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A NEW THIAZINEDIONE GLYCOSIDE FROM THE FRUIT OF *Xanthium sibiricum*

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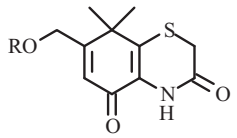
The fruits of *Xanthium sibiricum* Patr. (Compositae), also called "Cang-Er-Zi," are widely distributed in China. As a very important traditional Chinese medicine, they are mainly used for the treatment of chronic rhinitis, skin pruritus, arthritis, and headache due to cold [1, 2]. The chemical constituents of *X. sibiricum* generally include six types: fatty acid ester, sesquiterpene lactone, kaurene glycoside, phenolic acid, chrysophanol, and thiazinedione [3]. Among them, the thiazinediones are characteristic constituents in this plant, which bears sulfur and nitrogen in the chemical skeleton that have not been reported in other plants. In our investigation of the chemical constituents of this Chinese traditional medicine, a new thiazinedione glycoside, 7-hydroxymethyl-8,8-dimethyl-4,8-dihydrobenzo [1, 4] thiazine-3,5-dione-11-*O*-[*β*-D-apiofuranosyl-(1→6)-*O*-*β*-D-glucopyranoside] (**1**), containing not only a special chemical skeleton but also a rare sugar apiose, along with two known thiazinediones, xanthiside (**2**) and xanthiazone (**3**), were isolated and identified.

The fruits of *X. sibiricum* were from the Sichuan Neautus Ecological Medicinal Material Co. Ltd. The powdered dry fruits (27 kg) were extracted with 80% MeOH. The extracts (2200 g) were suspended in water and partitioned with petroleum ether, ethyl acetate, and *n*-butanol successively. The *n*-butanol fraction (200 g) was subjected to silica gel column chromatography eluted with $CHCl_3$–MeOH (100:0–0:100) gradient. Combining of similar fractions on the basis of TLC afforded 15 fractions (1–15). Fractions 3 and 8 afforded compounds **3** (1.5 g) and **2** (1.7 g), respectively, after repeated chromatography on silica gel ($CHCl_3$–MeOH) and recrystallization with methanol. Fraction 12 was subjected to silica gel eluted with (10:1–1:10) $CHCl_3$–MeOH and then to a C-18 column eluted with 30% MeOH, affording compound **1** (120 mg).

Compounds **2** and **3** were identified by comparison with the reported spectral data [4, 5].

Compound **1**, yellow powder, $[\alpha]_D^{25}$ –47° (*c* 1.0, MeOH). Its HR-ESI-MS showed a quasi-molecular ion peak at *m/z* 556.1488 $[M + Na]^+$ (calcd for $C_{22}H_{31}NO_{12}SNa$, 556.1459), suggesting the molecular formula $C_{22}H_{31}NO_{12}S$. The fragment ions at *m/z* 424 $[M + Na - 132]^+$ and 261 $[M + Na - 132 - 162]^+$ revealed two sugar moieties in **1**. TLC acid hydrolysis revealed two sugar spots, and one of them identical to glucose. Comparison of the ^{13}C NMR signals of **1** with those of **2** showed that **1** had one more pentose. The pentose was deduced as an apiose according to its ^{13}C NMR data [6–8] and confirmed by NOESY correlations between H-5″ (3.35)/H-2″ (3.72) and H-5″ (3.35)/H-4″ (3.83) (Fig. 1 and Table 1). The linkage of **1** was determined by HSQC and HMBC based on the correlations between C-11 and glucose-H-1, glucose-C-6, and pentose-H-1. The configuration of the apiofuranosyl unit was confirmed from the value of $[M]_D$. According to the Klyne rule [9], $\Delta C = [M]_D$(glycoside) – $[M]_D$(aglycone), –150.26 [calcd for *β*-D-Api*f* – 145.6] [10], the apiose should be *β*-D-apiofuranose. Therefore, the new compound **1** was identified as 7-hydroxymethyl-8,8-dimethyl-4,8-dihydrobenzo[1,4]-thiazine-3,5-dione-11-*O*-[*β*-D-apiofuranosyl-(1→6)-*O*-*β*-D-glucopyranoside].



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1: R = Api-(1→6)-Glc

2: R = Glc; **3:** R = H

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TABLE 1. ^{1}H NMR (600 MHz) and ^{13}C NMR (150 MHz) Data of **1** (DMSO-d_6, δ, ppm, J/Hz)

C atom	δ_H	δ_C	HMBC	NOESY
2	3.46 (2H, s)	29.0	H-4	
3		162.8	H-2	
4	9.27 (1H, s)			
4a		130.3	H-6	
5		175.5	H-4	
6	6.65 (1H, s)	122.0	H-11	H-1′
7		165.6	H-9, 10, 11	
8		42.0	H-6, 9, 10	
8a		141.4	H-2, 9, 10	
9	1.36 (3H, s)	27.2	H-10	H-11
10	1.35 (3H, s)	27.0	H-9	H-11
11	4.42 (1H, d, J = 16)	66.0	H-1′, 6	H-1′, 9, 10
	4.57 (1H, d, J = 16)			
Glc				
1′	4.20 (1H, d, J = 7.8)	102.5	H-11, 3′, 5′	H-6, 11, 3′, 5′
2′	3.05 (1H, m)	73.7	H-4′	H-6′
3′	3.15 (1H, br.s)	77.0	H-5′	H-1′, 1″
4′	3.00 (1H, m)	70.7	H-2′	H-6′
5′	3.28 (1H, m)	76.3	H-6′, 3′	H-1′, 1″
6′	3.30 (1H, m)	68.0	H-1′, 4″, 5″	H-5″, 4″, 1″
	3.83 (1H, br.s)			H-2′, 4′
Api				
1″	4.87 (1H, d, J = 2.9)	109.8	H-6′, 4″	H-4″, 5′, 6′, 3′
2″	3.72 (1H, d, J = 2.9)	76.4	H-5″, 4″	H-5″, 4″
3″		79.2	H-4″	
4″	3.56 (1H, d, J = 9.1)	73.9	H-1″, 2″, 5″	H-1″
	3.83 (1H, d, J = 9.5)			H-2″, 5″
5″	3.35 (2H, m)	63.6	H-4″	H-2″, 4″

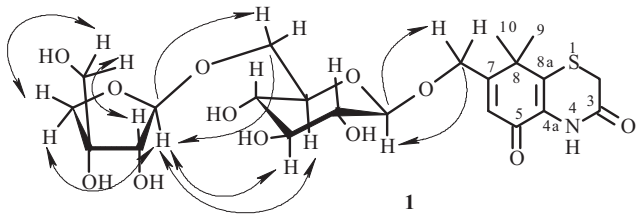

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Fig. 1. The key correlations of HMBC and NOESY of compound **1**.

Although the thiazinediones have not been found to have any activities, they may play some important role in this traditional medicine because they are the main components. To date, thiazinediones were found only from *Xanthium* species and could be used as marker compounds to identify this herb. It may be interesting to investigate the biosynthesis of these compounds because of their characteristic structure.

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