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XANTHONES FROM *Gentianopsis paludosa*

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Gentianopsis is a genus of the Gentianaceae family comprising about twenty-four species, which are distributed in Asia, Europe, and North America. *Gentianopsis paludosa* (Hook. f.) Ma grows at an altitude of 1180–4600 m in forest, floodplain, grassland slopes, swamps, and other wet areas, which are mainly distributed in the southeastern part of the Tibet Autonomous Region, the southeastern part of Qinghai Province, and the Gannan plateau of Gansu Province [1–3]. It has long been used in traditional Tibetan medicine for treating hepatitis, conjunctivitis, hypertension, and acute nephritis. It will be exploited intensively by Gansu and Qinghai provinces for its significant effect on hepatobiliary disease [4, 5]. To date, its chemical constituents have been investigated by three research groups [6–8]. Due to interest in the genus *Gentianopsis*, we investigated this plant collected from the Tibet Autonomous Region of China for the first time and obtained eight xanthones. In this paper, we report their isolation and structure elucidation.

From an alcoholic extract 1-hydroxy-3,7-dimethoxyxanthone (**1**), 1,8-dihydroxy-3,7-dimethoxyxanthone (**2**), 1-hydroxy-3,7,8-trimethoxyxanthone (**3**), 1,7-dihydroxy-3,8-dimethoxyxanthone (**4**), 7-hydroxy-3,8-dimethoxyxanthone-1-*O*-β-D-glucopyranoside (**5**), 8-hydroxy-3,7-dimethoxy-xanthone-1-*O*-β-D-glucopyranoside (**6**), 7-hydroxy-3,8-dimethoxyxanthone-1-*O*[β-D-xylosyl(1→6)]-β-D-glucopyranoside (**7**), and 3,7,8-trimethoxyxanthone-1-*O*[β-D-xylosyl(1→6)]-β-D-glucopyranoside (**8**) were isolated and purified by repeated chromatography over a silica gel column. The structures of all these compounds were proposed on the basis of spectroscopic data, together with comparison of their NMR data with those of the corresponding compounds reported in the literature. Among them, compounds **1–4** were obtained from this plant [9], and all the xanthone glycosides were obtained from this plant for the first time, but all the xanthone glycosides have been obtained from the genus *Swertia*, the genus *Gentianopsis*, and the genus *Gentiana* of the family Gentianaceae [10–13].

Plant Material. The plant material was collected from the Tibet Autonomous Region of China in August 2004 and was identified by Prof. You-Rui Suo holding office at the Northwest Institute of Plateau Biology. A voucher specimen has been deposited at the Laboratory for Natural Medicine and Tibetan Medicine of the Lanzhou Institute of Chemical Physics, Chinese Academy of Sciences, P. R. China.

Extraction, Isolation, and Purification of Compounds. Air-dried and ground whole plants of *Gentianopsis paludosa* (Hook. f.) Ma (5 kg) were extracted three times with 75% EtOH at room temperature, each time lasting seven days. The combined extracts were evaporated to dryness under reduced pressure. A quarter of the residue (1 kg) was then suspended in H_2O (1.5 L) and extracted with petroleum ether (1.5 L × 6), chloroform (1.5 L × 4), ethyl acetate (1.5 L × 4), and *n*-butanol (1.5 L × 4), successively. The chloroform extract (25 g) was subjected to column chromatography on silica gel (200–300 mesh, 300 g) using petroleum ether with increasing volume of ethyl acetate (v/v, from 30:1 to 1:1) as eluent to give five fractions (Fr. 1–Fr. 5). Fraction 2 (v/v, 20:1) was chromatographed on silica gel column using petroleum ether–ethyl acetate (v/v, 12:1) as eluent to yield pure compound **1** (3 mg) and crude compound **2** (75 mg). Pure compound **2** was obtained by recrystallization using petroleum ether–ethyl acetate as solvent. Fraction 3 (v/v, from 15:1 to 10:1) was eluted with petroleum ether–acetone (v/v = 15:1) to give pure compound **3** (750 mg). Fraction 4 (v/v, 8:1) was chromatographed on silica gel column with chloroform–methanol (v/v, 12:1) to give compound **4** (550 mg). The *n*-butanol extract (40 g) was subjected to column chromatography on

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silica gel (200–300 mesh, 400 g) using chloroform with increasing volume of methanol (v/v, from 20:1 to 1:1) as eluent to give four fractions (Fr. 1–Fr. 4). Fraction 1 (v/v, from 20:1 to 15:1) was chromatographed on silica gel column using chloroform–methanol (v/v, 10:1) as eluent to yield pure compound **5** (10 mg). Fraction 2 (v/v, from 15:1 to 10:1) was eluted with chloroform–methanol (v/v, 10:1) to give compound **6** (15 mg). Fraction 3 (v/v, from 8:1 to 6:1) was eluted with chloroform–methanol (v/v, 6:1) to give compound **7** (30 mg). Fraction 4 (v/v, from 5:1 to 1:1) gave compound **8** (30 mg) after CC on silica gel eluted with chloroform–methanol (v/v, 4:1).

1-Hydroxy-3,7-dimethoxyxanthone (1). Yellow crystals, mp 154–156°C [9].

1,8-Dihydroxy-3,7-dimethoxyxanthone (2). Yellow needle crystals, mp 180–182°C [9].

1-Hydroxy-3,7,8-trimethoxyxanthone (3). Yellow needle crystals, mp 160–161°C [6, 9].

1,7-Dihydroxy-3,8-dimethoxyxanthone (4). Yellow needle crystals, mp 195–197°C [6, 9].

7-Hydroxy-3,8-dimethoxyxanthone-1-*O*-β-D-glucopyranoside (5). Yellow powder, mp 136–138°C. ^{1}H NMR (400 MHz, TMS, DMSO-d_6, δ, ppm, J/Hz): 3.72–3.15 (5H, H-2″, 3″, 4″, 5″, 6″), 3.76 (3H, s, 3-OMe), 3.88 (3H, s, 8-OMe), 4.88 (1H, d, J = 7.6, H-1′), 6.72 (1H, d, J = 2.8, H-2), 6.76 (1H, d, J = 2.4, H-4), 7.16 (1H, d, J = 5.2, H-5), 7.28 (1H, d, J = 9.2, H-6), 9.39 (1H, s, 7-OH). ^{13}C NMR (100 MHz, TMS, DMSO-d_6, δ): 159.18 (C-1), 100.61 (C-2), 164.13 (C-3), 94.84 (C-4), 157.77 (C-4a), 146.87 (C-4b), 112.66 (C-5), 123.03 (C-6), 145.15 (C-7), 148.54 (C-8), 117.39 (C-8a), 107.55 (C-8b), 174.74 (C-9), 103.14 (C-1′), 73.54 (C-2′), 75.98 (C-3′), 69.87 (C-4′), 77.63 (C-5′), 60.83 (C-6′), 56.01 (3-OCH_3), 60.38 (8-OCH_3). The data were in accordance with those reported in [10, 13].

8-Hydroxy-3,7-dimethoxyxanthone-1-*O*-β-D-glucopyranoside (6). Yellow powder, mp 174–177°C. ^{1}H NMR (400 MHz, TMS, DMSO-d_6, δ, ppm, J/Hz): 3.73–3.17 (5H, H-2′–6′). 3.80 (3H, s, 3-OMe), 3.88 (3H, s, 7-OMe), 5.05 (1H, d, J = 7.6, H-1′), 6.72 (1H, s, J = 2.4, H-2), 6.74 (1H, s, J = 2.0, 6.0, H-4), 6.90 (1H, d, J = 9.2, H-5), 7.43 (1H, d, J = 8.8, H-6), 13.8 (1H, s, 8-OH). ^{13}C NMR (100 MHz, TMS, DMSO-d_6, δ): 159.33 (C-1), 99.00 (C-2), 165.64 (C-3), 94.69 (C-4), 158.98 (C-4a), 150.20 (C-4b), 108.52 (C-5), 120.38 (C-6), 142.47 (C-7), 148.16 (C-8), 104.57 (C-8a), 101.04 (C-8b), 181.19 (C-9), 104.75 (C-1′), 73.29 (C-2′), 76.46 (C-3′), 69.73 (C-4′), 77.42 (C-5′), 60.75 (C-6′), 56.19 (3-OCH_3), 56.53 (7-OCH_3). The data were in accordance with those reported in [10, 13].

7-Hydroxy-3,8-dimethoxyxanthone-1-*O*[β-D-xylosyl(1→6)]-β-D-glucopyranoside (7). Yellow powder. ^{1}H NMR (400 MHz, TMS, DMSO-d_6, δ, ppm, J/Hz): 4.90 (1H, H-1″), 4.92 (1H, d, H-1′), 6.71 (1H, d, J = 6.4, H-2), 6.76 (1H, s, J = 6.4, H-4), 7.14 (1H, d, J = 8.8, H-5), 7.28 (1 H, d, J = 9.2, H-6), 9.45 (1H, s, 7-OH). ^{13}C NMR (100 MHz, TMS, DMSO-d_6, δ): 159.07 (C-1), 100.08 (C-2), 164.19 (C-3), 94.85 (C-4), 157.78 (C-4a), 146.87 (C-4b), 112.68 (C-5), 123.01 (C-6), 145.16 (C-7), 148.54 (C-8), 117.42 (C-8a), 107.47 (C-8b), 174.66 (C-9), 104.19 (C-1′), 73.42 (C-2′), 75.90 (C-3′), 69.67 (C-4′), 76.60 (C-5′), 68.65 (C-6′), 102.63 (C-1″), 73.42 (C-2″), 75.90 (C-3″), 69.54 (C-4″), 65.69 (C-5″), 56.08 (3-OCH_3), 60.85 (8-OCH_3). The data were in accordance with those reported in [11].

3,7,8-Trimethoxyxanthone-1-*O*[β-D-xylosyl(1→6)]-β-D-glucopyranoside (8). Yellow crystals, mp 141–143°C. ^{1}H NMR (400 MHz, TMS, DMSO-d_6, δ, ppm, J/Hz): 3.83 (3H, s, 7-OCH_3), 3.87 (3H, s, 3-OCH_3), 3.79 (3H, s, 8-OCH_3), 5.21 (1H, d, H-1″), 5.40 (1H, d, H-1′), 6.69 (1H, d, J = 2.4, H-4), 6.74 (1H, d, J = 2.4, H-2), 7.25 (1H, d, J = 9.2, H-6), 7.50 (1H, d, J = 9.2, H-5). ^{13}C NMR (100 MHz, TMS, DMSO-d_6, δ): 159.07 (C-1), 99.89 (C-2), 164.32 (C-3), 94.81 (C-4), 157.78 (C-4a), 149.09 (C-4b), 112.37 (C-5), 119.54 (C-6), 147.34 (C-7), 149.24 (C-8), 117.54 (C-8a), 107.42 (C-8b), 174.54 (C-9), 104.20 (C-1′), 73.42 (C-2′), 75.90 (C-3′), 69.67 (C-4′), 76.60 (C-5′), 68.65 (C-6′), 102.35 (C-1″), 73.39 (C-2″), 75.96 (C-3″), 69.55 (C-4″), 65.69 (C-5″), 56.08 (3-OCH_3), 56.78 (7-OCH_3), 60.85 (8-OCH_3). The data were in accordance with those reported in [11].

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