A New Xanthone from *Garcinia oligantha* and Its Cytotoxicity

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A new xanthone, methyl 6-(2-acetoxyethyl)-4,8-dihydroxy-9-oxo-xanthene-1-carboxylate (1), was isolated from the stems of *Garcinia oligantha*. Its structure was elucidated by spectroscopic methods, including extensive 1D and 2D NMR techniques. Compound 1 was tested for its cytotoxicities against five human tumor cell lines (NB4, A549, SHSY5Y, PC3 and MCF7) and it exhibited moderate cytotoxicity against NB4, PC3 and MCF7 cell with IC₅₀ values of 6.2, 3.8 and 5.4 µM, respectively.

Keywords: Xanthone, *Garcinia oligantha*, Cytotoxicities.

INTRODUCTION

The species of *Garcinia oligantha* are one of the plants belonging to Garcinia genus. This species distributed in the south of Yunnan and Guangxi Province of China¹. Plants of the genus *Garcinia* (Guttiferae) has been extensively investigated from the phytochemical and biological points of view. Xanthones²,³, benzophenones⁴,⁵, depsidones⁶-⁸, flavonoids⁹-¹², biflavonoids¹³ and triterpenes¹⁴ have been reported from *Garcinia* species.

In our previous studies, some apoptotic compounds were isolated from the stems of *Garcinia oligantha*⁵. With the aim of multipurpose utilization of Garcinia plants and identify bioactive natural products from this genus, the phytochemical investigation on *G. oligantha* was carried out. As a result, a new xanthone (1) was isolated from this plant. The structure of 1 was elucidated on the basis of a comprehensive analysis of the ¹H NMR, ¹³C NMR and 2D NMR spectra. In addition, the cytotoxicities of 1 were evaluated. The details of the isolation, structure elucidation and cytotoxicities of 1 are reported in this article.

EXPERIMENTAL

UV spectra were obtained using a Shimadzu UV-2401A spectrophotometer. IR spectra were obtained in KBr disc on a Bio-Rad Winifred spectrophotometer. ESI-MS were measured on a VG Auto Spec-3000 MS spectrometer. ¹H, ¹³C and 2D NMR spectra were recorded on Bruker DRX-500 instrument with TMS as internal standard. Column chromatography was performed on silica gel (200-300 mesh), or on silica gel H (10-40 mm, Qingdao Marine Chemical Inc., China). The crude extract (115 g) was applied to silica gel (250 mm × 250 mm, 7 mm) column and DAD detector.

**Extraction and isolation:** The air-dried and powdered stems of *G. oligantha* (4.5 kg) were extracted four times with 70 % MeOH (4 × 5 L) at room temperature and filtered. The crude extract (115 g) was applied to silica gel (200-300 mesh) column chromatography, eluting with a CHCl₃-CH₃COCH₃ gradient system (20:1, 9:1, 8:2, 7:3, 6:4, 5:5), to give six fractions A-F. The further separation of fraction B (9:1, 2.94 g) by silica gel chromatography was performed on silica gel (200-300 mesh), or on silica gel H (3425, 3076, 2916, 2876, 1742, 1726, 1650, 1604, 1548, 1460, 1375, 1126, 1065, 876, 764; ESIMS m/z (positive ion mode) 395 [M+Na]⁺; HRESIMS (positive ion mode) m/z 395.0748 [M+Na]⁺ (calcd. C₁₀H₁₂O₆Na for 395.0743).

Methyl 6-(2-acetoxyethyl)-4,8-dihydroxy-9-oxo-9H-xanthene-1-carboxylate (1): Obtained as a yellow gum; UV (MeOH) λ max (log e) 210 (4.36), 242 (3.57), 308 (3.94) nm; IR (KBr, ν max, cm⁻¹) 3475, 3029, 2915, 1686, 1675, 1726, 1650, 1604, 1548, 1460, 1375, 1126, 1065, 876, 764; ESIMS m/z (positive ion mode) 395 [M+Na]⁺; HRESIMS (positive ion mode) m/z 395.0748 [M+Na]⁺ (calcd. C₁₀H₁₂O₆Na for 395.0743).
RESULTS AND DISCUSSION

A 70 % aq. methanol extract prepared from the stems of G. oligantha was subjected repeatedly to column chromatography on Silica gel, Sephadex LH-20, RP-18 and Preparative HPLC to afford compound 1. The structure of 1 was shown in Fig. 1. The 1H and 13C NMR data of 1 were listed in Table-1.

Compound 1 was isolated as a yellow gum. The HRESIMS of 1 gave the pseudomolecular [M+Na]+ ion at m/z 395.0748, corresponding to a molecular formula of C21H20O10. The 1H NMR spectra data (Table-1) showed the presence of two hydroxy groups, two ortho coupled aromatic protons, two meta coupled aromatic protons, two methylene protons and an acetoxy group. These signals could be attributed to a basic xanthone skeleton, an ethanol group and an acetoxy group. The appearance of the methylene protons (H-12) of the ethanol group at δH 2.59 together with J cross-peaks in the HMBC spectrum (Fig. 2) with two aromatic methine carbon (C-2, δC 110.9; C-4, δC 108.1) and a quaternary aromatic carbon (C-3, δC 143.6) suggested that the ethanol group was at C-3. The correlation between one of the ortho-coupled aromatic protons (H-7, δH 7.62) and C-7 in the HSQC spectrum established the attachment of this proton at C-7. Thus, the other ortho-coupled aromatic proton at δH 7.42 was attributed to H-6. H-7 also gave HMBC cross-peaks with C-11 (δC 168.0) of the ester carbonyl side chain and an aromatic carbon C-8 (δC 127.2) in the HMBC spectrum. Thus, the methoxycarbonyl group was placed at C-8. Two hydroxy groups were assigned to C-1 and C-5 on the basis of HMBC correlations between the hydroxy proton (δH 12.56) and C-1 (δC 162.0), C-2 (δC 110.9) and C-9a (δC 106.9), as well as those between the other hydroxy proton (δH 12.56) and C-5 (δC 152.0), C-6 (δC 120.2) and C-10a (δC 147.1). Finally, an acetoxy group attached to C-13 was supported by the HMBC correlation of H-13 (δH 4.37) with the carbonyl carbon (δC 169.8). Therefore, compound 1 was assigned as methyl 6-(2-acetoxyethyl)-4,8-dihydroxy-9-oxo-9H-xanthen-1-carboxylate.

Compound 1 was tested for its cytotoxicity against five human tumor cell lines (NB4, A549, SH-SY5Y, PC3 and MCF7) using the MTT method as reported previously16. Taxol was used as the positive control. The results shown that the compound 1 exhibited moderate cytotoxicity against NB4, PC3 and MCF7 cell with IC50 values of 6.2, 3.8 and 5.4 µM, respectively.

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TABLE-1

| No. | δH (m) | δC (m, J, Hz) | No. | δH (m) | δC (m, J, Hz) |
|-----|-------|---------------|-----|-------|---------------|
| 1   | 162.0 |               | 9a  | 106.9 |               |
| 2   | 110.9 | 7.09 s        | 10a | 147.1 |               |
| 3   | 143.6 |               | 11  | 168.0 |               |
| 4   | 108.1 | 7.21 s        | 12  | 38.0  | 2.59 (t, 7.2) |
| 5   | 152.0 |               | 13  | 66.7  | 4.37 (t, 7.2) |
| 6   | 120.2 | 7.42 (d, 9.0) | 1-OAc | 169.8 |               |
| 7   | 126.0 | 7.62 (d, 9.0) | 13-OAc | 69.8  |               |
| 8   | 127.2 |               |     |       |               |
| 9   | 181.8 |               |     |       |               |
| 4a  | 156.8 |               |     |       |               |
| 8a  | 118.9 |               |     |       |               |
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