Saponins from Bran of Quinoa, *Chenopodium quinoa* WILLD. II

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Grains of Quinoa, *Chenopodium quinoa* have been used as a staple food in the Andes, South America. In a continuing study on saponin constituents of this plant, seven oleanane saponins were isolated from brans of the grains. Two of them were identified as known saponins of oleanolic acid, chikusetsusaponin IVa (10) from rhizomes of *Panax* spp. and quinoside D (12) from seeds of this plant, respectively. The other five compounds (7, 8, 9, 11 and 13) are new saponins, being designated as quinoa-saponins-6—10. The structures of these saponins were elucidated as follows: 7, 8 and 9, 3-*O*-[β-glucopyranosyl(1→2)-β-glucopyranosyl(1→3)-α-arabinopyranoside]-28-*O*-β-glucopyranoside of 30-*O*-methyl spergulagenate, oleanolic acid and phytolaccagenic acid, respectively; 11, hederagenin 3-*O*-β-glucuronide-28-*O*-β-glucopyranoside; and 13; hederagenin 3-*O*-β-xylopyranosyl(1→3)-β-glucuronide-28-*O*-β-glucopyranoside.

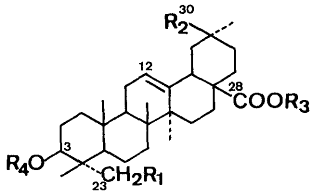
Keywords Quinoa; *Chenopodium quinoa*; Chenopodiaceae; food resource; saponin; oleanane triterpene; methyl spergulagenate; phytolaccagenic acid

Grains of "Quinoa," *Chenopodium quinoa* WILLD. (Chenopodiaceae) which grows in the Andes, South America, have attracted much attention as a valuable food resource.$^{1)}$ It is known that the seed-coat of this plant contains bitter principles which are effective for protection from noxious insects. Recently, we reported the isolation and structure elucidation of five new saponins named quinoa-saponins-1—5 (**1**—**5**) and one known saponin (**6**) from brans of this plant.$^{2)}$ These compounds account at least in part for bitterness of the seed-coat. The present paper reports the results of a further study on more polar saponins of the brans.

The methanolic extract of the defatted brans was subjected to repeated chromatography to give seven saponins (**7**—**13**) in yields of 0.08, 0.02, 0.16, 0.1, 0.02, 0.06 and 0.08% in addition to **1**—**6**. Of these saponins, **7**—**9**, **11** and **13** are new saponins, being designated as quinoa-saponins-6—10.

Quinoa-saponin-6 (**7**) exhibited four anomeric proton signals at δ 4.68 (1H, d, $J=8.0$ Hz), 5.06 (1H, d, $J=7.0$ Hz), 5.10 (1H, d, $J=7.3$ Hz) and 6.21 (1H, d, $J=7.2$ Hz) and four anomeric carbon signals (Table II). On acid hydrolysis, **7** afforded glucose and arabinose, while on enzymic hydrolysis with crude hesperidinase, **7** yielded an aglycone (**14**) which was identified as a known triterpene, 30-*O*-methyl spergulagenate.$^{3)}$ Comparison of the carbon-13 nuclear magnetic resonance (^{13}C-NMR) spectrum of **7** with that of **14** indicated the presence of glycosylation shifts$^{4,5)}$ for the signals due to 2-, 3- and 28-C of the aglycone moiety, disclosing that **7** must be a 3,28-bisdesmoside of **14**. On alkaline saponification,$^{6)}$ **7** afforded 1,6—anhydroglucose (**15**) and a prosapogenin (**16**). The formation of **15** by alkaline hydrolysis is characteristic of β-glucosyl esters of acidic di- and triterpenes.$^{7)}$ This evidence coupled with an anomeric carbon signal due to an ester type glucosyl linkage at δ 95.7 and the coupling constant of the anomeric proton signal at δ 6.21 (*vide supra*) demonstrated that **7** is a β-glucopyranosyl ester of **16**. The prosapogenin (**16**) showed three anomeric proton signals at δ 4.73 (1H, d, $J=7.4$ Hz), 5.10 (1H, d, $J=7.1$ Hz) and 5.17 (1H, d, $J=7.4$ Hz) and three anomeric carbon signals (Table II). The electron impact mass spectra (EI-MS) of a permethyl ether of **16** exhibited fragment ions due to the sugar moiety at m/z 219 (terminal Glc-Me_4), 423 [(Glc-Glc)Me_7] and 583 [(Glc-Glc-Ara)Me_9]. The methylation analysis of **16** by gas chromatography-mass spectrometry (GC-MS) revealed the presence of 3-linked arabinopyranoside, 2-linked glucopyranoside and terminal glucopyranoside units. Based on these results, **7** can be formulated as shown in Chart 1.

Quinoa-saponin-7 (**8**) afforded glucose, arabinose and oleanolic acid (**17**) on acid hydrolysis. Alkaline hydrolysis of **8** yielded **15**. The ^{1}H-NMR spectrum of **8** exhibited four anomeric proton signals at δ 4.64 (1H, d, $J=7.8$ Hz), 5.03 (1H, d, $J=6.4$ Hz), 5.07 (1H, d, $J=7.3$ Hz) and 6.20 (1H, d, $J=7.3$ Hz, –COO-β-Glc). In the ^{13}C-NMR spectrum of **8** (Table I), the glycosylation shifts of signals due to the aglycone moiety indicated the presence of glycoside linkages at both the 3-hydroxyl and 28-carboxyl groups and the signals due to the sugar moiety were almost super-



	R_1	R_2	R_3	R_4
6:	–OH	–CH_3	–Glc	–Ara
1:	–OH	–CH_3	–Glc	–Ara$\overset{3}{-}$Glc
2:	–OH	–CH_3	–Glc	–Gal$\overset{3}{-}$Glc
3:	–OH	–$COOCH_3$	–Glc	–Ara
4:	–OH	–$COOCH_3$	–Glc	–Ara$\overset{3}{-}$Glc
5:	–OH	–$COOCH_3$	–Glc	–Gal$\overset{3}{-}$Glc
7:	–H	–$COOCH_3$	–Glc	–Ara$\overset{3}{-}$Glc$\overset{2}{-}$Glc
14:	–H	–$COOCH_3$	–H	–H
16:	–H	–COOH	–H	–Ara$\overset{3}{-}$Glc$\overset{2}{-}$Glc
8:	–H	–CH_3	–Glc	–Ara$\overset{3}{-}$Glc$\overset{2}{-}$Glc
17:	–H	–CH_3	–H	–H
9:	–OH	–$COOCH_3$	–Glc	–Ara$\overset{3}{-}$Glc$\overset{2}{-}$Glc
18:	–OH	–$COOCH_3$	–H	–H
10:	–H	–CH_3	–Glc	–GlcA
11:	–OH	–CH_3	–Glc	–GlcA
19:	–OH	–CH_3	–H	–H
12:	–H	–CH_3	–Glc	–GlcA$\overset{3}{-}$Xyl
13:	–OH	–CH_3	–Glc	–GlcA$\overset{3}{-}$Xyl

Ara: α-L-arabinopyranosyl
Glc: β-D-glucopyranosyl
Gal: β-D-galactopyranosyl
GlcA: β-D-glucuronopyranosyl
Xyl: β-D-xylopyranosyl

The structures of these compounds were drawn incorrectly in the previous paper and are amended in this paper.

Chart 1

TABLE I. ^{13}C-NMR Chemical Shifts of the Aglycone Moieties in C_5D_5N

Carbon No.	**7**	**14**	**16**	**8**	**9**	**10**	**11**	**12**	**13**
1	38.8	38.9	38.7	38.8	38.9	38.7	38.6	38.8	38.6
2	26.8	28.1	26.7	26.8	26.1	26.5	26.1	26.4	26.1
3	89.0	78.1	89.0	89.1	82.5	89.0	82.1	89.3	82.1
4	39.6$^{a)}$	39.4$^{a)}$	39.6$^{a)}$	39.6$^{a)}$	43.5	39.4$^{a)}$	43.4	39.5$^{a)}$	43.5
5	55.9	55.9	56.0	55.9	47.8	55.8	47.5	55.9	47.4
6	18.5	18.8	18.4	18.6	18.3	18.5	18.1	18.6	18.2
7	33.2	33.3	33.2	33.4	32.9	33.1	32.8	33.1	32.7
8	39.9$^{a)}$	39.7$^{a)}$	39.8$^{a)}$	40.0$^{a)}$	40.0	39.8$^{a)}$	39.9	40.0$^{a)}$	39.9
9	48.1	48.1	48.1	48.1	48.3	48.0	48.1	48.1	48.1
10	37.0	37.4	37.0	37.0	37.0	36.9	36.8	37.0	36.8
11	23.6	23.8$^{b)}$	23.8$^{b)}$	23.9	23.9$^{a)}$	23.6	23.4$^{a)}$	23.7	23.6
12	123.5	123.2	123.0	122.9	123.5	122.9	122.8	122.9	122.9
13	143.7	144.5	144.8	144.1	143.8	144.0	144.1	144.1	144.1
14	42.0	42.1	42.1	42.2	42.1	42.1	42.1	42.2	42.1
15	28.3$^{b)}$	28.4	28.4$^{c)}$	28.3$^{b)}$	28.3	28.1	28.2	28.2	28.3
16	23.6	23.9$^{b)}$	23.9$^{b)}$	23.9	23.7$^{a)}$	23.6	23.6$^{a)}$	23.7	23.6
17	46.5	46.2	46.3	47.0	46.6	46.9	46.9	47.0	47.0
18	43.2	43.4	43.4	41.8	43.2	41.7	41.7	41.8	41.7
19	42.5	42.7	43.2	46.2	42.5	46.2	46.1	46.3	46.2
20	43.9	44.2	44.1	30.8	44.0	30.7	30.7	30.7	30.8
21	30.6	30.9	31.2	34.1	30.7	34.0	33.9	34.1	34.0
22	34.0	34.5	34.8	33.4	34.0	33.5	33.0	33.1	33.1
23	28.1$^{b)}$	28.8	28.1$^{c)}$	28.1$^{b)}$	64.7	28.1	64.3	28.2	64.1
24	16.8	16.5	16.9	16.9	13.6	16.9	13.5	16.9	13.6
25	15.5	15.5	15.4	15.5	16.1	15.5	16.1	15.5	16.1
26	17.4	17.4	17.4	17.5	17.5	17.4	17.5	17.5	17.5
27	26.1	26.1	26.2	26.1	26.1	26.1	26.1	26.1	26.1
28	176.9	179.9	180.0	176.4	176.9	176.4	176.4	176.4	176.4
29	28.3	28.4	29.1	33.2	28.3	33.1	33.0	33.1	33.1
30	176.0	177.2	179.5	23.7	176.0	23.6	23.6	23.7	23.6
OCH_3	51.7	51.7			51.6				

a—c) These assignments may be interchanged in each column.

TABLE II. ^{13}C-NMR Chemical Shifts of the Sugar Moieties in C_5D_5N

Carbon No.	**7**	**16**	**8**	**9**	**10**	**11**	**12**	**13**
C-3-Sugar								
Ara-1	106.6	106.6	106.9	105.9				
-2	71.4	71.4	71.4	71.4				
-3	86.0	86.0	86.1	85.8				
-4	69.1	69.1	69.1	69.0				
-5	67.0	67.0	67.0	66.9				
Glc-1 (inner)	104.5	104.5	104.5	104.3				
-2	86.0	86.0	86.1	85.8				
-3	79.1	79.1	79.1	79.1				
-4	70.9$^{a)}$	70.9$^{a)}$	71.2	71.2$^{a)}$				
-5	77.7	77.8	77.8	77.8				
-6	61.9$^{b)}$	62.1$^{b)}$	62.2$^{a)}$	62.2$^{b)}$				
Glc-1 (outer)	107.1	107.1	107.2	107.0				
-2	76.4	76.5	76.5	76.4				
-3	78.3	78.3	78.9	78.2				
-4	70.9$^{a)}$	70.6$^{a)}$	71.2	71.2$^{a)}$				
-5	77.7	77.8	78.4	77.6				
-6	62.3$^{b)}$	62.3$^{b)}$	62.6$^{a)}$	62.4$^{b)}$				
GlcA-1					107.1	106.1	106.4	106.2
-2					75.4	75.3	74.4	74.5
-3					78.0	78.0	86.5	86.5
-4					73.4	73.3	71.4	71.4
-5					77.6	77.8	77.7	77.8
-6					173.3	172.7	172.4	172.2
Xyl-1							105.7	105.9
-2							74.8	75.3
-3							78.9	78.0
-4							70.7	71.1
-5							67.1	67.4
C-28-Sugar								
Glc-1	95.7		95.8	95.7	95.7	95.7	95.7	95.7
-2	74.0		74.2	74.1	74.0	74.0	74.0	74.1
-3	78.8		78.9	78.8	78.8	78.8	78.7	78.9
-4	70.5$^{a)}$		70.6	70.9$^{a)}$	71.1	71.1	71.4	70.9
-5	79.2		79.3	79.1	79.2	79.2	78.9	79.2
-6	62.0$^{b)}$		62.2$^{a)}$	62.2$^{b)}$	62.2	62.1	62.5	62.2

a, b) These assignments may be interchanged in each column.

imposable on those of **7**. It follows that the structure of **8** can be assigned as shown in Chart 1.

Quinoa-saponin-8 (**9**) yielded glucose and arabinose on acid hydrolysis. Alkaline hydrolysis of **9** gave **15**. The ^{1}H-NMR spectrum of **9** showed four anomeric proton signals at δ 4.87 (1H, d, $J=7.7$ Hz), 5.06 (1H, d, $J=7.7$ Hz), 5.08 (1H, d, $J=7.5$ Hz) and 6.24 (1H, d, $J=8.1$ Hz, –COO-β-Glc). The comparison of the ^{13}C-NMR signals due to the aglycone moiety (Table I) with those of **3**, **4** and **5** revealed that **9** is a bisdesmoside of phytolaccagenic acid (**18**).[8] The comparison of the ^{13}C-NMR signals due to the sugar moiety (Table II) indicated that the structure of the sugar moiety of **9** is identical with that of **7** and **8**. Thus, **9** can be formulated as shown in Chart 1.

Saponin **10** was identified as chikusetsusaponin IVa[9] which has been isolated from rhizomes of *Panax japonicus* C.A.MEYER and many other *Panax* species.

Quinoa-saponin-9 (**11**) yielded glucose, glucuronic acid and hederagenin (**19**) on acid hydrolysis, while alkaline hydrolysis of **11** yielded **15**. The ^{1}H-NMR spectrum of **11** exhibited two anomeric proton signals at δ 5.24 (1H, d, $J=6.4$ Hz) and 6.30 (1H, d, $J=7.1$ Hz, –COO-β-Glc). The comparison of the ^{13}C-NMR spectrum (Table I) with those of **10** and bisdesmosidic saponins of **19** in the previous paper[2] led to the assignment of the structure of **11** as shown in Chart 1 (23-hydroxy-chikusetsusaponin-IVa).

Saponin **12** yielded glucose, xylose, glucuronic acid and **17**, while alkaline hydrolysis of this saponin gave **15**. The ^{1}H-NMR spectrum of **12** showed three anomeric proton signals at δ 5.00 (1H, d, $J=7.9$ Hz), 5.35 (1H, d, $J=7.3$ Hz) and 6.30 (1H, d, $J=8.1$ Hz, –COO-β-Glc). The proton signals due to the sugar moiety of **12** were assigned by the proton–proton correlation spectroscopy (^{1}H–^{1}H COSY) procedure. Based on this assignment, sugar carbon signals of **12** were identified by carbon-13–proton COSY (^{13}C–^{1}H COSY) (Table I) and it was concluded that a signal at δ 86.5 is attributable to 3-C of a glucuronide unit. This downfield displacement of the 3-C signals from that of unsubstituted β-glucuronide (near δ 78) such as **10** or **11** (Table II) indicated the presence of a 3-linked β-glucuronide unit in **12**. This evidence coupled with the presence of carbon signals attributable to a terminal β-xylopyranosyl unit led to the formulation of **12** as shown in Chart 1.

Quinoa-saponin 10 (**13**) afforded glucose, xylose, glucuronic acid and **19** on acid hydrolysis. The ^{1}H-NMR spectrum of **13** showed three anomeric proton signals at δ 5.22 (1H, d, $J=7.1$ Hz), 5.28 (1H, d, $J=7.3$ Hz) and 6.31 (1H, d, $J=8.1$ Hz, –COO-β-Glc). In the ^{13}C-NMR spectrum of **13**, carbon signals due to the aglycone moiety were consistent with the formulation as a bisdesmoside of **19** and signals due to the sugar moiety were almost superimposable on those of **12**. It follows that **13** can be formulated as shown in Chart 1.

McLaughlin reported the isolation and structure elucidation of several saponins (quinosides A—E) of **17** from quinoa.[10] Of these saponins, the structure proposed for quinoside D is identical with that of **12** but no other saponin in his report has been isolated in the present study.

Experimental

General Procedures NMR spectra were recorded on JEOL FX-100 and GX-400 instruments in C_5D_5N. High performance liquid chromatography (HPLC) was conducted on a column of TSK-gel ODS-120T (21.5 mm × 30 cm), and detection was done with a differential refractometer.

Acid hydrolysis of saponins and identification of the resulting monosaccharides were carried out as described in the previous paper[6] and an aglycone formed in this reaction was identified by comparison of the optical rotation and ^{13}C-NMR spectrum with those of an authentic sample. Alkaline hydrolysis and identification of the resulting 1,6-anhydroglucose (**15**) and methylation analysis: see the previous paper.[6]

Extraction and Separation of Saponins The brans (1 kg) supplied by Maruzen Kasei Co., Ltd., Onomichi, Japan, were defatted with *n*-hexane and extracted with hot MeOH and the with hot 50%MeOH. A part (65 g) of the combined extract (total 253 g) was subjected to chromatography on DIAION HP-20 (highly porous polymer, Mitsubishi Kasei Co., Ltd., Tokyo) with H_2O, 50%MeOH, 85%MeOH, MeOH and then acetone as eluants. The 85%MeOH eluate (17 g) was chromatographed on silica gel with $CHCl_3$–MeOH–H_2O (30 : 10 : 1, 10 : 5 : 1, 6 : 4 : 1 and finally 4 : 6 :1) to give ten fractions, fr. 1—10. Four saponins (**1**, **3**, **4** and **6**) which have already been reported,[2] were obtained from frs. 1 and 3.

Fraction 4 was chromatographed on LiChroprep RP-8 (reverse phase, Merck) with 57, 62 and then 67%MeOH to give six fractions, frs. 1′—6′ and further elution with MeOH gave another fraction, fr. 7′. Saponins **5** and **4**[2] were obtained from also frs. 2′ and 4′, respectively by HPLC. By HPLC with 68%MeOH, fr. 5′ gave **7** in a yield of 0.08% together with **2**.[2] Fraction 6′ exclusively contained **1**.[2] Recrystallization of fr. 7′ from MeOH–H_2O afforded **8** in a yield of 0.03%.

Fraction 5 was chromatographed on LiChroprep RP-8 with 50 and then 60%MeOH to give **9** in a yield of 0.16%. Fraction 6 was chromatographed on LiChroprep RP-8 with 50%MeOH to afford **10** in a yield of 0.1%. Chromatography of fr. 7 on LiChroprep RP-8 with 40, 45, 50 and then 55%MeOH gave **11** and **12** in yields of 0.02 and 0.06%, respectively. Chromatography of fr. 8 on LiChroprep RP-8 with 35, 40, 45, 50 and then 55%MeOH afforded **13** in a yield of 0.08%.

Quinoa-saponin 6(**7**): A white powder, $[\alpha]_D^{24}$ +56.2° (c=0.93, C_5H_5N). *Anal.* Calcd for $C_{54}H_{86}O_{24} \cdot 2H_2O$: C, 56.14; H, 7.85. Found: C, 56.00; H, 7.87. A solution of **7** (52 mg) and crude hesperidinase (Tanabe Pharm. Ind. Co., Ltd., Osaka, 50 mg) in H_2O (3 ml) was incubated at 37 °C for 44 h. After heating at 100 °C for a few minutes, the reaction mixture was concentrated and chromatographed on DIAION HP-20 with H_2O, 90%MeOH, MeOH and acetone. The eluates with 90%MeOH and MeOH were combined and subjected to HPLC with 85%MeOH to give **14** (8 mg), colorless needles from MeOH, mp 257—259 °C, $[\alpha]_D^{24}$ +89.1° (c=0.51, C_5H_5N). This product was identified as methyl spergulagenate by the ^{1}H- and ^{13}C-NMR spectra and other physical constants.[3] A suspension of **7** (35 mg) in aqueous 5%KOH (2 ml) was heated on a boiling water bath for 2 h. The reaction mixture was neutralized with Amberlite MB-3 resin and then filtered. The filtrate was chromatographed on Diaion HP-20 with H_2O and then with MeOH. The MeOH eluate (29 mg) was subjected to HPLC with 71%MeOH to give **16** (26 mg) as a white powder, $[\alpha]_D^{25}$ +78.3° (c=0.89, C_5H_5N). *Anal.* Calcd for $C_{47}H_{74}O_{19} \cdot 3H_2O$: C, 56.61; H, 8.09. Found: C, 56.41; H, 7.87.

Quinoa-saponin-7(**8**): Colorless needles from MeOH–H_2O, mp 241—243 °C, $[\alpha]_D^{24}$ +26.9° (c=0.87, C_5H_5N). *Anal.* Calcd for $C_{53}H_{86}O_{22} \cdot 3H_2O$: C, 56.37; H, 8.21. Found: C, 56.51; H, 8.10.

Quinoa-saponin-8(**9**): A white powder, $[\alpha]_D^{16}$ +52.5° (c=1.01, MeOH). *Anal.* Calcd for $C_{54}H_{86}O_{25} \cdot 2H_2O$: C, 55.37; H, 7.75. Found: C, 55.25; H, 8.03.

Chikusetsusaponin IVa(**10**): Colorless needles from MeOH–H_2O, mp 218—220 °C, $[\alpha]_D^{17}$ +6.9° (c=0.97, MeOH). Identification was achieved by comparison of optical rotation, melting point and the ^{1}H- and ^{13}C-NMR spectra with those of an authentic sample.

Quinoa-saponin-9(**11**): A white powder, $[\alpha]_D^{19}$ +25.8° (c=0.67, C_5H_5N). *Anal.* Calcd for $C_{42}H_{66}O_{15} \cdot 2H_2O$: C, 59.56; H, 8.33. Found: C, 59.54; H, 8.42.

Quinoside D(**12**): A white powder, $[\alpha]_D^{17}$ +5.4° (c=1.12, MeOH). *Anal.* Calcd for $C_{47}H_{74}O_{18} \cdot H_2O$: C, 59.73; H, 8.11. Found: C, 59.74; H, 8.50.

Quinoa-saponin-10(**13**): A white powder, $[\alpha]_D^{19}$ +8.7° (c=0.83, C_5H_5N). *Anal.* Calcd for $C_{47}H_{74}O_{19} \cdot 2H_2O$: C, 57.65; H, 8.03. Found: C, 57.39; H, 8.19.

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