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3B QUANG TRUNG - HOAN KIEM - HANOI - VIETNAM
TEL: (+84-24) 38247058 FAX: (+84-24) 39348740
Email: tapchiduoclieu@nimm.org.vn; tapchiduoclieu@gmail.com

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PHENOLIC CONSTITUENTS FROM THE LEAVES OF *CAMELLIA HAKODAE* NINH WITH THEIR α-GLUCOSIDASE INHIBITORY ACTIVITY

Pham Hai Yen[1], Nguyen Thi Cuc[2], Nguyen Huy Hoang[1], Phan Van Kiem[1], Do Thi Ha[3], Bui Huu Tai[1,*]

[1]*Institute of Marine Biochemistry, Vietnam Academy of Science and Technology, Hanoi, Vietnam;*
[2]*Hanoi Irradiation Centre, Ministry of Science and Technology of Vietnam, Hanoi, Vietnam;*
[3]*National Institute of Medicinal Materials (NIMM), Hanoi, 12110, Vietnam*
*Corresponding author: bhtaiich@gmail.com
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Summary

Phenolic Constituents from the Leaves of *Camellia hakodae* Ninh with their α-Glucosidase Inhibitory Activity

Six phenolic compounds, including camelliquercetiside D (**1**), tsubakioside A (**2**), stachyanthuside A (**3**), rutin (**4**), kaempferol 3-rutinoside (**5**), and kaempferol 3-*O*-β-D glucopyranoside (**6**), were isolated from the methanol extract of *Camellia hakodae* Ninh. Their chemical structures were identified by HR-ESI-MS, 1D and 2D NMR spectra and compared with the published data in the literature. The compounds were screened for their α-glucosidase inhibitory activity. Compounds **1**, **2**, **4**-**6** showed significant inhibition with IC_{50} values of 35.41 ± 0.02, 15.43 ± 0.39, 10.64 ± 0.23, 17.21 ± 0.34, and 19.42 ± 0.25 µM, respectively, compared to that of positive control, acarbose, which showed IC_{50} value of 47.10 ± 1.40 µM.

Keywords: *Camellia hakodae* Ninh; *Flavonoid glycoside; α-Glucosidase inhibitory activity*.

1. Introduction

Camellia hakodae Ninh (Theaceae family) is an endemic ornamental plant in Tam Dao, Vinh Phuc Province, Vietnam (local name: Trà hoa vàng hakoda). This species is a shrub that grows in valleys at altitudes of 400 to 500 meters. Green tea from *C. hakodae* Ninh is used as a social, medicinal, and health drink [1]. Phytochemical studies on members of the genus *Camellia* have led to the detection of more than 300 compounds originating from flavonoid, terpenoid, alkaloid, and phenolic groups [2],[3], exhibiting cytotoxic and anti-inflammatory properties [4],[5]. Because of an endemic plant, a few phytochemical studies on *C. hakodae* Ninh has been reported by Vietnamese scientists. Results indicated that its leaves contain flavonoids [6] and pentacyclic triterpenes [7] meanwhile various flavonoid sub-types including flavone, flavan, and flavanone derivatives are identified from the flowers. These isolated compounds showed weak activities in both anti-microbial and cytotoxic *in vitro* experiments. Besides, the ethanol extract from the leaves possessed anti-hyperlipidemic effect in an *in vivo* rat model [8]. Our previous studies revealed that *Camellia* species produced potential α-glucosidase inhibitors [2],[12]. In contribution to the enrichment phytochemical data of this plant, herein, we report the isolation and structural elucidation of six phenolic compounds from *C. hakodae* Ninh and the evaluation of their α-glucosidase inhibitory effect.

2. Materials and methods

2.1. Plant material

The leaves of *Camellia hakodae* Ninh (Theaceae) were collected at Tam Dao National Park, Vinh Phuc province, Vietnam, in April 2023 and taxonomically identified by Dr. Nguyen The Cuong, Institute of Ecology and Biological Resources, VAST. Voucher specimens (NCCT-P181) were kept at the Institute of Marine Biochemistry, VAST. Fresh samples were cut into small pieces (3-5 cm) and dried overnight at 60°C. Dried samples were then fine powdered before extraction.

2.2. General experimental procedures

Column chromatography (CC) was carried out with Kieselgel 60 *silica gel* (70-230 and 230-400 mesh, Merck, Darmstadt, Germany) and C18-reversed phase (150 µm, YMC Chemical Ltd., Kyoto, Japan). Thin layer chromatography (TLC) was performed using a pre-coated *silica gel* 60 F_{254} (0.25 mm, Merck) and RP-18 F_{254S} plates (0.25 mm, Merck). Preparative HPLC using Agilent HPLC 1100 system, J-sphere ODS H-80 column (250 mm length ×20 mm ID) column, a flow rate of 3 mL/min, and detector DAD at wavelengths of 205, 254, and 280 nm. NMR spectra were recorded on a Bruker 500 or 600 MHz spectrometer. Extraction was performed using

an Elma S300H (30 L) ultrasonic bath. *α*-Glucosidase assay was performed at the laboratory of Applied Biochemistry, Institute of Chemistry.

2.3. Extraction and isolation

The dried powders of *C. hakodae* Ninh (8.0 kg) were sonicated with hot methanol (3 times × 10 L, each 3 h) to obtain a MeOH extract (550.0 g) after evaporation of the solvent. The extraction was suspended in water and successively partitioned with organic solvents to obtain *n*-hexane (CH1A, 15.2 g), dichloromethane (CH1B, 20.3 g), ethyl acetate (CH1C, 70.1 g), and water (CH1D).

CH1D was chromatographed on a Diaion HP-20 column, eluting with water to remove sugar components. Elution was then used methanol/water (25, 50, 75, and 100% methanol, 1.5 L each step) to obtain four fractions, CH2A-CH2D. CH2C (62.4 g) was fractionated using *silica gel* CC and eluted with a gradient of EtOAc-MeOH (20:1 – 0:1, *v*/*v*) to obtain five fractions, CH3A-CH3E. Fraction CH3B (10.3 g) was isolated by an RP-18 column, eluting with MeOH-water (1:2.0, v/v), resulting in three fractions, CH4A-CH4C. Fraction CH4B was chromatographed on an HPLC using 28% ACN to yield compound **1** (7.1 mg). Fraction CH3C (15.6 g) was chromatographed on an RP-18 column, eluting with MeOH/water (1:3, v/v), resulting in four fractions, CH5A-CH5D. Fractions CH5A (3.6 g) and CH5B (5.4 g) were chromatographed on an HPLC using 18% ACN to yield compounds **4** (40.3 mg) and **5** (31.0 mg), respectively. Fraction CH5C (0.4 g) was purified on Sephadex LH-20 CC, eluting with MeOH:H_2O (1:1, *v*/*v*) to yield compound **3** (100.1 mg). Fraction CH3D (18.2 g) was isolated by an RP-18 column, eluting with MeOH/water (1:2.4, v/v), resulting in four fractions, CH6A-CH6D. Fraction CH6A was chromatographed on an HPLC using 18% ACN to yield compound **2** (31.6 mg).

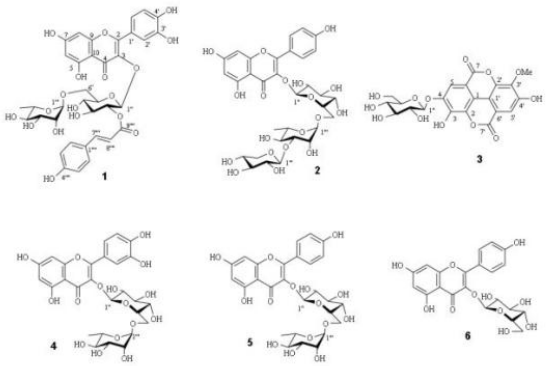

Fig. 1. Chemical structures of compounds (**1**–**6**) isolated from *C. hakodae*

Fraction CH1B (20.3 g) was fractionated using *silica gel* CC and eluted with a gradient of *n*-hexane-acetone (100:0 – 0:1, *v*/*v*) to obtain four fractions, CH7A-CH7D. Fraction CH7C (5.6 g) was isolated by an RP-18 column, eluting with acetone-water (1.8:1, v/v), resulting in three fractions, CH8A-CH8C. Fraction CH8B was chromatographed on an HPLC using 25% ACN to yield compound **6** (23.3 mg).

Table 1. ^{1}H (600 MHz) and ^{13}C NMR (150 MHz) spectral data of compounds **1–3**

C	**1**		**2**		C	**3**	
	δ_C[a]	δ_H (*J* in Hz)[a]	δ_C[a]	δ_H (*J* in Hz)[a]		δ_C[a]	δ_H (*J* in Hz)[a]
2	158.8	-	159.5	-	1	114.9	-
3	134.9	-	135.5	-	2	136.3	-
4	179.1	-	179.4	-	3	146.0	-
5	163.1	-	163.0	-	4	148.0	-
6	99.9	6.17 (d, 2.4)	100.1	6.24 (d, 1.8)	5	113.3	7.71 (s)
7	166.1	-	166.3	-	6	114.9	-
8	94.8	6.35 (d, 2.4)	95.1	6.43 (d, 1.8)	7	158.7	-
9	158.4	-	158.7	-	1′	111.6	-
10	105.7	-	105.7	-	2′	142.0	-
1′	123.2	-	122.8	-	3′	140.0	-
2′	117.4	7.60 (d, 2.4)	132.6	8.10 (d, 9.0)	4′	152.5	-
3′	145.9	-	116.1	6.91 (d, 9.0)	5′	111.2	7.50 (s)
4′	149.7	-	161.5	-	6′	113.0	-
5′	116.2	6.89 (d, 8.4)	116.1	6.91 (d, 9.0)	7′	159.0	-
6′	123.6	7.58 (dd, 2.4, 8.4)	132.6	8.10 (d, 9.0)	**4-*O*-glucose**		
3-*O*-glucose			**3-*O*-glucose**		1″	103.1	4.86 (d, 7.2)
1″	100.9	5.54 (d, 7.8)	104.5	5.14 (d, 7.2)	2″	73.4	3.33 (dd, 9.0, 7.2)
2″	75.8	5.06 (dd, 7.8, 9.0)	75.8	3.48 (m)	3″	75.9	3.31 (t, 9.0)
3″	76.3	3.64 (t, 9.0)	78.2	3.43 (m)	4″	69.6	3.20 (t, 9.0)
4″	71.7	3.39 (m)	71.7	3.23 (m)	5″	77.3	3.36 (m)

C	1		2		C	3	
	δ_C[a]	δ_H (*J* in Hz)[a]	δ_C[a]	δ_H (*J* in Hz)[a]		δ_C[a]	δ_H (*J* in Hz)[a]
5″	77.4	3.44 (m)	77.2	3.38 (m)	6″	60.7	3.53 (dd, 12.0, 5.4) 3.72 (dd, 12.0, 1.8)
6″	68.3	3.47 (m)/3.90 (m)	69.0	3.84 (m) 3.41 (m)	OCH_3	60.9	4.03 (s)
6″-*O*-rhamnose			**6″-*O*-rhamnose**				
1‴	102.3	4.58 (d, 1.8)	102.3	4.53 (d, 1.2)			
2‴	72.1	3.68 (dd, 1.8, 3.6)	71.7	3.80*			
3‴	72.3	3.56 (dd, 3.6, 9.6)	82.5	3.56 (dd, 9.0, 3.0)			
4‴	73.9	3.29 (m)	72.7	3.44*			
5‴	69.8	3.50 (m)	69.4	3.51*			
6‴	17.9	1.15 (d, 6.0)	17.9	1.13 (d, 6.0)			
2″-*O*-coumaroyl			**3‴-*O*-arabinose**				
1‴′	127.4	-	106.4	4.36 (d, 7.8)			
2‴′	131.2	7.47 (d, 8.4)	75.3	3.26 (dd, 9.0, 7.8)			
3‴′	116.8	6.83 (d, 8.4)	77.5	3.36 (t, 9.0)			
4‴′	161.2	-	71.1	3.50 (m)			
5‴′	116.8	6.83 (d, 8.4)	66.9	3.80* 3.15 (dd, 11.4, 10.8)			
6‴′	131.2	7.47 (d, 8.4)					
7‴′	147.0	7.71 (d, 15.6)					
8‴′	115.3	6.39 (d, 15.6)					
9‴′	168.6	-					

*[a]Recorded in CD_3OD, [b]Recorded in DMSO-d_6, *Overlapped signals.*

Compound **1** (camelliquercetiside D): yellow amorphous powder; HR-ESI-MS: *m/z* 755.1818 $[M-H]^-$, calcd. for $[C_{36}H_{35}O_{18}]^-$ 755.1829 (Δ=-1.5 ppm). ^{1}H-NMR (600 MHz, CD_3OD) and ^{13}C-NMR (150 MHz, CD_3OD) data see Table 1.

Compound **2** (tsubakioside A): yellow amorphous powder; ^{1}H-NMR (600 MHz, CD_3OD) and ^{13}C-NMR (150 MHz, CD_3OD) data see Table 1.

Compound **3** (stachyanthuside A): white powder; HR-ESI-MS: *m/z* 477.0676 $[M-H]^-$, calcd. for $[C_{21}H_{17}O_{13}]^-$: 477.0675, Δ=+0.2 ppm. ^{1}H-NMR (600 MHz, DMSO-d_6) and ^{13}C-NMR (150 MHz, DMSO-d_6) data see Table 1.

Compound **4** (rutin): yellow amorphous powder. ^{1}H-NMR (600 MHz, CD_3OD) and ^{13}C-NMR (150 MHz, CD_3OD) data see Table 2.

Compound **5** (kaempferol 3-rutinoside): yellow amorphous powder. ^{1}H-NMR (600 MHz, CD_3OD) and ^{13}C-NMR (150 MHz, CD_3OD) data see Table 2.

Compound **6** (kaempferol 3-*O*-*β*-D glucopyranoside): yellow amorphous powder. ^{1}H-NMR (600 MHz, CD_3OD) and ^{13}C-NMR (150 MHz, CD_3OD) data see Table 2.

2.4. α-Glucosidase inhibitory activity assay

The *α*-glucosidase (G0660, Sigma-Aldrich, St. Louis, MO) enzyme inhibition assay was performed according to the previously described method [9]. In brief, 20 µL of sample solution and 40 µL of *α*-glucosidase solution were well mixed with 100 µL of 0.1 M phosphate buffer (pH 7.0) in a 96-well plate. After 5 min pre-incubation at 37°C, the substrate, *p*-nitrophenyl-*α*-D-glucopyranoside solution (40 µL) was added, and the reaction mixture was incubated at 37°C for 30 min. The absorbance was then measured at 405 nm by using an ELISA Bio-Rad microplate reader. Acarbose was used as a positive control.

3. Results and discussion

3.1. Structure elucidation

Phytochemical study on the methanol extract of *C. hakodae* Ninh (Fig. 1) led to the isolation of six compounds. Their chemical structures were elucidated using HR-ESI-MS and NMR spectra in comparison with the published data.

Compound **1** was obtained as a yellow amorphous powder. Its molecular formula was determined to be $C_{36}H_{36}O_{18}$ based on its HR-ESI-MS (found *m/z* 755.1818 $[M-H]^-$, calcd. for $[C_{36}H_{35}O_{18}]^-$: 755.1829, Δ=-1.5 ppm). The ^{1}H NMR spectrum of compound **1** suggested a *para*-substituted benzene ring at δ_H 7.47 and 6.83 (*each* 2H, d, J = 8.4 Hz); three protons of an ABX system at δ_H 7.60 (1H, d, J = 2.4 Hz), 7.58 (1H, dd, J = 8.4, 2.4 Hz), and 6.89 (1H, d, J = 8.4 Hz), two *meta*-coupling aromatic protons at δ_H 6.35 and 6.17 (each 1H, d, J = 2.4 Hz), a *trans* double bond at δ_H 7.71 and 6.39 (each 1H, d, J = 15.6 Hz), and two anomeric protons at δ_H 5.54 (1H, d, J = 7.8 Hz) and 4.58 (1H, d, J = 1.8 Hz). The ^{13}C NMR spectrum of compound **1** showed signals for 36 carbons (Table 1). These included a carbonyl group at δ_C 168.6, a vinyl group at δ_C 147.0 and 115.3, and signals of a *para*-substituted benzene ring at δ_C 161.2, 131.2×2C, 127.4, and 116.8×2C, which were assigned to the presence of a

coumaroyl moiety. Other signals of 15 sp^2-hybridized carbons (δ_C 94.8–166.1) were assigned for the flavone skeleton. The sugar moieties were identified as a glucose (δ_C 100.9, 75.8, 76.3, 71.7, 77.4, and 68.3) and a rhamnose (δ_C 102.3, 72.1, 72.3, 73.9, 69.8, and 17.9) with the aid of HSQC spectrum. The above evidence suggested compound **1** was a flavonoid glycoside bearing a coumaroyl moiety, similar to the isolated compounds from other *Camellia* species [10]. The HMBC correlations from H-1″ glc (δ_H 5.54) to C-3 (δ_C 134.9) confirmed the position of the glucose moiety at C-3. The coumaroyl moiety was linked to C-2″ glc by an ester linkage, as confirmed by HMBC correlation from glc H-2″ (δ_H 5.06) to C-9‴ (δ_C 168.6). The HMBC correlation from H-1‴ rha (δ_H 4.58) to C-6″ glc (δ_C 68.3) confirmed the position of the rhamnose moiety at C-6″ glc (Fig. 2). The large J value (7.8 Hz) of an anomeric proton (glucose) at δ_H 5.54 suggested β-form and the small J value (1.8 Hz) of an anomeric proton (rhamnose) at δ_H 4.58 suggested α-form of the glycosidic linkages. Thus, the chemical structure of compound **1** was determined to be camelliquercetiside D [10]. This compound has been isolated from *C. sinensis* and exhibited significant alcohol dehydrogenase (ADH, IC_{50} = 41.5 ± 1.1 μM) and radical scavenging (DPPH, IC_{50} = 29.2±0.1 μM) activities [10].

Compound **2** was isolated as a yellow amorphous powder. The ^{1}H NMR spectrum showed a *para*-substituted benzene ring at δ_H 8.10 and 6.91 (each 2H, d, J = 9.0 Hz); two *meta*-coupling aromatic protons at δ_H 6.43 and 6.24 (each 1H, d, J = 1.8 Hz), and three anomeric protons at δ_H 5.14 (1H, d, J = 7.2 Hz), 4.53 (1H, d, J = 1.2 Hz), and 4.36 (1H, d, J = 7.8 Hz), suggesting a kaempferol glycoside. The ^{13}C NMR and HSQC spectra of **2** indicated 32 carbons, including 6 from a glucopyranoside, 6 from a rhamnopyranoside, 5 from a xylopyranoside, and 15 from a flavonoid, a main substance class of *Camellia* species [2],[11],[12]. The sugar moiety linked to C-3 as indicated by the HMBC correlation from glc H-1″ (δ_H 5.14) to C-3 (δ_C 135.5). The HMBC correlations from glc H-1‴ (δ_H 4.53) to C-6″ (δ_C 69.0) and from xyl H-1⁗ (δ_H 4.36) to rha C-3‴ (δ_C 82.5) proved the sugar linkages, xylopyranosyl-(1→3)-rhamnopyranosyl-(1→6)-glucopyranoside.

Therefore, compound **2** was suggested to be tsubakioside A [13]. The NMR data of **2** (in cluding J values of the anomeric protons) were compared to those of tsubakioside A and found to perfectly match.

Table 2. ^{1}H (600 MHz) and ^{13}C NMR (150 MHz) spectral data of compounds **4–6**

C	4		5		6	
	δ_C[a]	δ_H (J in Hz)[a]	δ_C[a]	δ_H (J in Hz)[a]	δ_C[a]	δ_H (J in Hz)[a]
2	158.6	-	161.5	-	156.3	-
3	135.6	-	135.5	-	133.2	-
4	179.4	-	179.4	-	177.5	-
5	163.0	-	163.0	-	161.2	-
6	100.1	6.22 (s)	100.1	6.22 (d, 1.8)	98.8	6.21 (d, 1.8)
7	166.5	-	166.2	-	164.4	-
8	95.0	6.40 (s)	95.0	6.41 (d, 1.8)	93.7	6.40 (d, 1.8)
9	159.3	-	158.6	-	156.4	-
10	105.5	-	105.6	-	103.9	-
1′	123.1	-	122.8	-	120.9	-
2′	116.1	7.69 (s)	132.4	8.08 (d, 9.0)	130.9	8.07 (d, 9.0)
3′	145.9	-	116.1	6.91 (d, 9.0)	115.1	6.91 (d, 9.0)
4′	149.8	-	159.4	-	160.0	-
5′	117.7	6.90 (d, 8.4)	161.5	-	115.1	6.88 (d, 9.0)
6′	123.6	7.65 (d, 8.4)	135.5	-	130.9	8.04 (d, 9.0)
3-Glucose			**3-Glucose**		**3-Glucose**	
1″	104.8	5.12 (d, 7.8)	104.6	5.14 (d, 7.8)	100.9	5.25 (d, 7.8)
2″	75.7	3.28-3.29*	75.8	3.27-3.48*	74.2	3.35*
3″	78.2	3.28-3.29*	78.2	3.27-3.48*	76.4	3.40-3.50*
4″	71.4	3.40-3.50*	71.5	3.27-3.48*	69.9	3.40-3.50*
5″	77.2	3.30-3.32*	77.2	3.27-3.48*	77.5	3.23 (m)
6″	68.6	3.83 (br d, 10.8) 3.58 (dd, 10.8, 3.0)	68.6	3.81 (br d, 10.8) 3.56 (dd, 10.8, 3.0)	60.9	3.54 (dd, 12.0, 5.4) 3.71 (br d, 12.0)

C	4		5		6	
	δ_C[a]	δ_H (*J* in Hz)[a]	δ_C[a]	δ_H (*J* in Hz)[a]	δ_C[a]	δ_H (*J* in Hz)[a]
6″-Rhamnose			**6″-Rhamnose**			
1‴	102.4	4.55 (br s)	102.4	4.53 (br s)		
2‴	72.1	3.78 (br s)	72.1	3.65 (br d, 3.0)		
3‴	72.2	3.40-3.52*	72.3	3.27-3.48*		
4‴	73.9	3.40-3.52*	73.9	3.27-3.48*		
5‴	69.7	3.40-3.52*	69.7	3.27-3.48*		
6‴	17.9	1.15 (d, 6.0)	17.9	1.15 (d, 6.0)		

[a]*Recorded in CD_3OD, *Overlapped signals.*

Compound **3** was isolated as a white powder. Its molecular formula, $C_{21}H_{18}O_{13}$, was confirmed by HR-ESI-MS (*m/z* 477.0676 $[M-H]^-$, calcd. for $[C_{21}H_{17}O_{13}]^-$ 477.0675). The ^1H NMR spectrum of **3** revealed two protons as singlets at δ_H 7.71 and 7.50 (each 1H, s), an aromatic methoxy group at δ_H 4.03 (3H, s), and one anomeric proton at δ_H 4.86 (1H, d, J = 7.2 Hz). The ^{13}C NMR spectrum showed 21 carbon atoms, including 12 quaternary carbons, 7 methines, one methylene, and one methyl carbon, as observed in the HSQC spectrum. Six carbon signals at δ_C 103.1, 77.3, 75.9, 73.4, 69.6, and 60.7 were assigned to a glucose unit. The remaining 14 carbon signals suggested that compound **3** is ellagic acid. The HMBC interaction between the methoxy group (δ_H 4.03) and C-3′ (δ_C 140.0) of ellagic acid indicated the location of the methoxy group at carbon C-3′. The location of glucopyranosyl group at C-4 was demonstrated by the HMBC interaction from H-1″ glc (δ_H 4.86) to C-4 (δ_C 148.0) of ellagic acid. Thus, compound **3** was determined to be stachyanthuside A [14]. This compound has been reported to have good chemical reduction properties [15].

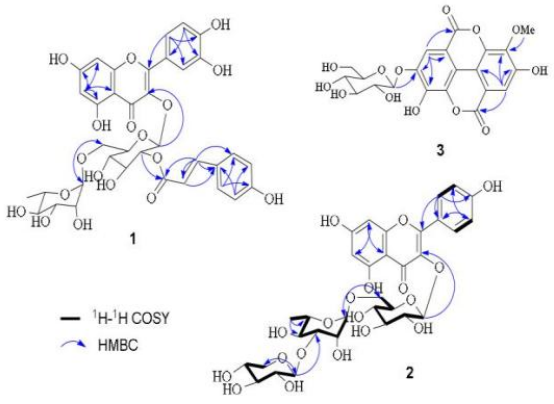

Fig. 2. Key HMBC and ^1H-^1H COSY correlations of compounds **1**-**3**

Compound **4** was obtained as a yellow amorphous powder. The ^1H NMR and ^{13}C NMR spectra showed signals for 27 carbons, including 15 carbons from a flavonoid, six carbons from a glucopyranoside unit, and six carbons from a rhamnopyranoside unit. The NMR data for **4** were similar to those of **1** except for the loss of a coumaroyl group. The NMR data for **4** matched well with those of rutin [16] (Table 2).

Compounds **5** and **6** were identified as kaempferol 3-rutinoside [17] and kaempferol 3-*O*-*β*-D glucopyranoside [18], respectively, by comparing their physical data with the previous literature and found to match.

3.2. α-Glucosidase inhibitory activity

Compounds **1**–**6** were evaluated for *α*-glucosidase inhibitory activity at a concentration of 500 μM. Except for compound **3**, other isolated compounds exhibited significant *α*-glucosidase inhibitory activity, showing over 50% inhibition (data not shown). Consequently, these compounds were selected for further evaluation at serial concentrations ranging from 0 to 500 μM to determine their IC_{50} values. As a result, compounds **1**, **2**, **4**–**6** exhibited significant *α*-glucosidase inhibitory activity, with IC_{50} values of 35.41 ± 0.02, 15.43 ± 0.39, 10.64 ± 0.23, 17.21 ± 0.34, and 19.42 ± 0.25 μM, respectively. The obtained IC_{50} values are smaller than that of the positive control, acarbose (47.10 ± 1.40 μM) indicating potential *α*-glucosidase inhibitors. In addition, the active compounds possessed either quercetin or kaempferol glycosides. Quercetin glycoside (**4**) exhibited higher inhibitory activity compared to kaempferol glycosides (**2**, **5**, and **6**), however, its courmaroylated derivative (**1**) displayed weaker inhibitory activity. Overall, the results suggested that these phenolic compounds may play an important role in the anti-diabetic effects of some teas made from *C. hakodae* Ninh. Further studies should be carried out such as enzyme kinetic, *in silico*, and *in vivo* evaluations to confirm the potential *α*-glucosidase inhibitory activity of those compounds.

4. Conclusion

In this study, six phenolic compounds, including camelliquercetiside D (**1**), tsubakioside A (**2**), stachyanthuside A (**3**), rutin (**4**), kaempferol 3-rutinoside (**5**), and kaempferol 3-*O*-*β*-D glucopyranoside (**6**), were isolated from the methanol extract of *C. hakodae* Ninh. This is the first report on the isolation of these compounds from *C. hakodae* Ninh. Notably, compound **5** was also first isolated from the *Camellia* genus. Compounds **1**, **2**, **4**, **5**, and **6** exhibited *α*-glucosidase inhibitory activity with IC_{50} values of 35.41 ± 0.02, 15.43 ± 0.39, 10.64 ± 0.23, 17.21 ± 0.34, and 19.42 ± 0.25 μM, respectively. This is also the first report on the *α*-glucosidase inhibitory activity of compounds from *C. hakodae* Ninh. The results suggest that this plant could be useful for the development of anti-diabetic products.

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