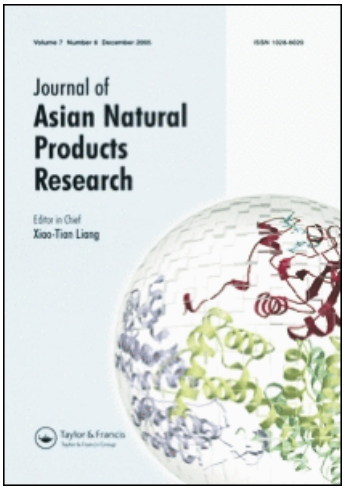

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New Tetracyclic Triterpene Glycosides from *Picria fel-tarrae* Lour

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NEW TETRACYCLIC TRITERPENE GLYCOSIDES FROM *PICRIA FEL-TARRAE* LOUR.

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Four tetracyclic triterpene glycosides picfeltarraenins VI(**4**), VII(**5**), VIII(**6**) and IX(**7**) along with three known compounds picfeltarraenins I_A, I_B and II were isolated from the water soluble part of *Picria fel-tarrae*. Their structures were elucidated on the basis of chemical and spectroscopic methods.

Keywords: *Picria fel-tarrae* Lour.; Scrophulariaceae; Triterpene glycosides; Picfeltarraenins VI VII VIII and IX

INTRODUCTION

Picria fel-tarrae Lour. is a plant belonging to the family Scrophulariaceae [1]. It grows widely in Southern China, namely Guangdong, Guangxi, Yunnan and Guizhou Provinces. It has long been used as a herbal medicine by local people for the treatment of inflammation [2] and the dry powdered extract of this plant has been prepared as an antibacterial medicament by Wuzhou Chinese Pharmaceutical Company [3].

Previously Gan *et al.* have isolated six cucurbitacin aglycones picfeltarraegenin I–VI from the alcoholic extract of *P. fel-tarrae* after acid hydrolysis [4] and they also isolated three main glycosides Pf I_A, Pf I_B and Pf II from ethanol extract of the plant [5].

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The cucurbitacin triterpenes exhibited potent biological actions [6], and the raw material of *P. fel-tarrae* has long been used as a medicament in China. Therefore we are interested in the further study of chemical constituents.

In a previous paper, we reported the isolation of three triterpene glycosides picfeltarraenins III, IV and V [7]. This paper deals with the isolation and structural elucidation of four new monose glycosides from the water soluble part of the total plant.

RESULTS AND DISCUSSION

From the water soluble part of *P. fel-tarrae*, in addition to the known tetracyclic triterpene glycosids Pf I_A, Pf I_B and Pf II, four new monose glycosides Pf VI (**4**), VII (**5**), VIII (**6**) and IX (**7**), were isolated (see Fig. 1). Their structures were elucidated on the basis of spectroscopic analysis including 2D NMR techniques. The structure of Pf VI (**4**) and Pf VII (**5**) were established by spectroscopic methods as picfeltarraegenin I-3-O-β-D-glucopyranoside (**4**) and picfeltarraegenin I-3-O-β-D-xylopyranoside (**5**), which have been prepared by partial hydrolysis of Pf I_A and Pf I_B [5] and were first found directly in nature.

Pf VIII (**6**), was obtained as colorless powder. It showed a violet spot with 1% vanillin H_2SO_4 after heating. Pf VIII showed a C-22 unconjugated carbonyl group absorption at 1750 cm^{-1} in IR and absence of conjugated carbonyl absorption 261 nm in UV spectrum indicating an unsaturated ring E.

FAB-MS of Pf VIII exhibited a molecular ion peak at m/z 664 and a fragment at m/z 502 $[M-162]^+$ suggesting the molecular formula $C_{36}H_{56}O_{11}$ with a hexose moiety.

Micro acid hydrolysis of Pf VIII led to picfeltarraegenin II and glucose spot on TLC. ^{13}C-NMR data of Pf VIII (see Table II) showed six signals at δ104.45d, 76.20d, 78.85d, 71.44d, 78.71d and 62.75t of glucose and 30 other carbon signals of aglycone for picfeltarraegenin II (**2**). ^1H-NMR chemical shifts of Pf VIII were assigned (Table I) in comparison with those of picfeltarraegenin II by $^1H-^1H$ COSY NMR spectrum.

The β-configuration at the anomeric center of the glucopyranosyl moiety was suggested by the large coupling constant ($J_1-J_2 = 7.8$ Hz) of the anomeric proton in the ^1H-NMR spectrum. Consequently the structure of picfeltarraenin VIII was elucidated as picfeltarraegenin II-3-O-β-D-glucopyranoside (**6**).

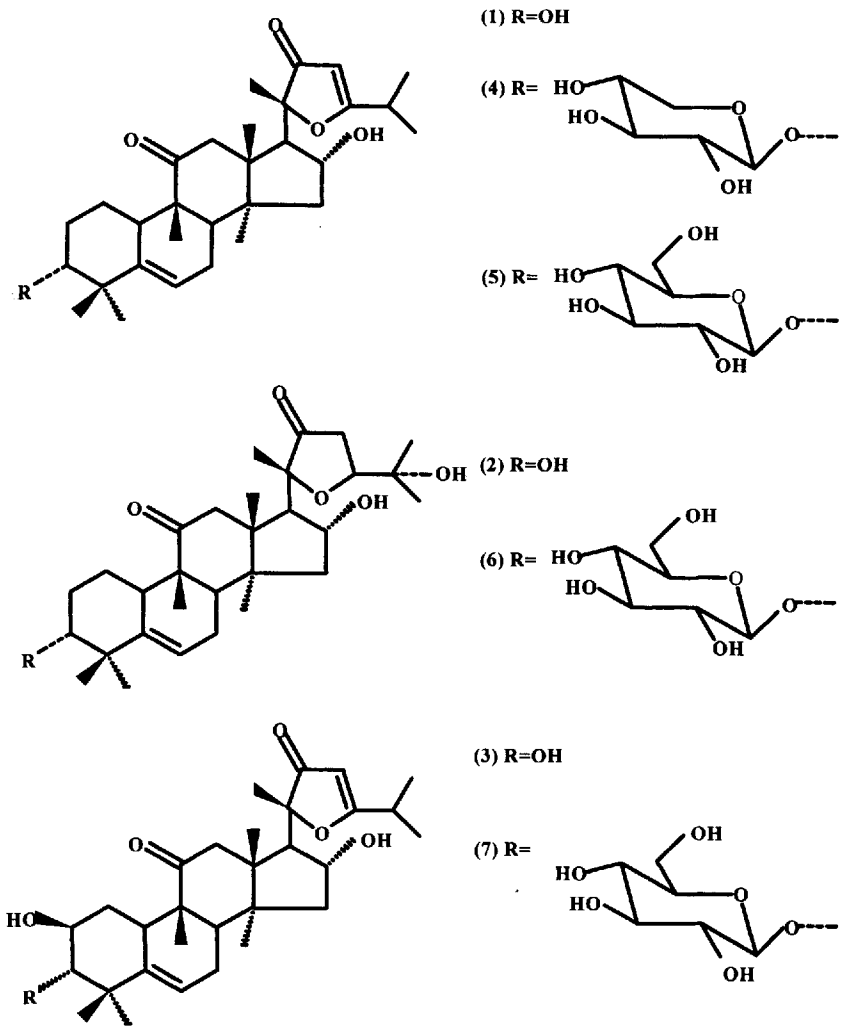

FIGURE 1

Pf IX (7) was obtained as colorless powder. It showed also a violet spot with vanillin-H_2SO_4 reagent. Its UV spectrum showed absorption at 261 nm (log ε 3.8) which indicated the presence of an α,β-unsaturated carbonyl group on ring E. Its IR absorption bands at 3240, 1685, 1585 cm^{-1} revealed the presence of hydroxyl, keto-carbonyl and α,β-unsaturated carbonyl groups.

TABLE I ^{1}H-NMR data of compounds **1**, **2**, **4**, **5**, **6** and **7**

	1 (C_5D_5N)	**2** (C_5D_5N)	**4** ($CDCl_3$)	**5** (C_5D_5N)	**6** (C_5D_5N)	**7** (C_5D_5N)
H-1	1.95m	1.86m	1.80m	1.84m	1.86m	1.84m
	2.61m	2.56m	2.54m	2.56m	2.62m	2.61brdd (13.8, 6.8)
H-2	2.34m	2.28m	2.29m	2.26m	2.26m	5.48brdd (8.1, 13.2)
H-3	3.48dd (4.1, 11.1)	3.47dd (4.5, 11.5)	3.55dd (4.0,11.0)	3.56dd (4.1, 11.1)	3.48m	3.84d (8.1)
H-6	5.68d (6.0)	5.68d (5.6)	5.69brd	5.62d (5.6)	5.64br	5.64brs
H-7	1.86m	1.86m	1.82m	1.84m	1.88m	1.84m
H-8	1.78dd (12.3, 2)	1.82m	1.68m	1.82m	1.82m	1.82m
H-10	1.90m	1.90m	1.86m	1.88m	1.90m	1.88m
H-12	2.46d (14.5)	2.46d (14.1)	2.44d (14.0)	2.40d (14.6)	2.58d (14.5)	2.44d (14.6)
	3.22d (14.5)	3.22d (14.1)	3.18d (14.0)	3.14d (14.6)	3.26d (14.5)	3.08d (14.6)
H-15	1.72d (10.9)	1.68d (11.5)	1.44d (12.0)	1.70d (10.3)	1.86d (12.0)	1.72d (11.2)
	1.98dd (11.2, 3.4)	1.98dd (3.8, 11.4)	1.92brd (13.00)	1.92m	1.92brd	1.95dd
H-16	4.78dd (6.8, 6.8)	5.36dd (7.1, 7.1)	5.00m	4.73dd (7.1, 7.1)	4.89dd	4.74dd (7.1, 7.1)
H-17	3.01d (6.7)	2.92d (7.1)	3.08d	2.92d (6.9)	2.91d (6.3)	2.90d (6.7)
H-18	0.98s	1.04s	0.85s	0.94s	1.04s	0.94s
H-19	1.15s	1.16s	0.90s	1.16s	1.16s	1.09s
H-21	1.59s	1.48s	1.34s	1.57s	1.46s	1.55s
H-23	5.58s	2.84d (14.3)	5.40s	5.53s	2.84d (15.4)	2.58m
		3.18dd			3.10brd (12.2)	
H-24		4.16dd (5.4, 11.3)			3.86dd (6.4, 13.2)	
H-25	2.58m		2.70m	2.56m		2.58m
H-26	1.07d (6.5)	1.56s	1.19d (7.0)	1.07d (6.1)	1.56s	1.07d (6.4)
H-27	1.08d (6.5)	1.46s	1.21d (7.0)	1.08d (6.1)	1.40s	1.08d (6.4)
H-28	1.47s	1.44s	1.28s	1.41s	1.40s	1.47s
H-29	1.24s	1.24s	1.01s	1.17s	1.28s	1.32s
H-30	1.43s	1.36s	1.13s	1.40s	1.40s	1.39s
G-1				4.90d (7.6)	5.18d (7.8)	5.18d (7.8)
G-2				4.38dd	4.42brd (11.8)	4.42dd
G-3				4.22dd	4.32dd (9.7, 6.5)	4.36dd
G-4				4.16m	4.16brt	4.12dt
G-5				4.02m	4.04m	4.06m
G-6				4.52dd	4.52dd	4.52dd
				4.22m	4.26dd (8.0, 8.6)	4.24dd
X-1			4.88d (7.5)			
X-2			4.22m			
X-3			3.92m			
X-4			3.84m			
X-5			3.82m			
			3.58m			

The FAB-MS of Pf IX exhibited a molecular ion peak at m/z 662 and a fragment at 500 $[M-162]^+$ suggesting the molecular formula $C_{36}H_{54}O_{11}$, and also with a hexose moiety.

Micro hydrolysis of Pf IX led to the identification of picfeltarraegenin VI (**3**) and glucose spot on TLC. The ^{13}C-NMR data (see Table II) showed six

TABLE II ^{13}C-NMR data and DEPT analysis of compounds **4**, **5**, **6** and **7**

C	**4** (*CDCl*$_3$)	**5** (*C*$_5$*D*$_5$*N*)	**6** (*C*$_5$*D*$_5$*N*)	**7** (*C*$_5$*D*$_5$*N*)
1	26.18t	25.11t	25.46t	34.90t
2	29.58t	27.19t	28.85t	77.54d
3	81.77d	82.87d	80.11d	78.47d
4	41.39s	41.83s	42.10s	47.87s
5	141.62s	142.46s	141.00s	140.45s
6	118.50d	118.35d	120.70d	120.06d
7	23.83t	23.95t	24.43t	23.84t
8	35.44d	35.51d	34.46d	33.89d
9	47.67s	47.91s	49.39s	48.56s
10	43.94d	43.11d	42.97d	42.72d
11	213.35s	212.72s	211.86s	211.35s
12	48.41t	48.44t	49.24t	48.38t
13	48.68s	48.81s	51.22s	50.24s
14	50.36s	50.46s	51.91s	51.37s
15	45.35t	46.32t	46.56t	46.15t
16	70.79d	69.52d	70.59d	69.38d
17	58.01d	58.90d	58.95d	58.84d
18	19.87q	19.87q	19.69q	19.77q
19	20.22q	20.26q	20.19q	20.01q
20	91.04s	90.76s	80.35s	90.54s
21	22.73q	22.73q	22.21q	22.75q
22	208.31s	206.62s	216.30s	206.39s
23	100.51d	100.88d	38.80t	103.89d
24	197.35s	194.94s	79.02d	197.84s
25	30.28d	30.12d	69.32s	30.05d
26	19.40q	19.40q	28.85q	19.33q
27	19.87q	19.87q	29.21q	19.61q
28	25.30q	25.11q	25.47q	25.01q
29	21.74q	21.73q	21.83q	21.44q
30	19.16q	19.16q	19.29q	19.08q
G-1		102.45d	104.45d	100.81d
G-2		74.98d	76.20d	75.68d
G-3		78.43d	78.85d	78.32d
G-4		71.77d	71.44d	70.95d
G-5		78.01d	78.71d	78.19d
G-6		62.97t	62.75t	62.24t
X-1	100.14d			
X-2	73.12d			
X-3	76.06d			
X-4	69.80d			
X-5	65.29t			

signals of glucose at δ100.81d, 75.68d, 78.32d, 70.95d, 78.15d and 62.24t, and 30 other signals of aglycone for picfeltarraegenin VI.

In ^{1}H–^{1}H COSY NMR spectrum of Pf IX, the proton signal at δ5.48 (br dd, J = 8.1, 13.2, H-2) showed cross peaks with δ1.84m and δ2.61 (br dd, J = 13.8, 6.8 Hz, H-1) and 3.84 (d, J = 8.1, H-3). It indicated the presence of a hydroxyl group at position 2 as picfeltarraegenin VI. All the ^{1}H-NMR signals are identical with those of picfeltarraegenin VI and assigned by means of 2D ^{1}H–^{1}H NMR spectrum in Table I. Therefore Pf IX was identified as picfeltarraegenin VI-3-O-β-D-glucopyranoside (**7**).

EXPERIMENTAL SECTION

General experimental procedures UV and IR spectra were recorded on Shimadzu M-250 and Perkin-Elmer 559-B spectrophotometer. ^{1}H- and ^{13}C-NMR spectra were measured on Bruker AM-400 and Varian Gemini-300 spectrometer in $CDCl_3$ or C_5D_5N with TMS as internal standard. EI-MS and FAB-MS were taken on MAT-711 and Finnigan MAT-8430. Optical rotations were measured on JASCO DIP-181 polarimeter. TLC and PTLC were performed on silica gel F_{254} glass or alumina plates (Merck) using solvent system $CHCl_3$/MeOH (4 : 1 or 6 : 1) or $CHCl_3$/MeOH/H_2O (6 : 3 : 0.5).

Plant material Plant materials of *P. fel-tarrae* Lour. were cultivated at the suburb of Wuzhou, Guangxi Province and collected in June 1992. A voucher specimen was deposited at the Herbarium of the Department of Phytochemistry, Shanghai Institute of Materia Medica, Chinese Academy of Sciences.

Extraction and isolation The whole plant of *P. fel-tarrae* was powdered and extracted three times with boiling water. The water solution was distilled under vacuum to dryness for preparing Yanjianning tablet, an antibacterial medicament produced by Wuzhou Chinese Pharmaceutical Company.

The dry extract 1 kg (corresponding to plant materials 10 kg) was dissolved in water and centrifuged. The water solution was adsorbed on a macroporous resin D-1300 (Yangzhou Pharmaceutical Company) column and then eluted with 95% ethanol. The alcohol elution was evaporated to obtain a dark residue (90 g), which was then decolorized by alumina to yield a brown crude glycoside (50 g). The crude glycoside was subjected to column chromatography on silica gel (1 kg, 6 × 100 cm) eluted with (1) $CHCl_3$, (2) $CHCl_3$/MeOH 90 : 10, (3) $CHCl_3$/MeOH 80 : 20, (4) $CHCl_3$/MeOH 50 : 50 and (5) $CHCl_3$/MeOH 20 : 80.

The fraction (2) was further separated by column chromatography on silica gel to give Pf VI (**4**, 110 mg), Pf IX (**7**, 25 mg). The fraction (3) was subjected to repeated column chromatography on silica gel to yield Pf I_A (5.6 g), Pf VII (**5**, 30 mg), Pf VIII (**6**, 40 mg) and fraction (4) was repeatedly chromatographed on silica gel to afford Pf I_B (2.4 g) and Pf II (70 mg).

Pf I_A, $C_{41}H_{62}O_{13}$, colorless needles, m.p. 190–191°C, $[\alpha]_D^{24}$ +25.89 (EtOH, c 0.045). UV(EtOH) λ_{max} nm (log ε): 261(4.1) nm. IR (KBr) ν_{max}: 3421, 1685, 1580, 1169 cm^{-1}. ^{1}H- and ^{13}C-NMR data are the same as that of an authentic sample. FAB-MS *m/z*: 785 $[M + Na]^+$, 763 $[M + 1]^+$, 617 $[M + 1\text{-}146]^+$, 485 $[M + 1\text{-}146\text{-}132]^+$.

Pf I_B, $C_{42}H_{64}O_{14}$, colorless needles, m.p. 211–212°C, $[\alpha]_D^{24}$ +29.33 (EtOH, c 0.054). UV(EtOH) λ_{max} nm (log ε): 261(3.9) nm. IR (KBr) ν_{max}: 3400, 1685, 1580, 1160 cm^{-1}. ^{1}H- and ^{13}C-NMR data are the same as that

of an authentic sample. FAB-MS *m/z*: 815 $[M+Na]^+$, 793 $[M+1]^+$, 647 $[M+1\text{-}146]^+$, 485 $[M+1\text{-}146\text{-}162]^+$.

Pf II, $C_{42}H_{66}O_{15}$, colorless crystalline, m.p. 220–223°C, $[\alpha]_D^{24}+22.7$ (EtOH, c 0.05). IR (KBr) ν_{max}: 3420, 1750, 1685, 1160 cm^{-1}. ^1H- and ^{13}C-NMR data are the same as that of an authentic sample. FAB-MS *m/z*: 833 $[M+Na]^+$, 811 $[M+1]^+$, 793 $[M+1\text{-}H_2O]^+$, 647 $[M+1\text{-}H_2O\text{-}146]^+$, 485 $[M+1\text{-}H_2O\text{-}146\text{-}162]^+$.

Pf VI (**4**) $C_{35}H_{52}O_9$, white amorphous powder, m.p. 172–173°C. UV (EtOH) λ_{max} nm ($\log\varepsilon$): 261(3.8) nm. IR (KBr) ν_{max}: 3400, 1680, 1580, 1160 cm^{-1}. ^1H- and ^{13}C-NMR data, see Tables I and II. FAB-MS *m/z*: 635 $[M+Na]^+$, 617 $[M+1]^+$, 485 $[M+1\text{-}132]^+$.

Pf VII (**5**) $C_{36}H_{54}O_{10}$, white amorphous powder, m.p. 206–209°C. UV (EtOH) λ_{max} nm ($\log\varepsilon$): 259(3.99) nm. IR (KBr) ν_{max}: 3420, 1678, 1575, 1160 cm^{-1}. ^1H- and ^{13}C-NMR, see Tables I and II. FAB-MS *m/z*: 669 $[M+Na]^+$, 647 $[M+1]^+$, 485 $[M+1\text{-}162]^+$.

Pf VIII (**6**), $C_{36}H_{54}O_{11}$, white amorphous powder, m.p. 268–270°C. IR (KBr) ν_{max}: 3420, 1715, 1685, 1160 cm^{-1}. ^1H- and ^{13}C-NMR, see Tables I and II. FAB-MS *m/z*: 704 $[M+1+K]^+$, 664 M^+, 502 $[M\text{-}162]^+$, 484 $[M\text{-}162\text{-}H_2O]^+$.

Pf IX (**7**), $C_{36}H_{54}O_{11}$, white amorphous powder, m.p. 258–261°C. UV (EtOH) λ_{max} nm($\log\varepsilon$): 261(3.80) nm. IR (KBr) ν_{max}: 3420, 1685, 1585, 1160 cm^{-1}. ^1H- and ^{13}C-NMR, see Tables I and II. FAB-MS *m/z*: 685 $[M+Na]^+$, 662 M^+, 500 $[M\text{-}162]^+$.

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