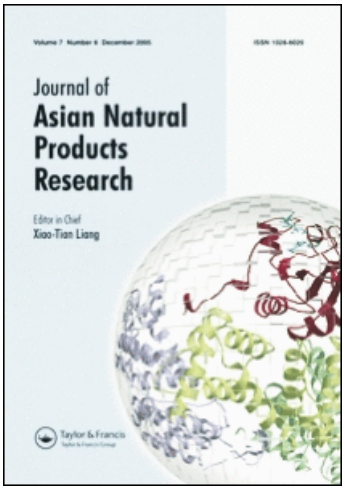

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A new thiaziedione from the fruits of *Xanthium sibiricum*

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A novel sulphur-containing compound named xanthiazinone (**1**) was isolated from the ethanolic extract of the fruits of *Xanthium sibiricum*, along with four known compounds, xanthiazone (**2**), xanthiside (**3**), xanthienopyran (**4**) and 5-hydroxypyrrolidin-2-one (**5**). Their structures were determined on the basis of spectroscopic techniques.

Keywords: Compositae; *Xanthium sibiricum*; xanthiazinone; thiaziedione

1. Introduction

The genus *Xanthium* (Compositae) is represented by a relatively limited number of species distributed from America over the whole world.[1] *Xanthium* is a source plant, growing in warm, arid parts in China. Its fruits have long been used as traditional folk medicine for treating leucoderma, fever, scrofula, sinusitis, headache, herpes and cancer.[2–5] *Xanthium* is known to be rich in sesquiterpene lactones of the xanthanolide-type.[6] In previous studies on *X. strumarium*, carboxyatractyloside, xanthanol, isoxanthanol, hydroquinone, alkaloids,[7,8] and caffeoylquinic acids[9] were identified. In continuation of our phytochemical studies of this genus, a new sulphur-containing compound, xanthiazinone (**1**) was isolated from the fruits of *X. sibiricum*, along with four known compounds **2**–**5**. Their structures were elucidated by spectroscopic methods and comparing their NMR data with those of corresponding compounds in the literature (see Figure 1). Compounds **3**, **4** and **5** were first isolated from this plant.

2. Results and discussion

By using a combination of silica gel, Sephadex LH-20 and reverse-phase column chromatography in various solvent systems, five compounds were isolated from the 70% ethanolic extract of *X. sibiricum*, including four known compounds: xanthiazone (**2**), xanthiside (**3**), xanthienopyran (**4**) and 5-hydroxypyrrolidin-2-one (**5**). Their structures were identified respectively by comparing their spectral data with literature values.[10–13]

Compound **1** was obtained as colourless needle crystals (MeOH), with a formula $C_{15}H_{18}N_2O_4S$ determined by the HRESI–MS ($[M + H]^+$, $m/z = 323.1105$), mp 190–192°C. The positive ESI–MS afforded an $[M + H]^+$ peak at *m/z* 323 and the fragmentation patterns at *m/z* 340 $[M + NH_4]^+$, 101 $[M—C_{11}H_{12}O_2SN]^+$, 645 $[2M + H]^+$. IR spectrum showed the presence of hydroxyl (3438 cm^{-1}) and a secondary amide group (1675 cm^{-1}). The ^1H NMR spectrum revealed signals for an olefinic proton which appeared as a broad singlet at δ 6.46 (H-6), two sets of methylene protons at δ 4.30/4.42 (each 1H, d, $J = 15.4$ Hz, H-11) and 3.47 (2H, broad singlet, H-2), and two methyls of a gem-dimethyl group (δ 1.45, 6H, s, H-9, 10). The ^{13}C NMR spectrum of the matrix displayed 11 carbon signals. These signals were assigned by HMQC spectrum analysis as one tri- and one tetra-substituted double bonds [(δ 122.9, C-6 and 167.2, C-7), and (δ 131.0, C-4a and 143.3, C-8a)], a secondary oxygenated methylene (δ 66.3, C-11), an aliphatic methylene (δ 29.7, C-2), two tertiary methyls of gem-dimethyl group (δ 27.5, 27.4, C-9 and C-10), an aliphatic quaternary carbon (δ 43.4, C-8) and two quaternary carbons at δ 164.6 (C═O, C-3) and 176.9 (C═O, C-5). Comparison of these data with xanthiazone, which was previously isolated from *X. strumarium*[10], suggested that **1** was a derivative of thiazinedione.

From NMR spectral data analysis, the overall structure of side chain was nearly identical to that of compound **5**. The positive ESI–MS afforded the fragmentation patterns at *m/z* 101 $[M—C_{11}H_{11}O_2SN]^+$. From the HMBC spectrum (see Figure 2), the important correlations were observed between H-11 and C-5′ (δ 87.8), C-6 (δ 122.9), C-7 (δ 167.2), C-8 (δ 43.4), between the proton H-5′ (δ 5.10) and C-11 (δ 66.3), C-3′ (δ 29.3), C-4′ (δ 29.1), C-2′ (δ 181.6), between the proton H-3′ (δ 2.50, 2.25) and C-2′ (δ 181.6), C-5′ (δ 87.8) and

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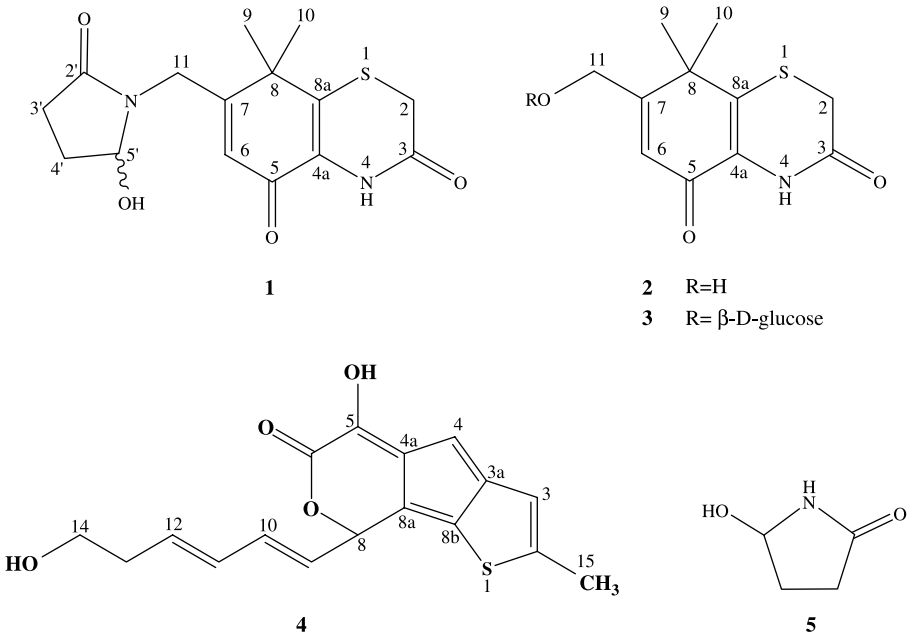

Figure 1. Structures of compounds **1**–**5**.

between the proton H-4′ (δ 2.35, 2.17) and C-2′ (δ 181.6), C-5′ (δ 87.8). The above data suggested that C-11 was connected with nitrogen and the side chain was identified as 5′-hydroxypyrrolidin-2′-one (see Figure 1). Therefore, the structure of **1** was elucidated as 7-(5-hydroxy-2-pyrrolidinon-1-yl-methyl)-8,8-dimethyl-4,8-dihydrobenzo[1,4]thiazine-3,5-dione and named xanthiazinone.

3. Experimental

3.1 General experimental procedures

Melting points were measured on a Yanaco micro-hot-stage apparatus without correction. 1D and 2D NMR spectra were recorded on a Bruker-ARX-300 or an AV-600 spectrometer, using TMS as an internal standard. The ESI–MS was determined by Finnigan LCQ spectrometer. Column chromatography was carried out on silica gel (200–300 mesh, Qingdao Haiyang Chemical Factory) and Sephadex LH-20 (Beijing Jingke Biology Co.).

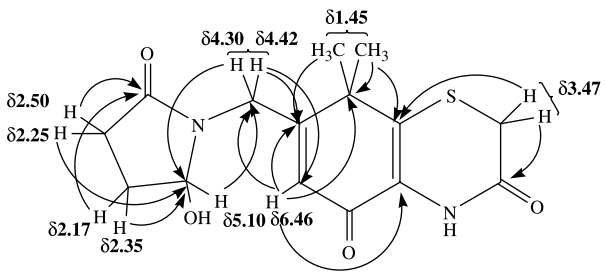

Figure 2. Key HMBC correlations of compound **1**.

3.2 Plant material

The fruits of *Xanthium sibiricum* were purchased from Shi-Ye Chinese Medicine Co. in Shenyang, China, in September 2005 and were identified by Professor Zheng Cui (one of the authors of this paper), Department of Pharmacognosy, Shenyang Pharmaceutical University. The voucher specimen has been deposited in the Department of Pharmacognosy, Shenyang Pharmaceutical University (No. 0500911).

3.3 Extraction and isolation

The fruits of *X. sibiricum* (10 kg) were ground into powder and refluxed with 70% ethanol three times for 3 h each. The ethanolic extraction were combined and concentrated to obtain 800 g residue. The residue was suspended in water, and then fractionated successively with petroleum ether, ethyl acetate and *n*-butanol. The *n*-butanolic soluble fraction was evaporated under reduced pressure to give 180 g residue. The *n*-butanolic extract was subjected to column chromatography over silica gel, eluting with gradient CH_2Cl_2/MeOH. The eluates were examined by TLC and 10 groups of eluting fractions were obtained. Fraction 10 was further separated on Sephadex LH-20 and eluted with MeOH to afford four subfractions. From the subfraction 4, compound **1** (3 mg) was obtained as colourless crystal. The subfraction 3 was purified by Sephadex LH-20 and eluted with MeOH to give compound **4** (6 mg) as yellow amorphous powder. Fraction 7 was subjected to column chromatography over silica gel, eluting with

Table 1. ^{1}H NMR (600 MHz) and ^{13}C NMR (125 MHz) spectral data of compounds **1** and **2**.

	1		**2**	
Position	δ_H	δ_C	δ_H	δ_C
2	3.47 (2H, s)	29.7	3.47 (2H, s)	28.6
3		164.6		162.5
4a		131.0		130.0
5		176.9		175.2
6	6.46 (1H, s)	122.9	6.38 (1H, s)	122.0
7		167.2		170.2
8		43.4		41.7
8a		143.3		140.9
9	1.45 (3H, s)	27.5	1.36 (3H, s)	26.9
10	1.45 (3H, s)	27.4	1.36 (3H, s)	26.9
11	4.30 (1H, d, $J = 15.4$ Hz)	66.3	4.30 (1H, d, $J = 5.4$ Hz)	59.4
	4.42 (1H, d, $J = 15.4$ Hz)		4.30 (1H, d, $J = 5.4$ Hz)	
2′		181.6		
3′	2.25 (1H, m) 2.50 (1H, m)	29.3		
4′	2.35 (1H, m) 2.17 (1H, m)	29.1		
5′	5.10 (1H, d, $J = 5.7$ Hz)	87.8		

gradient CH_2Cl_2/MeOH, 10 subfractions were obtained. From the subfraction 7, compound **3** (200 mg) was obtained. The ethyl acetate extract (70 g) was subjected to column chromatography over silica gel and eluted with CH_2Cl_2/MeOH (70:1–1:1) to yield 12 fractions. Fraction 6 was purified by Sephadex LH-20 and eluted with MeOH to give compound **2** (16 mg) and compound **5** (8 mg).

3.3.1 Compound *1*

Colourless needle crystals (MeOH); $C_{15}H_{18}N_2O_4S$; $[\alpha]_D^{25}$ − 3.75 (*c* 0.04, MeOH); mp 190–192°C; UV (MeOH) λ_{max}: 339, 248 nm; IR (KBr) cm^{-1}: 3438, 2924, 1675, 1383, 1154, 1114, 1062; Positive-ion ESI–MS *m/z*: 323 $[M + H]^+$. ^{1}H NMR (600 MHz, CD_3OH) and ^{13}C NMR (125 MHz, CD_3OH) spectral data are given in Table 1; HRESI–MS: *m/z* 323.1105 $[M + H]^+$ (calcd for $C_{15}H_{19}N_2O_4S$, 323.1066).

3.3.2 Compound *2*

Colourless cubic crystal (MeOH); $C_{11}H_{13}NO_3S$; mp 158–159°C; Positive-ion EI–MS *m/z*: 239 $[M]^+$. ^{1}H NMR (300 MHz, DMSO-d_6) and ^{13}C NMR (75 MHz, DMSO-d_6) spectral data are given in Table 1.

3.3.3 Compound *3*

Colourless cubic crystals (MeOH); $C_{17}H_{23}NO_8S$; mp 218–220°C; Positive-ion EI–MS *m/z*: 401 $[M]^+$. ^{1}H NMR (300 MHz, DMSO-d_6) δ: 1.36 (1H, s, H-9, H-10), 3.46 (2H, s, H-2), 4.40 (1H, d, $J = 16.4$ Hz, H-11a), 4.60 (1H, d, $J = 16.4$ Hz, H-11b), 5.24 (1H, d, $J = 4.8$ Hz, H-1′), 6.57 (1H, s, H-6), 9.32 (1H, s, N-H); ^{13}C NMR (75 MHz, DMSO-d_6) δ: 26.6 (C-10), 27.0 (C-9), 28.7 (C-2), 41.7 (C-8), 61.3 (C-6′), 65.7 (C-11), 70.2 (C-4′), 73.6 (C-3′), 76.7 (C-2′), 77.2 (C-5′), 102.3 (C-1′), 121.5 (C-6), 130.0 (C-4a), 141.0 (C-8a), 162.5 (C-3), 165.4 (C-7), 175.2 (C-5).

3.3.4 Compound *4*

Yellow amorphous powder; $C_{17}H_{16}O_4S$. By comparison of NMR and IR spectral data with those in the literature [12], compound **4** was identified as xanthienopyran.

3.3.5 Compound *5*

White amorphous powder; $C_4H_7NO_2$; EI–MS *m/z*: 101 $[M]^+$; ^{1}H NMR (300 MHz, DMSO-d_6) δ: 1.79 (1H, m, H-4a), 1.99 (1H, m, H-3a), 2.31 (1H, m, H-4b), 2.40 (1H, m, H-3b), 5.02 (1H, d, $J = 5.2$ Hz, H-5), 8.59 (1H, s, OH); ^{13}C NMR (75 MHz, DMSO-d_6) δ: 28.1 (C-3), 28.2 (C-4), 82.6 (C-5), 177.5 (C═O).

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