Vietnam Journal of Science and Technology ***58*** *(5) (2020) 517-525*

doi:10.15625/2525-2518/58/5/14712

PHENOLIC CONSTITUENTS FROM THE STEM BARKS OF *RHIZOPHORA APICULATA* BLUME

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Received: 19 December 2019; Accepted for publication 11 July 2020

Abstract. Using various chromatographic separations, seven phenolic derivatives (**1-7**) were isolated from a methanolic extract of the stem barks of *Rhizophora apiculata* Blume. Their structures were elucidated to be dunnianoside E (**1**), (+)-dihydroquercetin (**2**), 2,6-dimethoxy-[1,4]benzoquinone (**3**), 2,4,6-trimethoxyphenol (**4**), 3,4,5-trimethoxybenzyl alcohol (**5**), hydroxytyrosol (**6**), and methyl 3,4-dihydroxycinnamate (**7**) by a detailed analysis via spectroscopic techniques (1D-, 2D-NMR, and ESI-MS data) as well as comparison with those previously reported. This is the first report of compounds **1** and **4-7** from the *Rhizophora* genus.

Keywords: *Rhizophora apiculata*, Rhizophoraceae, phenolic.

Classification numbers: 1.1.1; 1.1.6.

1. INTRODUCTION

More than 84 species in 24 genera from 16 families of mangrove plants have been discovered across the world, which is composed of a large group of different salt-tolerant plants. These species are distributed worldwide, especially in tropical and subtropical intertidal estuarine areas [1, 2]. Of the recognized mangrove species, the family Rhizophoraceae constitutes a true mangrove, which contains 24 species in four genera, including *Bruguiera* (7 species), *Ceriops* (5 species), *Kandelia* (2 species), and *Rhizophora* (10 species) [1, 3]. In recent years, *Rhizophora* plants have attracted extensive scientific interests due to their chemical and pharmacological properties and proved to be a rich source of benzoquinones, flavonoids, terpenoids, and phenolic compounds [4 - 9].

Previous phytochemical investigations on *Rhizophora apiculata* Blume (synonym *R. candelaria* DC.) have resulted in the isolation of various classes of compounds including aliphatic alcohols [10], alkaloids [6, 11], flavonoids [6], phenolic derivatives [6], and terpenoids [5, 12, 13]. Some of these compounds have shown interesting biological properties including antibiotics [11], anticancer [4], antimicrobial [4], antioxidant [4, 14-17], antiviral [18], and hepatoprotective effects [19].

In our continuing search for phenolic compounds from the Vietnamese mangrove plants [20-22], the stem barks of *R. apiculata* were investigated on the chemical constituents. The current paper discusses the detailed structure elucidation of seven phenolic derivatives (**1**-**7**, Figure 1) from this plant.

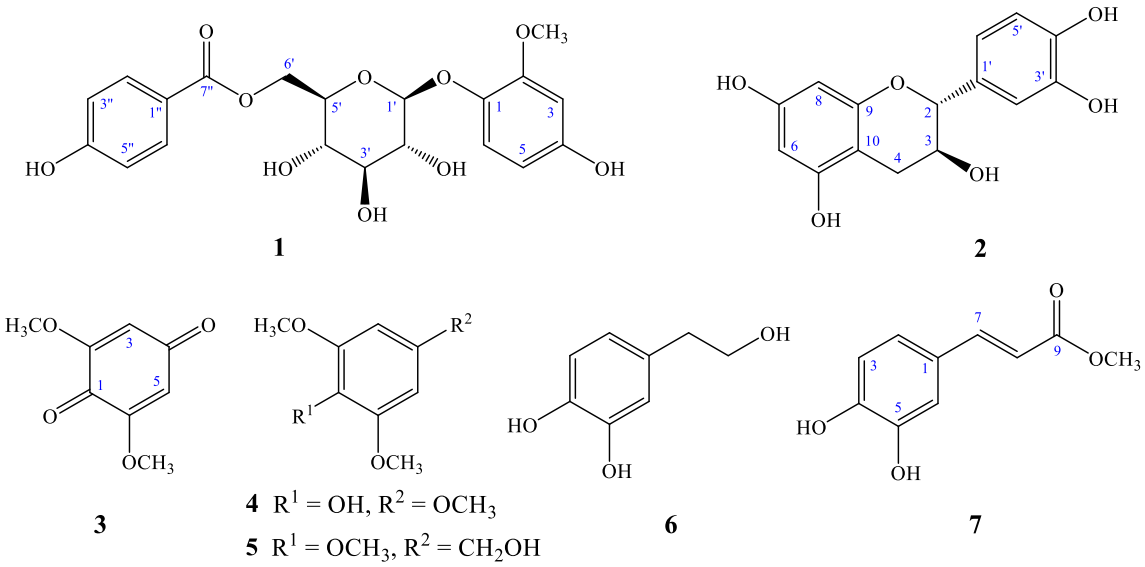

Figure 1. Structures of compounds **1**-**7** isolated from *R. apiculata*.

2. EXPERIMENTAL

2.1. General experimental procedures

The instruments used to isolate compounds, measure optical rotation, and record IR, NMR, ESI-MS data collection, TLC, and MPLC were carried out in a manner similar to procedures described in a previous paper [23].

2.2. Plant material

The stem barks of *Rhizophora apiculata* Blume were collected at Ca Mau National Park, Ca Mau province, Viet Nam in May 2018, and taxonomically identified by Dr. Nguyen The Cuong (Institute of Ecology and Biological Resources, VAST). A voucher specimen (TĐPCCC-2018.02) was deposited at the Herbarium of Institute of Marine Biochemistry (IMBC) and Institute of Ecology and Biological Resources, VAST.

2.3. Extraction and isolation

The dried stem barks of *R. apiculata* (2.5 kg) were cut into pieces and extracted with 95 % aqueous MeOH by percolation at room temperature to obtain 250 g of extract. The concentrated methanol extract was suspended in water and defatted with *n*-hexane and then was partitioned into an ethyl acetate-soluble fraction.

The EtOAc-soluble fraction (E, 21.5 g) was separated on silica gel MPLC (column: Biotage SNAP Cartridge, KP-SIL, 100 g) using a mobile phase of CH_2Cl_2-EtOAc (0 - 5 min 50 % EtOAc, 6 - 65 min 50 – 75 % EtOAc, 66 - 75 min 100 % EtOAc, 76 - 90 min 100 % MeOH, 15 mL/min, 90 min) to give ten fractions (E-1 to E-10). This MPLC procedure was repeated 5 times using the same conditions before further isolation. By TLC monitoring, fractions E-5 was further separated on a silica gel column chromatography (CC), using dichloromethane-acetone (10:1:1, v/v) as the mobile phase, to give four subfractions (E-5.1 to E-5.4). Precipitates from fraction E-5.1 eluted by dichloromethane-acetone (60:1) were collected, dissolved in MeOH, and purified on Sephadex LH-20 (eluted with MeOH) to yield **3** (5.5 mg) and **4** (10 mg). In a similar process to that described above, subfraction E-5.2 was chromatographed over an open ODS column eluted with acetone-water (2:3, 3:2, v/v) to give one subfraction E-1.2.1 and compounds **5** (2.1 mg) and **7** (2.5 mg). Similarly, subfraction E-8 was separated by separation on a Sephadex LH-20 column and was eluted with a gradient solvent mixture of MeOH-H_2O (gradient 1:3, 1:1, 2:1, 3:1, to pure MeOH) to yield three fractions (E-8.1 to E-8.3), based on TLC analysis. The fractionation W-8.2 was separated via silica gel CC and eluted repeatedly with *n*-hexane-acetone (1:1, v/v) to yield two subfractions (E-8.2a to E-8.2b). Subfraction E-8.2b was subjected to a silica gel CC (Φ20 mm, L800 mm with a solvent mixture of *n*-hexane-EtOAc, 1:1.2), and then an open YMC*GEL column (Φ15 mm, L800 mm, 65 → 100 %, H_2O-MeOH) to afford compound **6** (2.2 mg). Finally, when the same steps were repeated as per above, compounds **1** (3.6 mg) and **2** (6.5 mg) were also obtained by purifying subfraction E-10 on YMC*GEL column (Φ20 mm, L 700 mm) and followed by passage over a Sephadex LH-20 column (Φ15 mm, L900 mm) using a mixture of MeOH-H_2O (1:2).

Dunnianoside E (1): White, amorphous powder; $[\alpha]_D^{24}$ –22.6 (*c* 0.15, MeOH); UV (MeOH) λ_{max} (log ε) 204 (4.17) and 258 (3.87) nm; IR (KBr) ν_{max} 3350, 2943, 1680, 1610, 1521, 1458, 1334, 1290, 1205, 1167, 1086, 975, and 851 cm^{-1}; ^{1}H-NMR (500 MHz, CD_3OD) and ^{13}C-NMR (125 MHz, CD_3OD) spectroscopic data, see Table 1; ESI-MS *m/z* 423 $[M + H]^+$ ($C_{20}H_{23}O_{10}^+$) and 445 $[M + Na]^+$ ($C_{20}H_{22}NaO_{10}^+$), $C_{20}H_{22}O_{10}$, M = 422.

(+)-Dihydroquercetin (2): Yellow, amorphous solid; $[\alpha]_D^{24}$ +28.7 (*c* 0.15, MeOH); UV (MeOH) λ_{max} 277 nm; ^{1}H-NMR (500 MHz, CD_3OD) and ^{13}C-NMR (125 MHz, CD_3OD) spectroscopic data, see Table 2; ESI-MS *m/z* 291 $[M + H]^+$ ($C_{15}H_{15}O_6^+$), $C_{15}H_{14}O_6$, M = 290.

2,6-Dimethoxy-[1,4]benzoquinone (3): Yellow, amorphous powder; mp. 254 – 256 ^oC; IR (KBr) 1600, 1645, 1696, and 1320 cm^{-1}; ^{1}H-NMR (500 MHz, DMSO-d_6): δ_H 3.77 (6H, s, 2-OCH_3 and 6-OCH_3), and 5.94 (2H, s, H-3 and H-5); ^{13}C-NMR (125 MHz, DMSO-d_6): δ_C 186.3 (C-1), 157.0 (C-2 and C-6), 106.8 (C-3 and C-5), 175.7 (C-4), and 56.0 (2-OCH_3 and 6-OCH_3); $C_8H_8O_4$, M = 168.

2,4,6-Trimethoxyphenol (4): White, amorphous powder; mp. 62 – 64 ^oC; ^{1}H-NMR (500 MHz, CD_3OD): δ_H 3.69 (3H, s, 4-OCH_3), 3.78 (6H, s, 2-OCH_3 and 6-OCH_3), and 6.11 (2H, s, H-3 and H-5); ^{13}C-NMR (125 MHz, CD_3OD): δ_C 132.2 (C-1), 154.9 (C-2 and H-6), 94.01 (C-3 and H-5), 155.4 (C-4), 56.4 (2-OCH_3 and 6-OCH_3), and 61.3 (4-OCH_3); ESI-MS *m/z* 185 $[M + H]^+$ ($C_9H_{13}O_4^+$), $C_9H_{12}O_4$, M = 184.

3,4,5-Trimethoxybenzyl alcohol (5): White, amorphous powder; mp. 36 – 38 ^{o}C; UV (MeOH) λ_{max} 264 nm; IR (KBr) ν_{max} 3400, 2945, 1594, 1461, 1425, 1330, 1238, 1128, 1059, 1010, and 831 cm^{-1}; ^{1}H-NMR (500 MHz, CD_3OD): δ_H 3.84 (3H, s, 4-OCH_3), 3.87 (6H, s, 3-OCH_3 and 5-OCH_3), 4.64 (2H, s, H-7), and 6.61 (2H, s, H-2 and H-6); ^{13}C-NMR (125 MHz, CD_3OD): δ_C 136.6 (C-1), 103.9 (C-2 and C-6), 153.4 (C-3 and C-5), 137.5 (C-4), 65.0 (C-7), 56.1 (3-OCH_3 and 5-OCH_3), and 60.8 (4-OCH_3); ESI-MS *m/z* 197 $[M - H]^-$ ($C_{10}H_{13}O_4^-$), $C_{10}H_{14}O_4$, M = 198.

Hydroxytyrosol (6): Brown oil; IR (KBr) ν_{max} 3376, 2946, 1605, and 1448 cm^{-1}; ^{1}H-NMR (500 MHz, CD_3OD): δ_H 2.68 (2H, t, *J* = 7.0 Hz, H-7), 3.69 (2H, t, *J* = 7.0 Hz, H-8), 6.55 (1H, dd, *J* = 8.0, 2.0 Hz, H-6), 7.05 (1H, d, *J* = 2.0 Hz, H-2), and 7.56 (1H, d, *J* = 15.5 Hz, H-7); ^{13}C-NMR (125 MHz, CD_3OD): δ_C 131.8 (C-1), 117.0 (C-2), 144.6 (C-3), 146.1 (C-4), 116.3 (C-5), 121.2 (C-6), 39.6 (C-7), and 64.5 (C-8); ESI-MS *m/z* 155 $[M + H]^+$ ($C_8H_{11}O_3^+$), $C_8H_{10}O_3$, M = 154.

Methyl 3,4-dihydroxycinnamate (7): White, amorphous powder; mp. 158 ^{o}C; IR (KBr) ν_{max} 3500, 3450, 3320, 3019, 1705, 1258, and 1178 cm^{-1}; ^{1}H-NMR (500 MHz, CD_3OD): δ_H 3.77 (3H, s, 9-OCH_3), 6.27 (1H, d, *J* = 15.5 Hz, H-8), 6.80 (1H, d, *J* = 8.0 Hz, H-5), 6.96 (1H, dd, *J* = 8.0, 2.0 Hz, H-6), 7.05 (1H, d, *J* = 2.0 Hz, H-2), and 7.56 (1H, d, *J* = 15.5 Hz, H-7); ^{13}C-NMR (125 MHz, CD_3OD): δ_C 127.7 (C-1), 115.1 (C-2), 146.8 (C-3), 149.6 (C-4), 116.5 (C-5), 122.9 (C-6), 146.9 (C-7), 114.8 (C-8), 169.7 (C-9), and 51.9 (9-OCH_3); ESI-MS *m/z* 195 $[M + H]^+$ ($C_{10}H_{11}O_4^+$), $C_{10}H_{10}O_4$, M = 194.

3. RESULTS AND DISCUSSION

Compound **1** was obtained as a white, amorphous powder, with a negative optical rotation $[\alpha]_D^{24}$ - 22.6 (*c* 0.15, MeOH). Its molecular formula was found to be $C_{20}H_{22}O_{10}$ (10 indices of hydrogen deficiency) via the ^{13}C NMR spectroscopic data and positive ESI-MS ions at *m/z* 423 $[M + H]^+$ and 445 $[M + Na]^+$. The ^{1}H-NMR spectroscopic data showed three aromatic protons attributed to a 1,2,4-trisubsituted aromatic ring [δ_H 6.46 (1H, d, *J* = 2.5 Hz, H-3), 6.19 (1H, dd, *J* = 8.5, 2.5 Hz, H-5), and 6.97 (1H, d, *J* = 8.5 Hz, H-6), fragment A], two doublets assignable to a symmetrical 1,4 disubstituted aromatic ring [δ_H 7.88 (2H, d, *J* = 8.5 Hz, H-2" and H-6") and 6.86 (2H, d, *J* = 8.5 Hz, H-3" and H-5"), fragment B], an aromatic methoxy signal [δ_H 3.79 (3H, s, 3-OCH_3), together with one glucosidic moiety as evidenced by the presence of an anomeric proton signal [δ_H 4.73 (1H, d, *J* = 7.5 Hz, H-1')], and other proton signals [δ_H 3.50 (1H, dd, *J* = 9.0, 7.5 Hz, H-2'), 3.53 (1H, overlapped signal, H-3'), 3.46 (1H, overlapped signal, H-4'), 3.68 (1H, m, H-5'), 4.66 (1H, dd, *J* = 11.5, 2.0 Hz, H-6'a), and 4.35 (1H, dd, *J* = 11.5, 5.0 Hz, H-6'b) (Table 1). Moreover, the anomeric proton signal of H-1' was attributed to a *β*-glucosyl unit (a *trans*-diaxial configuration of H-1' and H-2') from the large coupling constant ($^3J_{1',2'}$ = 7.5 Hz).

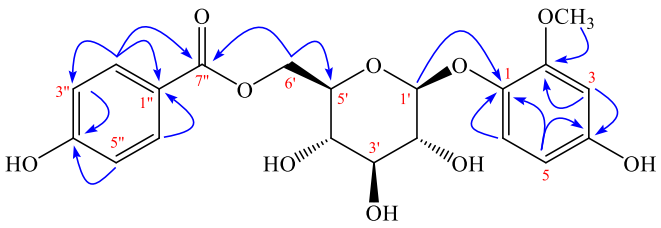

Figure 2. Key HMBC correlations of **1**.

Table 1. ^{1}H- and ^{13}C-NMR spectroscopic data for **1** and reference compound (in CD_3OD).

Position	$^{\#}\delta_C$	**1**	
		δ_C [a]	δ_H [b] mult. (*J* in Hz)
1	140.6	140.8	-
2	152.0	152.1	-
3	101.6	101.9	6.46 d (2.5)
4	154.9	154.9	-
5	107.0	107.5	6.19 dd (8.5, 2.5)
6	120.7	120.7	6.97 d (8.5)
1'	104.0	104.2	4.73 d (7.5)
2'	74.7	75.0	3.50 dd (9.0, 7.5)
3'	77.7	77.8	3.53*
4'	71.6	72.0	3.46*
5'	75.2	75.6	3.68 m
6'	64.6	64.9	4.66 dd (11.5, 2.0) 4.35 dd (11.5, 5.0)
1"	122.2	122.2	-
2", 6"	132.5	132.9	7.88 d (8.5)
3", 5"	116.1	116.2	6.86 d (8.5)
4"	163.0	163.5	-
7"	166.4	167.9	-
3-OCH_3	56.3	56.5	3.79 s

[a]125 MHz, [b]500MHz. *Overlapped signals. $^{\#}\delta_C$ of dunnianoside E [24]. Assignments were confirmed by HMQC and HMBC experiments.

The ^{13}C-NMR and HSQC spectroscopic data of **1** revealed the presence of 20 carbon signals, including a carbonyl (δ_C 167.9), a methoxyl group (δ_C 56.5), and 12 aromatic carbon atoms, as well as signals from one glycoside moiety [δ_C 104.2 (C-1'), 75.0 (C-2'), 77.8 (C-3'), 72.0 (C-4'), 75.6 (C-5'), and 64.9 (C-6')] (Table 1). The sugar moiety was confirmed as *β*-D-glucose, which was linked to the aglycone at C-1 (fragment A) and C-7' (fragment B) positions in **1**. This relationship was supported by the HMBC experiments, in which correlations were observed for the resonances between δ_H 4.73 (H-1')/4.66/4.35 (H-6') with the signals of C-1 (δ_C 140.8) and C-7' (δ_C 167.9). On the other hand, the locations of two hydroxyl groups and a methoxyl group were assigned to C-4, C-4", and C-2 by the HMBC correlations between δ_H 6.46 (H-3)/6.19 (H-5) and δ_C 154.9 (C-4); δ_H 6.86 (H-3"/H-5") and δ_C 163.5 (C-4"), as well as between δ_H 3.79 (OCH_3), 6.46 (H-3), and 6.97 (H-6) with C-2 (δ_C 152.1), respectively (Figure 2). These spectroscopic data suggested that **1** is a phenolic glycoside which indicated the presence of a glucosyl unit, a 2-methoxyl,4-hydroxyphenyl, and a 4-hydroxybenzoyl moiety [24].

By comparing the NMR spectroscopic data of **1** with reported literature which found that they were similar, it was suggested that **1** was dunnianoside E [24] (Table 1). Furthermore, the ESI-MS data of **1** exhibited a protonated molecular ion peak at *m/z* 423 $[M + H]^+$ and a sodium adduct molecular ion peak at *m/z* 445 $[M + Na]^+$, determining the molecular formula of $C_{20}H_{22}O_{10}$. From the above evidence, the structure of **1** was determined as 4-hydroxy-2-methoxylphenyl 1-*O*-*β*-D-[6'-O-(*p*-hydroxybenzoyl)]glucopyranoside (named dunnianoside E). This compound was previously obtained from the roots of *Illicium dunnianum* [24].

Compound **2** was isolated as a yellow, amorphous solid. Its molecular formula was determined to be $C_{15}H_{14}O_6$ based on a protonated molecular ion peak at *m/z* 291 $[M + H]^+$ and ^{13}C-NMR spectroscopic data, consistent with nine degrees of unsaturation. Analysis of the ^{1}H-,

Table 2. ^{1}H- and ^{13}C-NMR spectroscopic data for **2** (in CD_3OD) and reference compound.

Position	$^{\$}\delta_C$	$^{\#}\delta_C$	**2**	
			δ_C [a]	δ_H [b] mult. (*J* in Hz)
2	80.0	83.0	82.8	4.59 d (7.5)
3	67.7	69.0	68.7	4.00 m
4	29.4	28.7	28.4	2.87 dd (16.5, 5.5) 2.53 dd (16.5, 8.0)
5	157.9	157.7	157.7	-
6	96.0	96.4	96.3	5.95 d (1.5)
7	158.2	158.0	157.2	-
8	96.5	95.6	95.5	5.88 d (1.5)
9	157.9	157.1	156.8	-
10	100.2	100.9	100.8	-
1'	132.5	132.4	132.2	-
2'	115.5	115.4	115.2	6.86 d (2.0)
3'	146.1	146.4	146.1	-
4'	146.0	146.4	146.2	-
5'	116.0	116.2	116.1	6.77 d (8.0)
6'	119.5	120.2	120.0	6.75 dd (8.0, 2.0)

[a]125 MHz. [b]500MHz. $^{\#}\delta_C$ of (+)-catechin [25] and $^{\$}\delta_C$ of (−)-epicatechin [25]. Assignments were confirmed by HMQC and HMBC experiments.

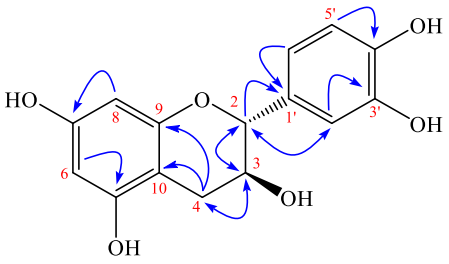

Figure 3. Key HMBC correlations of **2**.

^{13}C-NMR, and HSQC spectroscopic data of **2** displayed signals for all 15 carbons and 14 protons, suggesting the presence of the following partial structures: an AB spin system appearing as two doublet signals [δ_H 5.95 (1H, d, *J* = 1.5 Hz, H-6)/δ_C 96.3 (C-6) and 5.88 (1H, d, *J* = 1.5 Hz, H-8)/δ_C 95.5 (C-8)], typical of a *meta*-dihydroxylated A-ring; an ABX spin system [δ_H 6.86 (1H, d, *J* = 2.0 Hz, H-2')/δ_C 115.2 (C-2'), 6.77 (1H, d, *J* = 8.0 Hz, H-5')/δ_C 116.1 (C-5'), and 6.75 (1H, dd, *J* = 8.0, 2.0 Hz, H-6')/δ_C 120.0 (C-6')], characteristic of a 3,4-dihydroxylated B-ring, along with the occurrence of a flavan-3-ol skeleton in the molecule could be determined from the characteristic signals at δ_H 4.59 (1H, d, *J* = 7.5 Hz, H-2)/δ_C 82.8 (C-2), 4.00 (1H, m, H-3)/δ_C 68.7 (C-3), and 2.87 (1H, dd, *J* = 16.5, 5.5 Hz, H-4a), 2.53 (1H, dd, *J* = 16.5, 8.0 Hz, H-4b)/δ_C 28.4 (C-4)] (Table 2). Furthermore, a large coupling constant of H-2 and H-3 ($J_{2,3}$ = 7.5 Hz) and on the basis of the optical rotation ($[\alpha]_D^{24}$ +28.7), confirmed a 2,3-*trans* configuration in **2** [25, 26]. Based on the above analysis, the relative configuration was assigned for **2**. The comparison NMR spectroscopic data of **2** (Table 2) were similar to those of (+)-dihydroquercetin [25]. Detailed analysis of other HMBC correlations (Figure 3) confirmed the structure of **2** as (+)-dihydroquercetin (named (+)-catechin). Compound **2** was previously isolated from the stems and twigs of *R. stylosa* [27].

Based on the spectroscopic analysis and comparison with literature values, the remaining compounds were identified as 2,6-dimethoxy-[1,4]benzoquinone (**3**) [28], 2,4,6-trimethoxyphenol (**4**) [29], 3,4,5-trimethoxybenzyl alcohol (**5**) [30], hydroxytyrosol (**6**) [31], and methyl 3,4-dihydroxycinnamate (7) [32].

4. CONCLUSIONS

Seven phenolic compounds, including dunnianoside E (**1**), (+)-dihydroquercetin (**2**), 2,6-dimethoxy-1,4-benzoquinone (**3**), 2,4,6-trimethoxyphenol (**4**), 3,4,5-trimethoxybenzyl alcohol (**5**), hydroxytyrosol (**6**), and methyl 3,4-dihydroxycinnamate (**7**), were isolated from a methanolic extract of *Rhizophora apiculata* stem barks. This is the first report of phenolic derivatives **1** and **4-7** from the *Rhizophora* genus. The structures of these isolates were accomplished using comprehensive spectroscopic methods and comparison with those reported.

Acknowledgments. This research is funded by a grant from the Vietnam Academy of Science and Technology (code: TĐPCCC.04/18-20). The authors are grateful to MSc. Dang Vu Luong (Institute of Chemistry, VAST) for measurement of the NMR spectra and Dr. Nguyen The Cuong (Institute of Ecology and Biological Resources, VAST) for taxonomic classification of plant.

REFERENCES

1. Wu J., Xiao Q., Xu J., Li M. Y., Pana J. Y., Yang M. H. - Natural products from true mangrove flora: source, chemistry and bioactivities, Natural Product Reports **25** (2008) 955-981.
2. Chen Y., Hou Y., Guo Z., WenqingWang, Zhong C., Zhou R., Shi S. - Applications of multiple nuclear genes to the molecular phylogeny, population genetics and hybrid identification in the mangrove genus *Rhizophora*, Plos One (2015) e0145058.
3. Nebula M., Harisankar H. S., Chandramohanakumar N. - Metabolites and bioactivities of Rhizophoraceae mangroves, Natural Products and Bioprospecting **3** (2013) 207-232.
4. V. Ramalingam, R. Rajaram - Enhanced antimicrobial, antioxidant and anticancer activity of *Rhizophora apiculata*: an experimental report, Biotech **8** (2018) 1-13.
5. Gao M. Z., Yuan X. Y., Cheng M. C., Xiao H. B., Bao S. X. - A new diterpenoid from *Rhizophora apiculata*, Journal of Asian Natural Products Research **13** (2011) 776-779.
6. Selvaraj G., Kaliamurthi S., Thirugnasambandan R. - Effect of glycosin alkaloid from *Rhizophora apiculata* in non-insulin dependent diabetic rats and their mechanism of action: *in vivo* and *in silico* studies, Phytomedicine **23** (2016) 632-640.
7. Rahima A. A., Rocca E., Steinmetz J., Kassima M. J., Ibrahima M. S., Osman H. - Antioxidant activities of mangrove *Rhizophora apiculata* bark extracts, Food Chemistry **107** (2008) 200-207.
8. Huong P. T. T., Thanh N. V., Diep C. N., Thao N. P., Cuong N. T., Cuong N. X., Nam N. H., Minh C. V. - Antimicrobial compounds from *Rhizophora stylosa*, Vietnam Journal of Science and Technology **53** (2015) 205-210.
9. Huong P. T. T., Thanh N. V., Diep C. N., Cuong N. T., Cuong N. X., Nam N. H., Thai T. H., Kiem P. V., Minh C. V. - Five lignans from the mangrove *Rhizophora stylosa* Griff, Vietnam Journal of Chemistry **53** (2015) 42-47.

10. Kokpol U., Chavasiri W., Chittawong V., Bruce M., Cunningham G. N., Miles D. H. - Long chain aliphatic alcohols and saturated carboxylic acids from heartwood of *Rhizophora apiculata*, Phytochemistry **33** (1993) 1129-1131.
11. Moovendhan M., Ramasubburayan R., Vairamani S., Shanmugam A., Palavesam A., Immanuel G. - Antibiotic susceptibility of genistein and alkaloids from *Rhizophora apiculata*, Biocatalysis and Agricultural Biotechnology **3** (2014) 323-327.
12. Saxena E., Garg H. S. - Apiculol, 1β-hydroxy-13-epimanoyl oxide from roots of *Rhizophora apiculata* mangrove, Natural Product Letters **4** (1994) 149-154.
13. Kokpol U., Chavasiri W., Chittawong V., Miles D. H. - Taraxeryl *cis*-p-hydroxycinnamate, a novel taraxeryl from *Rhizophora apiculata*, Journal of Natural Products **53** (1990) 953-955.
14. Loo A. Y., Jain K., Darah I. - Antioxidant activity of compounds isolated from the pyroligneous acid, *Rhizophora apiculata*, Food Chemistry **107** (2008) 1151-1160.
15. Gao M., Xiao H. - Activity-guided isolation of antioxidant compounds from *Rhizophora apiculat*a. Molecules **17** (2012) 10675-10682.
16. Rahim A. A., Rocca E., Steinmetz J., Kassim M. J., Ibrahim M. S., Osman H. - Antioxidant activities of mangrove *Rhizophora apiculata* bark extracts, Food Chemistry **107** (2008) 200-207.
17. Vijayavel K., Anbuselvam C., Balasubramanian M. P. - Free radical scavenging activity of the marine mangrove *Rhizophora apiculata* bark extract with reference to naphthalene induced mitochondrial dysfunction, Chemico-Biological Interactions **163** (2006) 170-175.
18. Premanathan M., Arakaki R., Izumi H., Kathiresan K., Nakano M., Yamamoto N., Nakashima H. - Antiviral properties of a mangrove plant, *Rhizophora apiculata* Blume, against human immunodeficiency virus, Antiviral Research **44** (1999) 113-112.
19. Zhang H., Jacob J. A., Jiang Z., Xu S., Sun K., Zhong Z., Varadharaju N., Shanmugam A. - Hepatoprotective effect of silver nanoparticles synthesized using aqueous leaf extract of *Rhizophora apiculata*, International Journal of Nanomedicine **14** (2019) 3517-3524.
20. Dat L. D., Thao N. P., Tai B. H., Luyen B. T. T., Kim S., Koo J. E., Koh Y. S., Cuong N. T., Thanh N. V., Cuong N. X., Nam N. H., Kiem P. V., Minh C. V., Kim Y. H. - Chemical constituents from *Kandelia candel* with their inhibitory effects on pro-inflammatory cytokines production in LPS-stimulated bone marrow-derived dendritic cells (BMDCs), Bioorganic & Medicinal Chemistry Letters **25** (2015) 1412-1416.
21. Dat L. D., Thao N. P., Tai B. H., Luyen B. T. T., Yang S. Y., Kim S., Koo J. E., Koh Y. S., Cuong N. T., Nam N. H., Thanh N. V., Kiem P. V., Minh C. V., Kim Y. H. - Anti-inflammatory triterpenes and glyceryl glycosides from *Kandelia candel* (L.) Druce, Natural Product Sciences **21** (2015) 150-154.
22. Vinh L. B., Nguyet N. T. M., Thanh C. D., Huong T. T., Tram L. H., Thong N. V., Minh N. H., Thao N. P., Hwang I., Yang S. Y., Kim Y. H. - Chemical constituents of Vietnamese mangrove *Hibiscus tiliaceus* with antioxidant and alpha-glucosidase inhibitory activity, Natural Product Research (2019)

    https://doi.org/10.1080/14786419.14782019.11672065.
23. Luyen N. T., Binh P. T., Tham P. T., Hung T. M., Dang N. H., Dat N. T., Thao N. P. - Wedtrilosides A and B, two new diterpenoid glycosides from the leaves of *Wedelia*

trilobata (L.) Hitchc. with α-amylase and α-glucosidase inhibitory activities, Bioorganic Chemistry **85** (2019) 319-324.

24. Bai J., Fang Z. F., Chen H., Yu S. S., Zhang D., Wei H. L., Ma S. G., Li Y., Qu J., Xu S., Ren J. H., Zhao F., Zhao N., Liu J. H. - Antioxidant phenolic glycosides from the roots of *Illicium dunnianum*, Carbohydrate Research **361** (2012) 206-211.
25. Choi J., Cho J. Y., Kim Y. D., Htwe K. M., Lee W. S., Lee J. C., Kim J., Yoon K. D. - Phenolic compounds and triterpenes from the barks of *Diospyros burmanica*, Natural Product Sciences **21** (2015) 76-81.
26. Slade D., Ferreira D., Marais J. P. J. - Circular dichroism, a powerful tool for the assessment of absolute configuration of flavonoids, Phytochemistry **66** (2005) 2177-2215.
27. Li D. L., Li X. M., Peng Z. Y., Wang B. G. - Flavanol derivatives from *Rhizophora stylosa* and their DPPH radical scavenging activity, Molecules **12** (2007) 1163-1169.
28. Kim Y. S., Chang H. M., Kadla J. F. - Polyoxometalate (POM) oxidation of lignin model compounds. Holzforschung **62** (2008) 38-49.
29. Parmar V. S., Gupta S., Bisht K. S., Mukherjee S., Boll P. M., Errington W. - Synthesis and X-ray structure of 2-(3-methyl-2-butenyl)-3,4,5-trimethoxyphenol: a potent anti-invasive agent against solid tumours, Acta Chemical Scandinavica **50** (1996) 558-560.
30. Baumert M., Albrecht M., Winkler H. D. F., Schalley C. A. - Tuning the polarity of hierarchically assembled helicates, Synthesis **6** (2010) 953-958.
31. Park C. H., Kim K. H., Lee I. K., Lee S. Y., Choi S. U., Lee J. H., Lee K. R. - Phenolic constituents of *Acorus gramineus*, Archives of Pharmacal Research **34** (2011) 1289-1290.
32. Zhu Y., Zhang L. X., Zhao Y., Huang G. D. - Unusual sesquiterpene lactones with a new carbon skeleton and new acetylenes from *Ajania przewalskii*, Food Chemistry **118** (2010) 228-238.