

SECONDARY METABOLITES FROM THE STEM BARKS OF *RHIZOPHORA MUCRONATA* LAM.

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Abstract. Using various chromatographic separations, three phenolic derivatives (**1–3**) and three phytosteryl glycosides (**4–6**) were isolated from a methanolic extract of *R. mucronata* Lam. stem barks. Their structures were elucidated to be cinchonain Ib (**1**), breynioside B (**2**), polystachyol (**3**), β -sitosterol 3-*O*- β -D-glucopyranoside (**4**), β -sitosterol 3-*O*- β -D-(6'-*O*-palmitoyl)glucopyranoside (**5**), and β -sitosterol 3-*O*- β -D-(6'-*O*-stearoyl)glucopyranoside (**6**) by detailed analysis *via* spectroscopic techniques (1D, 2D NMR, and ESI-MS data) as well as comparison with those reported. This is the first report of compounds **1–6** from the *Rhizophora* genus.

Keywords: *Rhizophora mucronata*, Rhizophoraceae, phenolic, phytosteryl glycoside.

Classification numbers: 1.1.1; 1.1.6.

1. INTRODUCTION

To date, more than 84 species belonging to 24 genera and 16 families of mangrove plants have been discovered across the world, which composed of a large group of different salt-tolerant plants [1, 2]. Among them, the family Rhizophoraceae belongs to a true mangrove family, 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 in the chemical and pharmacological properties [4 - 7].

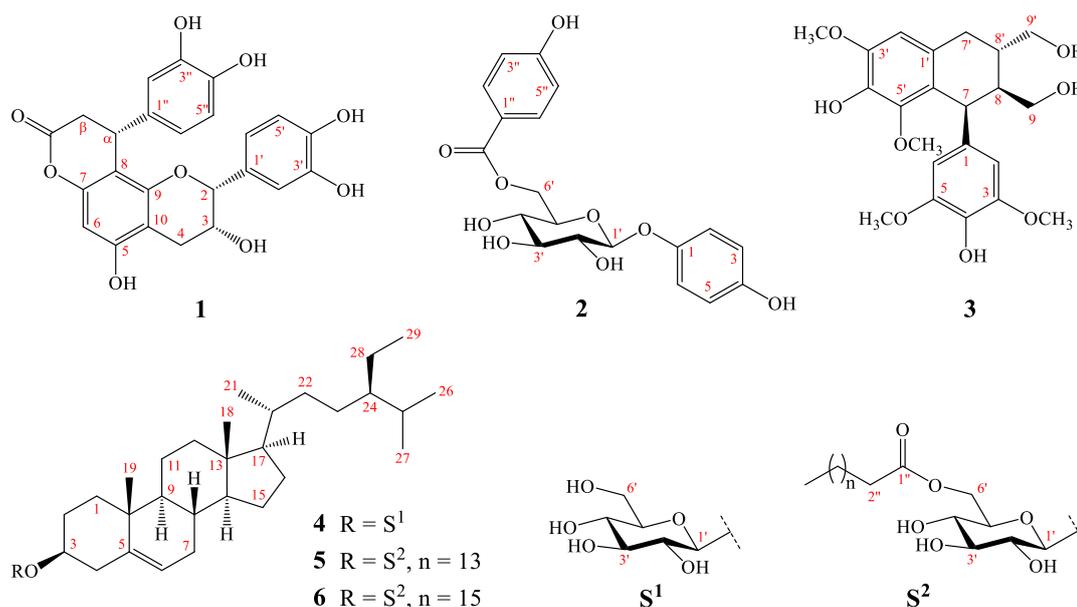


Figure 1. Structures of compounds 1–6 isolated from *R. mucronata*.

The true mangrove, *Rhizophora mucronata* Lam. is widely distributed in Southeast Asia along the coastlines of the Indian Ocean [8, 9]. This plant is used as a folk medicine in Southeast Asia to treat angina, constipation, diabetes, diarrhea, dysentery, haematuria, hemorrhage, nausea, and leprosy [10, 11]. Interestingly, the extracts and fractions of the leaves, fruits, and barks of this plant were reported to exhibit significant *in vitro* α -amylase and α -glucosidase inhibitory [12, 13], anti-arthritic [14], antibacterial [15 - 17], antidiabetic [18, 19], anti-inflammatory [14, 20, 21], anti-gastric cancer [22, 23], antihyperglycemic [24], and antioxidant [16, 18, 25 - 28] effects. According to previous phytochemical studies, besides being the source of tannins (up to 70 %) [18, 29], alkaloids [16, 21], phenolics [9], polysaccharides [30], and terpenoids [8, 22, 23, 31 - 34] have been reported from *R. mucronata*.

In our continuing search for secondary metabolites from the Vietnamese mangrove plants [35 - 37], an EtOAc fraction of *R. mucronata* stem barks was investigated on the chemical constituents. The current paper deals with detailed structure elucidation of six compounds (1-6, Figure 1) from this plant.

2. EXPERIMENTAL

2.1. General experimental procedures

The procedure and instruments used correspondingly to isolate compounds, measure optical rotation, and record Infra Red (IR), Nuclear Magnetic Resonance (NMR), Mass Spectroscopy (ESI-MS) data collection, TLC, and MPLC are similar to those described in a previous paper [38].

2.2. Plant material

The stem barks of *Rhizophora mucronata* Lam. 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-2018.03) was deposited at the Herbarium of Institute of Marine Biochemistry and Institute of Ecology and Biological Resources, VAST.

2.3. Extraction and isolation

The dried stem barks of *R. mucronata* (2.5 kg) were cut into pieces and extracted with 95 % aqueous MeOH by percolation at room temperature to obtain 210 g of extract. The concentrated methanol extract was suspended in water and defatted with *n*-hexane and then was partitioned into ethyl acetate-soluble fraction.

The EtOAc fraction (E, 60 g) was separated on silica gel MPLC (column: Biotage SNAP Cartridge, KP-SIL, 100 g) using the mobile phase of CH₂Cl₂-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, fraction E-6 was further separated on a silica gel column chromatography (CC), using CH₂Cl₂-MeOH (3.5 L, 50:1, 25:1, v/v) as the mobile phase, to give four subfractions (E-6.1 to E-6.4). Fractions E-6.1 and E-6.2 were combined (105 mg) and fractionated over Sephadex LH-20 (eluted with MeOH, 2.5 L) to give three subfractions (E-6.2a to E-6.2c). Compounds **3** (4.6 mg) and **5** (3.9 mg) were obtained from subfraction E-6.2b and compound **6** (5.5 mg) was obtained from subfraction E-6.2c by a silica gel CC (2L of CH₂Cl₂-MeOH, 4:1) and then by a Sephadex LH-20 column (1.5 L of CH₂Cl₂-MeOH, 1:3). In a similar process to that described above, fraction E-7 (1.05 g) was chromatographed over an open YMC*GEL column eluted with MeOH-H₂O (2.5L, 1 : 3, 1 : 2, v/v) to give subfraction E-7.1 and compound **4** (5.9 mg). Similarly, fraction E-10 was separated by a Sephadex LH-20 column and was eluted with a gradient solvent mixture of MeOH-H₂O (stepwise gradient 1 : 3, 1 : 1, 13 : 7, 3 : 1, MeOH, 4L) to yield five subfractions (E-10.1 to E-10.5), based on TLC analysis. Subfraction E-10.1 (180 mg) was separated *via* silica gel CC and eluted with EtOAc-MeOH (25:1, v/v) to yield three subfractions (E-10.1a to E-10.1c). Subfraction E-10.1b was subjected to 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 %, H₂O-MeOH) to afford compound **1** (10.7 mg). Finally, when the same steps were repeated as above, compound **2** (2.1 mg) was obtained by purifying subfraction E-10.3 on YMC*GEL column (Φ20 mm, L700 mm) and followed by passing a Sephadex LH-20 column (Φ15 mm, L900 mm) using a mixture of MeOH-H₂O (1.5L, 1:2).

Cinchonain Ib (1): Dark yellow, amorphous powder; $[\alpha]_D^{24} -19.6$ (*c* 0.15, MeOH); UV (MeOH) λ_{\max} (log ϵ) 214 (4.67), 283 (3.98), and 335 (3.39) nm; IR (KBr) ν_{\max} 3361, 1746, 1612, 1521, 1447, 1361, and 1199 cm⁻¹; ¹H NMR (500 MHz, CD₃OD) and ¹³C NMR (125 MHz, CD₃OD) spectroscopic data, see Table 1; ESI-MS *m/z* 453 [M + H]⁺ (C₂₄H₂₁O₉⁺) and 475 [M + Na]⁺ (C₂₄H₂₀NaO₉⁺), C₂₄H₂₀O₉, M = 452.

Breynioside A (2): Colorless needles; mp. 245 - 246 °C; $[\alpha]_D^{24} -21.5$ (*c* 0.15, MeOH); UV (MeOH) λ_{\max} (log ϵ) 216 (3.94), 258 (4.04) nm; IR (KBr) ν_{\max} 3370, 1698, 1605, 1510, 1280, 1210, and 1048 cm⁻¹; ¹H NMR (500 MHz, CD₃OD) and ¹³C NMR (125 MHz, CD₃OD) spectroscopic data, see Table 2; ESI-MS *m/z* 391 [M - H]⁻ (C₁₉H₁₉O₉⁻), C₁₉H₂₀O₉, M = 392.

Polystachyol (3): White, amorphous powder; UV λ_{\max} (MeOH) (log ϵ): 230 (4.02) and 276 (3.47) nm; IR(KBr) ν_{\max} 3393, 1695, 1605, 1517, 1504, 1368, 1464, 1221, and 1116 cm⁻¹; ¹H

NMR (500 MHz, CD₃OD): δ_{H} 6.40 (2H, br s, H-2/H-6), 4.33 (1H, d, $J = 5.5$ Hz, H-7), 1.99 (1H, m, H-8), 3.51 (2H, m, H-9), 6.60 (1H, br s, H-2'), 2.58 (1H, dd, $J = 15.5, 11.0$ Hz, H-7'a), 2.71 (1H, dd, $J = 15.5, 5.0$ Hz, H-7'b), 1.65 (1H, m, H-8'), 3.52 (1H, dd, $J = 11.0, 5.5$ Hz, H-9'a), 3.61 (1H, dd, $J = 11.0, 7.0$ Hz, H-9'b), 3.75 (6H, s, 3,5-OCH₃), 3.88 (3H, s, 3'-OCH₃), and 3.40 (3H, s, 5'-OCH₃); ¹³C NMR (125 MHz, CD₃OD): δ_{C} 139.3 (C-1), 106.9 (C-2/C-6), 149.0 (C-3/C-5), 134.5 (C-4), 42.3 (C-7), 49.3 (C-8), 64.2 (C-9), 130.2 (C-1'), 107.8 (C-2'), 148.7 (C-3'), 138.9 (C-4'), 147.7 (C-5'), 126.2 (C-6'), 33.5 (C-7'), 40.9 (C-8'), 66.8 (C-9'), 56.7 (3,5-OCH₃), 56.5 (3'-OCH₃), and 60.1 (5'-OCH₃); ESI-MS m/z 421 [M + H]⁺ (C₂₂H₂₉O₈⁺), C₂₂H₂₈O₈, M = 420.

β -Sitosterol 3-O- β -D-glucopyranoside (4): White, amorphous powder; mp. 284 - 285 °C; $[\alpha]_{\text{D}}^{24} - 29.7$ (c 0.20, MeOH); UV (MeOH) λ_{max} 200 and 192 nm; IR (KBr) ν_{max} 3401 - 3415, 2914, 2875, 1340-1465, and 1021-1160 cm⁻¹; ¹H NMR (500 MHz, pyridine-*d*₅): δ_{H} 0.91 (1H, m, H-1a), 1.68 (1H, m, H-1b), 1.71 (1H, m, H-2a), 2.11 (1H, m, H-2b), 3.94 (1H, m, H-3), 2.41 (1H, m, H-4a), 2.69 (1H, m, H-4b), 5.35 (1H, t, $J = 2.5$ Hz, H-6), 1.31 (1H, m, H-7a), 1.46 (1H, m, H-7b), 1.32 (1H, m, H-8), 0.82 (1H, m, H-9), 1.38 (2H, overlapped signals, H-11), 1.09 (1H, m, H-12a), 1.92 (1H, m, H-12b), 0.89 (1H, m, H-14), 0.99 (1H, m, H-15a), 1.49 (1H, m, H-15b), 1.20 (1H, m, H-16a), 1.79 (1H, m, H-16b), 1.06 (1H, m, H-17), 0.61 (3H, s, H-18), 0.89 (3H, s, H-19), 1.31 (1H, m, H-20), 0.93 (3H, d, $J = 6.5$ Hz, H-21), 1.01 (1H, m, H-22a), 1.32 (1H, m, H-22b), 1.19 (2H, overlapped signals, H-23), 0.92 (1H, m, H-24), 1.60 (1H, m, H-25), 0.84 (3H, d, $J = 7.0$ Hz, H-26), 0.87 (3H, d, $J = 7.0$ Hz, H-27), 1.22 (2H, overlapped signals, H-28), 0.81 (3H, t, $J = 7.5$ Hz, H-29); *Glc*: 4.95 (1H, d, $J = 7.5$ Hz, H-1'), 3.98 (1H, dd, $J = 9.0, 7.5$ Hz, H-2'), 4.23 (1H, t, $J = 9.0$ Hz, H-3'), 3.34 (1H, t, $J = 9.0$ Hz, H-4'), 4.21 (1H, m, H-5'), 4.27 (1H, dd, $J = 12.0, 5.0$ Hz, H-6'a), and 4.58 (1H, dd, $J = 12.0, 2.0$ Hz, H-6'b); ¹³C NMR (125 MHz, pyridine-*d*₅): δ_{C} 37.3 (C-1), 29.9 (C-2), 78.2 (C-3), 39.1 (C-4), 140.7 (C-5), 121.7 (C-6), 31.8 (C-7), 31.9 (C-8), 50.1 (C-9), 36.1 (C-10), 21.0 (C-11), 39.7 (C-12), 42.3 (C-13), 56.6 (C-14), 24.3 (C-15), 28.3 (C-16), 56.0 (C-17), 11.7 (C-18), 19.2 (C-19), 36.7 (C-20), 19.0 (C-21), 33.9 (C-22), 26.1 (C-23), 45.8 (C-24), 29.3 (C-25), 18.8 (C-26), 19.7 (C-27), 23.2 (C-28), 11.9 (C-29); *Glc*: 102.2 (C-1'), 74.8 (C-2'), 78.0 (C-3'), 71.3 (C-4'), 77.9 (C-5'), and 62.3 (C-6'); ESI-MS m/z 575 [M - H]⁻ (C₃₅H₅₉O₆⁻), C₃₅H₆₀O₆, M = 576.

β -Sitosterol 3-O- β -D-(6'-O-palmitoyl)glucopyranoside (5): White, amorphous powder; mp. 168 - 170 °C; $[\alpha]_{\text{D}}^{24} - 32.3$ (c 0.25, MeOH); IR (KBr) ν_{max} 3401 - 3410, 2985 - 2914, 2852, 1739, 1170, and 1022 cm⁻¹; ¹H NMR (500 MHz, CDCl₃): δ_{H} 1.06 (1H, m, H-1a), 1.84 (1H, m, H-1b), 1.29 (1H, overlapped signal, H-2), 3.56 (1H, m, H-3), 2.27 (1H, m, H-4a), 2.34 (1H, m, H-4b), 5.35 (1H, d, $J = 5.0$ Hz, H-6), 1.93 (1H, m, H-7a), 1.24 (1H, m, H-7b), 1.26 (1H, m, H-8), 0.89 (1H, m, H-9), 1.48 (2H, overlapped signals, H-11), 1.17 (1H, m, H-12a), 2.01 (1H, m, H-12b), 0.98 (1H, m, H-14), 1.38 (1H, m, H-15a), 1.59 (1H, m, H-15b), 1.27 (1H, m, H-16a), 1.83 (1H, m, H-16b), 1.15 (1H, m, H-17), 0.68 (3H, s, H-18), 1.00 (3H, s, H-19), 1.38 (1H, m, H-20), 0.91 (3H, d, $J = 6.5$ Hz, H-21), 1.02 (1H, m, H-22a), 1.36 (1H, m, H-22b), 1.57 (2H, overlapped signals, H-23), 0.91 (1H, m, H-24), 1.23 (1H, overlapped signal, H-25), 0.87 (3H, d, $J = 7.0$ Hz, H-26), 0.86 (3H, d, $J = 7.0$ Hz, H-27), 1.29 (2H, overlapped signals, H-28), 0.84 (3H, t, $J = 7.5$ Hz, H-29); *3-Glc*: 4.38 (1H, d, $J = 7.5$ Hz, H-1'), 3.40 (1H, dd, $J = 9.0, 7.5$ Hz, H-2'), 3.58 (1H, t, $J = 9.0$ Hz, H-3'), 3.34 (1H, t, $J = 9.0$ Hz, H-4'), 3.46 (1H, m, H-5'), 4.45 (1H, dd, $J = 12.0, 5.0$ Hz, H-6'a), and 4.26 (1H, dd, $J = 12.0, 2.0$ Hz, H-6'b); *6'-Palmitoyl*: 2.37 (2H, t, $J = 7.5$ Hz, H-2''), 1.62 (2H, overlapped signals, H-3''), 1.20 - 1.38 (overlapped signals, H-4'' - H-14''), 1.28 (2H, overlapped signals, H-15''), 0.85 (3H, t, $J = 7.0$ Hz, H-16''); ¹³C NMR (125 MHz, CDCl₃): δ_{C} 37.2 (C-1), 29.6 (C-2), 79.6 (C-3), 38.9 (C-4), 140.3 (C-5), 122.1 (C-6), 31.9 (C-7), 31.9 (C-8), 50.2 (C-9), 36.1 (C-10), 21.0 (C-11), 39.7 (C-12), 42.3 (C-13), 56.7 (C-14), 24.3 (C-15), 28.2 (C-16), 56.1 (C-17), 11.8 (C-18), 19.3 (C-19), 36.7 (C-20), 19.0 (C-21), 33.9 (C-22), 26.1 (C-

23), 45.8 (C-24), 29.1 (C-25), 18.8 (C-26), 19.8 (C-27), 23.0 (C-28), 11.9 (C-29); 3-*Glc*: 101.2 (C-1'), 73.5 (C-2'), 76.0 (C-3'), 70.1 (C-4'), 73.9 (C-5'), 63.2 (C-6'); 6'-*Palmitoyl*: 174.5 (C-1''), 34.2 (C-2''), 24.9 (C-3''), 29.2 - 29.7 (C-4'' - C-14''), 22.6 (C-15''), and 14.1 (C-16''); ESI-MS m/z 837 [M + Na]⁺ (C₅₁H₉₀NaO₇)⁺, 574 [M - C₁₆H₃₂O]⁺, 414 [M - palmitoyl - glucosyl]⁺, 397 [M - C₂₂H₄₁O₇]⁺, and 240 [M - C₃₆H₆₂O₅]⁺; C₅₁H₉₀O₇, M = 814.

β-Sitosterol 3-O-β-D-(6'-O-stearoyl)glucopyranoside (6): White, amorphous powder; mp. 288 - 290 °C; [α]_D²⁴ -11.9 (c 0.15, MeOH); IR (KBr) ν_{max} 3400 - 3410, 2986 - 2910, 2851, 1739, 1169, and 1023 cm⁻¹; ¹H NMR (500 MHz, pyridine-*d*₅): δ_H 0.93 (1H, m, H-1a), 1.69 (1H, m, H-1b), 1.71 (1H, m, H-2a), 2.12 (1H, m, H-2b), 3.92 (1H, m, H-3), 2.45 (1H, m, H-4a), 2.70 (1H, m, H-4b), 5.32 (1H, d, *J* = 5.0 Hz, H-6), 1.33 (1H, m, H-7a), 1.20 (1H, m, H-7b), 1.89 (1H, m, H-8a), 1.21 (1H, m, H-8b), 0.87 (1H, m, H-9), 1.39 (2H, overlapped signals, H-11), 1.06 (1H, m, H-12a), 1.97 (1H, m, H-12b), 0.92 (1H, m, H-14), 1.01 (1H, m, H-15a), 1.52 (1H, m, H-15b), 1.23 (1H, m, H-16a), 1.31 (1H, m, H-16b), 1.07 (1H, m, H-17), 0.63 (3H, s, H-18), 0.90 (3H, s, H-19), 1.34 (1H, m, H-20), 0.95 (3H, d, *J* = 6.5 Hz, H-21), 1.03 (1H, m, H-22a), 1.39 (1H, m, H-22b), 1.22 (2H, overlapped signals, H-23), 0.96 (1H, m, H-24), 1.63 (1H, overlapped signal, H-25), 0.82 (3H, d, *J* = 7.0 Hz, H-26), 0.97 (3H, d, *J* = 7.0 Hz, H-27), 1.24 (2H, overlapped signals, H-28), 0.63 (3H, t, *J* = 7.0 Hz, H-29); *Glc*: 4.99 (1H, d, *J* = 7.5 Hz, H-1'), 4.01 (1H, dd, *J* = 9.0, 7.5 Hz, H-2'), 4.26 (1H, t, *J* = 9.0 Hz, H-3'), 4.19 (1H, t, *J* = 9.0 Hz, H-4'), 4.25 (1H, m, H-5'), 4.50 (1H, dd, *J* = 12.0, 2.5 Hz, H-6'a), 4.32 (1H, dd, *J* = 12.0, 5.5 Hz, H-6'b); 6'-*Stearoyl*: 2.48 (2H, t, *J* = 7.5 Hz, H-2''), 1.02 (1H, m, H-3''a), 1.53 (1H, m, H-3''b), 1.25 - 1.39 (overlapped signals, H-4''-H-16''), 1.41 (2H, overlapped signals, H-17''), 0.83 (3H, t, *J* = 7.0 Hz, H-18''); ¹³C NMR (125 MHz, pyridine-*d*₅): δ_C 37.4 (C-1), 29.8 (C-2), 78.2 (C-3), 39.2 (C-4), 140.8 (C-5), 121.8 (C-6), 32.0 (C-7), 31.9 (C-8), 50.2 (C-9), 36.3 (C-10), 21.2 (C-11), 39.8 (C-12), 42.4 (C-13), 56.7 (C-14), 24.4 (C-15), 28.4 (C-16), 56.1 (C-17), 11.8 (C-18), 19.3 (C-19), 36.8 (C-20), 19.1 (C-21), 34.1 (C-22), 26.3 (C-23), 45.9 (C-24), 29.4 (C-25), 18.9 (C-26), 19.8 (C-27), 23.3 (C-28), 11.8 (C-29); *Glc*: 102.4 (C-1'), 75.0 (C-2'), 78.1 (C-3'), 71.4 (C-4'), 78.1 (C-5'), 62.5 (C-6'); 6'-*Stearoyl*: 174.5 (C-1''), 34.1 (C-2''), 24.9 (C-3''), 29.4 - 29.8 (overlapped signals, C-4''-C-16''), 22.6 (C-17''), 14.1 (C-18''); ESI-MS m/z 574 [M - C₁₈H₃₆O]⁺, 397 [M - C₂₄H₄₅O₇]⁺, and 268 [M - C₃₆H₆₂O₅]⁺, C₅₃H₉₄O₇, M = 842.

3. RESULTS AND DISCUSSION

Compound **1** was isolated as a dark yellow, amorphous powder. Its molecular formula was determined to be C₂₄H₂₀O₉ based on a protonated molecular ion peak at m/z 453 [M + H]⁺ and a sodium adduct molecular ion peak at m/z 475 [M + Na]⁺ in the ESI-MS data (consistent with 15 degrees of unsaturation). Analysis of the ¹H, ¹³C NMR, and HSQC spectroscopic data of **1** (Table 1) displayed signals for all 20 protons and 24 carbons, suggesting the presence of a flavan-3-ol skeleton in the molecule which could be determined from the characteristic signals of an AMX₂-type [δ_{H} 4.91 (1H, br s, H-2)/ δ_{C} 80.2 (C-2), 4.22 (1H, m, H-3)/ δ_{C} 67.0 (C-3), and 2.84 (1H, dd, *J* = 17.0, 2.5 Hz, H-4a), 2.95 (1H, dd, *J* = 17.0, 4.5 Hz, H-4b)/ δ_{C} 29.2 (C-4)], while the presence of an aromatic singlet signal [δ_{H} 6.23 (s, H-6)/ δ_{C} 96.4 (C-6)] was attributed to a pentasubstituted system in the flavan A-ring. Additionally, the occurrence of two ABX spin-spin systems [δ_{H} 6.85 (1H, d, *J* = 2.0 Hz, H-2')/ δ_{C} 115.0 (C-2'), 6.70 (1H, d, *J* = 8.5 Hz, H-5')/ δ_{C} 115.9 (C-5'), 6.63 (1H, dd, *J* = 8.5, 2.0 Hz, H-6')/ δ_{C} 119.3 (C-6'), and 6.64 (1H, d, *J* = 2.0 Hz, H-2'')/ δ_{C} 115.03 (C-2''), 6.71 (1H, d, *J* = 8.5 Hz, H-5'')/ δ_{C} 116.5 (C-5''), 6.56 (1H, dd, *J* = 8.5, 2.0 Hz, H-6'')/ δ_{C} 119.4 (C-6'')] demonstrates the characteristics of two 1,3,4-trisubstituted phenyl groups which exhibited the presence of the 3',4'-dihydroxyflavan B-ring. Based on these data,

the presence of the flavan-3-ol skeleton related to that of (-)-epicatechin (fragment A) [39 - 42], along with signals for a dehydrocaffeoyl group [δ_{H} 4.47 (1H, dd, $J = 7.0, 2.0$ Hz, H- α)/ δ_{C} 35.1 (C- α)], a methylene [δ_{H} 2.89 (1H, dd, $J = 16.0, 2.0$ Hz, H- β a), 3.01 (dd, $J = 16.0, 7.0$ Hz, H- β b)/ δ_{C} 38.3 (C- β)] (fragment B, phenylpropanoid-substituted), was also observed in the 1D NMR data.

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

Position	1		Position	2	
	$\delta_{\text{C}}^{\text{a}}$	$\delta_{\text{H}}^{\text{b}}$ mult. (J in Hz)		$\delta_{\text{C}}^{\text{a}}$	$\delta_{\text{H}}^{\text{b}}$ mult. (J in Hz)
2	80.2	4.91 br s	1	152.3	-
3	67.0	4.22 m	2,6	119.6	6.96 d (9.0)
4	29.2	2.95 dd (17.0, 4.5) 2.84 dd (17.0, 2.5)	3,5	116.6	6.63 d (9.0)
5	157.2	-	4	153.9	-
6	96.4	6.23 s	1'	103.7	4.75 d (7.5)
7	152.0	-	2'	74.9	3.48 dd (9.0, 7.5)
8	106.1	-	3'	78.2	3.50 dd (9.0, 9.0)
9	153.5	-	4'	72.1	3.45 t (9.0)
10	105.2	-	5'	75.5	3.74 ddd (9.0, 7.0, 2.0)
1'	131.6	-	6'	65.1	4.70 dd (11.5, 2.0) 4.36 dd (11.5, 7.0)
2'	115.0	6.85 d (2.0)	1''	122.2	-
3'	146.3	-	2'',6''	132.9	7.92 d (9.0)
4'	145.9	-	3'',5''	116.2	6.88 d (9.0)
5'	115.9	6.70 d (8.5)	4''	163.6	-
6'	119.3	6.63 dd (8.5, 2.0)	7''	167.9	-
1''	135.2	-			
2''	115.3	6.64 d (2.0)			
3''	145.8	-			
4''	145.1	-			
5''	116.5	6.71 d (8.0)			
6''	119.4	6.56 dd (8.0, 2.0)			
α	35.1	4.47 dd (7.0, 2.0)			
β	38.3	3.01 dd (16.0, 7.0) 2.89 dd (16.0, 2.0)			
-COO-	170.7	-			

^a125 MHz, ^b500 MHz. Assignments were confirmed by HMQC and HMBC experiments.

Moreover, the signal for a carbonyl carbon (δ_{C} 170.7) was conspicuously observed in the ^{13}C NMR data and was assigned through a $^2J_{\text{C-H}}$ correlation between the carbonyl signal (δ_{C} 170.7) and H- β (δ_{H} 2.89/3.01). This relationship was supported by the HMBC experiments, in which correlations were observed for the resonances between δ_{H} 4.47 (1H, dd, $J = 7.0, 2.0$ Hz, H- α) and 2.89 (1H, dd, $J = 16.0, 2.0$ Hz, H- β a)/3.01 (dd, $J = 16.0, 7.0$ Hz, H- β b) with δ_{C} 170.7 (C=O). On the other hand, the location of a pyranone ring fused to the A-ring at C-8 and C-7 was further observed by the HMBC correlations between δ_{H} 4.47 (1H, dd, $J = 7.0, 2.0$ Hz, H- α) with δ_{C} 152.0 (C-7)/106.1 (C-8), between δ_{H} 2.89 (1H, dd, $J = 16.0, 2.0$ Hz, H- β a)/3.01 (dd, $J = 16.0, 7.0$ Hz, H- β b) with δ_{C} 106.1 (C-8), as well as between δ_{H} 6.23 (1H, s, H-6) with δ_{C} 152.0 (C-7) and δ_{C} 106.1 (C-8) (Figure 2). The β -configuration of H- α on the pyranone ring in **1** was determined by analyzing its spin-coupling pattern and based on the generally comparable NMR data with previous reports [39 - 42]. The chemical shifts of C- α (δ_{C} 35.1)/ δ_{H} 4.47 (1H, dd, $J = 7.0, 2.0$ Hz,

H- α) and C- β (δ_C 38.3)/ δ_H 2.89 (1H, dd, $J = 16.0, 2.0$ Hz, H- β a)/3.01 (dd, $J = 16.0, 7.0$ Hz, H- β b) in **1** corresponded well to signals observed in the NMR spectra of corbulain Ia [δ_C 35.3 (C- α)/ δ_H 4.44 (1H, dd, $J = 7.0, 1.5$ Hz, H- α) and 38.4 (C- β)/ δ_H 2.85 (1H, dd, $J = 16.0, 1.5$ Hz, H- β a)/3.01 (dd, $J = 16.0, 7.0$ Hz, H- β b)] and different from the NMR spectra of corbulain Ib with α -configuration [δ_C 35.5 (C- α)/ δ_H 4.52 (1H, dd, $J = 7.0, 1.5$ Hz, H- α) and 38.6 (C- β)/ δ_H 2.85 (1H, dd, $J = 16.5, 1.5$ Hz, H- β a)/3.01 (dd, $J = 16.5, 7.5$ Hz, H- β b)] [40]. These data indicated the presence of a β -configuration of H- α in **1**. Moreover, cinchonain Ia and cinchonain Ib were first described by Nonaka and Nishioka [41] and their structures were revised by Chen et al. [42] based on NOESY experiments and CD data. To date, the structure of cinchonanin Ib was accepted to show in Figure 1. From the above evidence, the structure of **1** was determined as cinchonain Ib. This compound was previously obtained from the barks of *Cinchona succirubra* [41], *Castanopsis hystrix* [42], and *Trichilia catigua* [40].

Compound **2** was obtained as colorless needles, with a negative optical rotation [$\alpha_D^{24} - 21.5$ (c 0.5, MeOH)]. Its molecular formula was found to be $C_{19}H_{20}O_9$ (10 indices of hydrogen deficiency) via the ^{13}C -NMR spectroscopic data and a negative ESI-MS ion peak at m/z 391 [M-H] $^-$. Analysis of the 1H -NMR spectroscopic data of **2** showed four doublets assignable to a symmetrical 1,4-disubstituted aromatic ring [δ_H 6.96 (2H, d, $J = 9.0$ Hz, H-2/H-6)/6.63 (2H, d, $J = 9.0$ Hz, H-3/H-5) (fragment A) and 7.92 (2H, d, $J = 9.0$ Hz, H-2"/H-6")/6.88 (2H, d, $J = 9.0$ Hz, H-3"/H-5") (fragment B)], together with one glucosidic moiety [δ_C 103.7 (C-1'), 74.9 (C-2'), 78.2 (C-3'), 72.1 (C-4'), 75.5 (C-5'), and 65.1 (C-6')] as evidenced by the presence of an anomeric proton signal [δ_H 4.75 (1H, d, $J = 7.5$ Hz, H-1')], and other proton signals [δ_H 3.48 (1H, dd, $J = 9.0, 7.5$ Hz, H-2'), 3.50 (1H, dd, $J = 9.0, 9.0$ Hz, H-3'), 3.45 (1H, t, $J = 9.0$ Hz, H-4'), 3.74 (1H, m, H-5'), 4.36 (1H, dd, $J = 11.5, 7.0$ Hz, H-6'a), and 4.70 (1H, dd, $J = 11.5, 2.0$ Hz, H-6'b)].

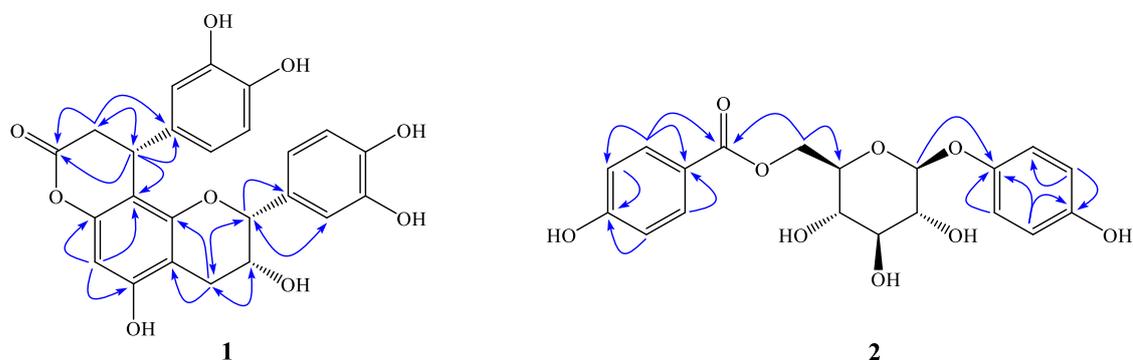


Figure 2. Key HMBC correlations of **1** and **2**.

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 coupling constant ($^3J_{1,2'} = 7.5$ Hz). Furthermore, analysis of the ^{13}C -NMR and HSQC spectroscopic data of **2** revealed the presence of 19 carbon signals, including a carbonyl (δ_C 167.9) and 12 aromatic carbon atoms, along with signals from one hexose moiety (Table 1). The sugar moiety was confirmed as β -D-glucose, which was linked to the aglycones at C-1 (fragment A) and C-7" (fragment B) positions in **2**. This assignment was supported by the HMBC experiments, in which correlations were observed for the resonances between δ_H 4.75 (H-1')/4.36/4.70 (H-6') with C-1 (δ_C 152.3) and C-7' (δ_C 167.9). Additionally, the locations of two hydroxyl groups were assigned to C-4 and C-4" positions, respectively, which were implied by the HMBC correlations between δ_H 6.96 (H-2/H-6) and 6.63 (H-3/H-5) with δ_C 153.9 (C-4); δ_H 7.92 (H-2"/H-6") and 6.88 (H-3"/H-5") with δ_C 163.6 (C-4") (Figure 2).

These spectroscopic data suggested that **2** was a phenolic glycoside with a glucosyl unit and two 4-hydroxybenzoyl moieties [43]. By comparing the NMR spectroscopic data of **2** with reported literature, **2** was determined as 4-hydroxyphenyl 1-*O*- β -D-[6'-*O*-(*p*-hydroxybenzoyl)] glucopyranoside (breynioside A) [43]. This compound was previously obtained from the leaves of *Breynia officinalis* [43].

Compound **5** was obtained as a white, amorphous powder with the molecular formula $C_{51}H_{90}O_7$, as determined by the positive-ion sodiated HR-ESI-MS peak (m/z 837.6586 ($[M + Na]^+$, calcd. for $C_{51}H_{90}NaO_7^+$, 837.6584). The IR spectrum of **5** showed characteristic hydroxyl ($3401 - 3410\text{ cm}^{-1}$), ester (1739 cm^{-1}), and C-O (1170 and 1022 cm^{-1}) group absorption bands. The ^1H NMR spectrum of **5** indicated the presence of six methyl groups and a trisubstituted double bond. The anomeric proton [δ_{H} 4.38 (1H, d, $J = 7.5\text{ Hz}$, H-1')] suggested a sugar moiety bonded to the aglycone via a β -glycosidic linkage. Additionally, the presence of a long-chain aliphatic moiety was indicated by an overlapped triplet methyl signal [δ_{H} 0.85 (1H, t, $J = 7.0\text{ Hz}$, H-16'')] and methylene groups. These findings show that **5** is a C-29 steroidal glucoside derivative [44, 45]. The ^{13}C NMR spectrum of **5** revealed 51 carbon signals, 29 of which were assigned to a steroidal moiety, six to one monosaccharide moiety, and the remaining fatty acid group. The presence of six methyl groups, an oxymethine group, a pair of olefinic methine carbons, together with one glucoside moiety was observed in the ^{13}C NMR spectrum. The ^{13}C NMR data together with the spin-coupling pattern of the sugar proton signals ($J_{1'-2'} = 9.0\text{ Hz}$, $J_{2'-3'} = 9.0\text{ Hz}$, and $J_{3'-4'} = 9.0\text{ Hz}$), indicated a β -D-glucopyranosyl moiety. Moreover, signals at δ_{C} 174.5 (C=O, C-1''), 34.2 (CH_2 , C-2''), 24.9 (CH_2 , C-3''), 29.2 - 29.7 (CH_2 , overlapped signals, C-4'' - C-14''), 22.6 (CH_2 , C-5''), and 14.1 (CH_3 , C-6'') were assigned to a long aliphatic chain of a fatty acid.

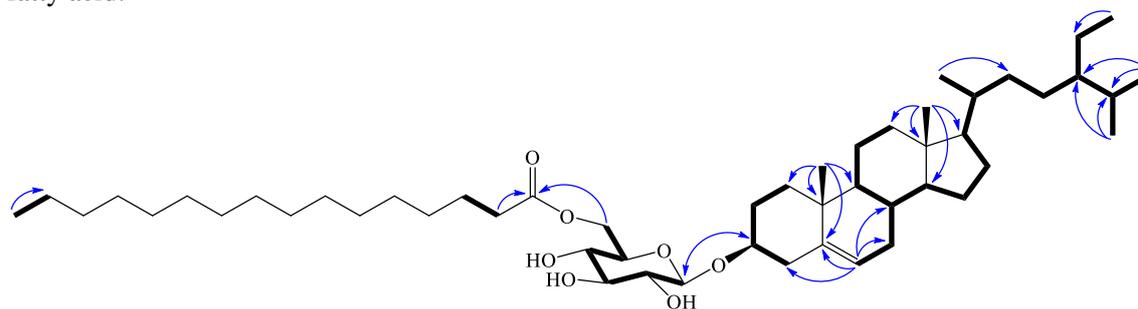


Figure 3. Key HMBC (\rightarrow) and COSY (\blacksquare) correlations of **5**.

Three partial fragments of **5** were revealed using a combination of 2D NMR HMBC and ^1H - ^1H COSY spectrum. A downfield shift was observed for δ_{C} 63.2 (C-6'), as well as an HMBC correlation of δ_{H} 4.45/4.26 (H-6') with δ_{C} 174.5 (C=O) confirming (6' \rightarrow 1'') glycosidic linkage between the glucosyl moiety and the aliphatic chain at C-6' position. Finally, the obvious downfield shift of δ_{C} 79.6 (C-3) suggested that the glucosyl moiety was at C-3, which was verified by an HMBC correlation between δ_{H} 4.38 (H-1') and δ_{C} 79.6 (C-3) and the proton sequence H-1/H-2/H-3/H-4 in the ^1H - ^1H COSY spectrum (Figure 3). The prominent fragment ions in the (+)-EI-MS spectrum at m/z 574 $[M - C_{16}H_{32}O]^+$ (6'-deoxy-sitosterolglucoside), 414 $[M - \text{palmitoyl} - \text{glucosyl}]^+$, 397 $[M - C_{22}H_{41}O_7]^+$ (3-deoxysitosterol), and 240 $[M - C_{36}H_{62}O_5]^+$ (deoxy-C16 fatty acid part) were observed. These NMR spectroscopic and mass data showed the presence of one sitosterol-type glucoside and one palmitoyl group in the structure of **5**. By comparing the NMR spectroscopic data of **5** with reported literature, **5** was determined to be β -sitosterol 3-*O*- β -D-(6'-*O*-palmitoyl)glucopyranoside [45].

Based on the spectroscopic analysis and comparison with literature values, the remaining compounds were identified as polystachyol (**3**) [46], β -sitosterol 3-*O*- β -D-glucopyranoside (**4**) [47], and β -sitosterol 3-*O*- β -D-(6'-*O*-stearoyl)glucopyranoside (**6**) [45]. Compound **3** is widely distributed throughout the plants, e.g, *Aphanamixis polystachya* [46], *Sorbus lanata* (D. Don.) Schauer [48], *Byttneria aspera* Colebr [49]. It is not usually of systematic significance but could be important in helping differentiate *R. mucronata* from other species of *Rhizophora*. Of the three phytosteryl glycosides (**4–6**) isolated from *R. mucronata*, compound **4** was previously isolated from *Brassica rapa* sb. sp. *campestris* and *Aloe barbadensis* [47], *Humulus lupulus* [50], while compound **6** was previously isolated from *Typha latifolia* [51] and *Lycium chinense* [45].

4. CONCLUSIONS

Six compounds, including cinchonain Ib (**1**), breynioside B (**2**), polystachyol (**3**), β -sitosterol 3-*O*- β -D-glucopyranoside (**4**), β -sitosterol 3-*O*- β -D-(6'-*O*-palmitoyl)glucopyranoside (**5**), and β -sitosterol 3-*O*- β -D-(6'-*O*-stearoyl)glucopyranoside (**6**), were isolated from a methanolic extract of *R. mucronata* stem barks. The structure determination of these isolates was accomplished using comprehensive spectroscopic methods and comparison with those reported. This is the first report of compounds **1–6** from the *Rhizophora* genus.

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