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FLAVONOL AND LIGNAN GLYCOSIDES FROM *Datura metel* L.

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ABSTRACT

Chemical investigation of an acidic methanol extract of the whole plants of *D. metel* resulted in the isolation of five compounds, including kaempferol 3-*O*-*β*-D-glucosyl(1→2)-*β*-D-galactoside 7-*O*-*β*-D-glucoside (**1**), kaempferol 3-*O*-*β*-glucopyranosyl(1→2)-*β*-glucopyranoside-7-*O*-*α*-rhamnopyranoside (**2**), pinoresinol *O*-*β*-D-glucopyranoside (**3**), (7*R*,8*S*,7′*S*,8′*R*)-4,9,4′,7′-tetrahydroxy-3,3′-dimethoxy-7,9′-epoxylignan-4-*O*-*β*-D-glucopyranoside (**4**), and (7*S*,8*R*,7′*S*,8′*S*)-4,9,4′,7′-tetrahydroxy-3,3′-dimethoxy-7,9′-epoxylignan-4-*O*-*β*-D-glucopyranoside (**5**). Their structures were elucidated by 1D and 2D NMR and MS spectroscopic analyses as well as comparing with the data reported in the literature. The absolute configurations of compounds **4** and **5** were determined by CD spectra. It is noted that (7*R*,8*S*,7′*S*,8′*R*)-4,9,4′,7′-tetrahydroxy-3,3′-dimethoxy-7,9′-epoxylignan-4-*O*-*β*-D-glucopyranoside and (7*S*,8*R*,7′*S*,8′*S*)-4,9,4′,7′-tetrahydroxy-3,3′-dimethoxy-7,9′-epoxylignan-4-*O*-*β*-D-glucopyranoside were isolated for the first time from the *Datura* genus.

Keywords: Datura metel, *Solanaceae*, Flavonol glycoside, Lignan glycoside.

1. INTRODUCTION

Datura metel L. is an annual herb of the Solanaceae family and is widely cultivated in many tropical and temperate regions. In the Vietnamese traditional medicine, *D. metel* has been used for the treatment of coughs, bronchial asthma, and rheumatism [1]. Its leaves have been used as anesthetics in surgery, a fumigant in bronchial asthma, and anti-contractive agents in the stomach ulcers [1]. The flowers of *D. metel* have been used widely in the Chinese traditional medicine for the treatment of asthma, convulsions, pain, and rheumatism for centuries [2]. Previous pharmacological studies have showed that the *D. metel* seeds have hypoglycemic activity in normal and alloxan-induced diabetic rats [3], the chloroform extract of *D. metel* exhibits an antifungal effect toward several pathogenic species of *Aspergillus* [4], and the seeds and fruit pulps of *D. metel* show high antioxidant activity [5]. Previous chemical studies have demonstrated that the major chemical components of *D. metel* are with anolide-type steroids [6 – 12], which have been shown to suppress NO production in lipopolysaccharide (LPS)-stimulated RAW264.7 cells [11, 12] and exhibit cytotoxicity against HCT-116, A549, DLD-1, BGC-823,

and K562 cancer cell lines [6, 7, 10]. In addition, some megastigmane sesquiterpenes and amide alkaloids from *D. metel* were also reported [13, 14]. In the present study, we report the isolation and structural elucidation of two flavonol glycosides (**1** and **2**) and three lignan glycosides (**3-5**) from the acidic methanol extract of the whole plants of *D. metel*.

2. MATERIAL AND METHODS

2.1. General experimental procedures

All NMR spectra were recorded on a Bruker AM500 FT-NMR spectrometer (500 MHz for ^{1}H and 125 MHz for ^{13}C-NMR), chemical shifts are reported in ppm using TMS as an internal standard. ESIMS spectra were recorded on Agilent 1100 spectrometer. Circular dichroism (CD) spectra were measured on a Chirascan CD spectrometer (Applied Photophysics Ltd., Surrey, UK). Column chromatography (CC) was performed on silica gel 230 - 400 mesh or reversed phase (RP) C_{18} resins (150 μm, Fuji Silysia Chemical Ltd.). Compounds were visualized by spraying with aqueous 10 % H_2SO_4 and heating for 5 minutes.

2.2. Plant material

The whole plants of *D. metel* were collected in Thai Binh province, Vietnam during May 2015, and identified by Dr. Bui Van Thanh, Institute of Ecology and Biological Resources. A voucher specimen (NCCT-CDM-5.2015) was deposited at the Herbarium of the Institute of Marine Biochemistry, VAST.

2.3. Extraction and isolation

The dried whole plants of *D. metel* (5 kg) were ground and extracted with MeOH/acetic acid (pH = 5.0) under sonication at room temperature. After concentration under reduced pressure, the MeOH extract (300 g) was suspended in water and partitioned with $CHCl_3$ to give $CHCl_3$- and water-soluble fractions. The water-soluble fraction was alkalinized by adding NH_4OH until pH = 9.0, and then partitioned successively with CH_2Cl_2 and EtOAc to provide CH_2Cl_2-, EtOAc-, and water-soluble fractions, respectively. The water-soluble fraction was neutralized and subjected to fractionation through a Diaion HP-20 column, eluted with a gradient of MeOH in water (25–100 %) to give four fractions (DMW1–DMW4). Fraction DMW2 was separated using RP C_{18} column chromatography (CC), eluting with MeOH-H_2O (1:3, v/v) to yield subfractions DMW21–DMW25. Subfraction DMW22 was then separated by silica gel CC, eluting with CH_2Cl_2-MeOH-H_2O (5:1:0.05, v/v/v) to give **1** (25 mg) and **4** (6 mg). Subfraction DMW23 was separated by silica gel CC, eluting with CH_2Cl_2-MeOH-H_2O (6:1:0.05, v/v/v) and further purified by a RP C_{18} CC, eluting with MeOH-H_2O (1:3, v/v) to yield **5** (6 mg). Subfraction DMW25 was separated using silica gel CC, eluting with CH_2Cl_2-MeOH-H_2O (6:1:0.05, v/v/v) and subsequently purified by RP C_{18} CC, eluting with MeOH-H_2O (1:2, v/v) to release **2** (20 mg). Fraction DMW42 was separated by silica gel CC, eluting with CH_2Cl_2-MeOH-H_2O (6:1:0.05, v/v/v) to provide four subfractions (DMW421–DMW424). Subfraction DMW424 was separated by RP C_{18} CC, eluting with acetone-H_2O (1:3, v/v) to obtain **3** (5 mg).

Kaempferol 3-O-β-D-glucosyl(1→2)-β-D-galactoside 7-O-β-D-glucoside (1): yellow, amorphous powder; $C_{33}H_{40}O_{21}$, M = 772; ESI-MS *m/z*: 795 $[M+Na]^+$; ^{1}H NMR (DMSO-d_6, 500 MHz) δ_H: 6.43 (d, *J* = 2.0 Hz, H-6), 6.80 (d, *J* = 2.0 Hz, H-8), 8.11 (d, *J* = 8.5 Hz, H-2′ and H-6′), 6.90 (d, *J* = 8.5 Hz, H-3′ and H-5′), 5.68 (d, *J* = 7.5 Hz, H-1″), 4.58 (d, *J* = 8.0 Hz, H-1‴), 5.07 (d, *J* = 7.0 Hz, H-1⁗); ^{13}C NMR (DMSO-d_6, 125 MHz): see Table 1.

Table 1. ^{13}C NMR data (500 MHz) for compounds **1**–**5.**

C	**1**		**2**		**3**		**4**		**5**	
	δ_C [#1]	δ_C [a]	δ_C [#2]	δ_C [b]	δ_C [#3]	δ_C [b]	δ_C [#4]	δ_C [a,b]	δ_C [#5]	δ_C [a,b]
1					53.7	55.5	133.5	138.5	133.8	137.8
2	156.2	156.2	159.5	159.4	85.1	87.5	110.6	111.7	110.9	111.8
3	133.2	133.2	135.2	135.1			147.4	150.8	147.4	150.9
4	177.7	177.7	180.0	179.7	71.0	72.6	145.8	147.1	145.6	147.6
5	160.9	160.9	163.0	163.0	53.5	55.3	115.1	117.8	115.1	117.8
6	99.4	99.4	100.7	100.5	84.9	87.0	118.9	120.0	118.9	120.4
7	162.8	162.8	163.6	163.4			83.4	84.6	82.8	85.4
8	94.5	94.5	95.6	95.5	71.0	72.6	53.9	53.7	51.9	55.9
9	156.0	156.0	158.2	158.0			61.6	62.4	60.4	63.3
10	105.6	105.6	107.6	107.5						
1′	120.8	120.8	122.7	122.5	132.3	133.7	138.4	136.0	138.3	136.2
2′	131.2	131.2	132.5	132.4	110.6	110.9	111.1	111.5	110.4	111.4
3′	115.4	115.4	116.4	116.3	146.0	147.0	148.7	148.9	148.7	149.0
4′	160.2	160.2	161.7	161.8	147.5	149.1	145.8	147.3	145.8	148.5
5′	115.4	115.4	116.4	116.3	115.2	116.0	114.9	115.9	114.7	115.9
6′	131.2	131.2	132.5	132.4	118.6	119.7	119.4	120.7	118.7	120.8
7′							74.8	76.6	73.7	77.4
8′							50.6	50.8	49.3	52.7
9′							69.5	71.6	69.5	71.3
1″	98.3	98.4	100.9	100.8	135.4	136.0	100.7	102.9	100.2	102.8
2″	80.5	80.5	82.8	82.6	110.8	111.5	73.3	74.9	73.3	74.9
3″	73.4	73.4	78.0	77.8	146.0	147.4	77.1	77.8	77.0	77.8
4″	67.7	67.7	71.3	71.2	149.1	150.9	69.7	71.3	69.7	71.3
5″	75.9	75.9	78.4	78.1	115.6	117.9	76.9	78.2	76.9	78.2
6″	60.0	60.0	62.6	62.4	118.2	120.0	60.7	62.5	60.7	62.5
1‴	104.3	104.3	104.8	104.7	100.4	102.8				
2‴	74.5	74.4	75.7	75.5	73.3	74.8				
3‴	76.5	76.5	78.0	77.8	76.8	77.8				
4‴	69.7	69.7	71.4	71.2	70.0	71.3				
5‴	77.0	77.0	78.3	78.2	77.0	78.2				
6‴	60.7	60.7	62.7	62.5	60.7	62.4				
1⁗	99.8	99.8	99.9	99.7						
2⁗	73.1	73.1	71.8	71.6						
3⁗	76.6	76.6	72.2	72.0						
4⁗	69.7	69.7	73.7	73.5						
5⁗	77.2	77.2	71.3	71.1						
6⁗	60.8	60.9	18.1	18.0						
OCH_3					55.7	56.3	55.7	56.7	55.6	56.7
					55.9	56.7	55.8	56.4	55.7	56.4

[a] Recorded in DMSO-d_6, [b] in CD_3OD; [#1] δ_C of 3-O-β-D-glucosyl(1→2)-β-D-galactoside 7-O-β-D-glucoside in DMSO-d_6 [16]; *[#2] δ_C of kaempferol 3-O-β-D-glucopyranosyl(1→2)-β-D-glucopyranoside-7-O-α-L-rhamnopyranoside in CD_3OD* [17]; *[#3] δ_C of pinoresinol O-β-D-glucopyranoside in DMSO-d_6* [1]; *[#4] δ_C of (7R,8S,7′S,8′R)-4,9,4′,7′-tetrahydroxy-3,3′-dimethoxy-7,9′-epoxylignan-4-O-β-D-glucopyranoside in DMSO-d_6* [15];

[#5] δ_C of (7S,8R,7′S,8′S)-4,9,4′,7′-tetrahydroxy-3,3′-dimethoxy-7,9′-epoxylignan-4-O-β-D-glucopyranoside in DMSO-d_6 [15].

Kaempferol 3-O-β-D-glucopyranosyl(1→2)-β-D-glucopyranoside-7-O-α-L-rhamnopyranoside (2): yellow, amorphous powder; $C_{33}H_{40}O_{20}$, M = 756; ESI-MS *m/z*: 779 $[M+Na]^+$; ^{1}H NMR (CD_3OD, 500 MHz) δ_H: 6.47 (s, H-6), 6.76 (s, H-8), 8.08 (d, *J* = 8.5 Hz, H-2′ and H-6′), 6.93 (d, *J* = 8.5 Hz, H-3′ and H-5′), 5.50 (d, *J* = 7.5 Hz, H-1″), 4.79 (d, *J* = 7.5 Hz, H-1‴), 5.59 (br s, H-1⁗), 1.27 (d, *J* = 6.5 Hz, H_3-6⁗); ^{13}C NMR (CD_3OD, 125 MHz): see Table 1.

Pinoresinol O-β-D-glucopyranoside (3): white, amorphous powder; $C_{26}H_{32}O_{11}$, M = 520; ESI-MS *m/z*: 543 $[M+Na]^+$; ^{1}H NMR (CD_3OD, 500 MHz) δ_H: 4.57 (H-2), 4.73 (H-6), 6.97 (s, H-2′), 6.95 (d, *J* = 8.5 Hz, H-5′), 6.79 (d, *J* = 8.5 Hz, H-6′), 7.05 (s, H-2″), 7.17 (d, *J* = 8.5 Hz, H-5″), 6.84 (d, *J* = 8.5 Hz, H-6″), 4.85 (d, *J* = 7.5 Hz, H-1‴), 3.87 and 3.89 (each s, OCH_3); ^{13}C NMR (CD_3OD, 125 MHz): see Table 1.

(7R,8S,7'S,8'R)-4,9,4',7'-Tetrahydroxy-3,3'-dimethoxy-7,9'-epoxylignan-4-O-β-D-glucopyranoside (4): white, amorphous powder; $C_{26}H_{34}O_{12}$, M = 538; ESI-MS *m/z*: 561 $[M+Na]^+$; CD (MeOH) λ_{max} ($\Delta\varepsilon$) 279 (–7.23) and 231 (–16.11) nm [15]: λ_{max} ($\Delta\varepsilon$) 277 (–1.84) and 231 (–5.34) nm]; ^{1}H NMR (CD_3OD, 500 MHz) δ_H: 7.03 (d, *J* = 2.0 Hz, H-2), 7.16 (d, *J* = 8.0 Hz, H-5), 6.94 (dd, *J* = 2.0, 8.0 Hz, H-6), 4.70 (d, *J* = 7.0 Hz, H-7), 1.91 (m, H-8), 3.33 (m, H-9a), 3.88 (m, H-9b), 6.88 (d, *J* = 2.0 Hz, H-2′), 6.76 (d, *J* = 8.0 Hz, H-5′), 6.74 (dd, *J* = 2.0, 8.0 Hz, H-6′), 4.49 (d, *J* = 8.5 Hz, H-7′), 2.55 (m, H-8′), 3.98 (m, H-9′a), 4.28 (dd, *J* = 4.5, 8.0 Hz, H-9′b), 4.91 (d, *J* = 7.5 Hz, H-1″), 3.88 (s, 3-OCH_3), 3.83 (s, 3′-OCH_3); ^{13}C NMR (CD_3OD, 125 MHz): see Table 1.

(7S,8R,7'S,8'S)-4,9,4',7'-Tetrahydroxy-3,3'-dimethoxy-7,9'-epoxylignan-4-O-β-D-glucopyranoside (5): white, amorphous powder; $C_{26}H_{34}O_{12}$, M = 538; ESI-MS *m/z*: 561 $[M+Na]^+$; CD (MeOH) λ_{max} ($\Delta\varepsilon$) 284 (+0.52), 233 (+17.45) nm [15]: λ_{max} ($\Delta\varepsilon$) 281 (+0.88) and 234 (+1.19) nm]; ^{1}H NMR (CD_3OD, 500 MHz) δ_H: 7.03 (br s, H-2), 7.16 (d, *J* = 8.5 Hz, H-5), 6.93 (br d, *J* = 8.5 Hz, H-6), 4.60 (d, *J* = 8.5 Hz, H-7), 2.29 (m, H-8), 3.67 (m, H_2-9), 7.01 (br s, H-2′), 6.80 (d, *J* = 8.0 Hz, H-5′), 6.85 (dd, *J* = 1.5, 8.0 Hz, H-6′), 4.50 (d, *J* = 9.0 Hz, H-7′), 2.64 (m, H-8′), 3.67 (m, H-9′a), 3.77 (dd, *J* = 6.5, 9.0 Hz, H-9′b), 4.86 (d, *J* = 7.5 Hz, H-1″), 3.89 (s, 3-OCH_3 and 3′-OCH_3); ^{13}C NMR (CD_3OD, 125 MHz): see Table 1.

3. RESULTS AND DISCUSSION

Compound **1** was obtained as a yellow, amorphous powder. Its molecular formula was established as $C_{33}H_{40}O_{21}$ by an ion peak $[M+Na]^+$ at *m/z* 795 in the ESIMS and the ^{13}C NMR spectroscopic analysis. The ^{1}H NMR of **1** showed signals for two meta coupled aromatic protons at δ_H 6.43 (d, *J* = 2.0 Hz, H-6) and 6.80 (d, *J* = 2.0 Hz, H-8) and a *para*-substituted aromatic ring at δ_H 8.11 (d, *J* = 8.5 Hz, H-2′ and H-6′) and 6.90 (d, *J* = 8.5 Hz, H-3′ and H-5′). The ^{1}H NMR spectrum further showed signals for three anomeric protons at δ_H 5.68 (d, *J* = 7.5 Hz, H-1″), 4.58 (d, *J* = 8.0 Hz, H-1‴), and 5.07 (d, *J* = 7.0 Hz, H-1⁗), revealing that **1** has three sugar units. Analysis of ^{13}C NMR and HSQC spectra indicated the presence of 33 carbons, including one carbonyl carbon at δ_C 177.7 (C-4), eight non-protonated aromatic carbons (of which five were oxygenated), and six aromatic methine carbons, suggesting that **1** possesses the flavonol skeleton (Table 1). The 18 remaining carbons were assigned to three sugar units, which were identified as two glucopyranoses and one galactopyranose by comparison with those reported in the literature [16]. The relatively large spin couplings of the three anomeric protons ($J \geq 7.0$ Hz) are characteristic features of the β-configurations for the glucose and galactose units. In the HMBC spectrum, the HMBC correlations from δ_H 4.58 (H-1‴) to δ_C 80.5 (C-2″) and from δ_H

5.68 (H-1″) to δ_C 98.4 (C-3) suggested that the *β*-glucopyranosyl-(1→2)]-*β*-D-galactopyranoside sugar chain was located at C-3 position (Figure 2). The remaining *β*-glucopyranose was attached to C-7 by the HMBC correlation observed from δ_H 5.07 (H-1‴″) to δ_C 162.8 (C-7). On the basis of the above analysis, along with comparison with those of the reported flavonol glycoside [16], the structure of **1** was established as kaempferol 3-*O*-*β*-D-glucosyl(1→2)-*β*-D-galactoside 7-*O*-*β*-D-glucoside.

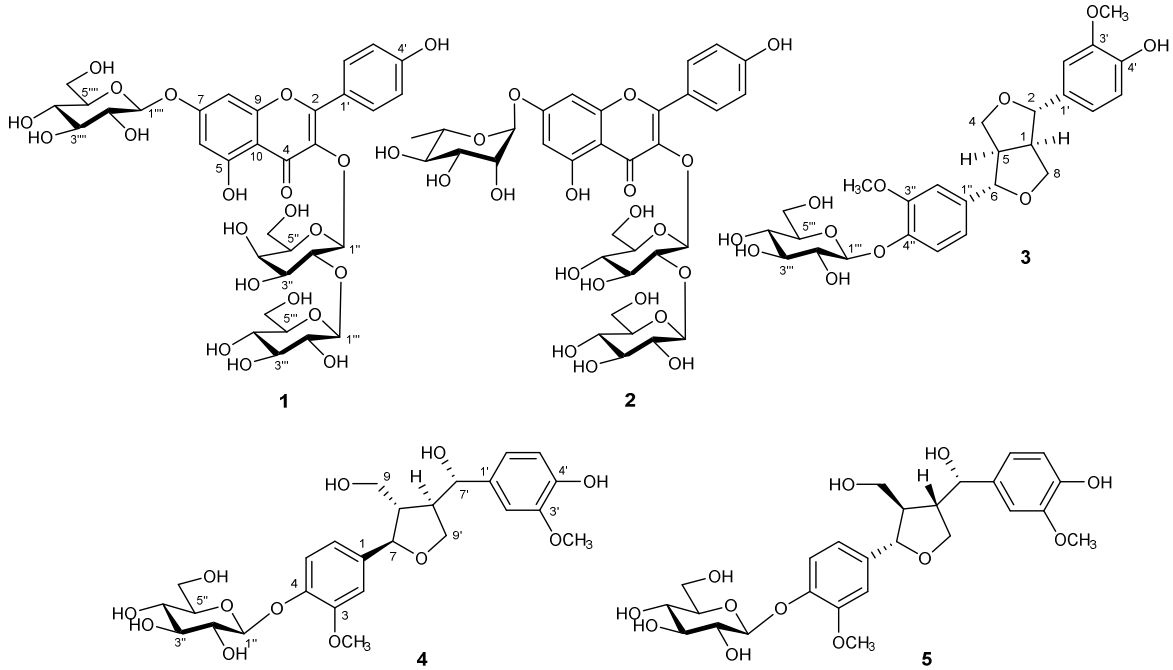

Figure 1. Chemical structures of compounds **1–5** from *D. metel*.

The molecular formula of compound **2** was determined to be $C_{33}H_{40}O_{20}$ by the presence of an ion $[M+Na]^+$ at *m/z* 779 in the ESIMS. The ^{1}H NMR spectrum contained signals for an AX spin system [δ_H 6.47 (s, H-6) and 6.76 (s, H-8)] and an AA′BB′ pattern at δ_H 8.08 (d, *J* = 8.5 Hz, H-2′ and H-6′) and 6.93 (d, *J* = 8.5 Hz, H-3′ and H-5′). The signals for three anomeric protons at δ_H 5.50 (d, *J* = 7.5 Hz, H-1″), 4.79 (d, *J* = 7.5 Hz, H-1‴), and 5.59 (br s, H-1‴″) observed in the ^{1}H NMR spectrum indicated the presence of three sugars in the structure. The ^{13}C NMR spectrum comprised 33 carbon signals, including 15 carbons of the aglycone and 18 carbons belonging to the sugar moiety (Table 1). Comparison of the ^{1}H and ^{13}C NMR data of **2** with those of **1** revealed that these compounds have the same aglycone but different sugar moieties. The sugar moiety of **2** was found to consist of two glucose units and one rhamnose by detailed analysis of ^{13}C NMR and HSQC spectra in comparison with the previously reported values [17]. The *β*-configurations for the anomeric protons of the glucopyranoses were deduced based on the relatively large coupling constants (*J* = 7.5 Hz), while the α-oriented anomeric proton of the rhamose was determined by its carbon chemical shift values of C-3 and C-5 positions [19]. The sugar chain at C-3 of the aglycone was identified as *β*-D-glucopyranosyl(1→2)-*β*-D-glucopyranoside by the HMBC correlations from δ_H 4.79 (H-1‴) to δ_C 82.6 (C-1″) and from δ_H 5.50 (H-1″) to δ_C 135.1 (C-3) (Figure 2). The location of the rhamnose at C-7 position was deduced by the HMBC cross-peak between δ_H 5.59 (H-1‴″) to δ_C 163.4 (C-7). Thus, the

structure of **2** was identified as kaempferol 3-*O*-*β*-D-glucopyranosyl(1→2)-*β*- D-glucopyranoside-7-*O*-*α*-L-rhamnopyranoside.

Compound **3** was isolated as a white, amorphous powder. Its molecular formula, $C_{26}H_{32}O_{11}$ was deduced by the observation of an ion peak $[M+Na]^+$ at *m/z* 543 in the ESIMS and ^{13}C NMR spectroscopic analysis. The ^1H NMR spectrum exhibited signals for two ABX spin systems at δ_H 6.97 (s, H-2′), 6.95 (d, *J* = 8.5 Hz, H-5′), 6.95 (d, *J* = 8.5 Hz, H-6′), 7.05 (s, H-2″), 7.17 (d, *J* = 8.5 Hz, H-5″), and 6.84 (d, *J* = 8.5 Hz, H-6″) and two methoxy groups at δ_H 3.87 and 3.89 (each s, 4′-OCH_3 and 4″-OCH_3). The signal of an anomeric proton at δ_H 4.85 (d, *J* = 7.5 Hz, H-1‴) observed in the ^1H NMR of **3** implied the presence of a sugar unit. The ^{13}C NMR and DEPT spectra displayed 26 carbon signals, of which six nonprotonated aromatic carbons (including four were oxygenated), six aromatic methines, two oxymethines at δ_C 87.5 (C-2) and 87.0 (C-6), two oxymethylenes at δ_C 72.6 (C-4 and C-8), two methines at δ_C 55.5 (C-1) and 55.3 (C-5), suggesting that **3** is a lignan derivative (Table 1). The six remaining carbon signals at δ_C 102.8, 74.8, 77.8, 71.3, 78.2, and 62.4 could be assigned to a glucopyranose. Comparison of the ^1H and ^{13}C NMR data of **3** with those of the reported lignan, pinoresinol *O*-*β*-D-glucopyranoside, revealed that the structures of these compounds are identical [18]. Therefore, the structure of compound **3** was identified as shown in Figure 1.

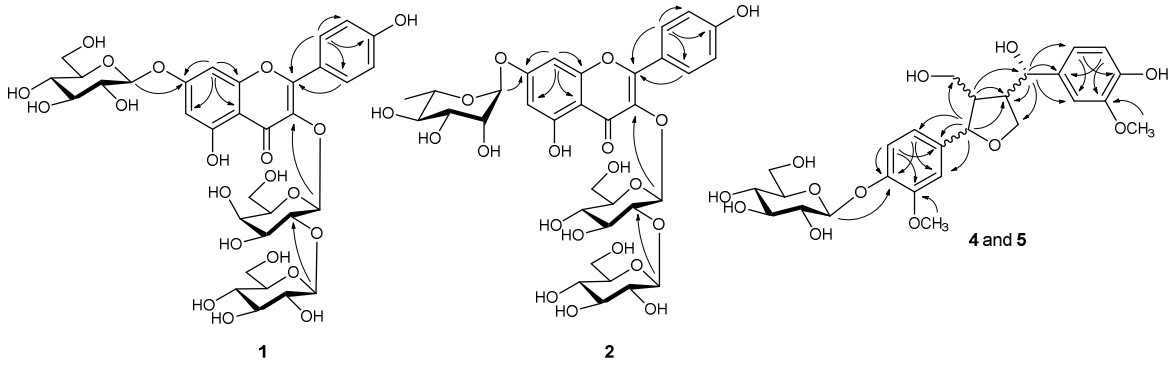

Figure 2. Selected HMBC correlations of compounds **1**, **2**, **4**, and **5.**

The ESIMS of compound **4** exhibited an ion $[M+Na]^+$ at *m/z* 561, corresponding with the molecular formula $C_{26}H_{34}O_{12}$. The ^1H NMR spectrum showed signals for two ABX spin systems at δ_H 7.03 (d, *J* = 2.0 Hz, H-2), 7.16 (d, *J* = 8.0 Hz, H-5), 6.94 (dd, *J* = 1.5, 8.5 Hz, H-6), 6.88 (d, *J* = 2.0 Hz, H-2′), 6.76 (d, *J* = 8.0 Hz, H-5′), and 6.74 (dd, *J* = 2.0, 8.0 Hz, H-6′) and two methoxy groups at δ_H 3.88 (s, 3-OCH_3) and 3.83 (3′-OCH_3). Compound **4** was found to have one sugar unit by the observation of an anomeric proton at δ_H 4.91 (d, *J* = 7.5 Hz, H-1″) in the ^1H NMR spectrum. Analysis of ^{13}C NMR and HSQC spectra indicated the presence of 26 carbons, including six non-protonated aromatic carbons (of which four were oxygenated), six aromatic methines, two oxymethines at δ_H 4.70/δ_C 84.6 (C-7) and δ_H 4.49/δ_C 76.6 (C-7′), two oxymethylenes at δ_H 3.33 and 3.88/δ_C 62.4 (C-9) and δ_H 3.98 and 4.28/δ_C 71.6 (C-9′), suggesting that **4** belongs to the lignan skeleton (Table 1). The sugar was suggested to be *β*-glucopyranose by the observation of six carbon signals at δ_C 102.9, 74.9, 77.8, 71.3, 78.2, and 62.5 and the large coupling constant of the anomeric proton (*J* = 7.5 Hz). Comparison of the ^1H and ^{13}C NMR data of **4** with those of the reported lignan glycoside, tetrahydroxy-3,3′-dimethoxy-7,9′-epoxylignan-4-*O*-*β*-D-glucopyranoside resulted in the close similarity [15]. In the HMBC

spectrum, the HMBC correlations from δ_H 4.70 (H-7) to δ_C 138.5 (C-1), 111.7 (C-2), and 120.0 (C-6) and from δ_H 4.49 (H-7′) to δ_C 136.0 (C-1′), 111.5 (C-2′), and 120.7 (C-6′) allowed to fix the location of the two 1,3,4-trisubstituted aromatic rings at C-7 and C-7′, respectively (Figure 2). The HMBC correlations from δ_H 3.88 to δ_C 150.8 (C-3) and from δ_H 3.83 to δ_C 148.9 (C-3′) indicated that the two methoxyl groups are located at C-3 and C-3′ positions. The position of the *β*-glucopyranose was determined to be at C-4 based on the HMBC correlations observed from δ_H 6.94 (H-2) to δ_C 147.1 (C-4) and from δ_H 4.91 (H-1″) to δ_C 147.1 (C-4). Based on the above analysis, the planar structure of **4** was established. The CD spectrum of **4** showed the negative Cotton effects at 279 nm ($\Delta\varepsilon$ -7.23) and 231 nm ($\Delta\varepsilon$ -16.11), which were in good agreement with those of the related compound, indicating the absolute configuration of **4** to be 7*R*,8*S*,7′*S*,8′*R* [15]. Thus, the structure of **4** was established as (7*R*,8*S*,7′*S*,8′*R*)-4,9,4′,7′-tetrahydroxy-3,3′-dimethoxy-7,9′-epoxylignan-4-*O*-*β*-D-glucopyranoside.

The molecular formula of compound **5**, $C_{26}H_{34}O_{12}$ was deduced by its ESIMS ion at *m/z* 561 $[M+Na]^+$ and ^1H and ^{13}C NMR spectra. The ^1H and ^{13}C NMR data of **5** were found to be very similar with those of **4**, except for the carbon chemical shift values of C-8 (**5**: δ_C 55.9 vs **4**: δ_C 53.7) and C-8′ (**5**: δ_C 52.7 vs **4**: δ_C 50.8), suggesting that these compounds are stereoisomers at C-8 and C-8′ (Table 1). This was supported by comparing the CD spectrum of **5** with that of the reported lignan glycoside, (7*S*,8*R*,7′*S*,8′*S*)-4,9,4′,7′-tetrahydroxy-3,3′-dimethoxy-7,9′-epoxylignan-4-*O*-*β*-D-glucopyranoside [**5**: λ_{max} ($\Delta\varepsilon$) 284 (+0.52) and 233 (+17.45) nm vs. λ_{max} ($\Delta\varepsilon$) 281 (+0.88) and 234 (+1.19) nm [15]. Hence, the structure of **5** was identified as shown in Figure 1.

4. CONCLUSION

Our chemical study of the acidic methanol extract of the *D. metel* whole plants led to the isolation and identification of five compounds, namely: kaempferol 3-*O*-*β*-D-glucosyl(1→2)-*β*-D-galactoside 7-*O*-*β*-D-glucoside (**1**), kaempferol 3-*O*-*β*-D-glucopyranosyl(1→2)-*β*-D-glucopyranoside-7-*O*-*α*-L-rhamnopyranoside (**2**), pinoresinol *O*-*β*-D-glucopyranoside (**3**), (7*R*,8*S*,7′*S*,8′*R*)-4,9,4′,7′-tetrahydroxy-3,3′-dimethoxy-7,9′-epoxylignan-4-*O*-*β*-D-glucopyranoside (**4**), and (7*S*,8*R*,7′*S*,8′*S*)-4,9,4′,7′-tetrahydroxy-3,3′-dimethoxy-7,9′-epoxylignan-4-*O*-*β*-D-glucopyranoside (**5**). Among the isolates, (7*R*,8*S*,7′*S*,8′*R*)-4,9,4′,7′-tetrahydroxy-3,3′-dimethoxy-7,9′-epoxylignan-4-*O*-*β*-D-glucopyranoside and (7*S*,8*R*,7′*S*,8′*S*)-4,9,4′,7′-tetrahydroxy-3,3′-dimethoxy-7,9′-epoxylignan-4-*O*-*β*-D-glucopyranoside were reported for the first time from the *Datura* genus.

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REFERENCES

1. Chi V. V. - Dictionary of medicinal plants in Vietnam, Vietnamese Publisher of Medicine, Vol. 1, 2012, pp. 284.
2. Xiao P. G. - Modern Chinese Materia Medica. Chemical Industry Publishing House, Beijing, 2002, pp. 757.
3. Krishna Murthy B., Nammi S., Kota M. K., Krishna Rao R. V., Koteswara Rao N., Annapurna A. - Evaluation of hypoglycemic and antihyperglycemic effects of *Datura*

metel (Linn.) seeds in normal and alloxan-induced diabetic rats, J. Ethnopharmacol. **91** (2004) 95-98.

4. Rajesh Sharma G. L. - Studies on antimycotic properties of *Datura metel,* J. Ethnopharmacol. **80** (2002) 193-197.
5. Roy S., Pawar S., Chowdhary A. - Evaluation of In Vitro Cytotoxic and Antioxidant Activity of *Datura metel* Linn. and *Cynodon dactylon* Linn, Extracts. Pharmacognosy Res. **8** (2016) 123-127.
6. Ma L., Xie C. M., Li J., Lou F. C., Hu L. H. - Daturametelins H, I, and J: three new withanolide glycosides from *Datura metel* L. Chem. Biodivers. **3** (2006) 180-186.
7. Pan Y., Wang X., Hu X. - Cytotoxic withanolides from the flowers of *Datura metel,* J. Nat. Prod. **70** (2007) 1127-1132.
8. Yang B. Y., Xia Y. G., Wang Q. H., Dou D. Q., Kuang H. X. - Baimantuoluosides D-G, four new withanolide glucosides from the flower of *Datura metel* L, Arch. Pharm. Res. **33** (2010) 1143-1148.
9. Kuang H. X., Yang B. Y., Xia Y. G., Wang Q. H. - Two new withanolide lactones from flos daturae, Molecules **16** (2011) 5833-5839.
10. Bellila A., Tremblay C., Pichette A., Marzouk B., Mshvildadze V., Lavoie S., Legault J. - Cytotoxic activity of withanolides isolated from Tunisian *Datura metel* L, Phytochemistry **72** (2011) 2031-2036.
11. Yang B. Y., Guo R., Li T., Liu Y., Wang C. F., Shu Z. P., Wang Z. B., Zhang J., Xia Y. G., Jiang H., Wang Q. H., Kuang H. X. - Five withanolides from the leaves of *Datura metel* L. and their inhibitory effects on nitric oxide production, Molecules **19** (2014) 4548-4559.
12. Yang B. Y., Guo R., Li T., Wu J. J., Zhang J., Liu Y., Wang Q. H., Kuang H. X. - New anti-inflammatory withanolides from the leaves of *Datura metel* L, Steroids **87** (2014) 26-34.
13. Kuang H. X., Yang B. Y., Xia Y. G., Feng W. S. - Chemical constituents from the flower of *Datura metel* L, Arch. Pharm. Res. **31** (2008) 1094-1097.
14. Yang B. Y., Xia Y. G., Wang Q. H., Dou D. Q., Kuang H. X. - Two new amide alkaloids from the flower of *Datura metel* L, Fitoterapia **81** (2010) 1003-1005.
15. Yang Y. N., Huang X. Y., Feng Z. M., Jiang J. S., Zhang P. C. - Hepatoprotective activity of twelve novel 7'-hydroxy lignan glucosides from *Arctii Fructus,* J. Agric. Food Chem. **62** (2014) 9095-9102.
16. Han Y., Nishibe S., Noguchi Y., Jin Z. - Flavonol glycosides from the stems of *Trigonella foenum-graecum,* Phytochemistry **58** (2001) 577-580.
17. Kite G. C., Veitch N. C., Boalch M. E., Lewis G. P., Leon C. J., Simmonds M. S. - Flavonol tetraglycosides from fruits of *Styphnolobium japonicum* (Leguminosae) and the authentication of Fructus Sophorae and Flos Sophorae, Phytochemistry, **70** (2009) 785-794.
18. Deyama T. - The Constituents of *Eucommia ulmoides* OLIV. I. Isolation of (+)-Medioresinol Di-O-b-D-glucopyranoside, Chem. Pharm. Bull. **31** (1983) 2993-2997.
19. Kasai R., Okihara M., Asakawa J., Mizutani K., Tanaka O. - ^{13}C nmr study of alpha- and beta-anomeric pairs of d-mannopyranosides and l-rhamnopyranosides, Tetrahedron **35** (1979) 1427-1432.