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Flavonoids and amides from *Melodorum fruticosum* L. stem bark and their α-glucosidase inhibitory activity

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Abstract. *Melodorum fruticosum* Lour. (Annonaceae), a small tree or climber, is widely distributed in Central and Southern Viet Nam. The leaves of *M. fruticosum* L. have been used as fork remedies for the treatment of digestive diseases and swelling of the breast, and the roots of the plant have been used to treat abdominal dyspepsia in women after giving birth. The dried powder of the stem of *M. fruticosum* L. collected in Lam Dong province was extracted with ethanol at room temperature and evaporated under reduced pressure to yield a crude ethanol residue. From ethyl acetate extract, six compounds, including (+)-taxifolin (**1**), quercetin (**2**), (−)-eriodictyol (**3**), paprazine (**4**), *N-trans*-caffeoyltyramine (**5**), and *N-trans*-feruloyltyramine (**6**), were isolated. The structures of these compounds were elucidated by NMR and ESI-MS as well as compared with data in the literature. All the isolated compounds, *n*-hexane, ethyl acetate, and ethanol extracts were evaluated for their *in vitro* α-glucosidase inhibition, with acarbose as a positive control.

Keywords: Melodorum fruticosum L., flavonoid, amide, α-glucosidase.

Classification numbers: 1.1.1, 1.1.6

1. INTRODUCTION

The genus *Melodorum* (family Annonaceae) includes about 55 species, distributed in tropical Asia [1]. *Melodorum fruticosum* L., known as “Du de trau” in Viet Nam, is a shrub or climber with fragrant yellow flowers. This plant has been used as a tonic, a mild cardiac stimulant, antipyretic, and as a hematinic to resolve dizziness [2]. The essential oil from the flowers is used in aromatherapy and as traditional medicine in Thailand [3]. The flower extract of *M. fruticosum* possesses antifungal, antioxidant, and cytotoxic activities [3, 4]. Previous studies of the chemical constituents of *M. fruticosum* revealed the presence of terpenoids, aromatic compounds, amides, heptenoids, alkaloids, and flavonoids [4 - 8]. Some of the isolates

displayed significant antioxidant, anti-inflammatory, cytotoxic, antiphytopathogenic, and antifungal activities [9 - 11]. In this paper, we report the isolation and structure elucidation of three flavonoids **1**-**3** and three amide compounds **4**-**6** (Figure 1) from the ethyl acetate extract of *M. fruticosum* stem bark, as well as the evaluation of *in vitro* α-glucosidase inhibition of the isolated compounds.

2. MATERIALS AND METHODS

2.1. Plant materials

The stem bark of *M. fruticosum* was collected in July 2017 in Lam Dong province, Viet Nam. The material was authenticated by Assoc. Prof. Dang Van Son – Institute of Life Sciences, Vietnam Academy of Science and Technology (VAST). A voucher specimen (No US-A012) was deposited at the Department of Organic Chemistry, Faculty of Chemistry, University of Science, National University–Ho Chi Minh City, Viet Nam.

2.2. General experimental procedures

The ESIMS spectra were recorded on an $X500_R$ QTOP model mass spectrometer (Sciex, Redwood City, CA, USA) and a Dionex Ultimate 3000 HPLC system hyphenated with a Q Exactive Hybrid Quadrupole Orbitrap MS (Thermo Fisher Scientific, Waltham, MA, USA). The NMR spectra were measured on a Bruker AvanceNEO 600 (Merck, Darmstadt, Germany). TLC (silica gel 60 F_{254}, Merck, Darmstadt, Germany) was used to monitor fractions from column chromatography (CC). Silica gel (70 - 230 mesh, Merck, Darmstadt, Germany) and Sephadex LH-20 gel (GE Healthcare Bio-Sciences AB, Uppsala, Sweden) were used for column chromatography.

2.3. Extraction and isolation

The dried powder of *M. fruticosum* stem bark (45.0 kg) was extracted with 95 % (v/v) EtOH (90 L × 3) at room temperature. The filtrated solution was evaporated under reduced pressure to afford a residue (1300 g). This EtOH crude extract was suspended in water and partitioned with *n*–-hexane, EtOAc then EtOAc–MeOH (4:1, v/v) to yield *n*-hexane (45.0 g), EtOAc (161.0 g) and EtOAc–MeOH (87.0 g) extracts. The water layer was evaporated to dryness. The residue was dissolved in methanol and the methanolic soluble portion was concentrated to obtain the methanolic extract (346 g); the remaining residue was concentrated to obtain the aqueous extract (550 g). The EtOAc extract was chromatographed on a silica gel column and eluted with *n*-hexane–EtOAc (4:1−0:1, v/v), EtOAc–MeOH (1:0 - 0:1, v/v) to give thirteen fractions (EA.1–EA.13).

Fraction EA.3 (15.2 g) was separated into seven subfractions EA.3.1–EA.3.7 by silica gel CC eluted with *n*-hexane–EtOAc (4:1, v/v). Purification of subfraction EA.3.7 (1.5 g) by CC with *n*-hexane-EtOAc (1:1, v/v), followed by CC on Sephadex LH-20 (100.0 g) eluted with $CHCl_3$–MeOH (1:4, v/v) to afford **2** (6.0 mg) and **3** (4.0 mg).

Fraction EA.4 (9.1 g) was fractionated over silica gel CC eluted with *n*-hexane–EtOAc (3:2, v/v) to give five subfractions EA.4.1–EA.4.5. Subfraction EA.4.3 (1.2 g) was chromatographed on a silica gel column using *n*-hexane–EtOAc (2:3, v/v) as eluent to yield **4** (7.0 mg), **5** (5.0 mg), and **6** (5.0 mg). Subfraction EA.4.5 (3.0 g) was further purified by silica gel CC eluted with $CHCl_3$–MeOH (90:10, v/v) to give **1** (4.0 mg).

(+)-Taxifolin (1): Pale yellow powder; $[\alpha]^{20}_D$ +24.4 (*c* 0.0001, $CHCl_3$). ESI-MS: *m/z* 305.08 $[M+H]^+$ (calcd for $C_{15}H_{13}O_7$, 305.07). ^{1}H-NMR (DMSO-d_6, 600 MHz): Table 1. ^{13}C-NMR (DMSO-d_6, 150 MHz): Table 2.

Quercetin (2): Yellow powder. ESI-MS: *m/z* 301.16 $[M-H]^-$ (calcd for $C_{15}H_9O_7$, 301.03). ^{1}H-NMR (DMSO-d_6, 600 MHz): Table 1. ^{13}C-NMR (DMSO-d_6, 150 MHz): Table 2.

(−)-Eriodictyol (3): White amorphous powder; $[\alpha]^{20}_D$ -59.2 (*c* 0.0001, $CHCl_3$). ESI-MS: *m/z* 287.09 $[M-H]^-$ (calcd for $C_{15}H_{11}O_6$, 287.06). ^{1}H-NMR (DMSO-d_6, 600 MHz): Table 1. ^{13}C-NMR (DMSO-d_6, 150 MHz): Table 2.

Paprazine (4): White amorphous powder. HRESI-MS: *m/z* 282.1121 $[M-H]^-$ (calcd for $C_{17}H_{16}NO_3$, 282.1130). ^{1}H-NMR (DMSO-d_6, 600 MHz): Table 1. ^{13}C-NMR (DMSO-d_6, 150 MHz): Table 2.

***N-trans*-caffeoyltyramine (5):** Colourless wax. ESI-MS: *m/z* 300.13 $[M+H]^+$ (calcd for $C_{17}H_{18}NO_4$, 300.12). ^{1}H-NMR (DMSO-d_6, 600 MHz): Table 1. ^{13}C-NMR (DMSO-d_6, 150 MHz): Table 2.

***N-trans*-feruloyltyramine (6):** Colourless wax. ESI-MS: *m/z* 314.15 $[M+H]^+$ (calcd for $C_{18}H_{20}NO_4$, 314.14). ^{1}H-NMR (DMSO-d_6, 600 MHz): Table 1. ^{13}C-NMR (DMSO-d_6, 125 MHz): Table 2.

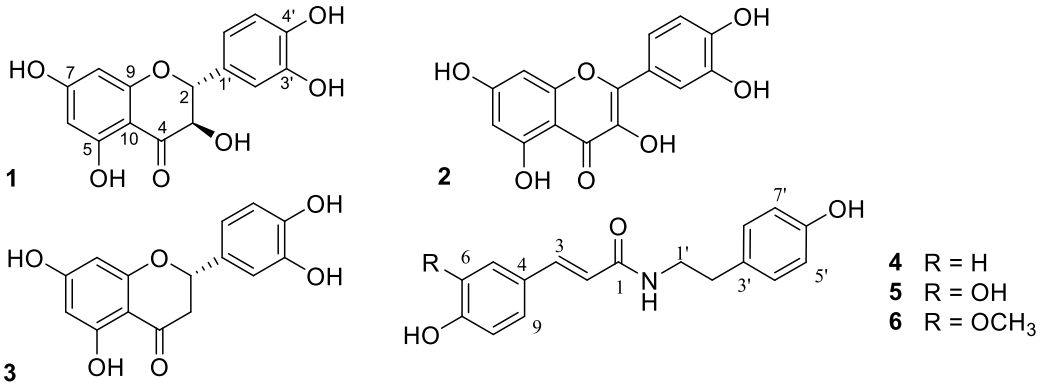

Figure 1. Chemical structures of the isolated compounds **1**-**6**.

2.4. α-Glucosidase inhibitory assay

The α-glucosidase inhibitory evaluation of the isolated compounds was conducted using the colorimetric method [12]. The principle of the method is that the enzyme *α*-glucosidase hydrolyzes the substrate *p*-nitrophenyl-*α*-D-glucopyranoside (pNPG) to give *α*-D-glucose and *p*-nitrophenol (pNP). The evaluation included the use of the positive control, acarbose (Bayer Vitol Leverkusen, Germany). Briefly, 0.2 U/mL of *α*-glucosidase (*Saccharomyces cerevisiae*, Sigma-Aldrich, St. Louis, USA) and substrate (5.0 mM *p*-nitrophenyl-*α*-D-glucopyranoside, Sigma-Aldrich) were dissolved in 100 mM pH 6.8 sodium phosphate buffer. The inhibitor (50 μL) was preincubated with *α*-glucosidase at 37 °C for 20 min, and then the substrate (40 μL) was added to the reaction mixture. The enzymatic reaction was carried out at 37 °C for 20 min and stopped by adding 0.2 M Na_2CO_3 (130 μL). Enzymatic activity was quantified by measuring absorbance at 410 nm. All samples were analyzed in triplicate at five different concentrations around the IC_{50} values, and the average values were recorded.

3. RESULTS AND DISCUSSION

3.1. Structural elucidation of the isolates

Compound **1** was isolated as a pale yellow powder. The ^{13}C-NMR spectrum displayed the presence of one conjugated carbonyl carbon, five aromatic methine carbons, five aromatic oxygenated carbons, two aromatic quaternary carbons, and two saturated methine carbons. The ^{1}H-NMR spectrum displayed resonances typical of the C-ring of a flavanonol at δ_H 4.96 (*d*, 11.4, H-2), 4.49 (*dd*, 11.4, 6.0, H-3) and 5.76 (*d*, 6.0, 3-OH), together with the ^{13}C-NMR data at δ_C 83.2 (C-2), 71.7 (C-3) and 197.8 (C-4). The presence of a characteristic signal of a hydrogen-bond hydroxy [δ_H 11.87 (*s*, 5-OH)] and two doublet signals of two *meta*-couple protons [δ_H 5.90 (*d*, 1.8, H-6) and 5.85 (*d*, 1.8, H-8)] determined that the A-ring had hydroxy groups at C-5 and C-7. An ABX pattern [δ_H 6.73 (*d*, 7.8, H-5′), 6.75 (*dd*, 7.8, 1.2, H-6′), and 6.87 (*d*, 1.2, H-2′)] was assigned to H-5′, H-6′, and H-2′ of the B-ring, respectively. The position of the hydroxyl group at C-5 was supported by the HMBC correlations of 5-OH (δ_H 11.87) with C-5 (δ_C 163.4), C-6 (δ_C 96.1), and C-10 (δ_C 100.6). The HMBC cross-peaks of H-2 (δ_H 4.96) to C-3 (δ_C 71.7), C-4 (δ_C 197.8), C-9 (δ_C 162.7), C-1′ (δ_C 128.1), C-2′ (δ_C 115.4), and C-6′ (δ_C 119.6); of H-3 (δ_H 4.49) to C-2 (δ_C 83.2), C-4 (δ_C 197.8), and C-1′ (δ_C 128.1); of 3-OH (δ_H 5.76) to C-2 (δ_C 83.2), C-3 (δ_C 71.7), and C-4 (δ_C 197.8) assigned the flavanonol skeleton of compound **1** (Figure 2). The absolute configurations of C-2 and C-3 were assigned as (2*R*,3*R*)-configuration through analysis of the optical rotation data of **1** ([α]$_D$ +24.4, $CHCl_3$) with the known compound (+)-taxifolin ([α]$_D$ +22.8, MeOH) [13]. Besides, the coupling constant (J = 11.4 Hz) of H-2 and H-3 indicated that they were in a *trans*-relationship. Compound **1** was assigned as (+)-taxifolin by comparison of the optical rotation and NMR data with those published in the literature [13].

Compound **2** was isolated as a yellow powder. The ^{13}C-NMR spectrum of **2** revealed the presence of 15 carbons, namely one conjugated carbonyl carbon, five aromatic methine carbons, seven aromatic oxygenated carbons, and two oxygenated olefinic carbons. The ^{1}H-NMR spectrum showed the presence of a hydrogen-bond hydroxy [δ_H 12.48 (*s*, 5-OH)], a pair of *meta*-protons [δ_H 6.18 (*d*, 2.4, H-6) and 6.40 (*d*, 2.4, H-8)], three protons of an ABX spin system [δ_H 7.67 (*d*, 1.8, H-2′), 6.88 (*d*, 8.4, H-5′) and 7.54 (*dd*, 8.4, 1.8, H-6′)]. The comparison of the ESIMS and NMR data of **2** and **1** showed similarities except that C-2 (δ_C 147.7) and C-3 (δ_C 135.5) of compound **2** were unsaturated and the chemical shift of the carbonyl carbon at C-4 (δ_C 175.8) was characteristic for a flavonol skeleton. Based on the NMR data and compared with those published in the literature [14], compound **2** was elucidated as quercetin.

Compound **3** was isolated as a white amorphous powder. The ^{1}H-NMR spectrum features of compound **3** resembled those of compounds **1** and **2**, including a signal of hydrogen-bond hydroxy [δ_H 12.14 (*s*, 5-OH)], two doublet signals of H-6 and H-8 of the A-ring [δ_H 5.87 (*d*, 2.4, H-6) and 5.88 (*d*, 2.4, H-8)], two singlet signals of three protons of the B-ring [δ_H 6.87 (*s*, H-2′), 6.74 (*s*, H-5′,6′)]. The flavanone skeleton of **3** was demonstrated by signals at δ_H 5.37 (*dd*, 12.6, 3.0, H-2), 3.18 (*dd*, 16.8, 12.6, H-3$_{ax}$), and 2.68 (*dd*, 16.8, 3.0, H-3$_{eq}$). The ^{13}C-NMR also confirmed the presence of a flavanone structure through the signals at δ_C 42.1 (C-3), 78.4 (C-2), and 196.3 (C-4). The negative optical rotation of **3** ([α]$_D$ –59.2, $CHCl_3$) was similar to that of (−)-eriodictyol ([α]$_D$ –21.6, MeOH) [13], so the absolute configuration of C-2 was assigned as *S*-configuration. Moreover, the 2*S*-configuration was also supported by comparing the coupling constant of H-2 and H-3 to the NMR data of (2*S*)- and (2*R*)-eriodictyol 7-*O*-*β*-D-glucopyranosiduronic acid [15]. As a result, compound **3** was determined as (−)-eriodictyol [13].

Compound **4** was isolated as a white amorphous powder. The ^{13}C-NMR spectrum displayed the presence of one conjugated carbonyl carbon, ten olefinic methine carbons, two aromatic oxygenated carbons, two aromatic quaternary carbons, and two aliphatic methylenes. The ^{1}H-NMR spectrum showed signals of one amide proton [δ_H 7.98 (*t*, 5.4, N-H)], two methylene groups [δ_H 3.33 (*m*, H-1′) and 2.65 (*t*, 7.2, H-2′)], a pair of doublet signals of two olefinic protons in *trans*-configuration [δ_H 7.31 (*d*, 15.6, H-3) and 6.40 (*d*, 15.6, H-2)], four doublet signals of two A_2B_2 systems [δ_H 7.38 (*d*, 8.4, H-5, H-9), 6.79 (*d*, 8.4, H-6, H-8), 7.01 (*d*, 8.4, H-4′, H-8′), and 6.68 (*d*, 8.4, H-5′, H-7′)]. The ^{1}H-^{1}H COSY experiment of **4** revealed the spin connection between H-2↔H-3, -N-H↔H-1′↔H-2′, H-5↔H-6, H-4′↔H-5′ (Figure 2). The HMBC spectrum exhibited correlations of N-H proton (δ_H 7.98) to C-1 (δ_C 165.3) and C-1′ (δ_C 40.7); of H-1′ (δ_H 3.33) and H-2′ (δ_H 2.65) to C-3′ (δ_C 129.5) and C-4′ (δ_C 129.4); of 6′-OH (δ_H 9.15) to C-6′ (δ_C 155.6) and C-5′ (δ_C 115.1). These correlations indicated the presence of a tyramine moiety. The HMBC cross-peaks of protons of the *trans*-double bond to the carbonyl carbon at C-1 (δ_C 165.3), C-4 (δ_C 125.9), and C-5 (δ_C 129.1) suggested the presence of a *trans*-coumaroyl moiety (Figure 2). Based on the spectral data and NMR comparison with the literature [16], compound **4** was elucidated as *N-p-trans*-coumaroyltyramine (paprazine).

Table 1. ^{1}H-NMR spectroscopic data of **1 – 6** recorded in DMSO-d_6 (δ in ppm, *J* in Hz).

Position	1	2	3	4	5	6
2	4.96 (d, 11.4)	-	5.37 (dd, 12.6, 3.0)	6.40 (d, 15.6)	6.31 (d, 15.6)	6.42 (d, 15.6)
3_{eq}	4.49 (dd, 11.4, 6.0)	-	2.68 (dd, 16.8, 3.0)	7.31 (d, 15.6)	7.22 (d, 15.6)	7.31 (d, 15.6)
3_{ax}			3.18 (dd, 16.8, 12.6)			
5	-	-	-	7.38 (d, 8.4)	6.93 (d, 1.8)	7.10 (d, 1.8)
6	5.90 (d, 1.8)	6.18 (d, 2.4)	5.87 (d, 2.4)	6.79 (d, 8.4)	-	-
8	5.85 (d, 1.8)	6.40 (d, 2.4)	5.88 (d, 2.4)	6.79 (d, 8.4)	6.74 (d, 7.8)	6.79 (d, 7.8)
9	-	-	-	7.38 (d, 8.4)	6.83 (dd, 7.8, 1.8)	6.98 (dd, 7.8, 1.8)
1′	-	-	-	3.33 (m)	3.31 (m)	3.33 (m)
2′	6.87 (d, 1.2)	7.67 (d, 1.8)	6.87 (s)	2.65 (t, 7.2)	2.63 (t, 7.2)	2.64 (t, 7.2)
3′	-	-	-	-	-	-
4′	-	-	-	7.01 (d, 8.4)	7.00 (d, 8.4)	7.01 (d, 9.0)
5′	6.73 (d, 7.8)	6.88 (d, 8.4)	6.74 (s)	6.68 (d, 8.4)	6.67 (d, 8.4)	6.68 (d, 9.0)
6′	6.75 (dd, 7.8, 1.2)	7.54 (dd, 8.4, 1.8)	6.74 (s)	-	-	-
7′	-	-	-	6.68 (d, 8.4)	6.67 (d, 8.4)	6.68 (d, 9.0)
8′	-	-	-	7.01 (d, 8.4)	7.00 (d, 8.4)	7.01 (d, 9.0)
NH	-	-	-	7.98 (t, 5.4)	8.02 (t, 5.4)	7.99 (t, 5.4)
3-OH	5.76 (d, 6.0)	-	-	-	-	-
5-OH	11.87 (s)	12.48 (s)	12.14 (s)	-	-	-
7-OH	-	10.76 (s)	10.77 (s)	9.80 (s)	9.22 (s)	9.45 (s)
3′-OH	9.01 (s)	9.34 (s)	9.01 (s)	-	-	-
4′-OH	9.06 (s)	9.55 (s)	9.06 (s)	-	-	-
6′-OH	-	-	-	9.15 (s)	9.22 (s)	9.23 (s)
6-OCH_3	-	-	-	-	-	3.80 (s)

Compound **5** was isolated as a colourless wax. The NMR spectral data of **4**, which were similar to **5**, indicated the presence of a tyramine moiety with signals of one amide proton [δ_H

8.02 (*t*, 5.4, N-H)], two methylene groups [δ_H 3.31 (*m*, H-1′), 2.63 (*t*, 7.2, H-2′); δ_C 40.8 (C-1′), 34.5 (C-2′)], two doublet signals of an A_2B_2 system [δ_H 7.00 (*d*, 8.4, H-4′, H-8′) and 6.67 (*d*, 8.4, H-5′, H-7′); δ_C 129.6 (C-4′, C-8′) and 115.3 (C-5′, C-7′)]. The appearance of an ABX spin system [δ_H 6.93 (*d*, 1.8, H-5), 6.74 (*d*, 7.8, H-8), 6.83 (*dd*, 7.8, 1.8, H-9)] and two doublet signals of two olefinic protons in *trans*-configuration [δ_H 7.22 (*d*, 15.6, H-3) and 6.31 (*d*, 15.6, H-2)] assigned a caffeoyl moiety. The ^{13}C-NMR spectrum displayed one conjugated carbonyl carbon, nine olefinic methine carbons, three aromatic oxygenated carbons, two aromatic quaternary carbons, and two aliphatic methylenes. The NMR data of compound **5** were similar to the literature [17], therefore, **5** was determined as *N-trans*-caffeoyltyramine.

Compound **6** was isolated as a colourless wax. The NMR data of **6** were found to be very similar to those of **5**, except for the appearance of a methoxy group at δ_H 3.80 (*s*, 6-OCH_3) and δ_C 55.7. The ^{13}C-NMR spectrum also showed one conjugated carbonyl carbon, nine olefinic methine carbons, three aromatic oxygenated carbons, two quaternary aromatic carbons, and two aliphatic methylenes. The ^{1}H-NMR spectrum exhibited signals of one amide proton [δ_H 7.99 (*t*, 5.4, N-H)], two methylene groups [δ_H 3.33 (*m*, H-1′), 2.64 (*t*, 7.2, H-2′)], two doublet signals of an A_2B_2 system [δ_H 7.01 (*d*, 9.0, H-4′, H-8′), 6.68 (*d*, 9.0, H-5′, H-7′)], three signals of an ABX spin system [δ_H 7.10 (*d*, 1.8, H-5), 6.79 (*d*, 7.8, H-8), and 6.98 (*dd*, 7.8, 1.8, H-9)] and a pair of *trans*-coupled doublets [δ_H 7.31 (*d*, 15.6, H-3) and 6.42 (*d*, 15.6, H-2). Compound **6** was determined as *N-trans*-feruloyltyramine based on the good compatibility of its NMR data with those published in the literature [18].

Table 2. ^{13}C NMR spectroscopic data of **1 – 6** recorded in DMSO-d_6 (δ in ppm).

Position	**1**	**2**	**3**	**4**	**5**	**6**
1	-	-	-	165.3	165.7	165.7
2	83.2	147.7	78.4	118.7	118.6	119.1
3	71.7	135.7	42.1	138.5	139.3	139.2
4	197.8	175.8	196.3	125.9	126.5	126.6
5	163.4	160.7	163.5	129.1	114.1	110.9
6	96.1	98.2	95.7	115.7	145.6	148.3
7	166.9	163.9	166.6	158.7	147.4	148.0
8	95.1	93.3	94.9	115.7	115.9	115.8
9	162.7	156.1	162.9	129.1	120.5	121.7
10	100.6	103.0	101.8	-	-	-
1'	128.1	121.9	129.4	40.7	40.8	40.8
2'	115.4	115.0	114.3	34.4	34.5	34.5
3'	145.9	145.0	145.7	129.5	129.7	129.7
4'	145.1	146.8	145.2	129.4	129.6	129.6
5'	115.3	115.6	115.3	115.1	115.3	115.3
6'	119.6	119.9	117.9	155.6	155.7	155.7
7'	-	-	-	115.1	115.3	115.3
8'	-	-	-	129.4	129.6	129.6
6-OCH_3	-	-	-	-	-	55.7

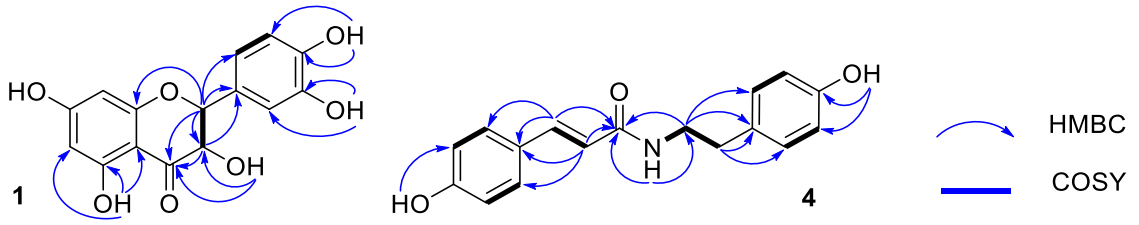

Figure 2. Key COSY and HMBC correlations for compounds **1** and **4**.

3.2. α-Glucosidase inhibitory activity

The α-glucosidase inhibitory activity of all isolated compounds, *n*-hexane, ethyl acetate, and ethanol extracts from *M. fruticosum* stem bark was evaluated, with acarbose being employed as a positive control. The IC_{50} values (Table 3) indicated that all tested compounds and extracts displayed significant α-glucosidase inhibitory activity, which were more potent than acarbose. As shown in Table 3, the *n*-hexane, ethyl acetate, and ethanol extracts possessed significant α-glucosidase inhibitory activity with IC_{50} values of 8.48, 2.93, and 1.89 μg/mL, respectively. Compounds **1-6** also showed strong α-glucosidase inhibitory activity with IC_{50} values ranging from 0.12 to 11.0 μM. Of these, compound **5** possessed the strongest α-glucosidase inhibitory activity with an IC_{50} value of 0.12 μM.

Table 3. α-Glucosidase inhibitory effects of stem bark extracts and compounds **1-6**.

Extract	IC_{50} (μg/mL)	Compound	IC_{50} (μM)	Compound	IC_{50} (μM)
Hexane extract	8.48 ± 0.46	**1**	1.17 ± 0.10	**4**	0.91 ± 0.14
EtOAc extract	2.93 ± 0.18	**2**	1.79 ± 0.20	**5**	0.12 ± 0.68
EtOH extract	1.89 ± 0.12	**3**	2.63 ± 0.50	**6**	11.00 ± 1.50
Acarbose	223.51 ± 6.33			Acarbose	179.65 ± 6.02

The inhibitory effects of six known compounds against α-glucosidase have been reported in previous articles (Table 4) but the α-glucosidase inhibitory activity was inconsistent among the literatures. According to Hang Su *et al.* [19], compound **1** exhibited good α-glucosidase inhibitory activity with an IC_{50} value of 0.038 mg/mL which was better than the positive control acarbose (IC_{50} value = 0.917 mg/mL). On the contrary, Qu-Jing Luo *et al.* [20] and Carina Proença *et al.* [21] reported that compound **1** showed weak activity against α-glucosidase. Compound **2** was reported to possess strong α-glucosidase inhibitory activity with IC_{50} values of 1.88±0.08 μM [20] or 15 ± 3 μM [21]. In comparison with acarbose, compound **3** was a stronger inhibitor with IC_{50} values of 57.5 μM [22], 22.1 μM [23]. The α-glucosidase inhibitory activity of three alkylamides (compounds **4-6**) were reported by Yeong Hun Song *et al.* [24], most of them had potent activities against α-glucosidase with IC_{50} values of 0.42, 1.86, 10.62 μM, respectively, which were better than positive control DNJ (IC_{50} = 21.26 μM). Likewise, Lu Zhang *et al.* [25] and Virayu Suthiphasilp *et al.* [26] reported about the good α-glucosidase inhibitory activity on compounds **4** and **6**. It could be seen that inhibition data of compounds **2-6** were consistent with experimental data from references, which mean they showed strong α-glucosidase inhibitory activity. However, the inhibition data of compound **1** was inconsistent among references as well as our data, so the inhibitory effects of **1** should be experimentally rechecked.

Table 4. α-Glucosidase inhibitory activity of compounds **1-6** reported in [19 - 26].

References	IC_{50} (μM)						
	1	**2**	**3**	**4**	**5**	**6**	**Positive control**
Su H. [19]	0.038 mg/mL	-	-	-	-	-	0.917 mg/mL
Luo Q. J. [20]	>20	1.88 ± 0.08	-	-	-	-	0.06
Proença C. [21]	-	15 ± 3	-	-	-	-	607 ± 56
Habtemariam S. [22]	-	-	57.5 ± 13.2	-	-	-	190.6 ± 16.1
Nguyen T. P. [23]	-	-	22.1	-	-	-	214.5
Song Y. H. [24]	-	-	-	0.42 ± 0.01	1.86 ± 0.04	10.62 ± 0.8	21.26 ± 0.8
Zhang L. [25]	-	-	-	4.47 ± 0.19	-	9.04 ± 1.18	169.0 ± 12.3
Suthiphasilp V. [26]	-	-	-	4.5	-	24.7	73.7

4. CONCLUSIONS

Phytochemical investigation of the ethyl acetate extract of *M. fruticosum* Lour. stem bark led to the isolation of three flavonoids including (+)-taxifolin (**1**), quercetin (**2**), (−)-eriodictyol (**3**) and three amides including paprazine (**4**), *N-trans*-caffeoyltyramine (**5**), and *N-trans*-feruloyltyramine (**6**). These compounds were isolated from *M. fruticosum* Lour. for the first time and their chemical structures were elucidated based on analysis of the NMR and ESIMS data as well as comparison to the published data. All the isolated compounds as well as extracts from *M. fruticosum* stem bark displayed significant α-glucosidase inhibitory activity. Among them, compound **5** demonstrated the most potent inhibitory activity against α-glucosidase (IC_{50} 0.12 μM).

CRediT authorship contribution statement. Nguyen Thi My Huong: research idea, isolation, structure elucidation. Do Thi My Lien: research idea, isolation, structure elucidation, writing.

Declaration of competing interest. The authors declare that they have no conflict of interest.

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