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Panaxfuraynes A and B, two new tetrahydrofuranic polyacetylene glycosides from *Panax ginseng* C. A. Meyer

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ABSTRACT

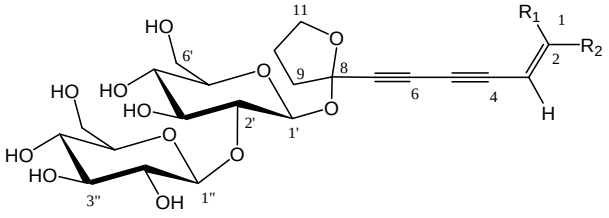
Panaxfurayne A (**1**), a tetrahydrofuranic polyacetylene glycoside, was isolated from the roots of *Panax ginseng* C. A. Meyer (Araliaceae) together with panaxfurayne B (**2**) as a geometric isomer of **1**. The chemical structures of these two compounds were ascertained by UV, Mass, 1D, and 2D NMR experiments. During these experiments, these tetrahydrofuranic polyacetylene compounds proved to be of biogenetically novel type.

The root of ginseng (*Panax ginseng* C. A. Meyer, Araliaceae) has been traditionally used as a precious medicine in Far East Asia, such as Korea, China, and Japan. Previous phytochemical investigations had shown the presence of several ginsenosides in water extract of ginseng and C_{17}-polyacetylene derivatives, that is, panaxynol,[1] panaxydol,[2] panaxytriol,[3] panaxyne, panaxyne epoxide,[4] and ginsenoyne-A ~ -K,[5–7] from petroleum etheral extract of this plant. In our further search of structurally unique and chemotaxonomically interesting ginseng polyacetylene, two new tetrahydrofuranic polyacetylene glycosides, panaxfuraynes A (**1**) and B (**2**), were isolated from the root of *P. ginseng*. The tetrahydrofuran-type polyacetylene was of a biogenetically novel type in nature. In this Letter, we describe the isolation and structure elucidation of **1** and **2**.

The water extract of the root of *P. ginseng*,[8] water soluble material removed by Diaion HP-20 adsorption, was repeatedly subjected to column chromatography over ODS (aq AcCN, 10→40%) to afford panaxfuraynes A (**1,** 10 mg) and B (**2,** 6 mg).[9] On the acid hydrolysis of **1** and **2** with 1 M HCl, it was hydrolyzed to give D-glucose as a sugar moiety.[10] By their spectroscopic data, these were identified as 2-(hepta-5-en-1,3-diynyl)-tetrahydrofuran glycosides and mutually geometric isomers (Fig. 1).

The characteristic UV absorption maxima of **1** and **2** at 205, 211, 227, 238, 251, 265, and 281 nm indicated an en-diyne-chromophore.[11] The compounds **1** and **2** showed a quasi-molecular ion peak at *m/z* 523 $[M+Na]^+$ at the positive FAB-MS spectra. These compounds were assigned the molecular formulas of $C_{23}H_{32}O_{12}$ in the positive HRESI-MS at *m/z* 523.1795 $[M+Na]^+$ (**1**), *m/z* 523.1793 $[M+Na]^+$ (**2**). The molecular structures of the compounds were determined by ^1H and ^{13}C NMR spectroscopies (Table 1) using DEPT, ^1H–^1H COSY, HMQC, and HMBC experiments. The ^1H and ^{13}C chemical shift parameter assignments and HMBC correlations of **1**, **2** are summarized in Table 1. Unfortunately, the enantiomeric determination of C-8 of **1**, **2** could not be deduced from ROESY spectra because of C-7, 6 did not have NOE correlative proton to $H_{a,b}$-9 and the protons on sugar moiety did not give any imformation of the stereochemistry of stereogenic center C-8.

Panaxfurayne A (**1**)[12] was obtained as a white amorphous powder. The ^1H NMR spectrum (800 MHz, pyridine-d_5) of **1** showed one



	R_1	R_2
Panaxfurayne A (**1**):	H	CH_3
Panaxfurayne B (**2**):	CH_3	H

Figure 1. Chemical structures of panaxfuraynes A and B.

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Table 1
NMR data of panaxfurayne A (**1**) and panaxfurayne B (**2**) in pyridine-d_5

No.	1		2		1, 2	
	δ_H[a]	δ_C[b]	δ_H[a]	δ_C[b]	HMBC (H→C)	COSY (H↔H)
1	1.57 (3H, dd, 7.2, 1.6 Hz)	19.1	1.78 (3H, br d, 6.4 Hz)	16.8	2, 3	2, 3
2	6.25 (1H, dq, 15.2, 7.2 Hz)	144.0	6.25 (1H, dq, 10.4, 6.4 Hz)	143.1	1	1, 3
3	5.58 (1H, br d, 15.2 Hz)	110.7	5.58 (1H, br d, 10.4 Hz)	109.9	1	1, 2
4, 5, 6, 7		84.2, 75.1, 74.5, 66.6		80.3, 2 × 66.4, 72.9		
8		84.9		86.4		
9	2.72 (1H, dt, 17.6, 7.2 Hz)	17.1	2.75 (1H, dt, 17.6, 7.2 Hz)	17.1	8, 10, 11	10
	2.65 (1H, dt, 17.6, 7.2 Hz)		2.67 (1H, dt, 17.6, 7.2 Hz)			
10	1.91 (2H, m)	29.6	1.91 (2H, m)	29.6	8, 9, 11	6, 11
11	4.08 (1H, dt, 9.6, 6.4 Hz)	68.6	4.08 (1H, dt, 9.6, 6.4 Hz)	68.6	8, 9, 10	10
	3.69 (1H, dt, 9.6, 6.4 Hz)		3.70 (1H, dt, 9.6, 6.4 Hz)			
1′	5.30 (1H, d, 8.0 Hz)	107.2	5.30 (1H, d, 8.0 Hz)	107.2	8, 2′, 3′, 5′	2′
2′	4.13 (1H, t, 8.8 Hz)	77.4	4.13 (1H, t, 8.8 Hz)	77.4	1′, 1″, 3′	1′, 3′
3′	4.26 (1H, t, 8.8 Hz)	78.5	4.26 (1H, t, 8.8 Hz)	78.5	4′	2′, 4′
4′	4.32 (1H, t, 8.8 Hz)	71.9	4.32 (1H, t, 8.8 Hz)	71.9	5′, 6′	3′, 5′
5′	3.96 (1H, m)	78.8	3.96 (1H, m)	78.8		4′, 6′
6′	4.56 (1H, dd, 12.0, 2.4 Hz)	62.9	4.56 (1H, br d, 12.0 Hz)	63.1	5′	5′
	4.45 (1H, dd, 12.0, 4.8 Hz)		4.45 (1H, br d, 12.0 Hz)			
1″	4.86 (1H, d, 7.2 Hz)	103.4	4.86 (1H, d, 8.0 Hz)	103.4	2′	2″
2″	4.14 (1H, t, 9.6 Hz)	85.0	4.14 (1H, t, 9.6 Hz)	84.9	1″, 3″	1″, 3″
3″	4.34 (1H, t, 8.8 Hz)	78.4	4.34 (1H, t, 8.8 Hz)	78.4	2″, 4″	2″, 4″
4″	4.23 (1H, t, 8.8 Hz)	71.7	4.23 (1H, t, 8.8 Hz)	71.7	3″, 6″	3″, 5″
5″	3.88 (1H, m)	79.2	3.88 (1H, m)	79.2		4″, 6″
6″	4.52 (1H, dd, 12.0, 2.4 Hz)	63.1	4.52 (1H, br d, 12.0 Hz)	62.9	5″	5″
	4.36 (1H, dd, 12.0, 5.6 Hz)		4.36 (1H, br d, 12.0 Hz)			

[a] Measured at 800 MHz.
[b] Measured at 201 MHz.

terminal methyl of en-diyne system at δ_H 1.57 (H-1, 3H, dd, 7.2, 1.6 Hz) and two olefinic protons δ_H 6.25 (H-2, 1H, dq, 15.2, 7.2 Hz), δ_H 5.58 (H-3, 1H, d, 15.2 Hz) from a trans-configurated olefine. These proton peaks were correlated with δ_c 19.1 (C-1), δ_c 144.0 (C-2), and δ_c 110.7 (C-3) by HMQC spectrum. On the ^{13}C NMR spectra (201 MHz, pyridine-d_5), the four carbons (C-4, 5, 6, and 7) of diyne system showed at δ_c 84.2, 75.1, 74.5, and 66.6, but the positional information of these peaks was not found on NMR spectra. On the tetrahydrofuran system, the proton H-$9_{a,b}$ showed at δ 2.72, 2.65 (each dt, 17.6, 7.2 Hz), H-$10_{a,b}$ showed at δ 1.91 (m), and H-$11_{a,b}$ showed at δ 4.08, 3.96 (each dt, 9.6, 6.4 Hz). The quaternary carbon (C-8) was correlated to H-9, 10, and an anomeric proton (H-1′) originated from glucose at HMBC spectra, therefore a sugar and acetylene units were linked at C-8 of tetrahydrofuran. The sugar moiety was easily discerned from its NMR spectra by observing the relative low field signals of the anomeric protons and carbons δ_H 5.30 (d, 8.0 Hz), δ_H 4.86 (d, 7.2 Hz) and (δ_c 107.2, 103.4). Other ^{13}C signals of sugar unit showed at δ_c 77.4, 78.5, 71.9, 78.8, 62.9, 85.0, 78.4, 71.7, 79.2, and 63.1. At the HMBC spectrum, H-2′ (δ_H 4.13) was correlated to the C-1″ (δ_c 103.4). These data were similar to a sophorosyl [β-D-glucopyranosyl(1→2)-β-D-glucopyranosyl]. Therefore, compound **1** was revealed as 2-((*E*)-hepta-5-en-1,3-diynyl)-tetrahydrofuran-2-β-D-glucopyranosyl(1→2)-β-D-glucopyranoside.

Panaxfurayne B (**2**)[13] was given as a white amorphous powder. The ^1H and ^{13}C NMR peaks and HMBC, ^1H–^1H COESY correlations of **2** were very similar to those of compound **1**. The ^1H NMR spectrum (800 MHz, pyridine-d_5) of **2** showed one terminal methyl of en-diyne system at δ_H 1.78 (H-1, 3H, br d, 7.2 Hz) and two olefinic protons δ_H 6.25 (H-2, 1H, dq, 10.4, 6.4 Hz), δ_H 5.58 (H-3, 1H, br d, 10.4 Hz). These proton peaks were correlated with δ_c 16.8 (C-1), δ_c 143.1 (C-2), and δ_c 109.9 (C-3) by HMQC spectrum. On the ^{13}C NMR spectra (201 MHz, pyridine-d_5), the four carbons (C-4, 5, 6, and 7) of diyne system showed at δ_c 80.3, 66.4, and 72.9. The peak at δ_c 72.9 was confirmed to overlap two quaternary carbons by HMBC spectrum. Particularly, the coupling constants (10.4 Hz) of two olefinic protons (2, 3-H) on the ^1H NMR proved to be cis-configurated protons. Therefore, compound **2** was revealed as 2-((*Z*)-hepta-5-en-1,3-diynyl)-tetrahydrofuran-2-β-D-glucopyranosyl (1→2)-β-D-glucopyranoside.

Acknowledgment

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8. The roots of *Panax ginseng* C. A. Meyer (Araliaceae) grown for six years were purchased from a farmer in Eumsung, Korea (voucher # KTNG 4800 GW).
9. Dried ginseng root (10 kg) was extracted with tap water (70 L, 70 °C for 3 days, twice) and filtrated after cooling. The water extract was subjected to Diaion HP-20 for the removal of water soluble material, and then eluted with MeOH (18 L), consecutively. The concentrated MeOH fraction (500 g) was chromatographed on ODS column, eluted with water–acetonitrile (1:4) to afford a mixture of compounds **1** and **2**. Sequential preparative liquid chromatography on ODS column led to the isolation of two new compounds, panaxfurayne A (**1**) and panaxfurayne B (**2**).
10. A solution of **1**, **2** (1 mg each) in 1.0 M HCl (dioxane–H_2O, 1:1, 2 ml) was heated at 95 °C for 1 h under Ar. After cooling, the reaction mixture was neutralized by passage through an Amberlite IRA-93ZU (Organo, Tokyo, Japan) and then passed through a Sep-Pak C_{18} cartridge (Waters, Milford, MA, USA) using MeOH–H_2O (1:4), giving a decomposed sugar fraction. Ion chromatography analysis of the sugar fraction under the following conditions showed the presence of D-glucose. Column, Carbopac PA 10 (4 mm i.d. × 250 mm, Dionex); solvent, 125 mM NaOH–H_2O (30:70); flow rate, 1.0 ml/min; detection, electrochemical detector (ECD); R_t, 7.1 min.
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12. *Panaxfurayne A* (**1**): A white amorphous powder; mp 190–192 °C; $[\alpha]_D^{25}$ +2.0 (*c* 0.213, 66% MeOH); UV (MeOH) λ_{max} (log ε): 281 (2.75), 265 (2.88), 251 (2.77), 238 (2.56), 227 (2.45), 211 (3.45), 205 (3.37); for ^{1}H and ^{13}C (pyridin-d_5) spectral data see Table 1; FAB-MS (positive) $[M+Na]^+$ *m/z* 523; HRESI-MS (positive) $[M+Na]^+$ *m/z* 523.1795, calcd for $C_{23}H_{32}O_{12}Na$, 523.1791.

13. *Panaxfurayne B* (**2**): A white amorphous powder, mp 170–171 °C; $[\alpha]_D^{25}$ +3.5 (*c* 0.200, 66% MeOH); UV (MeOH) λ_{max} (log ε): 281 (2.72), 265 (2.85), 251 (2.74), 238 (2.48), 227 (2.26), 211 (3.41), 205 (3.31); for ^{1}H and ^{13}C (pyridin-d_5) spectral data see Table 1; FAB-MS (positive) $[M+Na]^+$ *m/z* 523; HRESI-MS (positive) $[M+Na]^+$ *m/z* 523.1793, calcd for $C_{23}H_{32}O_{12}Na$, 523.1791.