Two New Dammarane-Type Bisdesmosides from the Fruit Pedicels of *Panax notoginseng*

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Two new dammarane-type triterpenoidal saponins, notoginsenosides FP_1 (**1**) and FP_2 (**2**), were isolated from the fruit pedicels of *Panax notoginseng*, along with 22 known compounds. Their structures were elucidated on the basis of spectroscopic evidences and chemical methods. The known compounds were identified as ginsenosides Rg_1 (**3**), Re (**4**), Rb_3 (**5**), Rc (**6**), Rd (**7**), Rb_2 (**8**), Rb_1 (**9**), F_2 (**10**), and F_1 (**11**); as notoginsenosides R_1 (**12**), Fa (**13**), and Fc (**14**); as vina-ginsenoside R_7 (**15**); as gypenosides IX (**16**), XVII (**17**), and XIII (**18**), and as chikusetsusaponin-L_5 (**19**), quercetin 3-*O*-*β*-D-glucopyranosyl-(1 → 2)-*β*-D-galactopyranoside (**20**), kaempferol 3-*O*-*β*-D-glucopyranosyl-(1 → 2)-*β*-D-galactopyranoside (**21**), benzyl-*β*-primeveroside (**22**), (*S*)-tryptophan (**23**), and icariside B_6 (**24**). Compounds **15**, **19** and **22**–**24** are reported for the first time from the title plant.

Introduction. – The roots of *Panax notoginseng* (BURK) F. H. CHEN (Araliaceae), commonly known as '*san-qi*', '*tian-qi*', and '*notoginseng*', is a well-known herb in traditional Chinese medicine (TCM), and has been widely used for the treatment of injuries from falls, for the activation of blood circulation to dissipate blood stasis, and against cardiovascular and cerebral vascular disease. Based on recent research, triterpenoidal saponins are considered as the main bioactive constituents of this herb. Currently, more than 60 dammarane-type saponins in the form of ginsenosides, notoginsenosides, and gypenosides have been isolated from the roots, flower buds, fruits, and leaves of this plant [1–4].

In continuation of our investigation on this herbal plant, we herein report the isolation and structural elucidation of two new dammarane-type bisdesmosides, notoginsenosides FP_1 (**1**) and FP_2 (**2**), which were isolated together with 17 known dammarane saponins (**3**–**19**) and five other known compounds (**20**–**24**) from the fruit pedicels of this plant.

Results and Discussion. – The MeOH extract of the air-dried fruit pedicels of *P. notoginseng* was chromatographed repeatedly to afford compounds **1**–**24**. The known compounds were identified as ginsenosides Rg_1 (**3**) [5], Re (**4**) [6], Rb_3 (**5**) [7], Rc (**6**) [8], Rd (**7**) [9], Rb_2 (**8**) [8], Rb_1 (**9**) [5], F_2 (**10**) [10], and F_1 (**11**) [11]; as notoginsenosides R_1 (**12**) [12], Fa (**13**) [13], and Fc (**14**) [13]; as vina-ginsenoside R_7 (**15**) [14]; as gypenoside IX (**16**) [13], XVII (**17**) [15], and XIII (**18**) [16]; and as chikusetsusaponin L_5 (**19**) [12], quercetin 3-*O*-*β*-D-glucopyranosyl-(1 → 2)-*β*-D-galac-

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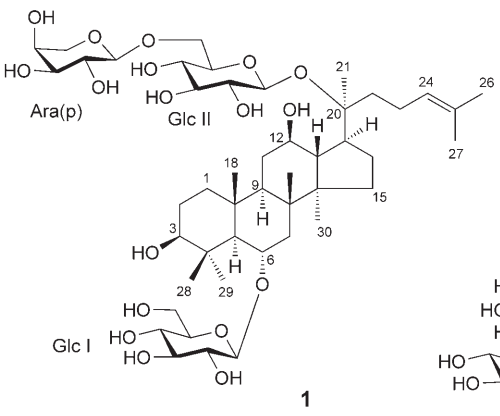

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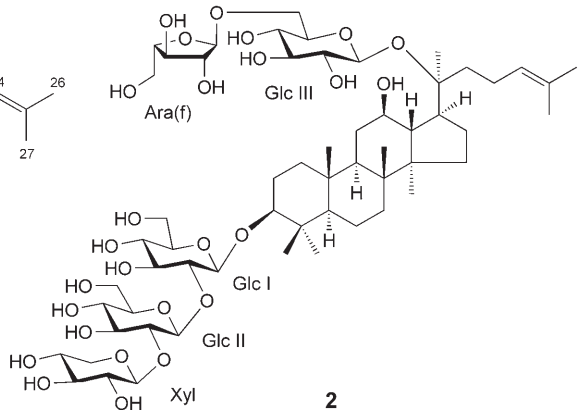

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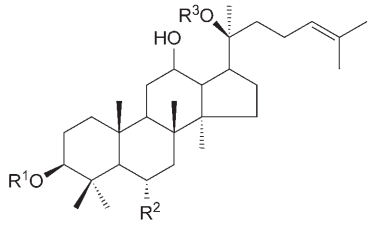
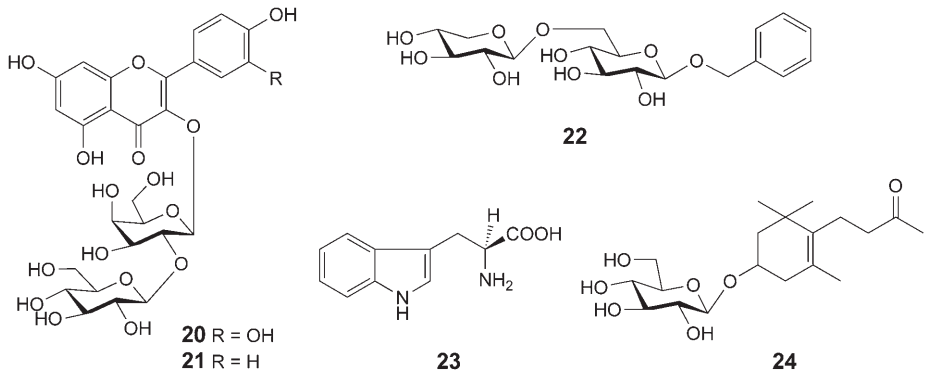


3 – 19

	R^1	R^2	R^3
3	H	Glc-O	Glc
4	H	Rha-(1→2)Glc-O	Glc
5	Glc-(1→2)-Glc	H	Xyl-(1→6)-Glc
6	Glc-(1→2)-Glc	H	Ara(f)-(1→6)-Glc
7	Glc-(1→2)-Glc	H	Glc
8	Glc-(1→2)-Glc	H	Ara(p)-(1→6)-Glc
9	Glc-(1→2)-Glc	H	Glc-(1→6)-Glc
10	Glc	H	Glc
11	H	OH	Glc
12	H	Xyl-(1→2)-Glc-O	Glc
13	Xyl-(1→2)-Glc-(1→2)-Glc	H	Glc-(1→6)-Glc
14	Xyl-(1→2)-Glc-(1→2)-Glc	H	Xyl-(1→6)-Glc
15	Xyl-(1→2)-Glc-(1→2)-Glc	H	Glc
16	Glc	H	Xyl-(1→6)-Glc
17	Glc	H	Glc-(1→6)-Glc
18	H	H	Xyl-(1→6)-Glc
19	H	OH	Xyl-(1→4)-Ara(p)-(1→6)-Glc

Ara(p) = L-Arabinopyranosyl, Ara(f) = L-arabinofuranosyl, Glc = D-glucopyranosyl, Rha = D-rhamnopyranosyl, Xyl = D-xylopyranosyl.



topyranoside (**20**) [17], kaempferol 3-*O*-*β*-D-glucopyranosyl-(1 → 2)-*β*-D-galactopyranoside (**21**) [16], benzyl-*β*-primeveroside (**22**) [18], (*S*)-tryptophan (**23**), and icariside B_6 (**24**) [19], by spectroscopic and physico-chemical comparison with authentic samples and literature data. Although saponins **15** and **19** have been found in other *Panax* species before [12][14], this is the first report of their occurrence in *P. notoginseng*. Compounds **22**–**24** were also isolated for the first time from the present plant.

Saponin **1** was obtained as a colorless, amorphous powder (m.p. 185–187°). Its molecular formula was assigned as $C_{47}H_{80}O_{18}$ on the basis of the quasi-molecular ion peak ($[M-H]^-$) in the high-resolution FAB mass spectrum (HR-FAB-MS) at *m*/*z* 931.5260 (calc. 931.5266). The ^{13}C-NMR spectrum of **1** (*Table*) exhibited 30 signals for the aglycone, which were identical to those of (20*S*)-protopanaxatriol. The signals at *δ*(C) 80.3 (C(6)) and 83.7 (C(20)) suggested that **1** was a bisdesmoside. In addition, the ^{1}H- and ^{13}C-NMR spectra of **1** showed the presence of two *β*-glucopyranosyl (Glc) units (*δ*(H) 5.01 (*d*, *J* = 7.8 Hz, 1 H), 5.09 (*d*, *J* = 7.5 Hz, 1 H); *δ*(C) 106.0, 98.2) and one *α*-arabinopyranosyl (Ara(p)) moiety (*δ*(H) 4.98 (*d*, *J* = 6.1 Hz, 1 H); *δ*(C) 104.8).

Acid hydrolysis of **1** with 2% HCl afforded D-glucose (D-Glc-OH) and L-arabinose (L-Ara-OH), as identified by GC analysis of their trimethylsilyl-imidazole derivatives [20]. The ^{13}C-NMR data of the sugar moieties of **1** were in good agreement with those of ginsenoside Rb_2 (**9**), except for the loss of a terminal *β*-D-Glc unit from the sugar chain on C(6) of the aglycone in **1**. The structure was further assigned by HMBC, HSQC, and HSQC-TOCSY experiments. In the HMBC spectrum of **1** (*Fig. 1*), the location and sequence of the sugar moieties was demonstrated, with key correlations from *δ*(H) 5.01 (H–C(1) of Glc I) to *δ*(C) 80.3 (C(6)), from 5.09 (H–C(1) of Glc II) to 83.7 (C(20)), and from *δ*(H) 4.98 (H–C(1) of Ara(p)) to 69.3 (C(6) of Glc II).

From the above data, the structure of the new saponin **1** was, thus, determined as (20*S*)-20-*O*-(*α*-L-arabinopyranosyl-(1 → 6)-*β*-D-glucopyranosyl)-6-*O*-(*β*-D-glucopyranosyl)protopanaxatriol[1]), and named *notoginsenoside FP$_1$*.

Saponin **2** was obtained as a colorless, amorphous powder (m.p. 166–168°). Its molecular formula was determined by HR-FAB-MS as $C_{58}H_{98}O_{26}$ from the $[M-H]^-$

[1]) For systematic names, see *Exper. Part*.

Table. *^{13}C-NMR Data of* **1** *and* **2**. At 125 MHz in (D_5)pyridine; δ in ppm. The terms (p) and (f) refer to pyranosyl and furanosyl, resp.

Atom	**1**	**2**	Atom	**1**	**2**
Aglycone:			Glc I:		
C(1)	39.8	39.3	C(1)	106.0	104.8
C(2)	28.0	26.7	C(2)	75.6	83.0
C(3)	78.8	89.1	C(3)	79.7	77.8
C(4)	40.5	39.8	C(4)	71.8	71.3
C(5)	61.5	56.5	C(5)	78.2	78.3
C(6)	80.3	18.5	C(6)	63.2	63.1
C(7)	45.2	35.2	Glc II:		
C(8)	41.2	40.1	C(1)	98.2	103.2
C(9)	50.1	49.8	C(2)	75.0	84.6
C(10)	39.6	37.0	C(3)	79.3	78.0
C(11)	30.9	30.9	C(4)	72.0	71.9
C(12)	70.4	70.4	C(5)	76.8	79.3
C(13)	49.2	49.5	C(6)	69.3	63.0
C(14)	51.5	51.5	Xyl:		
C(15)	30.7	30.8	C(1)		106.5
C(16)	26.8	26.8	C(2)		76.0
C(17)	51.7	51.8	C(3)		78.7
C(18)	17.7	16.1	C(4)		70.8
C(19)	17.7	16.4	C(5)		67.5
C(20)	83.7	83.5	Glc III:		
C(21)	22.4	22.5	C(1)		98.2
C(22)	36.3	36.3	C(2)		75.1
C(23)	23.3	23.3	C(3)		76.0
C(24)	126.1	126.1	C(4)		72.2
C(25)	131.3	131.1	C(5)		76.6
C(26)	25.9	25.9	C(6)		68.6
C(27)	18.0	18.0	Ara:	(p)	(f)
C(28)	31.9	28.2	C(1)	104.8	110.2
C(29)	16.5	16.8	C(2)	72.3	83.4
C(30)	17.3	17.5	C(3)	74.2	79.0
			C(4)	68.7	86.2
			C(5)	65.7	62.8

peak at *m*/*z* 1209.6245 (calc. 1209.6268), with characteristic fragment-ion peaks at *m*/*z* 1077 ($[M-132-H]^-$) and 945 ($[M-(2\times132)-H]^-$), which suggested the presence of two pentosyl units in the sugar moiety. The ^{1}H- and ^{13}C-NMR data (see *Exper. Part* and *Table*, resp.) were very similar to those of ginsenoside Rc (**7**) [9], except for the appearance of a set of additional signals in **2** ascribed to a xylopyranosyl (Xyl) unit (δ(H) 5.38 (*d*, $J=5.6$ Hz, 1 H); δ(C) 106.5).

Acid hydrolysis of compound **2** afforded D-Glc-OH, D-Xyl-OH, and L-Ara-OH as sugar residues, as determined by GC analysis. The sugars were fully assigned by HSQC and HSQC-TOCSY experiments, indicating the presence of three Glc, one Xyl, and one arabinofuranosyl (Ara(f)) residues. In the HMBC spectrum of **2** (*Fig. 2*), long-range correlations of δ(H) 4.91 (H–C(1) of Glc I) with δ(C) 89.1 (C(3)), of δ(H) 5.49 (H–C(1) of Glc II) with δ(C) 83.0 (C(2) of Glc I), of δ(H) 5.38 (H–C(1) of Xyl) with

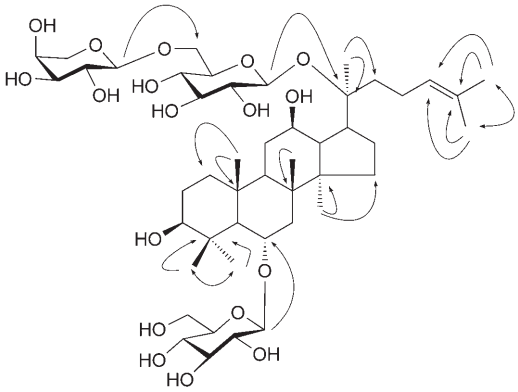


Fig. 1. *Key HMBC correlations of* **1**

δ(C) 84.6 (C(2) of Glc II), of δ(H) 5.12 (H–C(1) of Glc III) with δ(C) 83.5 (C(20)), and of δ(H) 5.64 (H–C(1) of Ara) with δ(C) 68.6 (C(6) of Glc III) were observed.

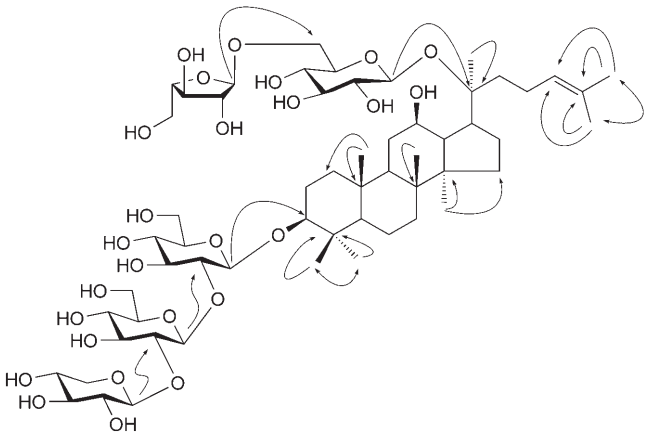


Fig. 2. *Key HMBC correlations of* **2**

From the above evidence, the structure of the new saponin **2** was elucidated as (20*S*)-20-*O*-(α-L-arabinofuranosyl-(1 → 6)-β-D-glucopyranosyl)-3-*O*-(β-D-xylopyranosyl-(1 → 2)-β-D-glucopyranosyl-(1 → 2)-β-D-glucopyranosyl)protopanaxadiol[1]), and named *notoginsenoside FP*$_2$.

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Experimental Part

General. Column chromatography (CC): on *Diaion HP-20SS* resin (*Mitsubishi Chemical Co., Ltd.*), *Sephadex LH-20* gel (25–100 μm, *Pharmacia Fine Chemical Co., Ltd.*), *MCI* gel *CHP20P* (75–100 μm, *Mitsubishi Chemical Co., Ltd.*), *RP-8* gel (40–63 μm; *Merck*), and silica gel (200–300 mesh, *Qingdao*

Haiyang Chemical Factory). Fractions were monitored by TLC on silica-gel plates sprayed with 10% H_2SO_4 in EtOH followed by heating. GC: *Agilent HP5890* gas chromatograph equipped with an H_2 flame-ionization detector and a *30QC2/AC-5* quartz capillary column (30 m × 0.32 mm). Optical rotations: *Horiba SEPA-3000* high-sensitive polarimeter. IR Spectra: *Bio-Rad FTS-135* spectrophotometer, with KBr; in cm^{-1}. NMR Spectra: *Bruker DRX-500* instrument; at 500 (^1H) and 125 MHz (^{13}C) in (D_5)pyridine at 25°; δ in ppm rel. to Me_4Si, *J* in Hz. FAB- and HR-FAB-MS: *VG AutoSpec-3000* mass spectrometer; glycerol as matrix; in *m/z*.

Plant Material. The fruit pedicels of *Panax notoginseng* (BURK) F. H. CHEN were collected in November 2005 in Wenshan, Yunnan Province, P. R. China, and identified by *C.-R. Y.*

Extraction and Isolation. The air-dried fruit pedicels (2.8 kg) were extracted repeatedly with MeOH (3 × 7 d) at r.t. The combined extracts were concentrated *in vacuo* to give a residue (350 g), which was subjected to CC (*Diaion HP-20SS*; H_2O/MeOH 1:0 → 0:1) to afford five fractions: *Fr. A – Fr. E. Fr. B* (32.5 g) was repeatedly purified by CC (*Sephadex LH-20* and *MCI* gel; H_2O/MeOH 1:0 → 0:1) to afford **20** (450 mg), **21** (23 mg), **22** (165 mg), **23** (361 mg), and **24** (10 mg). *Fr. C* (36.7 g) was subjected to CC (1. SiO_2, $CHCl_3$/MeOH/H_2O 9:1:0.1 → 6:4:1; 2. *RP-8* gel, 70–80% aq. MeOH) to afford **1** (14 mg), **2** (150 mg), **3** (461 mg), **4** (145 mg), **5** (285 mg), **6** (12 mg), **7** (71 mg), **12** (33 mg), **13** (194 mg), **14** (244 mg), and **19** (112 mg). Similarly, compounds **2** (194 mg), **9** (156 mg), **11** (155 mg), **13** (642 mg), and **14** (2399 mg) were isolated from *Fr. D* (59.8 g), and compounds **16** (434 mg), **17** (587 mg), **8** (400 mg), **10** (129 mg), **15** (271 mg), and **18** (150 mg) were obtained from *Fr. E* (19.3 g) by repeated CC (SiO_2 and *RP-8*).

Notoginsenoside FP$_1$ (= *(3β,6α,12β)-20-[(α-*L*-Arabinopyranosyl-(1 → 6)-β-*D*-glucopyranosyl)oxy]-6-(β-*D*-glucopyranosyl)oxy]dammar-24-ene-3,12-diol*; **1**). Colorless, amorphous powder. M.p. 185–187°. $[\alpha]_D^{17} = +12.08$ (*c* = 0.35, MeOH). IR (KBr): 3421, 1636, 1076. ^{1}H-NMR (500 MHz, (D_5)pyridine[2]): 0.79 (*s*, Me(30)); 1.01 (*s*, Me(19)); 1.15 (*s*, Me(18)); 1.64 (2*s*, Me(21), Me(29)); 1.69 (*s*, Me(26)); 1.71 (*s*, Me(27)); 2.05 (*s*, Me(28)); 4.98 (*d*, *J* = 6.1, H–C(1) of Ara(p)); 5.01 (*d*, *J* = 7.8, H–C(1) of Glc I); 5.09 (*d*, *J* = 7.5, H–C(1) of Glc II). ^{13}C-NMR: see *Table*. FAB-MS: 931 ($[M-H]^-$). HR-FAB-MS: 931.5260 ($[M-H]^-$, $C_{47}H_{79}O_{18}^-$; calc. 931.5266).

Notoginsenoside FP$_2$ (= *(3β,12β)-20-[(α-*L*-Arabinofuranosyl-(1 → 6)-β-*D*-glucopyranosyl)oxy]-3-[(β-*D*-xylopyranosyl-(1 → 2)-β-*D*-glucopyranosyl-(1 → 2)-β-*D*-glucopyranosyl)oxy]dammar-24-en-12-ol*; **2**). Colorless, amorphous powder. M.p. 166–168°. $[\alpha]_D^{17} = -2.94$ (*c* = 0.51, MeOH). IR (KBr): 3418, 1639, 1077. ^{1}H-NMR ((D_5)pyridine[2]): 0.77 (*s*, Me(19)); 0.93 (*s*, Me(18)); 0.93 (*s*, Me(30)); 1.08 (*s*, Me(29)); 1.25 (*s*, Me(28)); 1.60 (*s*, Me(26)); 1.62 (*s*, Me(21)); 1.65 (*s*, Me(27)); 4.91 (*d*, *J* = 6.4, H–C(1) of Glc I); 5.49 (*d*, *J* = 6.4, H–C(1) of Glc II); 5.12 (*d*, *J* = 5.1, H–C(1) of Glc III); 5.38 (*d*, *J* = 5.6, H–C(1) of Xyl); 5.64 (*s*, H–C(1) of Ara(f)). ^{13}C-NMR: see *Table*. FAB-MS: 1209 ($[M-H]^-$), 1077 ($[M-132-H]^-$), 945 ($[M-(2\times132)-H]^-$). HR-FAB-MS: 1209.6245 ($[M-H]^-$, $C_{58}H_{97}O_{26}^-$; calc. 1209.6268).

Acid Hydrolysis and GC Analysis. A soln. of **1** or **2** (*ca.* 10 mg) in 2% HCl/1,4-dioxane 1:1 (4 ml) was heated at 80° (reflux) for 8 h. The mixture was extracted with $CHCl_3$ (3 × 4 ml). The aq. layer was neutralized with *Amberlite IRA-401*, and the resin was removed by filtration. The filtrate was evaporated to dryness, and the resulting monosaccharides (*ca.* 2 mg) were dissolved in pyridine (2 ml). Then, L-cysteine methyl ester hydrochloride (1.5 mg) was added, and the mixture was kept at 60° for 1 h. Then trimethylsilyl imidazole (1.5 ml) was added, and the mixture was kept at 60° for another 30 min. An aliquot (4 µl) of the supernatant was removed and directly subjected to GC analysis under the following conditions: column temp. 180–280° at 3°/min, carrier gas N_2 (1 ml/min), injector and detector temp. 250°, split ratio 1:50. The configurations of D-Glc-OH, D-Xyl-OH, and L-Ara-OH were determined by comparison of the retention times of the corresponding derivatives [20] with those of authentic samples. The GC retention times of the standard D- and L-glucose, -xylose, and -arabinose derivatives were 19.450 and 19.943, 14.285 and 14.939, and 15.028 and 14.286 min, resp.

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[2]) Diagnostic signals only.

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