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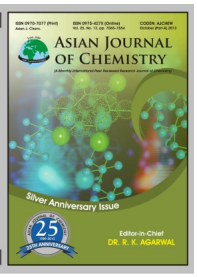

Antiviral Fluorenone Derivatives from *Arundina gramnifolia*

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A new fluorenone derivative, gramniphenol H (**1**), together with four known fluorenone derivatives (**2-5**) were isolated from the whole plant of *Arundina gramnifolia*. Their structures were determined by means of HRESIMS, extensive 1D and 2D NMR spectroscopic studies and chemical evidence. Compound **1** was tested for its cytotoxicity against five human tumor cell lines and it shows modest cytotoxicity against PC3 and SHSY5Y cell with IC_{50} values of 6.18 and 4.25 μM, respectively.

Key Words: *Arundina gramnifolia*, Fluorenone, Structural elucidation, Cytotoxicity.

INTRODUCTION

Arundina gramnifolia (D. Don) Hochr. (bamboo orchid) belongs to the orchid family (Orchidaceae). The plant is used in Chinese folkloric medicine as a detoxifying and diuretic agent, as well as for the treatment of arthritis and inflammation[1]. Previous phytochemical studies on *A. gramnifolia* has revealed the presence of stilbenoids[2-4], sterols[5,6], triterpenes[7,8] and phenols[5-10].

In our previous studies, some new phenols possessing antitobacco mosaic virus (anti TMV) property were isolated from *A. gramnifolia*[9,10]. Continuing the efforts to discover bioactive metabolites from local plants, we now investigated the chemical constituents of the whole plant of *A. gramnifolia* growing in the Xishuangbanna Prefecture, leading to the isolation of a new fluorenone derivative (**1**) and four known fluorenone derivatives (**2-5**). The structures of the isolated compounds were determined by means of spectroscopic methods including 1D and 2D NMR techniques. Compound **1** was tested for its cytotoxicity against five human tumor cell lines and it shows modest cytotoxicity against PC3 and SHSY5Y cell.

EXPERIMENTAL

General procedures: Optical rotations were measured in a Horiba SEPA-300 polarimeter. UV spectra were obtained on a Shimadzu UV-2401A spectrophotometer and CD spectra were measured on a JASCO J-810 spectropolarimeter. Tenor 27 spectrophotometer was used for scanning IR spectra (KBr pellets). 1D and 2D NMR spectra were recorded on a DRX-500 spectrometer with TMS as internal standard. Chemical shifts (δ) were expressed in ppm with reference to TMS. HRESIMS was performed on an API QSTAR spectrometer or a VG Autospec-3000 spectrometer. Preparative HPLC was performed on a Shimadzu LC-8A liquid chromatography equipped with ZORBAX PrepHT GF (21.2 mm × 25 cm, 7 μm) column or Venusil MP C_{18} (20 mm × 25 cm, 5 μm) column. Column chromatography was performed using Si gel (200-300 mesh, Qing-dao Marine Chemical, Inc., Qingdao, China), Lichroprep RP-18 gel (40-63 μM, Merck, Darmstadt, Germany), Sephadex LH-20 (Sigma-Aldrich, Inc, USA) or MCI gel (75-150 μM, Mitsubishi Chemical Corporation, Tokyo, Japan). Column fractions were monitored by TLC and the spots were visualized by heating the plates after spraying with 5 % H_2SO_4 in EtOH.

The whole plant of *Arundina gramnifolia* (D. Don)Hochr. was collected in the Xishuangbanna prefecture of Yunnan Province in in September 2010. The identification of plant material was verified by Prof. Ning Yuan. A voucher specimen (Ynni-10-09-22) has been deposited in the Key Laboratory of Chemistry of Ethnic Medicinal Resources, Yunnan University of Nationalities.

Extraction and isolation: The air-dried and powdered of whole plant of *A. gramnifolia* (2.0 kg) were extracted three times with 70 % aqueous acetone (3.0 L × 3.5 L) at room temperature and filtered to yield a filtrate, which was successively evaporated under reduced pressure to obtain a crude extract (152 g). The extract was applied to silica gel (150-200

mesh) column chromatography, eluting with $CHCl_3$-MeOH gradients (20:1, 9:1, 8:2, 7:3, 6:4, 5:5) to afford fractions A-F. Further separation of fraction B (35.4 g) by silica gel (300-400 mesh), eluted with $CHCl_3$-$CO(CH_3)_2$ (9:1-1:2), yielded fractions B1-B7. Fraction B3 (5.72 g), upon further separation on silica gel using petroleum ether-$CH_3COOC_2H_5$ and semi-preparative HPLC (55 % MeOH-H_2O, flow rate 12 mL/min), afforded **1** (18.2 mg), **2** (16.7 mg), **3** (21.4 mg) **4** (28.2 mg and **5** (29.7 mg).

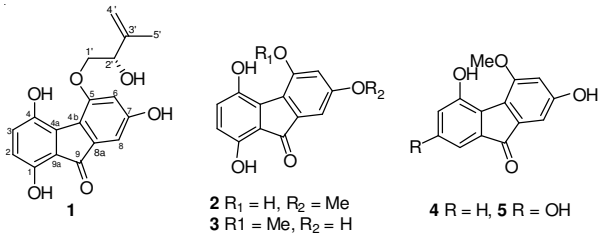
Gramniphenol H (1): Red gum; $[\alpha]_D^{25.0}$-16.8 (c 0.25, CH_3OH); UV (CH_3OH) λ_{max} (log ε) 210 (3.72), 267 (3.88), 320 (2.52), 346 (2.71) nm; IR (KBr, ν_{max}, cm^{-1}): 3325, 2970, 2892, 1694, 1612, 1547, 1455, 1184, 1119; ^1C and ^{13}H NMR data (C_5D_5N, 500 and 125 MHz) see Table-1; negative ESIMS *m/z* 327 $[M-H]^-$; negative HRESIMS *m/z* 327.0862 $[M-H]^-$ (calcd. (%) for $C_{18}H_{15}O_6$, 327.0869).

TABLE-1
^1H AND ^{13}C NMR DATA OF COMPOUND **1** (δ IN ppm, IN C_5D_5N)

Position	Compound **2**	
	δ_C	δ_H (*J* in Hz)
1	150.8 s	–
2	118.2 d	6.71 d (8.8)
3	129.5 d	7.06 d (8.8)
4	144.4 s	–
5	156.6 s	–
6	106.9 d	6.91 s
7	154.5 s	–
8	108.1 d	6.77 s
9	192.9 s	–
4a	125.0 s	–
4b	120.6 s	–
8a	137.1 s	–
9a	116.8 s	–
1'	71.0 t	3.97 dd (6.9, 10.0)
–	–	4.13 dd (9.5, 4.0)
2'	74.1 d	4.36 m
3'	145.8 s	
4'	113.4 t	4.89 s
–	–	5.18 s
5'	19.0 q	1.68 s
Ar-OH-1	–	11.02 s
Ar-OH-2	–	10.90 s
Ar-OH-4	–	10.50 s

RESULTS AND DISCUSSION

Gramniphenols H (**1**) and four known fluorenone derivatives (**2-5**) (Fig. 1) were isolated from the 70 % aqueous acetone extract of *A. gramnifolia*. Known compounds were identified as 1,4,5-trihydroxy-7-methoxy-9*H*-fluoren-9-one (**2**)[11], dendroflorin (**3**)[12], Dengibsin (**4**)[13], Denchrysan A (**5**)[14] by comparison of spectroscopic data with the literature.



1 **2** R_1 = H, R_2 = Me **3** R1 = Me, R_2 = H **4** R = H, **5** R = OH

Fig. 1. Structures of derivatives fluorenone from *A. gramnifolia*

Gramniphenol H (**1**) was obtained as red gum. The molecular formula $C_{18}H_{15}O_6$ was inferred by HRESI-MS at *m/z* 327.0862 $[M-H]^-$ (calcd. (%) for C $C_{18}H_{15}O_6$, 327.0869). The IR absorption bands indicated the presence of hydroxy (3325 cm^{-1}), carbonyl (1694 cm^{-1}) and aromatic ring (1612, 1547, 1455 cm^{-1}) and UV absorptions at 267, 320, 346 nm suggested a conjugated aromatic ring system. The ^1H and ^{13}C NMR spectra of **1** (Table-1) displayed signals for all **18** carbons and **16** protons, suggesting the presence of an 1,4,5,7-oxygenated fluorenone moiety[11] (H-2, H-3, H-6, H-8 and C-1-C-9a), three phenolic protons (δ_H 10.50, 10.90 and 11.02) and a 2-hydroxy-3-methylbut-3-enyloxy unit $[-OCH_2CH(OH)C(CH_2)(CH_3)]$[10] (H-1', H-2', H-4', H-5' and C-1'-C-5'). The location of the 2-hydroxy-3-methylbut-3-enyloxy unit at C-5 position was supported by the HMBC correlation observed between H-1' (δ_H 3.97 and 4.13) and C-5 (δ_C 156.6). The three phenolic groups were assigned to C-1, C-4 and C-7 positions on the basis of HMBC correlations (Fig. 2). The S configuration at C-2' was assigned by a comparison of NMR and optical rotation data with those of stachylines A[10], of which absolute configuration was established by the Mosher method.

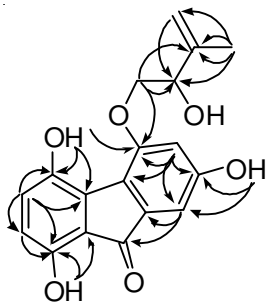


Fig. 2. Selected HMBC ( ) correlations of compound **1**

Since certain of the phenolic compounds exhibit potential cytotoxicity[15-17]. Compound **1** was tested for their cytotoxicity against five human tumor cell lines (NB4, A549, SHSY5Y, PC3 and MCF7) using the MTT method as reported previously[18]. Taxol was used as the positive control. The results revealed that compound **1** showed low active (IC_{50} values >10 μM) for NB4, A549 and MCF7 tumor cell and showed modest cytotoxicity against PC3 and SHSY5Y cell with IC_{50} values of 6.18 and 4.25 μM, respectively.

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