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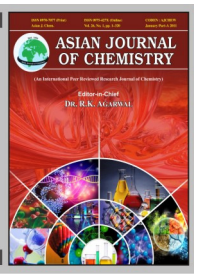

NOTE

New Chalcone from *Garcinia oligantha* and Its Cytotoxicity

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A new chalcone, (5,6-dimethoxybenzofuran-2-yl)(4-hydroxyphenyl)methanone was isolated from the stems of *Garcinia oligantha*. Its structure was elucidated by spectroscopic methods, including extensive 1D and 2D NMR. The new chalcone was tested for its cytotoxicity against five human tumor cell lines (NB4, A549, SHSY5Y, PC3 and MCF7) and it showed modest cytotoxicity against A549 and MCF7 cell with IC_{50} values of 6.2 and 4.8 μM.

Keywords: *Garcinia oligantha*, Chalcone, Cytotoxicity.

Garcinia is a plant genus of the family Clusiaceae native to Asia, Australia, tropical and southern Africa and Polynesia[1]. This genu is known to be a rich source of polyisoprenylated benzophenones and xanthones. Up to now, series of active components extracted from this genus displayed clear apoptosis-inducing effect against different cancer cells such as HeLa[2-4].

In previous studies, some apoptotic compounds were isolated from the stems of *Garcinia oligantha*[5]. Continuing the efforts to discover bioactive metabolites from local plants. We now reinvestigated the chemical constituents of the *G. oligantha* growing in Xishuangbanna Prefecture, leading to the isolation of a new chalcone. The structure of this new chalcone was determined by means of spectroscopic methods including 1D and 2D NMR techniques and this compound exhibited modest cytotoxicity against A549 and MCF7 cell with IC_{50} values of 6.2 and 4.8 μM.

IR spectra were obtained in KBr disc on a Bio-Rad Wininfmred spectrophotometer. ESI-MS were measured on a VG Auto Spec-3000 MS spectrometer. ^1H, ^{13}C 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 μm, Qingdao Marine Chemical Inc., China). Second separation was used an Agilent 1100 HPLC equipped with ZORBAX-C_{18} (21.2 mm × 250 mm, 7.0 μm) column and DAD detector.

The stems of *Garcinia oligantha* were collected in Xishuangbanna Prefecture, Yunnan Province, P.R. China, in September 2011. The identification of the plant material was verified by Prof. Y.J. Chen (Yunnan Nationalities University). A voucher specimen (YNNI 11-9-38) has been deposited in our laboratory.

Extraction and isolation: The air-dried and powdered stems of *G. oligantha* (4.5 kg) were extracted four times with 70 % methanol (4 × 5 L) at room temperature and filtered. The crude extract (218 g) was applied to silica gel (200-300 mesh) column chromatography, eluting with a chloroform-acetone gradient system (20:1, 9:1, 8:2, 7:3, 6:4, 5:5), to give six fractions A-F. Further separation of fraction C (8:2, 15.6 g) by silica gel column chromatography, eluted with chloroform-methanol (9:1, 8:2, 7:3, 6:4, 1:1), yielded mixtures C1-C5. Fraction C1 (9:1, 1.87 g) was subjected to preparative HPLC (48 % methanol, flow rate 12 mL/min) to give the new chalcone (11.8 mg).

(5,6-Dimethoxybenzofuran-2-yl)(4-hydroxyphenyl) methanone, obtained as a yellow gum; UV (MeOH), λ_{max} (log ε) 372 (3.86), 307 (3.65), 248 (3.59), 210 (4.36) nm; IR (KBr, λ_{max}, cm^{-1}): 3358 2960, 2912, 1675, 1612, 1563, 1486, 1268, 1145, 1052, 873, 758; ^1H and ^{13}C NMR data (C_5D_5N, 500 and 125 MHz, respectively), Table-1; ESIMS (positive ion mode) *m/z* 321 $[M + Na]^+$; HRESIMS (positive ion mode) *m/z* 321.0746 $[M + Na]^+$ (calcd. (%) 321.0739 for $C_{17}H_{14}O_5Na$).

A 70 % aq. methanol extract prepared from the stems of *G. oligantha* was subjected repeatedly to column chromatography on Si gel, Sephadex LH-20, RP-18 and Preparative HPLC to

TABLE-1
^{1}H AND ^{13}C NMR DATA OF THE NEW CHALCONE (IN C_5D_5N, 500 AND 125 MHz)

No.	δ_C (m)	δ_H(m, *J*, Hz)	No.	δ_C (m)	δ_H (m, *J*, Hz)
2	154.6 s	–	10	183.2 s	–
3	116.8 d	7.62, s	1'	124.2 s	–
4	106.4 d	7.18, s	2',6'	131.3 d	7.74, d, *J* = 8.6
5	148.8 s	–	3',5'	118.5 d	6.94, d, *J* = 8.6
6	149.6 s	–	4'	158.2 s	–
7	98.9 d	6.80, s	OMe-5	55.8 q	3.82, s
8	154.7 s	–	OMe-6	56.1 q	3.87, s
9	125.2 s	–	Ar-OH-4'	–	10.85, brs

afford the new chalcone. Its structure is shown in Fig. 1 and its ^{1}H and ^{13}C NMR data are listed in Table-1.

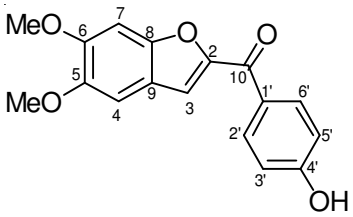

Fig. 1. Structure of new chalocone

Compound **1** was obtained as yellow gum. The HRESIMS showed a quasi-molecular ion peak at *m/z* 321.0746 $[M + Na]^+$, corresponding to a molecular formula of $C_{17}H_{14}O_5$. The ^{1}H and ^{13}C NMR spectrum of **1** (Table-1) displayed 17 carbon and 14 proton signals, respectively, corresponding to one aromatic ring [C-4 (δ_C 106.4 d), C-5 (δ_C 148.8 s), C-6 (δ_C 149.6 s), C-7 (δ_C 98.9 d), C-8 (δ_C 154.7 s), C-9 (δ_C 125.2 s)] with two aromatic proton [H-4 (δ_H 7.18 s) and H-7 (δ_H 6.80 s)], one aromatic ring (C-1' (δ_C 124.2 s), C-2',6' (δ_C 131.3 d), C-3',5' (δ_C 118.5), C-4' (δ_C 158.2 s)] with four aromatic proton [H-2',6' (δ_H 7.74, d, *J* = 8.6) and H-3',5' (δ_H 6.94, d, *J* = 8.6)], a carbonyl carbon (C-10, δ_C 183.2 s), a pair of double bond [C-2 (δ_C 154.6 s) and C-3 (δ_C 116.8 d); H-3 (δ_H 7.62 s)], two methoxy groups (δ_C 55.8 and 56.1; δ_H 3.82 and 3.87) and a phenolic hydroxy group (δ_H 10.85). Strong absorption bands accounting for hydroxy (3358 cm^{-1}), carbonyl (1675) and aromatic groups (1612, 1563, 1486 cm^{-1}) could be observed in its IR spectrum. The UV absorptions at 372, 307, 248 also suggested the presence of a conjugated aromatic ring system. The NMR data of C-2 (δ_C 154.6), C-3 (δ_C 116.8), C-10 (δ_C 183.2) and H-3 (δ_H 7.62, s), together with the HMBC correlations (Fig. 2) of H-3 (δ_H 7.62) with C-2 (δ_C 154.6)/C-4 (δ_C 106.4)/C-8 (δ_C 154.7)/C-9 (δ_C 125.2)/C-10 (δ_C 183.2), of H-4 (δ_H 7.18) with C-3 (δ_C 116.8) and of H-2',6' (δ_H 7.74) with C-10 (δ_C 183.2), suggested that **1** should be a chalcone derivative fused with a furan ring at C-2 and C-8[6]. The signals for four coupled aromatic protons at δ_H 6.94 (d, *J* = 8.6 Hz, 2H) and 7.74 (d, *J* = 8.6, 2H), suggested a 4'-monosubstituted for C ring[7] and the proton signals for two singlets at δ_H 7.18 (s, 1H) and δ_H 6.80 (s, 1H) also revealed that the substituents for B-ring should be located at C-5 and C-6[7]. The HMBC correlations (Fig. 2) between the methoxy proton signals (δ_H 3.82 and 3.89) and C-5 (δ_C 148.8)/C-6 (δ_C 149.6) suggested the positions of two methoxy groups at C-5 and C-6. On the other hand, the phenolic hydroxy group at C-4' was supported by the HMBC correlations observed between the hydroxy proton (δ_H 10.85) and C-4' (δ_C 158.2), C-3', 5' (δ_C 118.5), respectively. Two methoxy groups at C-6 and C-4' were also supported by the cross-peak between the methoxy proton signals (δ_H 3.82 and 3.87) and H-4 (δ_H 7.18)/H-7 (δ_H 6.80) in the NOESY experiment. On the basis of the above observations, the structure of new chalcone was elucidated as (5,6-dimethoxybenzofuran-2-yl)(4-hydroxyphenyl)-methanone.

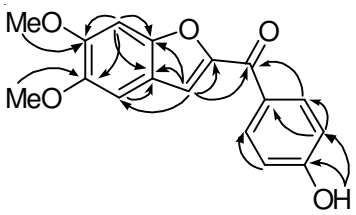

Fig. 2. Selected HMBC (↷) correlations of new chalcone

Since some of the flavonoids derivatives exhibit potential cytotoxicity[8-10]. The new chalcone was tested for its cytotoxicity against five human tumor cell lines (NB4, A549, SHSY5Y, PC3 and MCF7) using the MTT method as reported previously[11]. Taxol was used as the positive control. The results shown that the new chalcone exhibited modest cytotoxicity against A549 and MCF7 cell with IC_{50} values of 6.2 and 4.8 μM, respectively.

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