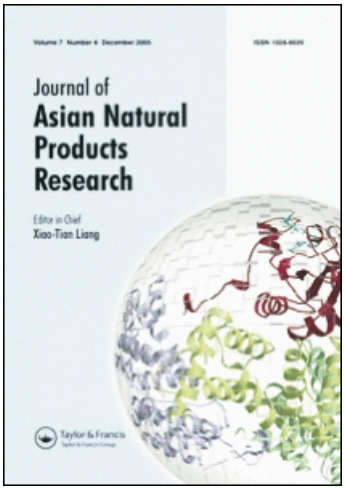

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New aromatic glucosides from *Carthamus tinctorius*

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Three new aromatic glucosides, 2,3-dimethoxy-5-methylphenyl-1-*O*-β-D-glucopyranoside (**1**), 2,6-dimethoxy-4-methylphenyl-1-*O*-β-D-glucopyranoside (**2**), and ethyl-3-(4-*O*-β-D-glucopyranosyl-3-methoxyphenyl)propionate (**3**), named as carthamosides B_1, B_2, and B_3, respectively, along with three known aromatic glucosides, methyl-3-(4-*O*-β-D-glucopyranosyl-3-methoxyphenyl)propionate (**4**), ethylsyringin (**5**), and methylsyringin (**6**), have been isolated from the air-dried flower of *Carthamus tinctorius*. Their structures were identified on the basis of chemical and spectroscopic methods.

Keywords: *Carthamus tinctorius*; aromatic glucosides; carthamoside B_1; carthamoside B_2; carthamoside B_3

1. Introduction

The dried flower of safflower, *Carthamus tinctorius* L., is a traditional Chinese medicine widely used in China, having the function of promoting blood circulation by removing blood stasis [1]. The chemical constituents from this plant have been examined, and the isolation of flavonoids [2,3], polyacetylenes [4], serotonin derivatives [5], steroids [6], lignans [7,8], alkanediol [9,10], and coloring matter [11] has been reported. During the course of our phytochemical investigation, three new aromatic glucosides, together with three known aromatic glucosides (Figure 1), were isolated from *C. tinctorius*. This paper describes the isolation and structure characterization of these compounds.

2. Results and discussion

Compound **1** was obtained as a white amorphous powder. The molecular formula was determined to be $C_{15}H_{22}O_8$ by the HRFABMS (*m/z* 331.1398 $[M + H]^+$). The IR spectrum of **1** showed absorption bands at 1580 and 1465 cm^{-1}, which indicated the presence of an aromatic ring. The ^1H NMR spectrum of **1** showed the presence of a methyl signal at δ 2.21 (3H, s, 5-CH_3), two methoxyl signals at δ 3.64, 3.73 (3H each, both s, 2, 3-OCH_3), and two aromatic protons at δ 6.50 (1H, s, H-4), 6.58 (1H, s, H-6). Acid hydrolysis indicated the existence of glucose, which was confirmed from the anomeric proton at δ 4.79 (1H, d, $J = 7.1$ Hz, H-1′) and the corresponding carbon signal for the anomeric carbon at δ 101.1 (C-1′). The coupling constant ($J = 7.1$ Hz) of the anomeric proton of glucose indicated that the anomeric configuration was β-oriented. The ^{13}C NMR spectrum displayed 15 carbons including six aromatic carbons, six carbon signals of a glucopyranosyl unit, two methoxyls, and one methyl. In the HMBC experiment of **1** (Figure 2), the correlations of

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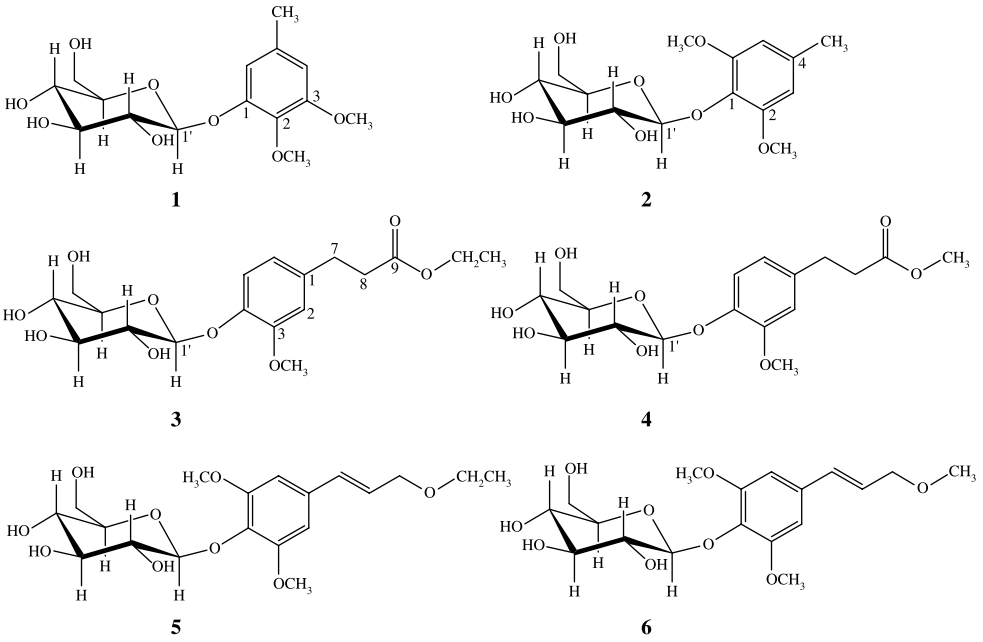

Figure 1. The structures of compounds **1**–**6**.

H-1′ and H-6 with C-1 (150.9) indicated that glucose was linked to C-1. The correlations of methoxyl signal at δ 3.64 with C-2 (δ 136.2) and another methoxyl signal at δ 3.73 with C-3 (δ 152.8) suggested that the two methoxyl groups were attached to C-2 and C-3, respectively. The correlations of the methyl signal at δ 2.21 with C-5 (δ 132.9), C-4 (δ 107.3), and C-6 (δ 109.8) indicated that it was substituted at C-5. On the basis of the above evidence, compound **1** was identified as 2,3-dimethoxy-5-methylphenyl-1-*O*-β-D-glucopyranoside.

Compound **2** was isolated as a white crystal, mp 185–187°C. The molecular formula was determined to be $C_{15}H_{22}O_8$ by HRFABMS (*m*/*z* 331.1405 $[M + H]^+$). The IR spectrum of **2** showed absorption bands at 1585 and 1490 cm^{-1}, indicating the presence of an aromatic ring. The ^1H NMR spectrum of **2** showed signals assignable to a methyl at δ 2.23 (3H, s, 4-CH_3), two methoxyls at δ 3.72 (6H, s, 2, 6-OCH_3), and two aromatic protons at δ 6.47 (2H, s, H-3, 5). Acid hydrolysis of **2** indicated the existence of the glucose unit, which was confirmed from the anomeric proton at δ 4.80 (1H, d, $J = 7.1$ Hz, H-1′) and the corresponding carbon signal at δ 102.9 (C-1′). The coupling constant ($J = 7.1$ Hz) of the glucose anomeric proton indicated that the anomeric configuration was β-oriented. The ^{13}C NMR spectrum displayed 15 carbon signals including six aromatic carbons, six carbon signals of a glucopyranosyl unit, two methoxyls, and one methyl. Furthermore, by comparison of its ^1H NMR and ^{13}C NMR

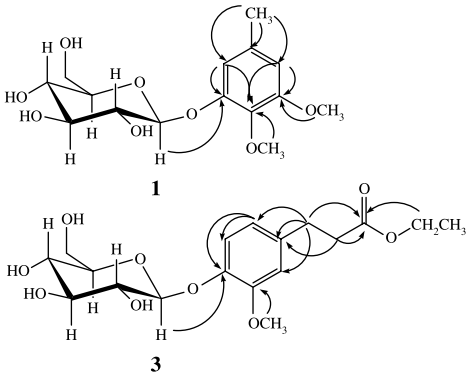

Figure 2. The key HMBC correlations of compounds **1** and **3**.

spectra with **1**, compound **2** was established to be 2,6-dimethoxy-4-methylphenyl-1-*O*-β-D-glucopyranoside.

Compound **3** was obtained as a white amorphous powder. The molecular formula was determined to be $C_{18}H_{26}O_9$ by HRFABMS (*m/z* 387.1668 $[M + H]^+$). The IR spectrum of **3** showed absorption bands at 3426, 1732, 1560, and 1458 cm^{-1}, suggesting the presence of hydroxyl, ester carbonyl, and aromatic ring. In the ^1H NMR spectrum of **3**, the ABX-type signals at δ 6.60 (1H, dd, $J = 8.2, 1.5$ Hz, H-6), 6.76 (1H, d, $J = 1.5$ Hz, H-2), and 6.88 (1H, d, $J = 8.2$ Hz, H-5) indicated the presence of a 1-, 3-, 4-trisubstituted benzene ring. In addition, the ^1H NMR spectrum showed a group signal of sugar, a methoxyl at δ 3.65 (3H, s, 3-OCH_3), an ethyl ester moiety at δ 1.07 (3H, t, $J = 7.0$ Hz), 3.95 (2H, q, $J = 7.0$ Hz), 9-OCH_2CH_3, and two methylenes at δ 2.50 (2H, t, $J = 7.5$ Hz, H-8), 2.69 (2H, t, $J = 7.5$ Hz, H-7), indicating the existence of a $-CH_2-CH_2-$ unit. Acid hydrolysis indicated the existence of glucose, which was confirmed from the anomeric proton at δ 4.74 (1H, d, $J = 7.1$ Hz, H-1′) and the corresponding carbon signal for the anomeric carbon at δ 100.3 (C-1′). The coupling constant ($J = 7.1$ Hz) of the glucose anomeric proton indicated that the anomeric configuration was β-oriented. The ^{13}C NMR spectrum displayed 18 carbons including six aromatic carbons, six carbon signals of a glucopyranosyl unit, a methoxyl, a methyl, three methylenes, and a carbonyl carbon. In the HMBC spectrum, the correlations of H-1′, H-6, and H-2 with C-4 (δ 145.0) suggested that the glucosyl was linked to C-4. The correlations of H-7 with C-1 (δ 134.3), C-2 (δ 112.9), and C-6 (δ 120.2), and H-8 with C-1 indicated that the $-CH_2-CH_2-$ unit was linked to C-1. The correlations of H-7 and H-8 with the carbonyl carbon (δ 172.4) indicated that the carbonyl carbon (C-9) was attached to C-8 (δ 35.4). The correlation of protons at δ 3.95 (2H, q, $J = 7.0$ Hz) with the carbonyl carbon suggested that the CH_3CH_2O- was attached to C-9. On the other hand, the correlation between 3-OCH_3 and C-3 (δ 148.9) indicated that the methoxyl was substituted at C-3. Furthermore, by comparison of its chemical shifts with the similar compound [12], compound **3** was identified as ethyl-3-(4-*O*-β-D-glucopyranosyl-3-methoxyphenyl)propionate.

The three known compounds methyl-3-(4-*O*-β-D-glucopyranosyl-3-methoxyphenyl) propionate (**4**), ethylsyringin (**5**), and methylsyringin (**6**) were identified by comparison of their spectral data (^1H NMR and ^{13}C NMR) with those reported in the literature [13–15].

3. Experimental

3.1 General experimental procedures

Melting points were obtained by using a Yanaco MP-S3 micro-melting-point apparatus and are uncorrected. The IR spectra were recorded on a Bruker IFS-55 infrared spectrophotometer. The NMR data were recorded on a Bruker AV-600 (600 MHz for ^1H and 150 MHz for ^{13}C) in DMSO-d_6 with TMS as an internal standard. The HRFABMS data were obtained on the Micross Mass Autospec-UltimaE TOF mass spectrophotometer. Chromatography was performed on silica gel (200–300 mesh; Qingdao Haiyang Chemical Factory, Qingdao, China), Sephadex LH-20 (Pharmacia, Piscataway, NJ, USA), and reverse-phase HPLC (Shimadzu LC-8A vp).

3.2 Plant material

Dried petals of *C. tinctorius*, cultivated in Xinjiang province of China, were bought from the Cooperation of Traditional Chinese Medicine of Shenyang, China, in June 2005. A voucher specimen was identified by Professor Qi-shi Sun and has been deposited in the School of Traditional Chinese Medicine of Shenyang Pharmaceutical University, China (No. 6025).

3.3 Extraction and isolation

Dried petals (5 kg) of *C. tinctorius* were extracted three times with hot 95% EtOH, every time for 2 h, and the combined solution

was concentrated *in vacuo* to a syrup (1200 g), followed by suspension in water. The suspension was extracted with petroleum ether, ethyl acetate, and *n*-butanol successively. The *n*-butanol fraction (200 g) was further chromatographed over a D101 macroporous resin column eluted with H_2O and 30, 70, and 95% EtOH gradually. The fraction (60 g) eluted with 30% EtOH was subjected to silica gel column chromatography (eluted with $CHCl_3$ and MeOH in increasing polarity) to obtain nine fractions (I–IX). Fraction III was purified by Sephadex LH-20 column chromatography and preparative HPLC to obtain compounds **1** (15 mg), **2** (30 mg), **3** (26 mg), **4** (12 mg), **5** (10 mg), and **6** (18 mg).

*3.3.1 2,3-Dimethoxy-5-methylphenyl-1-O-β-D-glucopyranoside (**1**)*

White amorphous powder. IR (KBr) ν_{max} (cm^{-1}) 1580, 1465; ^{1}H NMR (DMSO-d_6) δ: 2.21 (3H, s, 5-CH_3), 3.64, 3.73 (both s, 2,3-OCH_3), 6.50 (1H, s, H-4), 6.58 (1H, s, H-6), 4.79 (1H, d, $J = 7.1$ Hz, H-1′); ^{13}C NMR spectral data, see Table 1; HRFABMS *m/z*: 331.1398 $[M + H]^+$ (calcd for $C_{15}H_{23}O_8$, 331.1393).

*3.3.2 2,6-Dimethoxy-4-methylphenyl-1-O-β-D-glucopyranoside (**2**)*

White crystal, mp 185–187°C. IR (KBr) ν_{max} (cm^{-1}) 1585, 1490; ^{1}H NMR (DMSO-d_6) δ: 2.23 (3H, s, 4-CH_3), 3.72 (6H, s, 2,6-OCH_3), 6.47 (2H, s, H-3,5), 4.80 (1H, d, $J = 7.1$ Hz, H-1′); ^{13}C NMR spectral data, see Table 1; HRFABMS *m/z*: 331.1405 $[M + H]^+$ (calcd for $C_{15}H_{23}O_8$, 331.1393).

*3.3.3 Ethyl-3-(4-O-β-D-glucopyranosyl-3-methoxyphenyl)propionate (**3**)*

White amorphous powder. IR (KBr) ν_{max} (cm^{-1}) 3426, 1732, 1560, 1458; ^{1}H NMR (DMSO-d_6), δ: 6.60 (1H, dd, $J = 8.2$, 1.5 Hz, H-6), 6.76 (1H, d, $J = 1.5$ Hz, H-2), 6.88 (1H, d, $J = 8.2$ Hz, H-5), 2.69 (2H, t, $J = 7.5$ Hz, H-7), 2.50 (2H, t, $J = 7.5$ Hz, H-8), 1.07 (3H, t, $J = 7.0$ Hz), 3.95 (2H, q, $J = 7.0$ Hz), 3.65 (3H, s, 3-OCH_3), 4.74 (1H, d, $J = 7.1$ Hz, H-1′); ^{13}C NMR spectral data, see Table 1; HRFABMS *m/z*: 387.1668 $[M + H]^+$ (calcd for $C_{18}H_{27}O_9$, 387.1655).

Table 1. ^{13}C NMR spectral data of compounds **1**–**3** in DMSO (150 MHz).

Position	**1**	**2**	**3**
1	150.9	133.0	134.3
2	136.2	150.8	112.9
3	152.8	106.0	148.9
4	107.3	132.0	145.0
5	132.9	106.0	115.4
6	109.8	150.8	120.2
7			30.0
8			35.4
9			172.4
5-CH_3	21.5		
4-CH_3		21.4	
2-OCH_3	60.3	56.2	
3-OCH_3	55.9		55.7
6-OCH_3		56.2	
9-OC_2H_5			59.9
			14.2
Glc.			
1′	101.1	102.9	100.3
2′	73.5	74.3	73.3
3′	77.2	77.3	77.1
4′	69.9	70.1	69.8
5′	76.9	76.6	76.9
6′	60.8	61.0	60.8

3.4 Acid hydrolysis of 1, 2, and 3

Compound **1** (5 mg) was refluxed with 2 N HCl in aqueous MeOH (5 ml) for 8 h. The reaction mixture was diluted with water (10 ml) and extracted with EtOAc. The aqueous part was neutralized with saturated solution of Na_2CO_3 and filtered. The filtrate was concentrated under reduced pressure and examined for sugar identification by paper chromatography with an authentic sample of glucose. The methods of acid hydrolysis of **2** and **3** were the same as those of **1**.

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