Original Article

Chemical Constituents From the Bark of *Garcinia oblongifolia*

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Abstract

The phytochemical investigation of the methanol extract of bark of *Garcinia oblongifolia* yielded a new xanthone derivative 1,3,8-trihydroxy-6',6'-dimethylpyrano (2',3':5,6) xanthone (**5**) along with 8 known compounds, including 1,2,5-trihydroxy-6-methoxyxanthone (**1**), 1,3,6,7-tetrahydroxy-2,5-bis (3-methylbut-2-enyl) xanthen-9-one (**2**), xanthone V1 (**3**), isojacareubin (**4**), methyl protocatechuate (**6**), isoxanthochymol (**7**), euxanthone (**8**), and protocatechuic acid (**9**). The structures of these compounds were verified based on extensive spectroscopic data analysis as well as comparison with the literature data.

Keywords

xanthones, *Garcinia oblongifolia*, Clusiaceae, ethnomedicine, protocatechuic acid

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There are about 450 species of *Garcinia* (Clusiaceae) worldwide, with 21 species distributed in China.[1] *Garcinia* species grow primarily in tropical Asia, southern Africa, and Polynesia.[1] Many *Garcinia* species are valued for their edible fruits, like *Garcinia mangostana* which is widely cultivated, and its sweet pleasant-tasting fruits are eaten fresh or in processed food products like juices.

Garcinia oblongifolia is an Asian species used traditionally to relieve inflammation and pain, treat burns, wounds, and eczema.[2,3] An evergreen tree, *G. oblongifolia* is mainly distributed in tropical and subtropical regions.[4] In China, it is found in Hainan, Guangdong, and Guangxi provinces. It is used as a folk medicine to treat diseases such as indigestion, cacochylia, bleeding, periodontitis, stomatitis, and fever.[2,3] Previous studies have found that an extract of *G. oblongifolia* bark has significant anti-inflammatory activity, which may explain why it is used traditionally to treat burns, gastrointestinal ulcers, stomatitis, and periodontitis.[3] In 2017, Trinh et al isolated 3 new xanthones (oblongixanthone F-H) and 8 known xanthones from an ethylacetate extract of the twigs of *G. oblongifolia*. Among them, norcowanin was exhibited the most notable inhibitory effects on α-glucosidase and PTP1B, showing potent antidiabetic activity.[5] Therefore, understanding the constituents of *G. oblongifolia* may help us to further understand its traditional uses. Herein, we report the isolation and structural elucidation of 1 new xanthone and 8 known compounds from the bark of *G. oblongifolia*. Their structures were shown in Figure 1.

Results and Discussion

Compound **5** (Figure 2) was obtained as a methanol (MeOH)-soluble amorphous white solid. Its high-resolution electrospray ionization mass spectrometry (HRESIMS) (Supplemental Figure S1) revealed a $[M + H]^+$ ion peak at m/z 327.0862 (calculated as m/z 327.0869) with the molecular formula deduced as $C_{18}H_{14}O_6$, corresponding to 12 degrees of unsaturation. The nuclear magnetic resonance (NMR) spectroscopic data (Table 1) of compound **5** were similar to those of 1,3,5-trihydroxy-13,13-dimethyl-2H-pyran [6,7-b] xanthen-9-one,[6] indicating they had a similar structure. In detail, the ^{13}C NMR and distortionless enhancement by polarization transfer spectra (Supplemental Figure S2) of

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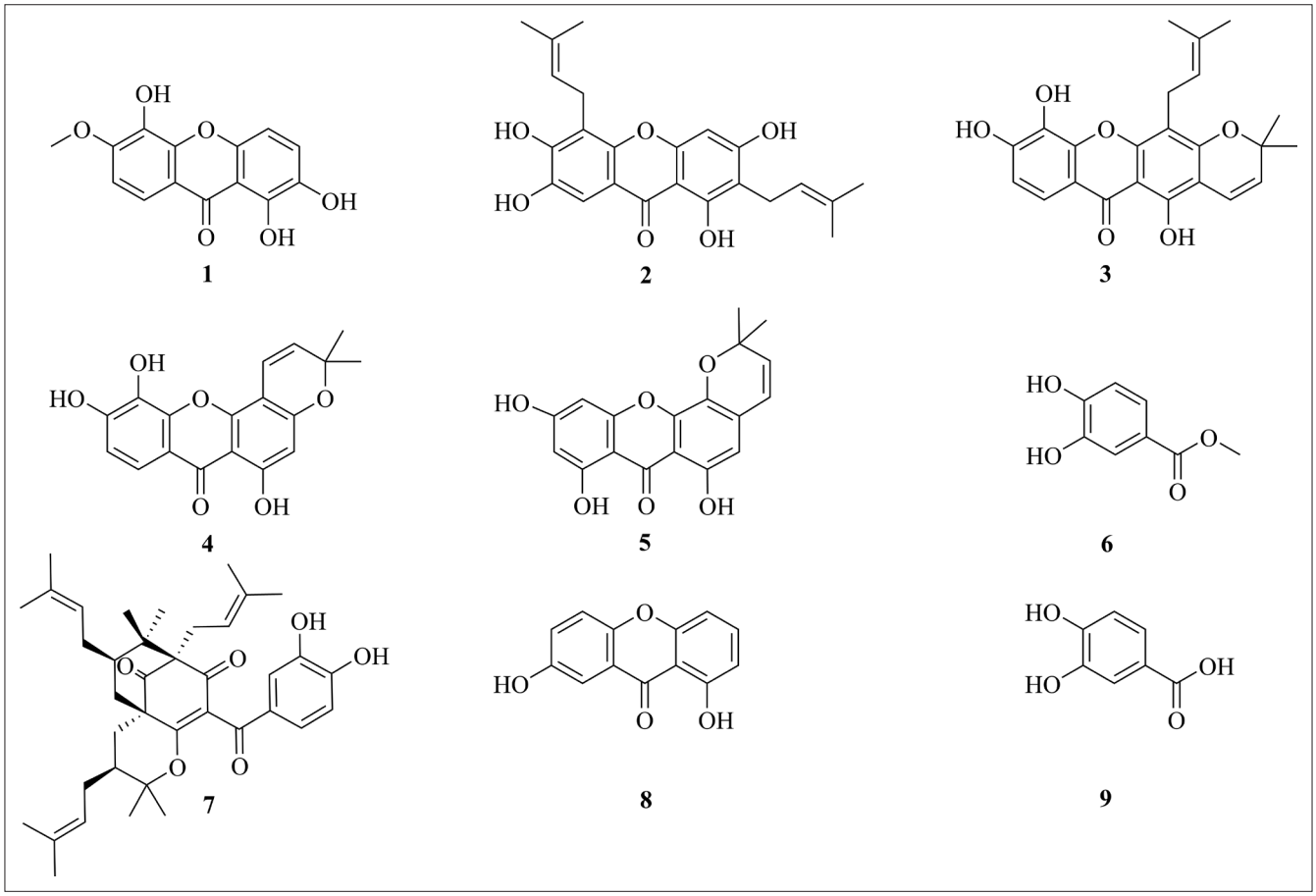

Figure 1. Chemical structures of compounds **1-9** obtained from *Garcinia oblongifolia*.

compound **5** exhibited 18 carbons signals corresponding to 11 quaternary carbons, 5 tertiary carbons, and 2 methyl carbons. Among these carbon resonances, 13 carbons were attributed to a xanthone skeleton, and 5 were attributed to the isoprene group. Two signals of aromatic proton displaying as a singlet at δ_H 6.16 (H-2) and δ_H 6.41 (H-4) (Table 1) were observed in the ^{1}H-NMR spectrum (Supplemental Figure S3), which coupled with carbon atoms δ_C 99.2 (C-2) and δ_C 95.2 (C-4) in the heteronuclear multiple quantum coherence (HMQC) spectrum (Supplemental Figure S4), respectively, in combination with the correlations of H-2/C-4, H-2/C-9a (δ_C 103.3), H-4/C-2, H-4/C-9a in the heteronuclear multiple bond correlation (HMBC) spectrum (Supplemental Figure S5) suggested that 2 hydroxy were attached to C-1 (δ_C 164.7) and C-3 (δ_C 167.2), respectively. The 2 ortho-coupled proton signals δ_H 6.48 (1H, d, J = 10.0 Hz, H-4') and δ_H 5.83 (1H, d, J = 10.0 Hz, H-5') (Table 1) were observed in the ^{1}H-NMR spectrum in combination with the correlation of H-4'/C-4' (δ_C 122.4) and H-5'/C-5' (δ_C 132.7) observed in the HMQC spectrum, and H-4'/H-5' observed in the ^{1}H-^{1}H correlation spectroscopy (COSY) spectrum (Supplemental Figure S6) confirmed the presence of cis-olefin double bonds. Furthermore, the correlations of H-8'/C-5', H-5'/C-6, H-4'/C-7, H-4'/C-6', and H-4'/C-5' observed in the HMBC spectrum suggested that the isoprene group at C-6 is cyclized with the hydroxy group at C-5 to form dimethylpyran. Moreover, the single aromatic proton signal at δ_H 7.36 (H-7) (Table 1) revealed in ^{1}H-NMR spectrum in combination with the correlation of H-7/C-5, H-7/C-8a, and H7/C-4' observed in HMBC spectrum suggested that the hydroxy posited at C-8 (δ_C 134.5). Therefore, compound **5** was

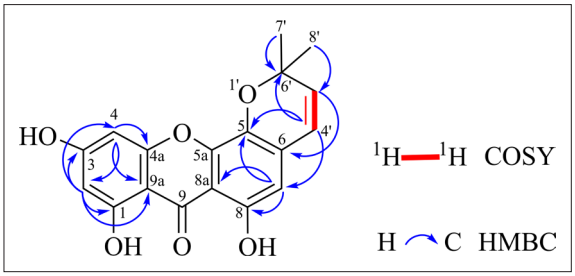

Figure 2. ^{1}H-^{1}H correlation spectroscopy (COSY, red lines) correlations and key heteronuclear multiple bond correlation (HMBC, blue arrows) of compound **5**. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

Table 1. NMR Spectroscopic Data Measured at 200 MHz for ^{13}C and 800 MHz for ^{1}H NMR in MeOD for Compound **5**.[a]

Position	δ_C type[b]	δ_H (J in Hz)[c]
1	164.7 C	
2	99.2 CH	6.16, d (2.4)
3	167.2 C	
4	95.2 CH	6.41, d (2.4)
5	147.3 C	
6	119.8 C	
7	113.5 C	7.36, s
8	134.5 C	
9	181.5 C	
9a	103.3 C	
4a	159.3 C	
5a	147.6 C	
8a	115.6 C	
4'	122.4 CH	6.48, d (10.0)
5'	132.7 CH	5.83, d (10.0)
6'	79.2 C	
7'	28.4 CH_3	1.50, s
8'	28.4 CH_3	1.50, s

HMBC, heteronuclear multiple bond correlation; HSQC, heteronuclear single quantum coherence; DEPT, distortionless enhancement by polarization transfer; COSY, correlation spectroscopy; NMR, nuclear magnetic resonance; MeOD, Deuterated methanol.
[a]Signal assignments were based on the results of DEPT, HSQC, HMBC, and ^{1}H-^{1}H COSY experiments. Chemical shifts are given in ppm.
[b]The δ_C values were referenced from the MeOD signals at δ_C 49.0.
[c]The δ_H values were referenced from the MeOD signals at δ_C 3.3.

established as 1,3,8-trihydroxy-6', 6'-dimethyl-2H-pyran [2',3':5,6] xanthen-9-one; the structure and the key HMBC and ^{1}H-^{1}H COSY correlation of compound **5** are shown in Figure 2.

Additionally, 8 known compounds (Figure 1) were isolated and identified as 1,2,5-trihydroxy-6-methoxyxanthone (**1**),[7] 1,3,6,7-tetrahydroxy-2,5-bis (3-methylbut- 2-enyl) xanthen-9-one (**2**),[8] xanthone V1 (**3**),[9] isojacareubin (**4**),[10] methyl protocatechuate (**6**),[11] isoxanthochymol (**7**),[12] euxanthone (**8**),[13] and protocatechuic acid (**9**)[14] through comparison of the spectroscopic data (Supplemental Figures S8–S24) with the corresponding reference data.

Experimental

General

Thin-layer chromatography was conducted on silica gel plates (Yantai Institute of Chemical Industry), and the compounds were visualized directly under ultraviolet (UV) light (Jiangsu Qilinbeier Co. Ltd). High-performance liquid chromatography (HPLC) separations were performed on an LC-20AP preparative liquid chromatography-UV detector (Shimin Company Ltd., China) and recycling preparative HPLC (Japan Analytical Industry Co. Ltd., Japan). Column chromatography (CC) was performed on silica gel (200-300 mesh; Qingdao Haiyang Chemical Co. China) and Sephadex LH-20 (Amersham Pharmacia Biotech, China). Mass spectra were measured on a YG AutoSpec 3000 mass spectrometer. All the NMR data were obtained at ambient temperature on a Bruker Avance 800 NMR spectrometer (Bruker Bio-Spin GmbH, Rheinstetten, Germany) with tetramethylsilane as an internal reference, and chemical shifts reported in δ (ppm). HRESIMS value was taken on Agilent 6540 Q-TOF spectrometer (Columbia, MD, USA).

Plant Material

The bark of *G. oblongifolia* was collected in Ledong County, Hainan Province of China (18°34'N, 108°59'E) in February 2016 and identified by Professor Chunlin Long at Minzu University of China. The voucher specimen numbered LCL1607 was deposited in the Laboratory of Ethnobotany, Minzu University of China, in Beijing.

Extraction and Isolation

The dried bark of *G. oblongifolia* (3.9 kg) was ground and extracted with 100% MeOH 4 times. After filtration and evaporation, a crude extract (900 g) was obtained. The extract was then dissolved via sonication in distilled water (900 mL) and partitioned with an equivalent volume of chloroform. The obtained chloroform extract (68.2 g) was separated by silica gel column chromatography eluting with chloroform-ethyl acetate gradient providing 16 fractions (Fr.1-16). Fr.3 (2.5 g) was further fractionated by silica gel column chromatography eluting with petroleum ether gradient to get 18 subfractions (Fr.3-1 to 3-18). And then Fr.3-8 and Fr.3-9 were purified using the preparative liquid chromatography equipped with a UV detector and preparative HPLC, to ultimately obtain compound **1** (1.0 mg) and **2** (2.1 mg). Fr.7 (1.4 g) was separated by silica gel column chromatography, with chloroform-methanol (1:1, V/V) as the solvent system to obtain 14 components (Fr.7-1 to Fr.7-14). Fr.7-10 was fractionated again over silica gel with chloroform-methanol (1:1, V/V) and then further purified by HPLC to obtain compounds **3** (17.3 mg) and **4** (1.0 mg). Compound **5** (1.2 mg) was obtained from Fr.8-18, and compound **6** (1.0 mg), compound **7** (2.0 mg), and compound **8** (4.4 mg) were derived from Fr.9-15. Fr.10 (2.18 g) was separated by silica gel column chromatography with petroleum ether-acetone gradient elution and then further purified via recrystallization to get compound **9** (57.2 mg).

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Declaration of Conflicting Interests

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Supplemental Material

Supplemental material for this article is available online.

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