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The chemical composition from the fruits of *Pandanus tonkinensis,* their NO production inhibitory and lipid peroxidation inhibitory activities

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Abstract

Seven known compounds, including two neolignans, four lignans, and one flavane were isolated from the methanol extract of *Pandanus tonkinenis* fruits. Their structures were determined to be ficusal (**1**), vladinol F (**2**), medioresinol (**3**), syringaresinol (**4**), lariciresinol (**5**), secoisolariciresinol (**6**), and luteoliflavan (**7**) by analysis of MS and NMR data as well as by comparison of their spectral data with those reported in the literature. All compounds were evaluated for NO production inhibitory and lipid peroxidative inhibitory activities. Compounds **5** and **7** showed significant NO production inhibitory with IC_{50} values of 5.3±0.4 and 7.1±0.4 μM, respectively. Compounds **6** and **7** showed significant lipid peroxidative inhibitory activity with IC_{50} values of 20.2±1.7 and 26.2±3.6 μM, respectively.

Keywords. *Pandanus tonkinenis,* anti-inflammatory activity, antioxidant activity.

1. INTRODUCTION

Pandanaceae is a family of flowering plants native to the tropics and subtropics, distributed from West Africa to the Pacific Ocean. Among them, *Pandanus* is the largest and the most important genus, with about 600 species, which could be used as a source of food and medicine. In Vietnam, the pineapple family (Pandanaceae) includes 23 species belonging to *Freycinetia* (3 species) and *Pandanus* (20 species). There are 9 *Pandanus* species that are used as medicine in Vietnam, mainly effective in kidney diseases (diuretics, treatment of kidney stones, gallstones, urinary tract infections, etc.), liver diseases (hepatitis, cirrhosis of the liver ascites), antipyretic, skin diseases, etc.[1,2] In Vietnam, the roots and fruits of some species such as *P. tectorius, P. odoratissimus, P. kaida* have been studied for their chemical composition and/or pharmacological effects.[3-5]

Pandanus tonkinensis Mart. B. ex Stone plant, also known as the Northern wild pineapple, widely distributed from the Northern midland mountains to the Southern central of Vietnam. According to the ancient knowledge, its buds, leaves, roots and fruits are commonly used as medicine.[1] Previously we reported the chemical constituents and their lipid peroxidative inhibitory activity from the roots of *P. tonkinensis*.[6] This paper continues to report the isolation and structural elucidation of seven known compounds from *P. tonkinensis* fruits. Their NO production inhibitory and lipid peroxidative inhibitory activities were also evaluated.

2. MATERIALS AND METHODS

2.1. Plant materials

Pandanus tonkinensis fruits were collected in Lai Chau province, Vietnam in April, 2021 and identified by Dr. Do Thi Xuyen, Department of Botany, Faculty of Biology, University of Science, Vietnam National University, Hanoi. A voucher specimen (HNU 024663) was deposited at the Museum of Biology, University of Science, Vietnam National University, Hanoi.

2.2. Experimental procedures

Thin layer chromatography (TLC) was performed on DC-Alufolien 60 F_{254} (Merck), RP-18 F_{254s} (Merck). Column chromatography (CC) was performed with either silica gel with a particle size of 0.040-0.063 mm or RP-18 (30-50 µm, Fuji Silysia Chemical Ltd.). Preparative liquid chromatography (HPLC) was performed on an HPLC Agilent 1100 system with a DAD detector, J'sphere ODS-H80 column (150 mm length × 20 mm ID), and the flow rate of 3.0 mL/min. NMR spectra were measured on a Bruker AM500 instrument (500 MHz for ^{1}H-NMR and 125 MHz for ^{13}C-NMR). High-resolution mass spectrometry was measured on an Agilent 6530 Accurate-Mass Q-TOF LC/MS.

2.3. Extraction and isolation

Pandanus tonkinensis fruits were sliced, dried and ground into powder. The total amount of 9.8 kg of dry powder was extracted with MeOH in an ultrasonic bath for 4 h (three times). After solvent evaporation, the crude methanol extract (250 g) was suspended in water (2 L) and then partitioned with dichloromethane and ethyl acetate to obtain the ethyl acetate extract (PTF, 215 g) and an aqueous solution. The PTF fraction (215 g) was separated on a silica gel column eluting with *n*-hexane/acetone (100/0, 40/1, 20/1, 10/1, and 5/1, v/v) and then dichloromethane/methanol (100/0, 20/1, 10/1, 5/1, 1/1, 100/0, v/v) to obtain 10 fractions (PTF1-PTF10). PTF6 (12.5 g) was chromatographed on an RP-18 column eluting with acetone/water (1/1.5, v/v) to obtain 6 fractions, PTF6A-PTF6F. PTF6B was chromatographed on a silica gel column eluting with dichloromethane/methanol (50/1, 35/1, 15/1, 10/1, v/v) to obtain six fractions (PTF6B1-PTF6B6). Compounds **1** (5.0 mg), **3** (6.0 mg), and **4** (23.6 mg) were obtained from PTF6B1 using an HPLC system eluting with 28% ACN in water. PTF6B3 was chromatographed on an HPLC system eluting with 28% ACN in water to yield compound **5** (20.1 mg). In addition, PTF6B4 was subjected to an HPLC system eluting with 24% ACN in water to give compounds **2** (28.9 mg) and **6** (20.1 mg). Using the same above condition, compound **7** (43.9 mg) was yielded from PTF6B6.

2.3.1. Ficusal (**1**): Yellow amorphous powder; $C_{18}H_{18}O_6$ (M = 330); $[\alpha]_D^{25}$ = +10.5 (*c* 0.1, MeOH); HR-ESI-MS *m/z* 331.1179 $[M+H]^+$ (Calcd. for $[C_{18}H_{19}O_6]^+$, 331.1176, Δ = +0.9 ppm); ^{1}H- and ^{13}C-NMR (CD_3OD) data, see table 1.

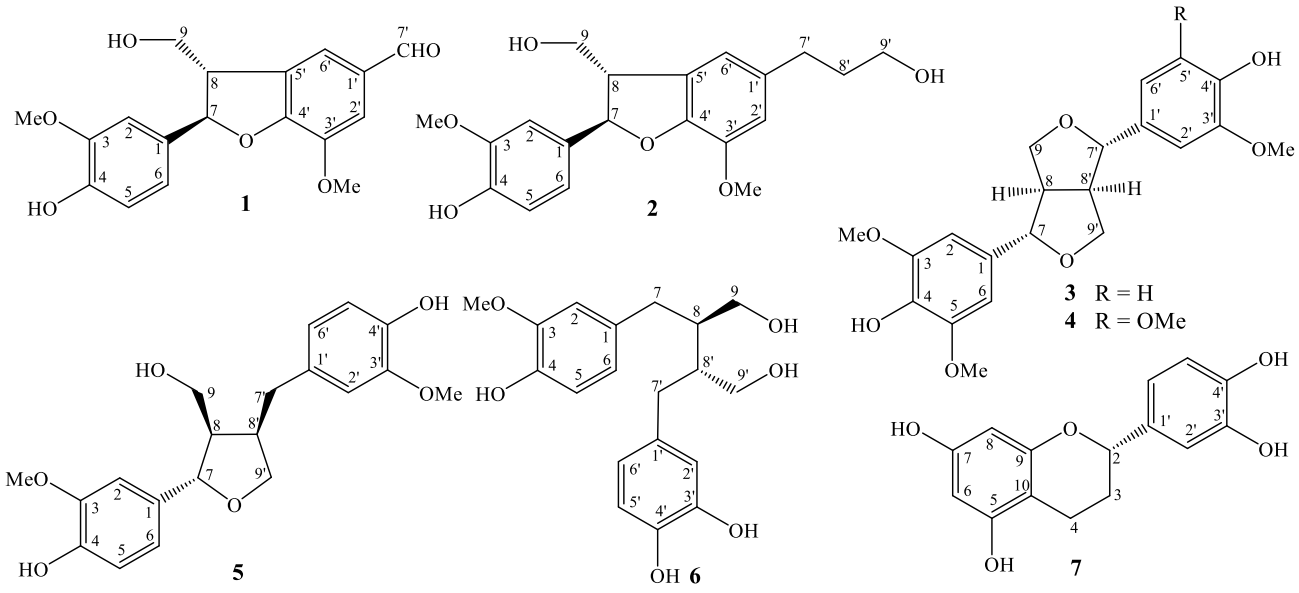

Figure 1: Chemical structures of compounds **1**-**7**

2.3.2. Vladinol F (**2**): Yellow oil; molecular formula: $C_{20}H_{24}O_6$ (M = 360); $[\alpha]_D^{25}$ = -6.1 (*c* 1.0, MeOH); HR-ESI-MS *m/z* 383.1457 $[M+Na]^+$ (Calcd. for $[C_{20}H_{24}O_6Na]^+$, 383.1465, *Δ* = -2.1 ppm); ^{1}H- and ^{13}C-NMR (CD_3OD) data, see table 1.

2.3.3. Medioresinol (**3**): Yellow amorphous powder; molecular formula: $C_{21}H_{24}O_7$ (M = 388); HR-ESI-MS *m/z* 411.1429 $[M+Na]^+$ (Calcd. for $[C_{21}H_{24}O_7Na]^+$, 411.1420, *Δ* = +2.2 ppm); $[\alpha]_D^{25}$ = +17,8 (*c* 0.49, MeOH); ^{1}H- and ^{13}C-NMR (CD_3OD) data, see table 1.

2.3.4. Syringaresinol (**4**): Yellow amorphous powder; molecular formula: $C_{22}H_{26}O_8$ (M = 418); HR-ESI-MS *m/z* 453.1313 $[M+Cl]^-$; (Calcd. for $[C_{22}H_{26}O_8Cl]^-$, 453.1322, *Δ* = -2.0 ppm); ^{1}H- and ^{13}C-NMR (CD_3OD) data, see table 1.

2.3.5. Lariciresinol (**5**): White amorphous powder; molecular formula: $C_{20}H_{24}O_6$ (M = 360); HR-ESI-MS *m/z* 383.1468 $[M+Na]^+$ (Calcd. for $[C_{20}H_{24}O_6Na]^+$, 383.1465, *Δ* = +0.8 ppm); $[\alpha]_D^{25}$= +32.0 (*c* 0.1, MeOH); ^{1}H- and ^{13}C-NMR (CD_3OD) data, see table 2.

2.3.6. Secoisolariciresinol (**6**): White amorphous powder; molecular formula, $C_{20}H_{26}O_6$ (M = 362); HR-ESI-MS *m/z* 395.1619 $[M+Na]^+$ (Calcd. for $[C_{20}H_{26}O_6Na]^+$, 395.1622, *Δ* = -0.6 ppm); $[\alpha]_D^{25}$ = 0 (*c* 0.1, MeOH, 4:1); ^{1}H- and ^{13}C-NMR (CD_3OD) data, see table 2.

2.3.7. Luteoliflavan (**7**): Yellow amorphous powder; molecular formula: $C_{15}H_{14}O_5$ (M = 274); HR-ESI-MS *m/z* 275.0922 $[M+H]^+$ (Calcd. for $[C_{15}H_{15}O_5]^+$, 275.0914, *Δ* = +2.9 ppm); $[\alpha]_D^{25}$= -26.0 (*c* 0.1, MeOH); ^{1}H- and ^{13}C-NMR (CD_3OD) data, see table 2.

2.4. Nitric oxide assay

The anti-inflammatory activity of the compounds was evaluated through the inhibitory activity of NO production on RAW 264.7 cells according to the method previously published.[7] In this trial, the inhibitory activity of NO production in LPS-stimulated RAW 264.7 cells was determined by nitrite (NO_2^-) content, which is considered as an indicator of NO generation. The positive control used was NG-Methyl-L-arginine acetate (L-NMMA).

2.5. Lipid peroxidative inhibitory assay

The antioxidant potential of the compounds was evaluated through their inhibitory activity on membrane lipid peroxidation (MDA test).[8] In this test, the lipid peroxidation inhibitory activity of the compounds was determined by the content of malondialdehyde (MDA), which is the product of the Fenton system-induced membrane lipid peroxidation of rat liver cell membranes. MDA is able to react with thiobarbituric acid to form trimethin complex (pink color) with maximum absorption peak at λ = 532 nm. The positive control used in the trial was Trolox.

3. RESULTS AND DISCUSSION

Compound **1** was obtained as a yellow amorphous powder. Its molecular structure was determined as $C_{18}H_{18}O_6$ based on the presence of a quasi-molecular ion peak at *m/z* 331.1179 $[M+H]^+$ (Calcd. for $[C_{18}H_{19}O_6]^+$, 331.1176). The ^{1}H-NMR spectrum showed proton signals of an aldehydic group at δ_H 9.81 (d, *J* = 4.0 Hz), three protons of a 1,3,4-trisubstituted aromatic ring with ABX coupling patterns at δ_H 6.81 (1H, d, *J* = 8.0 Hz), 6.85 (1H, dd, *J* = 2.0, 8.0 Hz), and 6.97 (1H, d, *J* = 2.0 Hz), two aromatic protons at δ_H 7.48 (1H, d, *J* = 4.0 Hz) and 7.54 (1H, d, *J* = 4.0 Hz), and two methoxy groups at δ_H 3.84 and 3.95 (each 3H, s). The ^{13}C-NMR and HSQC spectra of **1** showed the signals of 18 carbons, including one aldehydic group (δ_C 192.7), seven non-protonated carbons (δ_C 131.2, 132.8, 133.7, 146.3, 148.0, 149.0, and 155.0), seven methines (δ_C 54.3, 90.6, 110.7, 114.0, 116.3, 119.9, and 122.3), one methylene (δ_C 64.5), and two methoxy carbons (δ_C 56.7 and 56.4). Analysis of 1D- and 2D-NMR spectra suggested that compound **1** was a neolignan and further confirmed by the HMBC correlations between H-7 (δ_H 5.67) and C-1 (δ_C 1333.7)/C-2 (δ_C 110.7)/C-6 (δ_C 119.9)/C-8 (δ_C 54.3)/C-9 (δ_C 64.5)/C-4′ (δ_C 155.0)/C-5′ (δ_C 146.3). The HMBC correlations between H-2 (δ_H 6.97)/H-6 (δ_H 6.85) and C-4 (δ_C 148.0) and H-5 (δ_H 6.81)/ methoxy (δ_H 3.84) and C-3 indicated the position of hydroxyl and methoxy groups at C-3 and C-4, respectively. The HMBC correlations between H-7′ (δ_H 9.81) and C-1′ (δ_C 132.8)/C-2′ (δ_C 122.3)/C-6′ (δ_C 114.0) and between methoxy (δ_C 3.95) and C-3′ (δ_C 131.2) proved the aldehydic and methoxy groups at C-1′ and C-3′, respectively. Based on the above evidence, compound **1** was elucidated to be ficusal.[9]

Compound **2** was also obtained as a yellow amorphous powder. The ^{1}H-NMR spectrum of **2**

Table 1: ^{1}H- and ^{13}C-NMR data for compounds **1-4**

C	**1**		**2**		**3**		**4**	
	δ_C[a)]	δ_H[a)] (mult., *J* = Hz)	δ_C[a)]	δ_H[a)] (mult., *J* = Hz)	δ_C[a)]	δ_H[a)] (mult., *J* = Hz)	δ_C[a)]	δ_H[a)] (mult., *J* = Hz)
1	133.7	-	134.8		133.2	-	132.2	-
2	110.7	6.97 (d, 2.0)	110.0	6.97 (d, 2.0)	104.6	6.65 (s)	104.6	6.67 (s)
3	149.0	-	149.1	-	149.4	-	149.4	-
4	148.0	-	147.5	-	136.5	-	136.3	-
5	116.3	6.81 (d, 8.0)	116.1	6.78 (d, 8.0)	116.1	-	149.4	-
6	119.9	6.85 (dd, 8.0, 2.0)	119.7	6.84 (d, 8.0, 2.0)	120.1	6.65 (s)	104.6	6.67 (s)
7	90.6	5.68 (d, 6.0)	89.0	5.51 (5.51)	87.7	4.71 (d, 4.5)	87.6	4.73 (d, 4.5)
8	54.3	3.64 (m)	55.4	3.49 (dd, 9, 6.5)	55.3	3.14 (m)	55.5	3.14 (m)
9	64.5	3.88 (m)	65.0	3.75 3.85	72.7	3.86 (m) 4.25 (m)	72.8	4.27 (dd, 9.0, 6.5) 3.89 (dd, 9.0, 3.5)
1′	132.8	-	136.9	-	133.8	-	132.2	-
2′	122.3	7.54 (d, 4.0)	114.1	6.74 (s)	111.1	6.95 (d, 2.0)	104.6	6.67 (s)
3′	131.2	-	145.2	-	149.2	-	149.4	
4′	155.0*	-	147.5	-	147.4	-	136.3	
5′	146.3	-	129.9		116.1	6.77 (d, 8.0)	149.4	
6′	114.0	7.48 (d, 4.0)	117.9	6.74 (s)	120.1	6.81 (dd, 8.0, 2.0)	104.6	6.67 (s)
7′	192.7	9.81 (d, 4.0)	32.9	2.64 (t, 7.5)	87.5	4.71 (d, 4.5)	87.6	4.73 (d, 4.5)
8′			35.8	1.84 (m)	55.6	3.14 (m)	55.5	3.15 (m)
9′			62.2	3.59 (t, 7.5)	72.8	3.86 (m) 4.25 (m)	72.8	4.27 (dd, 9.0, 6.5) 3.89 (dd, 9.0, 3.5)
3-OMe	56.4	3.84 (s)	56.4	3.82 (s)	56.8	3.84 (s)	56.8	3.86 (s)
5-OMe					56.8	3.84 (s)	56.8	3.86 (s)
3′-OMe	56.7	3.95 (s)	56.8	3.86 (s)	56.5	3.85 (s)	56.8	3.86 (s)
5′-OMe							56.8	3.86 (s)

[a)]Recorded in CD_3OD. *The signal of carbon could not be observed in ^{13}C-NMR spectrum, deduced from HMBC spectrum.

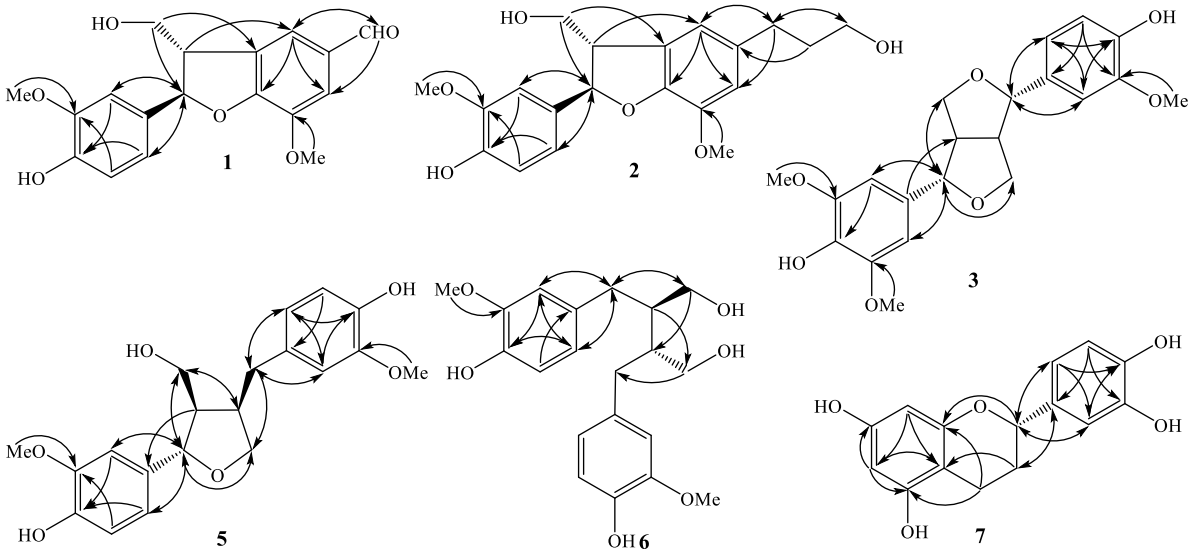

Figure 2: The key HMBC correlations of compounds **1-3** and **5-7**

showed signals of two aromatic rings at δ_H 6.74 (2H, s) and δ_H 6.84 (1H, dd, *J* = 8.0, 2.0 Hz), 6.78 (1H, d, *J* = 8.0 Hz), and 6.97 (d, *J* = 2.0 Hz), three methylene protons at δ_H 2.64 (2H, t, *J* = 7.5 Hz), 1.84 (2H, m), and 3.59 (2H, t, *J* = 7.5 Hz) together with two methoxy groups at δ_H 3.82 (3H, s) and 3.86 (3H, s). The ^{13}C-NMR and HSQC spectra of **2** exhibited 20 carbons, similar to those of **1** except for

the replacement of the aldehydic group by a 3-hydroxypropyl group at C-1′. The position of 3-hydroxypropyl group at C-1′ was further confirmed by HMBC correlations from H-7′ (δ_H 2.64) to C-2′ (δ_C 114.1)/C-6′ (δ_C 117.9). Analysis of 1D- and 2D-NMR data indicated the structure of **2** to be vladinol F.[10]

The ^{1}H-NMR spectrum of **3** (in CD_3OD) showed signals for aromatic protons of 1,3,4,5-tetrasubstitutedbenzene at δ_H 6.65 (each, 2H, s), 1,3,4-trisubstituted aromatic ring at δ_H 6.81 (1H, dd,J = 8.0, 2.0 Hz), 6.77 (1H, d, J = 8.0 Hz), and 6.95 (d, J = 2.0 Hz), and three methoxy groups at δ_H 3.84 (6H, s) and 3.85 (3H, s). Analysis of ^{13}C-NMR and HSQC spectra indicated the structure of **3** to be a lignan. In the HMBC spectrum of **3** (see figure 2), the correlations between H-7 (δ_H 4.71) and C-1 (δ_C 133.2)/C-2/C-6 (δ_C 104.6), between H-2/H-6 (δ_H 6.65) and C-4 (δ_C 136.5), and between the methoxy groups (δ_H 3.84) and C-3/C-5 (δ_C 149.4) indicated the presence of two methoxy groups at C-3 and C-5. The HMBC correlations from H-2′ (δ_H 6.95)/H-6′ (δ_H 6.81) to C-4′ (δ_C 147.4), from H-5′ (δ_H 6.77) and the methoxy protons (δ_H 3.85) to C-3′ (δ_C 149.2) indicated the position of hydroxyl and methoxy groups at C-3′ and C-4′. Consequently, the structure of **3** was determined to be (+)- medioresinol.[11]

Table 2: NMR data for compounds **5-7**

C	**5**		**6**		**7**	
	δ_C[a)]	δ_H[a)] (mult., J = Hz)	δ_C[a)]	δ_H[a)] (mult., J = Hz)	δ_C[a)]	δ_H[a)] (mult., J = Hz)
1	135.8		133.9	-		
2	110.7	6.93 (d, 1.5)	113.4	6.61 (d, 2.0)	78.8	4.79 (dd, 10.0, 1.5)
3	149.0	-	148.8	-	30.8	2.10 (m)/1.92 (m)
4	147.1	-	145.5	-	20.3	2.68 (m)/2.60 (m)
5	116.0	6.78[#]	115.8	6.68 (d, 8.0)	157.9	
6	119.8	6.79[#]	122.7	6.57 (dd, 8.0, 2.0)	96.0	5.94 (d, 2.0)
7	84.0	4.77 (d, 7.0)	36.1	2.58 (dd, 14.0, 8.0) 2.68 (dd, 14.0, 7.0)	157.4	-
8	54.0	2.39 (m)	44.2	1.92 (m)	96.0	5.86 (d, 2.0)
9	60.5	3.65 (dd,11.0, 6.5) 3.84 (dd, 11.0, 6.5)	62.1	3.61 (dd, 11.0, 5.0)	157.0	-
10					102.6	-
1′	133.6	-	133.9	-	135.1	-
2′	113.5	6.81 (d, 2.0)	113.4	6.61 (d, 2.0)	114.4	6.87 (d, 2.0)
3′	149.0	-	148.8	-	146.1	-
4′	145.8	-	145.5	-	145.8	-
5′	116.2	6.74 (d, 8.0)	115.8	6.68 (d, 8.0)	116.1	6.77 (d, 8.0)
6′	122.2	6.68 (dd, 8.0, 2.0)	122.7	6.57 (dd, 8.0, 2.0)	118.8	6.73 (dd, 8.0, 2.0)
7′	33.7	2.51 (dd, 13.5, 11.5) 2.94 (dd, 13.5, 5.0)	36.1	2.58 (dd, 14.0, 8.0) 2.68 (dd, 14.0, 7.0)		
8′	43.9	2.75 (m)	44.2	1.92 (m)		
9′	73.5	4.00 (dd, 8.0, 6.5) 3.74 (dd, 8.0, 6.0)	62.1	3.61 (dd, 11.0, 5.0)		
3-OMe	56.4	3.86 (s)	56.2	3.76 (s)		
3′-OMe	56.4	3.84 (s)	56.2	3.76 (s)		

[a)]Recorded in CD_3OD.

Compound **4** was obtained as a white powder. The HR-ESI-MS of **4** showed pseudo-ion peak at *m/z* 453.1313 deduced the molecular formula to be $C_{22}H_{26}O_8$. The ^{1}H- and ^{13}C-NMR spectral data showed symmetry, indicating the structure of **4** to be a lignan. Its NMR data was found to be identical with data in published literature,[12] the structure of **4** was established as syringaresinol.

Compound **5** was obtained as a white powder. The ^{1}H-NMR spectrum of **5** suggested signals of two aromatic rings with ABX-system. The ^{13}C-NMR and HSQC spectra of **5** showed signals of 20 carbons with two 1,3,4-aromatic rings. In addition, two oxygenated methylenes at δ_C 60.5 and 73.5, one oxygenated methine at δ_C 84.0, two methine carbons at δ_C 54.0 and 43.9, one methylene carbon at δ_C 33.7 and two methoxy carbons at δ_C 56.4. The above obtained NMR data showed the structure of **5** to be a

lignan with two methoxy groups. A comparison of the NMR spectral data of **5** with laricirecinol showed a similarity.[13] Finally, the specific rotation of **5** of $[\alpha]_D^{25}$ +32.0 is in full agreement with (+)-lariciresinol.[13]

Compound **6** was obtained as a white powder. The ^{1}H-NMR spectrum (table 2) displayed symmetric signals of two 1,3,4-trisubstituted benzene rings [δ_H 6.68 (2H, d, J = 8.0 Hz), 6.62 (2H, d, J = 2.0 Hz), 6.56 (2H, dd, J = 8.0, 2.0 Hz)] and two methyl groups at δ_H 3.76 (6H, s). The ^{13}C-NMR and HSQC spectra indicated signals of 20 carbons, including 2 methoxy groups, 4 methylenes, 8 methines, and 6 non-protonated carbons. Analysis of the spectral data indicated the structure of **6** was a lignan. Thus, compound **6** was concluded as secoisolariciresinol.[14]

The ^{1}H-NMR spectrum of **7** showed signals of two *meta*-aromatic protons at δ_H 5.86 (1H, d, J = 2.5 Hz) and 5.94 (1H, d, J = 2.5 Hz)] and three ABX aromatic protons at δ_H 6.87 (1H, d, J = 2.0 Hz), 6.77 (1H, d, J = 8.0 Hz), and 6.73 (1H, dd, J = 8.0, 2.0 Hz), and one oxygenated methine at δ_H 4.79 (dd, J = 10.0, 1.5 Hz). The ^{13}C-NMR and HSQC spectra of **7** showed signals of 15 carbons, including 12 carbon atoms of two aromatic rings (7 non-protonated carbons and 5 methine carbons) and 3 sp^2 carbons. In comparison with the reference,[20] compound **7** was identified as luteoliflavan.[15]

Table 3: Inhibition of NO production in LPS-stimulated macrophages RAW 264.7 by compounds **1-7**

Compound	Inhibition at the concentration of 100 µg/mL (%)	IC_{50} (µM)
1	87.9±5.7	17.4±1.9
2	88.7±6.2	21.4±2.1
3	85.8±7.9	39.3±3.3
4	68.1±3.9	125.8±7.7
5	84.6±6.5	5.3±0.4
6	77.8±7.2	23.0±1.4
7	82.4±6.4	7.1±0.4
L-NMMA	95.5±8.2	37.8±3.2

According to the publications related to the research on the genus *Pandanus* investigated in Vietnam until now, among the 7 isolated and identified compounds as mentioned above (+)-syringaresinol and (+)-medioresinol were already found in the chloroform or ethylacetate based extracts from the fruits of *P. odoratissimus, P. tectorius* and *P. kaida.*[3-5] Additionally, there were also the 2 further compounds (+)-isolariciresinol and (-) secoisolariciresinol clearly showed in the composition of the fruits of *P. kaida.*[3]

To evaluate the NO production inhibtory, all compounds were evaluated for cytotoxic activity. None of them showed cytotoxic activity (data not shown). Compounds **1-7** were further screened for NO production inhibitory at the concentration of 100 µg/mL. All compounds showed NO production inhibitory at this concentration (inhibitory percentage > 50%). Thus, compounds were evaluated at the smaller concentrations (20, 4, and 0.8 µg/mL) to get IC_{50} values. L-NMMA was used as a positive control with IC_{50} value of 37.8±3.2 µM. As the results, compounds **5** and **7** showed significant NO production inhibitory with IC_{50} values of 5.3±0.4 and 7.1±0.4 µM. The remaining compounds showed moderate activity with IC_{50} values ranging from 17.4 to 125.8 µM (table 3).

Compounds were also evaluated lipid peroxidative inhibitory activity. Trolox, a positive control, exhibited peroxidation inhibitory with IC_{50} value of 31.4±2.2 µM. The results indicated compounds **5** and **7** showed significant lipid peroxidative inhibitory activity with IC_{50} values of 20.2±1.7 and 26.2±3.6 µM (table 4).

Table 4: Lipid peroxidation inhibitory activity of compounds **1-7**

Compound	Inhibition at the concentration of 100 µg/mL (%)	IC_{50} (µM)
1	32.6±3.1	>100
2	75.8±5.9	84.8±6.7
3	80.7±7.5	>100
4	72.5±4.6	128.7±5.6
5	84.7±4.1	32.2±1.4
6	87.3±5.2	20.2±1.7
7	81.9±8.9	26.2±3.6
Trolox	87.1±5.8	31.4±2.2

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