)	35.3 (t)	C-14, 16, 17
15 β	1.43 (m)		C-8, 14, 16
16	4.39 (m)	70.9 (d)	C-13
17	1.64 (dd, 3.8, 7.4)	49.9 (d)	C-12, 13, 16, 20, 22, Me-18, Me-21
18	1.06 (s)	13.3 (q)	C-12, 13, 14, 17
19	0.70 (s)	15.1 (q)	C-1, 5, 9, 10
20	2.53 (m)	33.1 (d)	C-13, 16, 17, 22, 23
21	0.97 (d, 6.8)	12.3 (q)	C-17, 20, 22
22	4.61 (m)	79.6 (d)	Me-21
23 α	2.50 (m)	31.7 (t)	C-20, 24, 25, Me-28
23 β	2.15 (d, 2.4)		Me-28
24		152.8 (s)	
25		125.7 (s)	
26		166.5 (s)	
27a	4.34 (ABd, 12.6)	57.3 (t)	C-24, 25, 26
27b	4.40 (ABd, 12.6)		C-24, 25, 26
28	2.06 (s)	20.1 (q)	C-23, 25, 24
Ac	2.05 (s)	21.2 (q)	
		169.8 (s)	

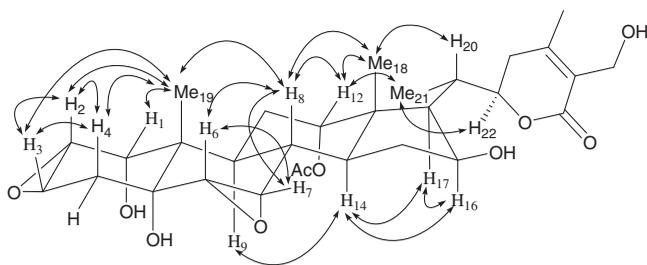
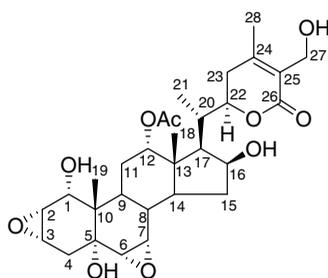


Figure 1. Significant ROESY correlations of plantagiolide F (1).

The acetoxy group was positioned at C-12 on the basis of HMBC correlations of H-12 (δ_{H} 5.12, brs) with C-9 (δ_{C} 28.3), C-14 (δ_{C} 43.1) and AcO (δ_{C} 169.8). Furthermore, the hydroxyl group was assigned to C-1 according to the upshift at 69.4 (C-1), which was confirmed by HMBC between H-2 (δ_{H} 3.46), H-3 (δ_{H} 3.31), and Me-19 (δ_{H} 0.70) and C-1 (δ_{C} 69.4).



The relative stereochemistry of **1** was elucidated by the ROESY experiment (Figure 1). In its ROESY spectrum, the correlations of H-8 with Me-18 and Me-19, H-14 with H-9 and H-17 indicated the B/C *trans* and C/D *trans* ring junctions. Furthermore, the correlations of H-1/Me-19, H-2/Me-19, H-3/Me-19, H-6/H-8, H-7/H-8 and H-12/Me-18 suggested that H-1, H-2, H-3, H-6, H-7 and H-12 were β -oriented. The configuration of H-16 was proved to be α -oriented judged by the ROESY correlations of H-16 with H-14 and H-17. NOE correlations from H-12 to Me-21 and H-20 to Me-18 (H-20 to both H-12 and Me-18) made it possible to confirm the 20*S* configuration. On the basis of the above evidence, the structure of compound **1** was established as (20*S*, 22*R*)-12 α -acetoxy-2 α ,3 α ,6 α ,7 α -diepoxy-1 α ,5 α ,16 β ,27-tetrahydroxywith-24-enolide, and named plantagiolide F.

3. Experimental

3.1. General experimental procedures

Melting points were recorded on an XRC-1 micro melting point apparatus and are uncorrected. Optical rotations were measured in a Jasco DIP-370 digital polarimeter. UV spectra were measured using a Shimadzu UV-2401 PC spectrophotometer. IR spectra were obtained on a Bio-Rad FTS-135 infrared spectrophotometer with KBr pellets. 1- and 2-D NMR experiments were performed on Bruker AM-400 and DRX-500 instruments with TMS as the internal standard.

Chemical shifts (δ) were expressed in ppm with reference to the solvent signals. The 2-D NMR experiments were carried out at 300 K with the following parameters: for HSQC spectrum, the experiment used 1024×128 data point matrices, SF01 500.030 MHz, SF02 125.743, NS 6, DS 16, AQ 0.0853 s, TE 300.0 K, D1 1.500 s, SWH 6009.6 Hz, SW 170.021 ppm, P16 1000 μ s; for HMBC spectrum, the experiment used 2048×128 data point matrices, SF01 500.030 MHz, SF02 125.743, NS 40, DS 16, AQ 0.170 s, TE 300.0 K, D1 1.400 s, SWH 6009.615 Hz, SW 224.964 ppm, P16 1000 μ s; for ROESY spectrum, the experiment used 1024×180 data point matrices, SF01 500.030 MHz, SF02 125.743, NS 8, DS 16, AQ 0.114 s, TE 300.0 K, D1 2.000 s, spin-lock pulse duration (P15) 285 ms, SWH 4496.403 Hz, SW 9.000 ppm. ESIMS and HRESIMS were recorded on an API QStar Pulsar LC/TOF spectrometer. Semi-preparative HPLC was carried out on Agilent 1100 apparatus equipped with a Zorbax SB-C-18 (Agilent, 9.4 mm \times 25 cm) column. Column chromatography was performed on silica gel (200-300 mesh, Qingda Marine Chemical Inc., China) or on silica gel H (10-40 μ m, Qingdao Marine Chemical Inc.) and Lichroprep Rp-18 (43-63 μ m, Merck). Fractions were monitored by TLC and spots were visualised by heating silica gel plates sprayed with 10% H₂SO₄ in EtOH.

3.2. Plant material

The whole plants *T. plantaginea* were collected in Guilin, Guangxi Zhuang Autonomous Region, P.R. China, in August 1999, and identified by Professor De-Ding Tao, Kunming Institute of Botany, the Chinese Academy of Sciences. A voucher was deposited in the Herbarium of the Kunming Institute of Botany, CAS.

3.3. Extraction and isolation

The powdered air-dried plants *T. plantaginea* (30 kg) were exhaustively extracted three times with 95% EtOH under reflux. After evaporation, the semi-solid residue (1.5 kg) was suspended in water and partitioned with CHCl₃ and *n*-butanol, successively. The CHCl₃ extract (700 g) was subjected to silica gel column chromatography, eluting with a petroleum ether:EtOAc gradient (1:0, 10:1, 7:1, 5:1, 1:1) to give five fractions. Fraction 4 (150 g) was repeatedly chromatographed over silica gel (CHCl₃/MeOH, 150:1) and semi-preparative HPLC (MeCN:H₂O, 30:70; flow rate: 3 mL min⁻¹) to afford compound **1** (4 mg).

3.3.1. Plantagiolide F (**1**)

C₃₀H₄₂O₁₀, colourless powder; m.p. = 258-260°C; $[\alpha]_D^{22} = +49.11$ ($c = 0.21$, CHCl₃); UV (CHCl₃) λ_{\max} (log ϵ): 240 (3.47) nm; IR (KBr) ν_{\max} (cm⁻¹): 3446, 2925, 1735, 1698, 1648, 1396, 1244 and 1028; ¹H-NMR (CDCl₃, 400 MHz) and ¹³C-NMR (CDCl₃, 100 MHz) (Table 1); Positive ESI-MS m/z : 585 [M + Na]⁺; HRESI-MS m/z : 585.2648 [M + Na]⁺ (C₃₀H₄₂O₁₀Na, Calcd 585.2675).

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