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LIGNANS FROM LEAVES OF *AMESIODENDRON CHINENSE* AND THEIR CYTOTOXIC ACTIVITY

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Abstract. Four lignans, (+)-aptosimon (**1**), (+)-isolariciresinol (**2**), (-)-cleomiscosin A (**3**), and (-)-cleomiscosin C (**4**) were isolated from the leaves of *Amesiodendron chinense* (Mer.) Hu. Their chemical structures were determined by spectroscopic analysis including MS, 1D and 2D NMR as well as by comparison with reported literatures. All compounds were evaluated for cytotoxic activity against five human cancer cell lines, KB, SK-LU-1, MCF-7, HepG-2, and SW-480. The compounds showed weak cytotoxic activity with IC_{50} values ranging from 32.61 to 95.18 µg/mL.

Keywords: Amesiodendron chinense, lignans, cytotoxic activity.

Classification numbers: 1.1.1, 1.2.1.

1. INTRODUCTION

Lignans, considered as phytoestrogens, are widely found in plant kingdom and they created an enormous class of pharmacological active compounds. The current evidences highlight the bioactive properties of lignans as human health-promoting molecules, especially cancer prevention [1 - 4]. The genus *Amesiodendron* (Sapindaceae) comprises three species, distributed in China and Southeast Asia, among which *Amesiodendron chinense* (Merr.) Hu, Vietnamese name "Truong sang", was listed in 2006 IUCN Red List of threatened species [5, 6]. The chemical and biological investigations of this plant have not been studied yet. As a part of our research on searching anticancer reagents from Vietnamese medicinal plants, the ethyl acetate extract of *A. chinense* was found to inhibit KB human cancer cell line (IC_{50} value of 20 µg/mL). We report herein the isolation and structural elucidation of four lignans from the leaves of *A. chinense* and evaluation of their cytotoxic effects.

2. MATERIALS AND METHODS

2.1. General experimental procedures

The NMR spectra were recorded on a Bruker AM500 FT-NMR spectrometer. The ESI-MS were measured on an Agilent 1100 Series LC/MSD Trap SL. The melting points were recorded on a Thermo Scientific 1402, Mel-Temp 3.0 USA. Optical rotations were recorded on a JASCO P-2000 Polarimeter. Column chromatography (CC) was performed using a silica gel 60 (230 - 400 mesh, Merck) or RP-18 resins (30 - 50 μm, Fuji Silysia Chemical Ltd, Aichi, Japan). Thin layer chromatography (TLC) used percolated silica gel 60 F254 (Merck) and RP-18 F254S plates (Merck).

2.2. Plant material

The leaves of *Amesiodendron chinense* (Merr.) Hu were collected at Sontra, Danang, Viet Nam in June 2018 and identified by Dr. Do Van Hai, Institute of Ecology and Biological Resources, VAST. A voucher specimen (PTH15032018) was deposited in the Institute of Ecology and Biological Resources, VAST.

2.3. *In vitro* cytotoxic assay

The effects of compounds on viability of cells were determined by sulforhodamine B (SRB) cytotoxic assay [7]. Cells were grown in 96-well microliter plates containing 190 μL of medium (DMSO 10 %) with 3.10^4 cell/ well then incubated at 37 ^oC and 5 % CO_2. After 24 h, the samples dissolved in DMSO (10 μL) was added to each well at concentrations of 100, 20, 4, and 0.8 μg/mL. The one plate without samples served as a day 0 (timezero) control. The cells were continuously cultured for additional 72 h. After incubating, cell monolayers were fixed with 20 % (wt/v) trichloroacetic acid and stained for 30 min and washed with 5 % (v/v) acetic acid (three times) to move excess SRB. The protein bound dye was dissolved in 10 mM Tris base solution. Optical density value (OD) was determined at 515 nm using ELISA Plate Reader (Biotek).

The percentage of cell-growth inhibition (GI) was calculated using the formulae below:

$$\% \text{ GI} = 100 - [(OD_{sample} - OD_0)/(ODc - OD_0)] \times 100,$$

in which: OD_{sample} is the average optical density value at 72 h; OD_0: the average optical density value at time-zero; and ODc: the average optical density value of the control sample (sample contains DMSO 10 %). IC_{50} values were calculated using TableCurve 2Dv4 software. All experiments were carried out in triplicate.

2.4. Extraction and isolation

Dried leaves of *A. chinense* (7.0 kg) were powdered and extracted with 85 % MeOH (three times at 50 ^oC, each 6 h). The extracts were collected and solvent was removed in reduced pressure to give a MeOH extract (2.5 L). The MeOH extract was suspended with H_2O (2.5 L) and then successively partitioned with *n*-hexane, and ethyl acetate (EtOAc) to give *n*-hexane (ACH, 70 g) and EtOAc (ACE, 50 g) residues and water layer (ACW). The ACE fraction was applied on a silica gel column eluting with CH_2Cl_2/EtOAc (10/1, v/v) to give ACE1 (6 g), ACE2 (8 g), ACE3 (13 g), ACE4 (11 g), and ACE5 (7 g). The ACE1 fraction was chromatographed on

a silica gel column eluting with CH_2Cl_2/EtOAc (4/1, v/v) to yield compound **1** (30.0 mg). The ACE2 fraction was applied on a silica gel column eluting with *n*-hexane/EtOAc (1/4, v/v) to give four smaller fractions, ACF2.1-ACF2.4. The ACE2.1 fraction was chromatographed on a silica gel column eluting with solvent of *n*-hexane/EtOAc (1/4, v/v) then purified on a sephadex LH-20 column eluting with MeOH to yield compound **2** (7.0 mg). The ACE5 fraction was applied on a silica gel column eluting with EtOAc/acetone (4/1, v/v) to give 5 sub-fractions (ACF5.1-ACF5.5). The ACE5.2 fraction was chromatographed on an RP-18 column, eluting with MeOH/H_2O (1/1, v/v) and then purified on a sephadex LH-20 column eluting with MeOH and crystalized by MeOH to yield compound **3** (9.0 mg). The ACE5.3 fraction was applied on a silica column eluting with CH_2Cl_2/acetone (6/1 v/v), and then purified on a sephadex LH-20 column to yield compound **4** (10.0 mg).

(+)-Aptosimon (1): white amorphous powder, $[\alpha]_D^{25}$: + 65^o (*c* 0.1, MeOH), UV λ_{max} (MeOH) nm: 205.6, 286.4. IR (KBr) ν_{max} = 3073, 2899, 1764, 1264, 1167, 1040, 926 cm^{-1}; Positive ESI-MS: *m/z* 369 $[M+H]^+$. ^{1}H-NMR ($CDCl_3$, 500 MHz): δ_H 3.20 (1H, m, H-1), 3.42 (1H, dd, *J* = 3.5, 9.0 Hz, H-5), 4.00 (1H, dd, *J* = 5.0, 9.5 Hz, H_β -8), 4.32 (1H, dd, *J* = 7.0, 9.5 Hz, H_α-8), 5.28 (1H, d, *J* = 4.0 Hz, H-2), 5.30 (1H, d, *J* = 3.5 Hz, H-6), 6.76 (1H, d, *J* = 6.5 Hz, H- 5'), 6.77 (H, d, *J* = 8.0 Hz, H- 5"), 6.80 (1H, br d, *J* = 6.5 Hz, H-6'), 6.81 (1H, br s, H- 2'), 6.84 (1H, br d, 8.0 Hz, H-6"), and 6.86 (1H, br s, H- 2"). ^{13}C-NMR ($CDCl_3$, 125 MHz): δ_C 49.9 (C-1), 53.3 (C-5), 72.7 (C-8), 83.4 (C-6), 84.3 (C-2), 101.4 and 101.2 (2 × OCH_2O), 105.7 (C-5'), 106.0 (C-5"), 108.3 (C-2'), 108.5 (C-2"), 118.8 (C-6'), 119.0 (C-2"), 133.1(C-1'), 134.4 (C-1"), 147.3, 148.0, 148.1, 148.4 (C-4', C-4", C-3', C-3"), and 176.6 (4-CO).

(+)-Isolariciresinol (2): white amorphous powder, $[\alpha]_D^{25}$: + 25^o (*c* 0.1, MeOH), UV λ_{max} (MeOH) nm: 211.6, 284.6. Positive ESI-MS: *m/z* 383 $[M+Na]^+$. ^{1}H-NMR ($CDCl_3$, 500 MHz): δ_H 1.80 (1H, ddt, *J* = 3.5, 4.5, 10.0 Hz, H-8), 2.02 (1H, m), 2.79 (2H, br d, *J* = 7.5 Hz, H-7'), 3.42(1H, dd, *J* = 4.5, 11.5 Hz, H_b-9), 3.65-3.72 (2 H, overlap, H_2-9' and H_a-9), 3.80 (3H, s, 3-OCH_3), 3.82 (1H, d, *J* = 10.0 Hz, H-7), 3.83 (3H, s, 3'-OCH_3), 6.21 (1H, s, H-5'), 6.63 (1H, dd, *J* = 1.5, 8.0 Hz, H-6), 6.68 (1H, s, H-2'), 6.70 (1H, br d, *J* = 1.5 Hz, H-2), and 6.76 (1H, dd, *J* = 8.0 Hz, H-5). ^{13}C-NMR ($CDCl_3$, 125 MHz): δ_C 33.6 (C-7'), 40.1 (C-8'), 48.0 (C-7/8), 56.4 (3-OCH_3), 56.4 (3'-OCH_3), 62.3 (C-9), 66.0 (C-9'), 112.4 (C-2'), 113.8 (C-2), 116.0 (C-5), 117.4 (C-5'), 123.2 (C-6), 129.0 (C-1'), 134.2 (C-6'), 138.6 (C-1), 145.3 (C-4'), 146.0 (C-4), 147.2 (C-3'), and 149.0 (C-3).

(-)-Cleomiscosin A (3): colorless needles, mp 249-250. $[\alpha]_D^{25}$ -34^o (*c* 0.1, MeOH). UV λ_{max} (MeOH) nm: 206.8, 324.8. ESI-MS (positive) *m/z* = 387 $[M + H]^+$. ^{1}H-NMR (500 MHz, DMSO-d_6), see Table 1. ^{13}C-NMR (125 MHz, DMSO-d_6), see Table 1.

(-)-Cleomiscosin C (4): white amorphous powder; $[\alpha]_D^{25}$ -23^o (*c* 0.1, MeOH). UV λ_{max} (MeOH) nm: 221.0, 321.6. ESI-MS (positive) *m/z* = 417 $[M + H]^+$. ^{1}H-NMR (500 MHz, DMSO-d_6), ^{13}C-NMR (125 MHz, DMSO-d_6), and ^{13}C-NMR (125 MHz, C_5D_5N), see Table 1.

3. RESULTS AND DISCUSSION

Compound **1** was isolated as a white amorphous powder. The UV absorption bands at 205.6 and 286.4 nm suggested the presence of a lignan. The IR spectrum of **1** showed absorption at 1764 cm^{-1} suggested the presence of a lactone group. The ESI-MS gave a molecular ion peak at *m/z* 369 $[M+H]^+$ and ^{13}C-NMR of **1** indicated a molecular formula of $C_{20}H_{16}O_7$ (M = 368). The ^{1}H-NMR spectrum of **1** showed proton signals of two set of ABX aromatic proton systems at δ_H 6.86 and 6.81 [each 1H, br s, H-2" and H-2′), 6.84 (1H, br d, *J* = 8.0 Hz, H-6"), 6.80 (1H,

br d, *J* = 6.5 Hz, H-6′), 6.77 (1H, d, *J* = 8.0 Hz, H-5") and 6.76 (1H, d, *J* = 6.5 Hz, H-5′); four protons of two dioxymethylene groups at δ_H 5.97 and 5.95 (each 2H, s); a bicyclooctane moiety with six protons including: two oximethine protons at δ_H 5.30 and 5.28 (each 1H, d, *J* = 4.0 Hz, H-6, H-2), two oximethylene protons at δ_H 4.32 (1H, dd, *J* = 9.5, 7.0 Hz, H_α-8) and 4.00 (1H, dd, *J*= 9.5, 5.0 Hz, H_β-8), and two methine protons at δ_H 3.41 (1H, dd, *J* = 9.0, 3.5 Hz, H-5) and 3.20 (1H, m, H-1). The small coupling constants (*J* = 4.0 Hz) of H-2 and H-6 revealed that configurations H-1 and H-2; H-5 and H-6 were *trans*. The ^{13}C-NMR spectrum showed signals of 20 carbons, including 12 aromatic carbons at δ_C 105.7, 106.0, 108.3, 108.5 ,118.8, 119.0, 133.1, 134.4, 147.3, 148.0, 148.1 and 148.4; 6 carbons of the bicyclooctane rings at δ_C 83.4 and 84.3 (two oxy linked methine carbons, C-6 and C-2), 49.9 and 53.3 (two methine carbons: C-1, C-5), 72.7 (one oxygenated methylene carbon, C-8), and at δ_C 176.6 (one carboxyl group); two dioxymethylene carbons at δ_C 101.4 and 101.2. In addition, the HMBC spectrum showed cross-peak between H-6 and C-1, C-5, C-6′′, C-1′, and C-4; H-2 and C-1, C-5, C-8, C-5′, C-6′, and C-4; H-8 and C-1, C-5, C-2, and C-6; H-5 and C-1, C-8, C-2, C-1′′, and C-4; and between H-1 and C-2, C-1′, and C-4. Based on the above spectral analysis, compound **1** was suggested the presence of a 4-oxofurofurane-*type* lignan with two benzyl moieties located at C-2 and C-6. By comparing the NMR data and the optical rotation $[\alpha]_D$ + 65^o (*c* 0.1, MeOH) of **1** with those reported in literature [8], the structure of **1** was determined as (+)-aptosimon. (+)-Aptosimon (**1**) was isolated from *Aptosimum spinescens* for the first time [9] and total synthesized by Yamaauchi *et. al*. [8].

Compound **2** was also isolated as a white amorphous powder. The ESI-MS showed a pseudo-molecular ion peak at *m/z* 383 $[M+Na]^+$ and ^{13}C-NMR spectrum indicated a molecular formula of $C_{20}H_{24}O_6$ (M = 360). The ^{1}H-NMR spectrum of **2** displayed proton signals of a ABX-trisubstituted aromatic ring at δ_H 6.76 (1H, d, *J* = 8.0 Hz, H-5), 6.70 (1H, br d, *J* = 1.5 Hz, H-2), 6.63 (1H, dd, *J* = 1.5, 8.0 Hz, H-6); two singlet protons of benzene ring at δ_H 6.68 (1H, s, H-2′) and 6.21 (1H, s, H-5′); three methine groups at δ_H 3.84 (H-7), 1.80 (1H, ddt, *J* = 3.5, 4.5, 10 Hz, H-8), and 2.02 (1H, m, H-8′); two methoxy groups at δ_H 3.83 (3H, s, 3′-OMe), 3.80 (3H, s, 3-OMe); two oxygenated methylene groups at δ_H (3.65-3.72) (3H, overlap, H_2-9′ and H_a-9) and 3.43 (1H, dd, *J* = 4.5, 11.5 Hz, H_b-9); a methylene group at δ_H 2.79 (2H, d, *J*= 7.5 Hz, H-7′). The ^{13}C-NMR and DEPT spectra of **2** showed signals of 20 carbons including twelve aromatic carbons (seven non-protonated carbons and five methines), six aliphatic carbons (three methylenes and three methines), and two methoxy carbons. In addition, the HMBC correlations were displayed between H-7 and C-1, C-2, C-6, C-8, C-6′, and C-8′; and between H-7′ and C-8′, C-9′, C-8, C-1′, C-2′, and C-6′. Above NMR analysis revealed that compound **2** could be a courmarinolignan [10]. The HMBC correlations between methoxy protons and C-3 and C-3′ and the NOESY correlations between 3-OMe and H-2, 3′-OMe and H-2′ confirmed the positions of the methoxy groups at C-3 and C-3′. Furthermore, the NOESY correlations of H-7 and H-8′ and H-2 and H-8 suggested the configuration of 3-methoxy-4hydroxyphenyl moiety at C-7 to be β. The large coupling constant between H-7 and H-8 (*J* = 10.0 Hz) indicated the configuration of the hydroxymethylene group at C-8 to be α. Thus, the structure of **2** was determined to be (+)-isolariciresinol.

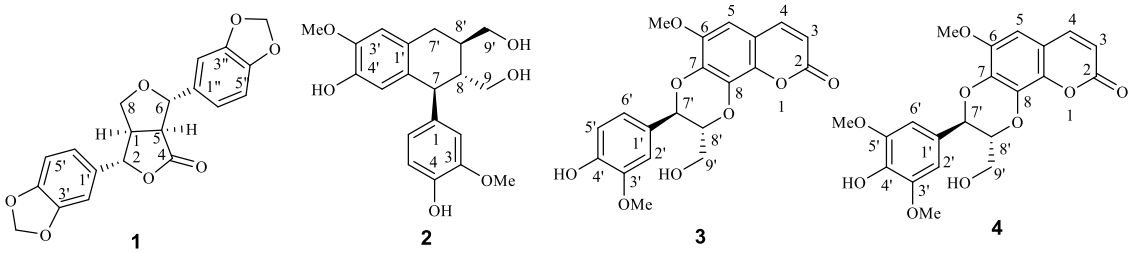

Figure 1. The chemical structures of compounds **1**-**4**.

Table 1. The NMR spectroscopic data for compounds **3** and **4**.

	3			**4**			
Position	δ_C [#]	δ_C [a,b]	δ_H [a,c]	δ_C [##]	δ_C [d,b]	δ_C [a,b]	δ_H [a,c]
2	160.0	160.0	-	160.8	160.9	160.1	-
3	113.2	113.2	6.34 d (9.5)	113.7	113.8	113.2	6.34 d (9.5)
4	144.7	144.8	-	144.5	144.6	144.8	-
5	100.6	100.8	6.91 s	101.0	101.2	100.9	6.91 s
6	145.3	145.2	-	146.3	146.4	145.3	-
7	137.1	137.1	-	138.1	138.4	137.1	-
8	131.6	131.6	-	132.5	133.0	131.7	-
9	110.7	111.2	-	139.2	139.3	138.0	-
10	138.3	138.0		111.9	112.0	111.3	-
6-OMe	55.7	55.7	3.79 s	56.2	56.2	55.9	3.79 s
1’	126.7	126.7	-	126.3	126.6	125.7	-
2’	112.0	112.1	7.02 d (2.0)	106.1	106.4	105.7	6.75 s
3’	147.2	147.2	-	149.1	149.7	148.0	-
4’	147.6	147.6	-	135.9	135.6	136.3	-
5’	117.4	115.4	6.82 d (8.0)	149.1	149.7	148.0	-
6’	121.3	120.8	6.88 dd (2.0, 8.0)	106.1	106.4	105.7	6.75 s
7’	76.2	76.2	4.99 d (8.0)	77.7	77.8	76.6	4.97 d (8.0)
8’	77.4	77.8	4.34-4.30 m	79.7	79.7	77.8	4.35-4.38 m
9’	59.9	59.8	3.66 dd (2.0, 5.0, 12.5, β) 3.41-336 m, α	60.7	60.7	59.9	3.67 br d (12.0, β) 3.42-338 m, α
3’-OMe	55.8	55.8	3.78	56.4	56.4	56.2	3.77 s
5’-OMe				56.4	56.4	56.2	3.77 s
4’-OH	9.18 s						
9’-OH	5.06 t (5.0)						

[a] recorded in DMSO-d_6, [b] 125 MHz, [c] 500 MHz, [d] in Pyridine (C_5D_5N), [#] δ_C of cleomiscosin A (in DMSO-d_6 at 100 MHz) [11], [##] δ_C of cleomiscosin C (in C_5D_5N at 60 MHz) [13].

Compound **3**, was obtained as colorless needles. The ^{1}H-NMR spectrum of **3** showed proton signals of a coumarin concluding two olefinic protons at δ_H 6.34 (d, J = 9.5 Hz) and 7.96 (d, J = 9.5 Hz) and one singlet aromatic methine proton at 6.91 (s). Proton signals of a phenylpropanoid

group including one 1,3,4-trisubstituted phenyl group with ABX protons system (7.02 (d, *J*= 2.0 Hz, H-2′), 6.82 (d, *J* = 8.0 Hz, H-5′), and 6.88 (dd, *J* = 8.0, 2.0 Hz, H-6′)), and proton signals at δ_H 4.99 (d, *J* = 8.0 Hz, H-7′), 4.34–4.30 (m, H-8′), 3.66 (ddd, *J* = 2.0, 5.0, 12.5 Hz, H_β-9′) and 3.41–3.36 (m, H_α-9′), and two aromatic methoxy groups at 3.78 (s, 3′-OMe) and 3.79 (s, 6-OMe). The analysis of ^{1}H-NMR spectrum suggested compound **3** to be a coumarinolignan. The ^{13}C-NMR and DEPT spectra of **3** also showed the signals of 20 carbons of a coumarinolignan including one lactone carbonyl at δ_C 160.0 (C-2); two olefinic carbons at δ_C 113.2 (C-3) and 144.8 (C-4); twelve aromatic carbons being 4 methine carbons at 100.8 (C-5), 115.4 (5′), 120.8 (C-6′) and 112.1 (C-2′); and 8 quaternary carbons at 145.2 (C-6), 137.1 (C-7), 131.6 (C-8), 111.2 (C-9), 138.0 (C-10), 126.7 (C-1′), 147.2 (C-3′) and 147.6 (C-4′), among which C-6, C-7, C-8, C-10, C-3′ and C-4′ are oxy linked quaternary carbons; three oxy linked aliphatic carbons at δ_C 76.2 (C-7′), 77.8 (C-8′) and at δ_C 59.8 (C-9′) and two methoxy carbons (OMe) at δ_C 55.8 and 55.7. The HMBC cross-peaks between H-7′ (δ_H 4.99)/C-8′(δ_C 77.8), C-2′(δ_C 112.1), C-6′(δ_C 120.8), C-1′ (δ_C 126.7), between H-2′(δ_H 7.02), H-6′ (δ_H 6.88), H_β-9′ (δ_H 3.66) and C-7′ (δ_C 76.2), proved the attachment of a phenylpropane moiety with a coumarin moiety through a dioxan bridge of coumarinolignan framework. In addition, the HMBC correlations between 3′-OMe (δ_H 3.78) and C-3′ (δ_C 147.2), and between 6-OMe (δ_H 3.79) and C-6 (δ_C 145.2) and as well as NOESY correlations between 3′-OMe (δ_H 3.78) and H-2′ (δ_H 7.02); 6-OMe (δ_H 3.79) and H-5 (6.91), confirmed the coumarinolignan bearing two methoxy groups at C-6 and C-3′. The above evidence suggested the structure of **3** could be cleomiscosin A or cleomiscosin B [11]. Therefore, the comparing melting point of compound **3** (253-255 ^{o}C) and cleomiscosin A (mp 247- 257 ^{o}C) and cleomiscosin B (mp 273 - 276 ^{o}C) confirmed compound **3** to be cleomiscosin A [12]. The optical rotation $[\alpha]_D^{20}$ - 34^o (*c* 0.1, MeOH) of compound **3** suggested compound **3** to be (-)-cleomiscosin A.

The ^{13}C-NMR and DEPT spectra of **4** showed 21 carbons including one lactone carbonyl carbon, two olefinic carbons, twelve aromatic carbons, three oxy linked aliphatic carbons at δ_C 76.6 (C-7′), 77.8 (C-8′) and 59.9 (C-9′) and three methoxy groups. Similar to **3**, analysis of 1D, 2D-NMR spectra suggested the structure of **4** was similar to cleomiscosin C. The spectral data of **4** was identical to those of cleomiscosin C [13, 14]. In addition, the optical rotation $[\alpha]_D^{25}$ -23^o (*c* 0.1, MeOH) of compound **4** suggested the structure of **4** to be (-)-cleomiscosin C.

3.5. Evaluation of cytotoxic potential of four lignans

Table 2. Cytotoxic effect of compounds **1**-**4**.

Compound	IC_{50} (µg/mL)				
	KB	SK-LU-1	MCF7	HepG2	SW480
1	32.61 ± 3.08	52.86 ± 3.94	51.62 ± 2.31	44.22 ± 2.54	36.47 ± 2.27
2	71.93 ± 2.46	95.18 ± 5.33	79.92 ± 8.62	70.16 ± 4.17	59.40 ± 6.76
3	45.59 ± 3.87	54.60 ± 5.73	56.42 ± 3.40	37.39 ± 4.91	43.65 ± 4.61
4	38.55 ± 2.86	58.12 ± 5.60	64.08 ± 5.69	53.24 ± 3.71	51.94 ± 5.73
Ellipticine	0.40 ± 0.05	0.43 ± 0.03	0.49 ± 0.05	0.45 ± 0.04	0.38 ± 0.050

The *in vitro* cytotoxic activity of compounds **1**–**4** was evaluated against five human cancer cell lines, KB, SK-LU-1, MCF-7, HepG-2, and SW-480 using SRB assay. The cytotoxic effect was described on Table 2. These results showed lignans, **1- 4,** possessing weak cytotoxic activity with IC_{50} values ranging from 32.61- 95.18 µg/mL. The results agreed to published researches on cytotoxic activity of (+)-aptosimon (**1**, IC_{50} >10 µg/mL for MCF7) [15], (+)-isolariciresinol (**2**, IC_{50} > 100 µg/mL for KB, MCF7, HepG2, and Lu) [16], (-)-cleomiscosin A (**3**, IC_{50} = 132 ± 112 µg/mL) and (-)-cleomiscosin C (**4**, IC_{50} > 250 µg/mL) for MCF7) [17].

4. CONCLUSIONS

This is the first report about chemical constituents and cytotoxic activity from the leaves of *Amesiodendron chinense* (Merr.) Hu. The structures of isolated compounds were determined as (+)-aptosimon (**1**), (+)-isolariciresinol (**2**), (-)-cleomiscosin A (**3**), and (-)-cleomiscosin C (**4**). Their structures and characteristics were elucidated by spectroscopic analysis including MS, 1D, 2D-NMR spectra, physical properties as well as by the comparison with reported data in literature. All isolated compounds showed weak cytotoxic activity with IC_{50} values ranging from 32.61- 95.18 µg/mL on five human cancer cell lines, KB, SK-LU-1, MCF-7, HepG-2, and SW-480.

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