Vietnam Journal of Science and Technology ***61*** *(5) (2023) 798-806*

doi:10.15625/2525-2518/17313

Polyprenyl phloroglucinols and methyl esters of citric acid from the fruits of *Garcinia multiflora*

Nguyen Nghia Vu[1, 3], Hoang Thi Minh Nguyet[2], Lo Van Nguyen[3], Tran Thi Thu Thuy[2, *], Phan Minh Giang[3, *]

[1]*Center for Research and Production of Vaccines and Biologicals, 135 Lo Duc, Ministry of Health, Hai Ba Trung, Ha Noi, Viet Nam*

[2]*Institute of Natural Products Chemistry, Vietnam Academy of Science and Technology, 18 Hoang Quoc Viet, Hai Ba Trung, Ha Noi, Viet Nam*

[3]*Faculty of Chemistry, Vietnam National University University of Science, Vietnam National University Hanoi, 19 Le Thanh Tong Street, Hai Ba Trung, Hoan Kiem, Ha Noi, Viet Nam*

[*]Emails: *1.thuy.tran@inpc.vast.vn, 2.phanminhgiang@yahoo.com*

Received: 14 July 2022; Accepted for publication: 11 February 2023

Abstract. *Garcinia multiflora* belonging to the Clusiaceae family is one of the medicinal plant species native to Viet Nam and southern China and its use is an ethno-medicinal remedy to treat acne, scabies, constipation, and inflammation. The major bioactive classes of secondary metabolites were found in different parts of this plant such as phloroglucinol, xanthone, bioflavonoid, organic acid… In this paper, the chemical investigation on the fruits of *Garcinia multiflora* growing in the north of Vietnam was reported. Six compounds including two polyprenyl phloroglucinols (garcinol (**1**), isogarcinol (**2**)), one triterpene (friedelin (**3**)), and three methyl esters of citric acid (1,5,6-trimethyl citrate (**4**), 1,5-dimethyl citrate (**5**) and 6-methyl citrate (**6**)) were isolated from the methanol extract of fresh fruit pericarp using repeated column chromatography on different absorbents (silica gel, RP-18 and Sephadex). Their chemical structures were determined using spectroscopic methods (ESI-MS, 1D and 2D NMR) and comparison with the spectroscopic data in the literature. The absolute configurations of two polyprenyl phloroglucinols **1** and **2** were determined by comparison of its experimental optical rotation and NMR data with the reported values of their stereoisomers. This is the first report on the occurrence of the phytochemicals **1**-**6** in the fruits of *Garcinia multiflora* growing in Viet Nam.

Keywords: Garcinia multiflora, polyprenyl phloroglucinol, methyl citrate, NMR data.

Classification numbers: 1.1.1, 1.1.6.

1. INTRODUCTION

Garcinia multiflora Champ.ex Benth of the family Clusiaceae is an evergreen tree that usually grows to 5 - 15 meters in height. The tree is harvested from the wild for local use of its edible fruit and is also cultivated as a fruit crop in southern China and Viet Nam. *G. multiflora*

has a wide distribution and large population, and its use is a remedy to treat acnes, scabies, constipation, and inflammation [1]. Many studies have been performed on different parts of *G. multiflora* such as fruits, leaves, twigs, and branches, demonstrating the ability to biosynthesize novel compounds from *G. multiflora* [2 - 8]. From the fruits, hydrocitric acids, benzophenones (e.g. polyprenyl acylphloroglucinol), coumarins, triterpenes, and steroids have been isolated [2 - 5], of which benzophenones are the most important group related to the biological activities they have demonstrated. However, in Viet Nam chemical studies on *G. multiflora* fruits have not been reported. The present study focused on isolating compounds from the MeOH extract of the fruit pericarp of *G. multiflora* with the perspective of examining their structures and biological activities.

2. MATERIALS AND METHODS

2.1. General experimental procedures

Silica gel (40 - 63 µm and 63 - 200 µm, Merck), Sephadex LH-20 (GE Healthcare, Sweden) and reversed-phase RP-18 (Merck, Germany) were used for column chromatography (CC). TLC was performed using silica gel 60 F_{254} on aluminum plates (Merck, Germany). Spots were detected by UV lights (254 and 365 nm) and 5 % vanillin-sulfuric acid in absolute ethanol solution. Solvents of industrial grade were used for the extraction and chromatographic separation. ESI-MS spectra were obtained from an Agilent 1100 LC-MS instrument (USA). NMR spectra were measured on a Bruker Avance 600 or 500 spectrometer (USA). Optical rotations were measured on a Perkin-Elmer 141 polarimeter (USA). Melting points were measured on a Büchi B-450 melting point apparatus (USA).

2.2. Plant material

Fresh fruits of *Garcinia multiflora* Champ.ex Benth (20.0 kg) were collected in Bac Kan province in December 2021. The voucher specimen (GM082021) was identified by Dr. Nguyen Quoc Binh, Vietnam National Museum of Nature, Vietnam Academy of Science and Technology, and deposited at the Institute of Natural Products Chemistry, Vietnam Academy of Science and Technology.

2.3. Extraction and isolation

The fresh fruits of *G. multiflora* (20.0 kg) were peeled and the pericarp was dried at 45 ^{o}C for two days. The dried pericarp (1.3 kg) was powdered and sonicated with 2 L of MeOH at 40 ^{o}C for 30 min. The sonication was repeated three times then the extracts were filtered and the solvent was evaporated under reduced pressure to obtain a concentrated methanol extract (308 g). The methanol extract was dissolved in water and successively partitioned with *n*-hexane (500 mL × 3) and ethyl acetate (500 mL × 3), then the solvents were removed under reduced pressure to obtain *n*-hexane (158 g) and ethyl acetate (70.6 g) extracts.

The *n*-hexane extract (158 g) was separated by silica gel CC with gradient *n*-hexane-acetone solvent systems (100:1→1:1) to obtain 10 fractions (F1-F10). Fraction F1 (54 g) was separated by silica gel CC with gradient *n*-hexane-acetone solvent systems (70:1→1:1) to give compounds **1** (50 mg) and **5** (15 mg). Fraction F5 was loaded onto a silica gel column with gradient *n*-hexane-acetone solvent systems (50:1→1:1) to give 5 fractions (F5.1-F5.5) and the

purification of fraction F5.5 by RP-18 CC with MeOH-H_2O (5:1) and Sephadex LH-20 CC with MeOH-dichloromethane (95:5) gave compound **3** (30 mg).

The ethyl acetate extract (70.6 g) was separated by silica gel CC with gradient *n*-hexane-acetone solvent systems (100:1→1:1) to obtain 12 fractions (E1-F12). Compound **4** (70 mg) was precipitated from fraction E1. Fraction E7 was separated by RP-18 CC with MeOH-H_2O (5:1) and further purified by Sephadex LH-20 CC with MeOH-dichloromethane (95:5) giving compound **5** (20 mg). Fraction E12 was purified by Sephadex LH-20 CC with MeOH giving compound **6** (60 mg).

Garcinol (1): yellow needles, m.p. 122 ^oC, $[\alpha]_D^{25}$ = -138 (*c* 0.1, $CHCl_3$). ESI-MS: *m/z* 603.2 $[M+H]^+$; *m/z* 601.3 $[M-H]^-$ ($C_{38}H_{50}O_6$). ^1H- (600 MHz, $CDCl_3$) and ^{13}C-NMR (150 MHz, $CDCl_3$): see Table 1.

Isogarcinol (2): yellow amorphous powder, $[\alpha]_D^{25}$ = -159 (*c* 1.0, $CHCl_3$). ESI-MS:*m/z* 601.6 $[M-H]^-$ ($C_{38}H_{50}O_6$). ^1H- (600 MHz, $CDCl_3$) and ^{13}C-NMR (150 MHz, $CDCl_3$): see Table 1.

Friedelin (3): white needles, m.p. 267 ^oC. ESI-MS: *m/z* 427.2 $[M+H]^+$ ($C_{30}H_{50}O$). ^1H-NMR (600 MHz, $CDCl_3$) δ (ppm): 2.38 (1H, *m*, H_a-2); 2.29 (1H, *m*, H_b-2); 2.25 (1H, *q*, *J* = 6.6 Hz, H-4); 1.96 (1H, *m*, H_a-1); 1.75 (1H, *m*, H_a-6); 1.69 (1H, *m*, H_b-1); 1.57 (1H, *m*, H_a-16); 1.56 (1H, *m*, H-18); 1.52 (1H, *m*, H-10); 1.51 (1H, *m*, H_a-22); 1.50 (1H, *m*, H_a-21); 1.49 (1H, *m*, H_a-7); 1.48 (1H, *m*, H_a-15); 1.45 (1H, *m*, H_a-11); 1.38 (2H, *m*, H-8, H_a-19); 1.35 (2H, *m*, H_b-7, H_b-16); 1.33 (1H, *m*, H_a-12); 1.32 (1H, *m*, H_b-12); 1.31 (1H, *m*, H_b-21); 1.29 (1H, *m*, H_b-6); 1.27 (1H, *m*, H_b-15); 1.25 (1H, *m*, H_b-11); 1.22 (1H, *m*, H_b-19); 1.18 (3H, *s*, H-28); 1.05 (3H, *s*, H-27); 1.01 (3H, *s*, H-26); 1.0 (3H, *s*, H-29); 0.95 (3H, *s*, H-30); 0.94 (1H, *m*, H_b-22); 0.88 (1H, *d*, *J* = 5.5 Hz, H-23); 0.87 (3H, *s*, H-25); 0.73 (3H, *s*, H-24). ^{13}C-NMR (150 MHz, $CDCl_3$) δ (ppm): 213.2 (C-3); 59.5 (C-10); 58.3 (C-4); 53.1 (C-8); 42.9 (C-18); 42.2 (C-5); 41.6 (C-2); 41.3 (C-6); 39.7 (C-13); 39.3 (C-22); 38.3 (C-14); 37.5 (C-9); 36.1 (C-16); 35.7 (C-11); 35.4 (C-19); 35.0 (C-29); 32.8 (C-21); 32.5 (C-15); 32.1 (C-28); 31.8 (C-30); 30.5 (C-12); 30.0 (C-17); 28.2 (C-20); 22.3 (C-1); 20.3 (C-26); 18.7 (C-27); 18.3 (C-7); 18.0 (C-25); 14.7 (C-24); 6.8 (C-23).

1,5,6-Trimethyl citrate (4): white amorphous powder. ESI-MS: *m/z* 256.8 $[M+Na]^+$ ($C_9H_{14}O_7$). ^1H-NMR (500 MHz, $CDCl_3$) δ (ppm): 4.12 (1H, *s*, OH); 3.83 (3H, *s*, H-7); 3.69 (6H, *s*, H-8, H-9); 2.91 (2H, *d*, *J* = 15.5 Hz, H_a-2, H_a-4); 2.81 (2H, *d*, *J* = 15.5 Hz, H_b-2, H_b-4). ^{13}C-NMR (125 MHz, $CDCl_3$) δ (ppm): 173.8 (C-6); 170.2 (C-1, C-5); 73.3 (C-3); 53.2 (C-7); 52.0 (C-8, C-9); 43.1 (C-2, C-4).

1,5-Dimethyl citrate (5): white amorphous powder. ESI-MS: *m/z* 242.8 $[M+Na]^+$; 218.8 $[M-H]^-$ ($C_8H_{12}O_7$). ^1H-NMR (500 MHz, acetone d_6) δ(ppm): 3.62 (6H, *s*, H-8, H-9); 3.26 (1H, *br s*, OH); 2.93 (2H, *d*, *J* = 15.5 Hz, H_a-2, H_a-4); 2.84 (2H, *d*, *J* = 15.5 Hz, H_b-2, H_b-4). ^{13}C-NMR (125 MHz, acetone-d_6) δ (ppm): 174.8 (C-6); 170.8 (C-1, C-5); 73.7 (C-3); 51.8 (C-8, C-9); 43.5 (C-2, C-4).

6-Methyl citrate (6): white amorphous powder. ESI-MS: *m/z* 228.8 $[M+Na]^+$, *m/z* 204.7 $[M-H]^-$ ($C_7H_{10}O_7$).^1H-NMR (600 MHz, acetone d_6) δ(ppm): 3.62 (3H, *s*, H-7); 2.91 (2H, *d*, *J* = 13.5 Hz, H_a-2, H_a-4); 2.80 (2H, *d*, *J* = 13.5 Hz, H_b-2, H_b-4). ^{13}C-NMR (150 MHz, acetone-d_6) δ(ppm): 174.4 (C-6); 171.6 (C-1, C-5); 74.0 (C-3); 52.7 (C-7); 43.4 (C-2,C-4).

3. RESULTS AND DISCUSSION

Compound **1** was isolated as yellow needles, m.p. 122 ^oC, $[\alpha]_D^{25}$ = -138 (*c* 0.1, $CHCl_3$). The ESI-MS pseudomolecular ion peaks at *m/z* 603.2 $[M+H]^+$ and *m/z* 601.3 $[M-H]^-$ suggested the

molecular formula of **1** to be $C_{38}H_{50}O_6$. The ^{1}H-NMR of compound **1** showed signals of two tertiary methyl groups at δ_H 1.16 (3H, *s*) and 1.01 (3H, *s*) (H-22 and H-23) and seven olefinic methyl groups at δ_H 1.54 (*s*, H-28 and H-33), 1.60, 1.67, 1.70, 1.73, and 1.80 (*s*, H-38, H-37, H-27, H-21, and H-20). Signals of a vinylic methylene at δ_H 4.38 and 4.42 (2H, s, H-32) and three olefinic protons at δ_H 4.93, 5.05, and 5.09 (*m*, H-25, H-35 and H-18), three protons of an ABX system at δ_H 6.62 (*d*, *J* = 7.8 Hz, H-15), 6.97 (*d*, *J* = 1.8 Hz, H-12), and 6.98 (*dd*, *J* = 7.8, 1.8 Hz, H-16)] were observed. The ^{13}C-NMR and HSQC spectra showed signals of six aromatic carbons (C-11-C-16, Table 1), a carbonyl group at δ_C198.7 (C-10), and one bicyclic [3,3,1]nonane-3,9-dione system containing 3 tertiary carbons at δ_C 57.9 (C-8), 69.8 (C-4), 49.6 (C-5), one methine at δ_C 46.9 (C-6), one methylene group at δ_C 42.7(C-7), two ketone carbons at δ_C 209.1 (C-9), 194.7 (C-3), and an oxygenated aromatic carbon at δ_C 193.9 (C-1). The ^{1}H-, ^{13}C-NMR spectroscopic data (Table 1) suggested that the bicyclic [3,3,1]nonane-3,9-dione system was connected to four prenyl and one 3,4-dihydroxybenzoyl groups in the structure of **1**. The ^{1}H-^{1}H COSY spectrum displayed correlations of the spin systems of H-29 (δ_H 2.13, 1.90)/H-30 (δ_H 2.75)/H-34 (δ_H 2.08)/H-35 (δ_H 5.05), H-6 (δ_H 1.44)/H-7 (δ_H 2.07), H-17 (δ_H 2.74, 2.59)/H-18 (δ_H 5.09), and H-6/H-24 (δ_H 2.15, 1.95)/H-25 (δ_H 4.93). The HMBC correlations of **1** between H-29 and C-1/C-8/C-30 (δ_C 43.6)/C-31 (δ_C 148.1)/C-34 (δ_C 32.7), H-30 and C-8/C-33 (δ_C 17.7)/C-34, and H-32 (δ_H 4.42, 4.38) and C-30/C-33 allowed the attachment of a complex of 2-isopropenyl-5-methylhex-4-enyl group from C-29 (δ_C 36.2) to C-38 (δ_C 18.0) to C-8 of the bicyclic system. The other HMBC correlations between H-18 and C-4 (δ_C 69.8), H-17 (δ_H 2.74, 2.59) and C-9 (δ_C 209.1)/C-3, H-24 and C-6/C-7 determined the location of two prenyl groups at C-5 and C-7. Two methyl groups C-22 (δ_C 22.7) and C-23 (δ_C 27.0) were attached to C-5 by HMBC correlations between H-22/H-23 and C-4/C-5/C-6. The NMR spectroscopic data of **1** agreed with those of garcinol. Further verification based on the specific optical rotation of **1** showed the coincidence with that of garcinol ($[\alpha]_D$: -138, *c* 0.1, $CHCl_3$) [9]. The other stereoisomers 7-*epi*-garcinol ($[\alpha]_D$: -86, *c* 1.0, $CHCl_3$) [10, 11] and guttiferone E ($[\alpha]_D$: +101, *c* 0.5, $CHCl_3$) [12] showed different signs or values of the optical rotations. Thus, compound **1** was concluded to be garcinol.

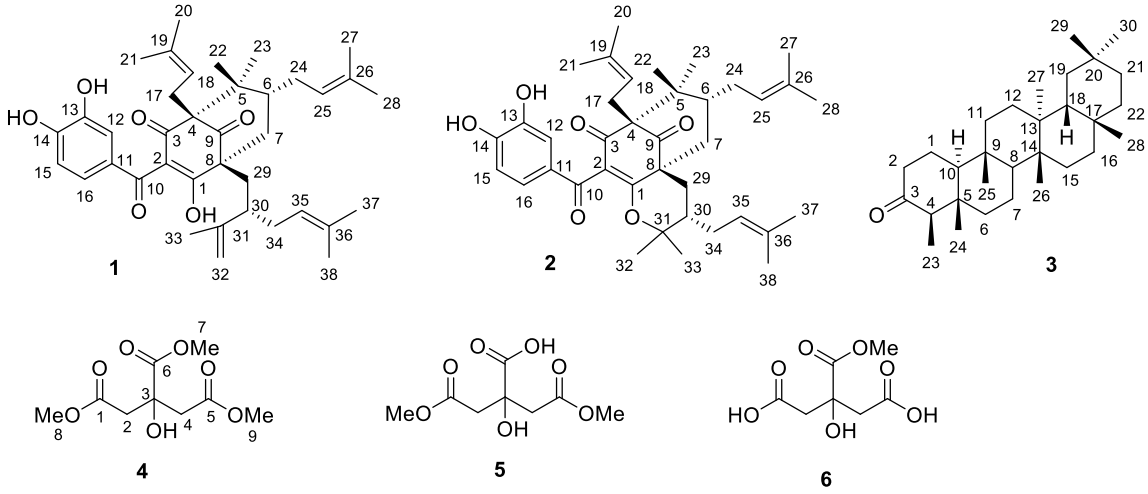

Figure 1. Chemical structures of compounds **1**-**6**.

Compound **2** was isolated as a yellow amorphous powder, $[\alpha]_D^{25}$ = -159 (*c* 1.0, $CHCl_3$). The ESI-MS pseudomolecular ion peak at *m/z* 601.6 $[M-H]^-$ suggested that the molecular formula of

2 was $C_{38}H_{50}O_6$. The ^{1}H-NMR of compound **2** showed signals of four tertiary methyl groups at δ_H 1.15 (*s*, H-22), 0.98 (*s*, H-23), 1.24 (*s*, H-32), 0.91 (*s*, H-33) and six methyl groups attached to the doubly bonded carbons at δ_H 1.60 (6H, *s*, H-20, H-21), 1.68 and 1.67 (6H, *s*, H-27, H-28), 1.77 and 1.58 (6H, *s*, H-37, H-38). In the downfield region, an ABX system at δ_H 6.75 (*d*, *J* = 7.8 Hz, H-15), 7.00 (*dd*, *J* = 7.8, 2.4 Hz, H-16), 7.35 (*d*, *J* = 2.4 Hz, H-12)] and three olefinic protons at δ_H 4.89 (*m*, H-18), 4.91 (*m*, H-25), 5.20 (*m*, H-35) were observed (Table 1). The ^{13}C-NMR and HSQC showed signals of six aromatic carbons (C-11-C-16, Table 1), three carbonyl groups at δ_C 207.3 (C-9), 194.4 (C-3), and 193.3 (C-10), and a bicyclic [3,3,1]nonane-3,9-dione system with three quaternary carbons at δ_C 51.2 (C-8), 68.2 (C-4), and 46.2 (C-5), one methine at δ_C 46.1 (C-6), one methylene at δ_C 39.4 (C-7), one isolated ketone group at δ_C 207.3 (C-9), and a conjugated double bond at δ_C 171.4 (C-1) and 194.4 (C-3).

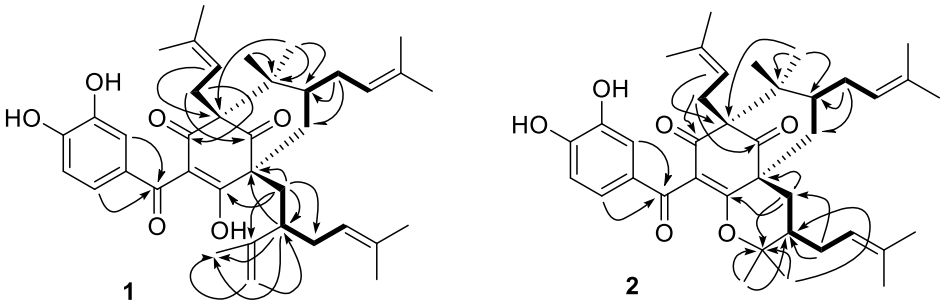

Figure 2. Key HMBC (arrows) and COSY (bold lines) correlations for compounds **1** and **2**.

Table 1. ^{1}H (600 MHz) and ^{13}C (150 MHz) NMR data of compounds **1** and **2 (**$CDCl_3$, *J* in Hz).

	1			**2**	
C/H	δ_H	δ_C		δ_H	δ_C
1		193.9			171.4
2		115.9			125.2
3		194.7			194.4
4		69.8			68.2
5		49.6			46.2
6	1.44 *m*	46.9		1.45 *m*	46.1
7	2.37 *d* (13.8) 2.07 *overlapped*	42.7		1.98 *dd* (14.4, 7.8) 2.26 *d* (14.4)	39.4
8		57.9			51.2
9		209.1			207.3
10		198.7			193.3
11		128.0			130.0
12	6.97 *d* (1.8)	116.5		7.35 *d* (2.4)	114.2
13		143.6			144.4
14		149.7			150.4
15	6.62 *d* (7.8)	114.4		6.75 *d* (7.8)	114.2
16	6.98 *dd* (7.8, 1.8)	124.1		7.00 *dd* (7.8, 2.4)	124.0
17	2.74 *overlapped* 2.59 *d* (12.6)	26.4		2.44 *dd* (13.2, 4.8) 2.63 *overlapped*	25.5

18	5.09 *m*	120.2		4.89 *m*	119.6
19		135.2			134.6
20	1.80 *s*	26.1		1.60 *s*	26.0
21	1.73 *s*	18.2		1.60 *s*	18.0
22	1.16 *s*	22.7		1.15 *s*	26.7
23	1.01 *s*	27.0		0.98 *s*	22.4
24	2.15 *overlapped* 1.95 *m*	29.0		2.16 *m* 2.63 *overlapped*	29.2
25	4.93 *m*	123.9		4.91 *m*	124.9
26		132.9			133.0
27	1.70 *s*	25.7		1.68 *s*	25.85
28	1.54 *s*	18.0		1.67 *s*	17.9
29	2.13 *overlapped* 1.90 *dd* (13.8, 4.2)	36.2		3.03 *dd* (14.4, 3.6) 0.92 *overlapped*	28.3
30	2.75 *overlapped*	43.6		1.40 *m*	42.8
31		148.1			86.6
32	4.42 *d* (2.4) 4.38 *d* (2.4)	112.7		1.24 *s*	21.2
33	1.54 *s*	17.7		0.91 *s*	28.6
34	2.08 *overlapped* 2.0 *overlapped*	32.7		2.03 *m* 1.79 *m*	29.6
35	5.05 *m*	122.7		5.20 *m*	121.4
36		132.0			133.6
37	1.67 *s*	25.7		1.77 *s*	25.7
38	1.60 *s*	18.0		1.58 *s*	17.9

The HMBC correlations from H-29 (δ_H 3.03; 0.92) to C-8 (δ_C 51.2), C-1 (δ_C171.4), C-30 (δ_C 42.8), and C-31 (δ_C 86.6) revealed the annexation of a tetrahydropyran ring to the bicyclic [3,3,1]nonane-3,9-dione system. Based on the NMR data, the structure of **2** consisted of a tricyclic pyrano[3,3,1]nonane-3,9-dione decorated with three prenyl groups and one 3,4-dihydroxybenzoyl group. The HMBC correlations between H-18 and C-4, H-17 (δ_H 2.44, 2.63) and C-9/C-3, H-24 (δ_H 2.16, 2.63) and C-6/C-7, H-34 (δ_H 2.03, 1.79) and C-29 (δ_C 28.3)/C-30 (δ_C 42.8) determined the location of three prenyl groups at C-4, C-6 and C-30. Further HMBC correlations between H-22/H-23 and C-4/C-5/C-6, H-32/H-33 and C-30/C-31 (δ_C 86.6) determined the attachment of C-22/C-23 methyl groups to C-5 and C-32/C-33 methyl groups to C-31. Compared with the values in the literature, the 1D and 2D NMR spectroscopic data of **2** were in agreement with the structure of isogarcinol. The specific optical rotation of **2** ($[\alpha]_D$ = -159) was similar to those of isogarcinol ($[\alpha]_D$ = -158) [10, 11]. The other stereoisomers 7-*epi*-isoxanthochymol ($[\alpha]_D$ = +98.4) [13] and isoxanthochymol ($[\alpha]_D$ = +181) [13] showed the opposite optical rotations. Thus, compound **2** was determined as isogarcinol.

Compound **3** was isolated as white needles, m.p. 267 ^oC. The ESI-MS pseudomolecular ion peak at *m/z* 427.2 $[M+H]^+$ suggested that the molecular formula of **3** was $C_{38}H_{50}O_6$. The ^{1}H-NMR spectrum of compound **3** showed the resonance of seven singlet tertiary methyl groups at δ_H 1.18 (3H, *s*, H-28), 1.05 (3H, *s*, H-27), 1.01 (3H, *s*, H-26), 1.0 (3H, *s*, H-29), 0.95 (3H, *s*, H-30), 0.87 (3H, *s*, H-25), 0.73 (3H, *s*, H-24) and a doublet secondary methyl group at δ_H 0.88 (1H, *d*, *J* = 5.5 Hz, H-23), in addition to methylene and methine groups in the upfield NMR range at δ_H 2.41-1.22. The ^{13}C-NMR showed the presence of 30 carbon signals including a ketone

carbonyl group at δ_C 213.2 (C-3), eight methyl signals at δ_C 35.0 (C-29), 32.1 (C-28), 31.8 (C-30), 20.3 (C-26), 18.7 (C-27), 18.0 (C-25), 14.7 (C-24), 6.8 (C-23) and 21 methine and methylene carbons at δ_C 59.5-18.3. The NMR data suggested the 3-oxofriedelane structure of **3** and the comparison of the spectroscopic data and the melting point of **3** with those of friedelin [14] confirmed the suggestion. Thus, compound **3** was identified as friedelin.

Compounds **4-6** were isolated as white amorphous powders. The ESI-MS pseudomolecular ion peaks at *m/z* 256.8 $[M+Na]^+$; 242.8 $[M+Na]^+$ and 218.8 $[M-H]^-$; 228.8 $[M+Na]^+$ and 204.7 [M-H] determined the molecular formulas of **4-6** to be $C_9H_{14}O_7$, $C_8H_{12}O_7$ and $C_7H_{10}O_7$, respectively. Their ^{1}H-NMR spectra showed the resonance of two coupling protons as doublets at δ_H 2.8-2.9 and from one to three methoxy groups at δ_H 3.62 (s), 3.69 (s), and 3.83 (s). The ^{13}C-NMR spectra of compounds **4-6** all showed the resonance of three acid or ester carbonyl groups at δ_C 175-170 including two chemically and magnetically equivalent carbonyl groups and from one to three methoxy groups. In addition, the presence of a tertiary carbon at δ_C 73.3 (C-3) and two symmetrical methylene groups at δ_C 43.1 (C-2, C-4) identified the structure of compound **4** as 1,5,6-trimethyl citrate which was in good agreement with the spectroscopic values of trimethyl citrate in the literature [15]. Consequently, the two other related esters were identified as 1,5-dimethyl citrate (**5**) (with two symmetrical ester carbonyl groups) and 6-methyl citrate (**6**) (with one central ester carbonyl group) [16, 17]. These three esters (**4-6**) form the basis of the sourness and flavor of the ripe fruits of *Garcinia multiflora.*

4. CONCLUSIONS

By chromatographic separation, six compounds (**1-6**) were isolated from the *n*-hexane and ethyl acetate extracts from the fruit pericarp of *Garcinia multiflora*. Their structures were identified as two polyprenylated phloroglucinols: garcinol (**1**) and isogarcinol (**2**), a triterpene: friedelin (**3**), and three methyl citrates: 1,5,6-trimethyl citrate (**4**), 1,5-dimethyl citrate (**5**), and 6-methyl citrate (**6**). This is the first report on the occurrence of phytochemicals **1-6** in *G. multiflora* fruits in Viet Nam.

Acknowledgement. One of the authors (Tran Thi Thu Thuy) is grateful to the Vietnam Academy of Science and Technology for financial supports (NVCC07.09/22-23).

CRediT authorship contribution statement. Nguyen Nghia Vu, Hoang Thi Minh Nguyet, Lo Van Nguyen: Experiment, data analysis. Tran Thi Thu Thuy, Phan Minh Giang: data analysis, methodology, manuscript preparation, supervision.

Declaration of competing interest. The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

REFERENCES

1. Pham H. H. - An Illustrated Flora of Vietnam, Vol. 1, Publisher Youth, Ho Chi Minh City, 1999, pp. 457-461 (Vietnamese).
2. Chen J. J., Ting C. W., Hwang T. L. and Chen I. S. - Benzophenone derivatives from the fruits of *Garcinia multiflora* and their anti-inflammation activity, J. Nat. Prod. **72** (2009) 253-258. https://doi.org/10.1021/np8006364.
3. Liu H., Gan F., Jin S., Li J., Chen Y. and Yang G. - Acylphloroglucinol and tocotrienol derivatives from the fruits of *Garcinia multiflora*, RSC Adv. **7** (2017) 29295-29301. https://doi.org/10.1039/C7RA04208F.

4. Teng H. D., Ren Y. S., Ma Z. Y., Tan X., Xu J., Chen Y. and Yang G. Z. - Homoadamantane polycyclic polyprenylated acylphloroglucinols from the fruits of *Garcinia multiflora*, Fitoterapia **137** (2019) 104245-104252. https://doi.org/10.1016/j.fitote.2019.104245.
5. Teng H., Li Q., Ma Z., Li X., Xie W., Chen Y. and Yang G. - Polyprenylated acylphloroglucinols with different carbon skeletons from the fruits of *Garcinia multiflora*, Front. Chem. **9** (2021) 1-12. https://doi.org/10.3389/fchem.2021.75.
6. Jiang G., Du F. and Fang G. - Two new proanthocyanidins from the leaves of *Garcinia multiflora*, Nat. Prod. Res. **28** (7) (2014) 449-453. http://dx.doi.org/10.1080/14786419.2013.873431.
7. Jing W. Y., Jiang C., Ji F., Hua H. M. and Li Z. L. - Chemical constituents from the stem barks of *Garcinia multiflora*, J. Asian Nat. Prod. Res. **15** (11) (2013) 1152-1157. http://dx.doi.org/10.1080/10286020.2013.819854.
8. Liu X., Gao X. M., Zhou Y., Qiao C. F., Peng Y., Chen S. L., Luo K. Q. and Xu H. X. - Apoptotic effects of polyprenylated benzoylphloroglucinol derivatives from the twigs of *Garcinia multiflora*, J. Nat. Prod. **73** (2010) 1355-1359. https://doi.org/10.1021/np100156w.
9. Sang S., Pan M. H., Cheng X., Bai N., Stark R. E., Rosen R. T., Lin-Shiau S. Y., Lin J. - K. and Ho C. T. - Chemical studies on antioxidant mechanism of garcinol: analysis of radical reaction products of garcinol and their antitumor activities, Tetrahedron **57** (2001) 9931-9938. https://doi.org/10.1016/S0040-4020(01)01015-8.
10. Marti G., Eparvier V., Moretti C., Susplugas S., Prado S., Grellier P., Retailleau P., Guerrite F. and Litaudon M. - Antiplasmodial benzophenones from the trunk latex of *Moronobea coccinea* (Clusiaceae), Phytochem.**70** (2009) 75-85. https://doi.org/10.1016/j.phytochem.2008.10.005.
11. Zheng D., Jiang J. M., Chen S. M., Wan S. J., Ren H. G., Chen G., Xu G., Zhou H., Zhang H. and Xu H. X. - Structural revision of guttiferone F and 30-*epi*-cambogin, J. Nat. Prod. **84** (2021) 1397-1402. https://doi.org/10.1021/acs.jnatprod.0c01031.
12. Nugroho A. E., Nakamura H., Inoue D., Hirasawa Y., Wong C., P., Kaneda T., Hadi H. A. and Morita H. - Polyisoorenylated acylphloroglucinols from *Garcinia nervosa*, Nat. Prod. Commun. **13** (3) (2018) 367-369. https://doi.org/10.1177/1934578X1801300324.
13. Gustafson K. R., Blunt J. W., Munro M. H. G., Fuller R. W., McKee T. C., Cardellina J. H., McMahon J. B., Cragg G. M. and Boyd M. R. - The guttiferones, HIV-inhibitory benzophenones from *Symphonia globulifera, Garcinia livingstonei, Garcinia ovalifolia* and *Clusia rosea*, Tetrahedron **48** (1992) 10093-10102. https://doi.org/10.1016/S0040-4020(01)89039-6.
14. Mann A., Ibrahim K., Oyewale A. O., Amupitan J. O., Fatope M. O. and Okogun J. I. - Antimycobacterial friedelane-terpenoid from the root bark of *Terminalia avicennioides*, Am. J. Chem. **1** (2011) 52-55. https://doi.org/10.5923/j.chemistry.20110102.11.
15. Garg B., Bisht T. and Ling Y. C. - Sulfonated graphene as highly efficient and reusable acid carbocatalyst for the synthesis of ester plasticizers, RCS Adv. **100** (4) (2014) 57297-57307. https://doi.org/10.1039/C4RA11205A.

16. Han Y. N., Choo Y., Lee Y. C., Moon Y. I., Kim S. D. and Choi J. W. - Monoamine oxidase B inhibitors from the fruits of *Opuntia ficus-indica* var. *saboten*, Arch. Pharm. Res. **24** (1) (2001) 51-54. https://doi.org/10.1007/BF02976493.
17. Hirota K., Kitagawa H., Shimamura M. and Ohmori S. - A facile preparation of *asym*-monomethyl, *sym*-monomethyl and *asym*-dimethyl citrate, Chem. Lett. **9** (1980) 191-194. https://doi.org/10.1246/cl.1980.191.