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A New Aminoglycoside from *Hylocereus polyrhizus*

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ABSTRACT

*A new aminoglycoside, pitayaoside A (2-((-5'-(aminomethoxy)-3',4'- dihydroxy-2'-(hydroxymethyl)tetrahydro-2 H-pyran-2'-yl)oxy)-6- (hydroxymethyl)tetrahydro-2 H-pyran-3,4,5-triol) (**1**) was isolated from the fruits of Hylocereus polyrhizus (pitaya). The structure was elucidated on the basis of physical and spectral analysis.*

Keywords

Hylocereus polyrhizus, Aminoglycoside, Pitayaoside A, Pitaya.

Pitaya, belonging to the genus *Hylocereus* of the order *Caryophyllales*, also called dragon fruit, is a kind of tropical fruits around the world, and there are at last 3 varieties classified as *Hylocereu polyrhizus* (red pitaya), *H. undatus* (white pitaya) and *H. megalanthus* (yellow pitaya) [1]. The antioxidant capacity of red pitaya juice has been proved by *in vitro* and *in vivo* assay [1-3]. Many beneficial effects of red pitaya are reported in experimental animal studies, including improvement of dyslipidemia and blood glucose in high-carbohydrate or high-fat diet-induced metabolic syndrome rats [3-6], retardation of alcoholic liver disease progression in mice [7], attenuation of inflammation, and modulation of gut microbiota in obese mice [8]. In this paper, we report the isolation and structural elucidation of this new aminoglycoside (pitayaoside A (**1**)).

Pitayaoside A (**1**) was obtained as pale yellow crystals from CH_3OH. Its molecular formula was deduced as $C_{13}H_{25}O_{11}N$ by HR-ESI-MS (*m/z* 394.1324 ($[M+Na]^+$; calc. 394.1325)). The IR spectrum show absorptions for hydroxyl group (3400 cm^{-1}) and amino group (3300 cm^{-1}). The ^1H NMR spectrum of **1** (Table 1) showed 8 oxymethine signals of two sets of glucopyranosyloxyls signals overlap between 3.69~5.66 ppm, four pair oxymethylenes [δ_H 3.91 (1H, dd, J = 12.0, 6.0 Hz, CH_2-7a)/4.04 (1H, dd, J = 12.0, 2.4 Hz, CH_2-7b), δ_H 3.86 (2H, t, J = 12.4 Hz, CH_2-6'), δ_H 3.93 (2H, m, CH_2-7') & δ_H 3.55 (2H, s, CH_2-8')] corroborated by ^{13}C NMR signals in Table 1. They were clarified and assigned based on COSY, NOESY, HSQC and HMBC spectra. The ^1H NMR signal at δ 5.66 (1H, d, J = 3.6 Hz, H-2) suggested the presence of one glucopyranosyl moiety. The HMBC correlations of H-2′ to C-2 (Table 1) showed that the glucopyranosyloxyl was bonded to C-2 and 2' by an oxygen atom. By the ^1H-^1H COSY and HSQC data, two contiguous structural sequence was derived from correlations from H-2 (δ_H 5.66; δ_C 93.8) to H-3 (δ_H 4.11; δ_C 74.9), from H-3 to H-4 (δ_H 3.70; δ_C 71.6), from H-4 to H-5 (δ_H 4.45; δ_C 75.8), from H-5 to H-6 (δ_H 4.46; δ_C 79.6), from H-6 to CH_2-7 (δ_H 3.91/4.04; δ_C 62.4), H-3' (δ_H 4.19; δ_C 74.8) to H-4' (δ_H 3.69; δ_C 73.4), from H-4' to H-5' (δ_H 4.04; δ_C 84.2), from H-5' to CH_2-6' (δ_H 3.86; δ_C 64.4), in accord with the presence of two spin systems corresponding to a CH(2)–CH(3)–CH(4)–CH(5)–CH(6)–CH_2(7)– and CH(3')–CH(4')– CH(5')–CH_2(6')– moiety. Two oxymethylene groups (δ_H 3.55 (2H, s) and 3.93 (2H, m)) located at the position were determined by ^{13}C-NMR signals at C-2' (δ 105.7) and C-5' (δ 84.2) and the HMBC correlations of H-7'/C-2', and H-8'/C-5'. The attachment of two oxymethylene groups at C-2' and C-5' was confirmed by the correlation between H-7'/H-3' and H-8'/H-5' in NOESY spectrum. The full assignment of **1** was further confirmed by COSY, HSQC, and HMBC spectra. The ^{1}H- and ^{13}C-NMR (Table 1), COSY, NOESY, HSQC and HMBC (Table 1) experiments confirmed the structure as 2-((-5′-(aminomethoxy)-3′,4′- dihydroxy-2′-(hydroxymethyl)-tetrahydro-2 *H*-pyran-2′-yl)oxy)-6-(hydroxymethyl)tetrahydro-2 *H*-pyran- 3,4,5-triol, and designated pitayaoside A (**1**).

Experimental

General:

IR spectra were measured on a Hitachi 260-30 spectrophotometer. ^{1}H NMR (400 MHz) and 2D spectra were obtained on Varian-Mercury-400 spectrometers. Low-resolution ESI-MS spectra were obtained on an API 3000 (Applied Biosystems) and high-resolution ESI-MS spectra on a Bruker Daltonics APEX II 30e spectrometer. The anion-exchange resin, di-ethyl-amino-ethyl (DEAE) sephacel™ (GE healthcare, USA) was used for column chromatography.

Plant Material:

Fresh red dragon fruits (*Hylocereus polyrhizus*) were obtained from a local market in Kaohsiung City, Daliao Dist., Taiwan, in June 2020. Plant material was identified by Dr. Su-Ling Liu (Experimental Forest College of Bioresources and Agriculture, National Taiwan University). A voucher specimen was deposited at the Department of Medical Technology, School of Medical and Health Sciences, Fooyin University, Kaohsiung, Taiwan.

Extraction and Isolation:

The primary isolation for pitayaoside (**1**) by two phase extraction was similar to the method of betalains purification [9]. Briefly, red dragon fruits were peeled, sliced and homogenized in a juicer (Vita Mix, VM0101B, USA) at maximum speed. The homogenate was centrifuged by a centrifuger (Hitech, CR21G, Japan) at 3500xg (30 min, 4°C), and then the supernatant was filtered by using qualitative filter paper No.2 (Advantec, Japan). The filtered 20 ml supernatant of juice was added 5 g of polyethylene glycol 6000 (PEG 6000; Merck, USA) and 2 g of ammonium sulfate ($(NH_4)_2SO_4$; Merck, USA). The mixtures were mixed thoroughly using a magnetic stirrer for 1 h, and then stood overnight at 4°C allowed to formation of aqueous *two-phase partition*, the bottom aqueous phase was discarded and the top phase was submitted to extraction with equal volume of chloroform. PEG 6000 was removed by an organic–aqueous extraction, which PEG 6000 was distributed to the organic (chloroform) phase (bottom phase). The top aqueous phase was harvested, and then was followed through a column packaged with DEAE resin (GE healthcare, USA). This column was washed with water by five volumes of column of water to remove other components. The fractions containing pitayaoside A (**1**) were gradually eluted by 0.001 N HCl and collected, and then were concentrated under reduced pressure by using a rotary evaporator (EYELA, N-1100S, Japan) at 60°C. Finally, the purified pitayaoside A (**1**) were further lyophilized by a freeze dryers (Labconco, freezone plus 6, USA), and the powders of pitayaoside A (**1**) were stored at -20°C until use.

Table 1. ^{13}C and ^{1}H HMR (Py-d_5 and CD_3OD) data of pitayaoside (**1**).

C#	δ_C	$_H$	mult., *J* (Hz)	HMBC (^{1}H → ^{13}C)
2	93.8	5.66	d, 3.6	C-3, C-4, C-2'
3	74.9	4.11	t, 9.2	C-2, C-4, C-5
4	71.6	3.70	t, 9.2	C-2, C-3, C-5, C-6
5	75.8	4.45	d, 12.0	C-3, C-4, C-6, C-7
6	79.6	4.46	t, 8.0	C-2, C-4, C-5, C-7
7a 7b	62.4	3.91 4.04	dd, 12.0, 6.0 dd, 12.0, 2.4	C-5, C-6 C-5, C-6
2'	105.7	-	-	-
3'	74.8	4.19	m	C-2', C-7', C-4', C-5'
4'	73.4	3.69	dd, 8.8, 1.2	C-2', C-3', C-5', C-6'
5'	84.2	4.04	m	C-3', C-4', C-6', C-8'
6'	64.4	3.86	t, 12.4	C-2', C-4', C-5'
7'	63.3	3.93	m	C-2', C-3'
8'	71.4	3.55	s	C-5'

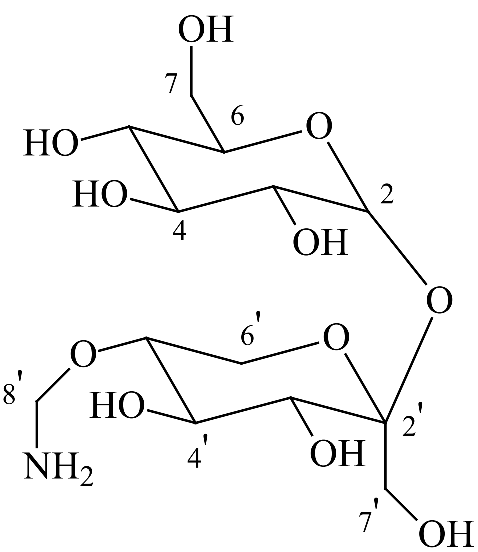

Figure 1: Structure of pitayaoside (**1**).

Pitayaoside A (1):

Pale yellow crystals. mp 201-203 °C. $[\alpha]^{25}_{D}$ + 33.6° (c 0.53, CH_3OH). IR (KBr, ν_{max}, cm^{-1}) ν_{max}: 3400 (OH), 3300 (NH_2) cm^{-1}. HR-EI-MS: *m/z* $[M+Na]^+$ calcd for $C_{13}H_{25}O_{11}N$: 394.1325; found: 394.1324. ^{1}H and ^{13}C NMR (400 MHz, Py-d_5 and CD_3OD, δ, ppm, J/Hz): see Table 1.

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