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Cytotoxic triterpenoid saponins from *Ardisia pusilla*

Hai Feng Tang [a,*], Hou Wen Lin [b], Xiao Li Chen [a], Guang Cheng [c], Yue Ping Zhao [a], Ai Dong Wen [a]

[a] *Department of Pharmacy, Xijing Hospital, Fourth Military Medical University, Xi'an 710032, China*
[b] *Department of Pharmacy, Changzheng Hospital, Second Military Medical University, Shanghai 200003, China*
[c] *Department of Neurosurgery, Xijing Hospital, Fourth Military Medical University, Xi'an 710032, China*

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Abstract

A new triterpenoid saponin, 3-*O*-{β-D-xylopyranosyl-(1 → 2)-β-D-glucopyranosyl-(1 → 4)-[β-D-glucopyranosyl-(1 → 2)]-α-L-arabinopyranosyl}-3β,16α,28α-trihydroxy-13β,28-epoxy-oleanan-30-al (ardipusilloside III, **1**), together with two known saponins, ardisiacrispins A (**2**) and B (**3**), were isolated from the whole plants of *Ardisia pusilla* A. DC. Their structures were elucidated by extensive spectral analysis and chemical evidences. Saponins **1** and **3** exhibited significant cytotoxicity against human glioblastoma U251MG cells.

Keywords: *Ardisia pusilla*; Triterpenoid saponin; Ardipusilloside III; Cytotoxic activities

Ardisia pusilla A. DC (Myrsinaceae) is a widely occurring shrub in southern China. Its whole plants, known as 'Jiu Jie Long' (Chinese name), have been used as an antidote in traditional medicine [1]. Previous chemical studies have led to the isolation of three triterpenoid saponins, ardipusillosides I, II and an unnamed saponin with significant antitumor effects in both Lewis pulmonary carcinoma and hepatocarcinoma [2–5]. In this paper, we report the isolation and structural elucidation of a new minor triterpenoid saponin named ardipusilloside III (**1**), along with two known saponins, ardisiacrispin A (**2**), 3-*O*-{β-D-xylopyranosyl-(1 → 2)-β-D-glucopyranosyl-(1 → 4)-[β-D-glucopyranosyl-(1 → 2)]-α-L-arabinopyranosyl} cyclamiritin A, and ardisiacrispin B (**3**), 3-*O*-{α-L-rhamnopyranosyl-(1 → 2)-β-D-glucopyranosyl-(1 → 4)-[β-D-glucopyranosyl-(1 → 2)]-α-L-arabinopyranosyl} cyclamiritin A (Fig. 1) [6,7]. Saponins **1** and **3** showed potential cytotoxicity against human glioblastoma U251MG cells.

Compound **1**, a colorless amorphous powder, mp 240–241 °C, $[\alpha]_D^{22}$ − 3.6 (*c* 0.15, MeOH), was positive to Liebermann–Burchard and Molish tests. The molecular formula was established as $C_{52}H_{84}O_{23}$ by the pseudomolecular ion $[M+Na]^+$ at *m/z* 1099.5310 (calcd. 1099.5301) in the positive HR–ESI–MS and pseudomolecular ion $[M-H]^-$ at *m/z* 1075 in the negative ESI–MS. Both the pseudomolecular ions were 16 mass units larger than those of the known saponin **2**. Its negative ESI–MS/MS (parent ion at *m/z* 1075) showed significant fragment peaks at *m/z* 943 $[1075–132]^-$, 913 $[1075–162]^-$, 781 $[943–162]^-$, 619 $[781–162]^-$, and 487 $[619–132]^-$. Compound **1** displayed

* Corresponding author.
E-mail address: tanghaifeng71@163.com (H.F. Tang).

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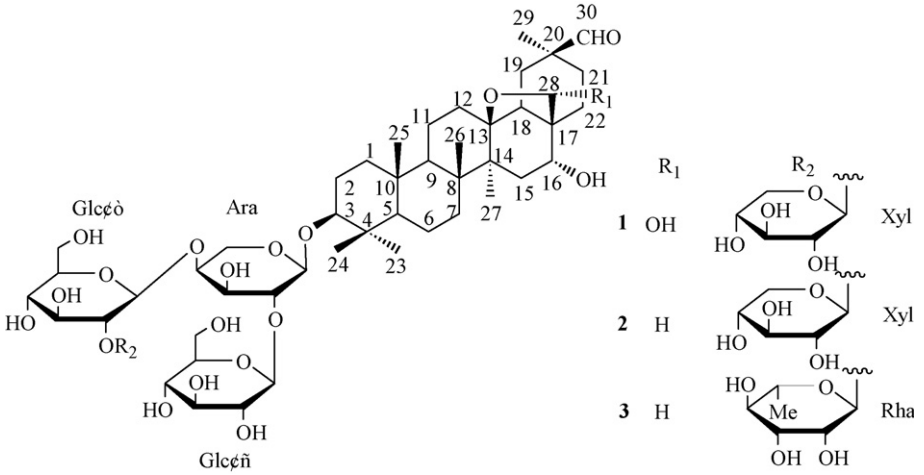

Fig. 1. Structures of saponin **1**, **2** and **3**.

52 carbon signals in its ^{13}C NMR spectrum, of which 30 could be assigned to the signals of the aglycone. It was evident that **1** was a triterpenoid saponin related to oleanane skeleton based on the ^{1}H NMR spectral signals (Table 1) assigned to six tertiary methyl groups at δ 0.81, 1.00, 1.06, 1.18, 1.29 and 1.55, together with six corresponding sp^3 carbon signals in the ^{13}C NMR spectrum (Table 1). The presence of an aldehyde group at C-30 was deduced from the NMR

Table 1
^{1}H (600 MHz) and ^{13}C NMR (150 MHz) data of ardipusilloside III (**1**) in C_5D_5N (δ in ppm, J in Hz).

Position	δ_H	δ_C	Position	δ_H	δ_C
1	1.60 brd (13.2), 0.79 m	39.1	Ara		
2	2.00 m, 1.81 m	26.5	1	4.80 d (5.4)	104.3
3	3.13 dd (11.4, 4.2)	89.0	2	4.51 m	79.9
4	–	39.5	3	4.25 m	73.5
5	0.64 d (11.4)	55.6	4	4.20 m	78.8
6	1.39 m	17.9	5	3.64 brd (10.8), 4.60 brd (12.0)	63.6
7	1.50 m, 1.18 m	34.2	Glc I		
8	–	42.5	1	5.48 d (7.8)	104.7
9	1.21 d (12.6)	50.4	2	4.04 m	76.2
10	–	36.7	3	4.21 m	78.2
11	1.66 m, 1.41 m	19.1	4	4.16 m	71.9
12	2.58 m, 2.04 m	31.1	5	3.97 m	78.0
13	–	87.2	6	4.50 m, 4.34 dd (11.4, 4.2)	62.8
14	–	44.9	Glc II		
15	2.18 dd (13.8, 4.8), 1.48 m	36.9	1	5.05 d (7.8)	104.1
16	4.20 m	76.1	2	3.92 t (9.0)	85.2
17	–	42.4	3	4.17 m	77.4
18	1.86 m	49.1	4	4.14 m	71.0
19	2.15 m	34.4	5	3.75 m	78.3
20	–	48.5	6	4.38 dd (11.4, 3.6), 4.24 m	62.2
21	2.57 m	30.8	Xyl		
22	1.99 m, 1.84 m	28.1	1	4.94 d (7.8)	107.5
23	1.18 s	28.0	2	3.96 m	75.9
24	1.00 s	16.6	3	3.99 m	77.6
25	0.81 s	16.3	4	4.08 m	70.6
26	1.29 s	18.5	5	4.53 m, 3.71 m	67.2
27	1.55 s	19.7			
28	5.12 s	99.2			
29	1.06 s	24.3			
30	9.70 s	207.9			