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Research Article

Phenolic compounds from the bark of *Aglaia lawii* and their cytotoxic activity against HepG2

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ABSTRACT

Introduction: *Aglaia lawii* is a large tree belonging to the Meliaceae family. In traditional medicine, stem bark is used as a vermicide, whereas leaves are used for the treatment of headache. Studies on the chemical constituents of this species in Vietnam and its biological activity, especially its ability to treat liver cancer, are still limited. This work describes the isolation and structural elucidation of six phenolic compounds from an ethyl acetate extract of the bark of *A. lawii* as well as the evaluation of their cytotoxic activity against HepG2. **Methods:** Extracts were prepared by extracting dried ground bark via Soxhlet extraction. Isolation was performed via column chromatography over silica gel, RP-18, and via gel permeation chromatography over Sephadex LH-20. Chemical structures were elucidated via spectroscopic methods (1D- and 2D-NMR, HR-ESI-MS and IR), and the spectral data were compared with those in the literature. Cytotoxic activity against HepG2 human liver cancer cells was evaluated in vitro via the MTT assay. **Results:** Six phenolic compounds, palmarumycin JC2 (**1**), 5-hydroxy-4',7-dimethoxyflavone (**2**), coniferaldehyde (**3**), 3-hydoxy-1-(4'-hydroxy-3'-methoxyphenyl)propan-1-one (**4**), *p*-hydroxybenzaldehyde (**5**), and vanillin (**6**), were isolated from an ethyl acetate extract of the bark of *A. lawii* collected in Dong Nai Province. Compounds **1-3** were evaluated for their cytotoxicity against HepG2 cells, and the results showed that the compounds exhibited weak effects or no activity. **Conclusion:** All the isolated compounds have been reported from this species for the first time. This is also the first report on the cytotoxicity of **1-2** against HepG2 cells, although the compounds displayed weak effects.

Key words: Aglaia lawii, phenolic compounds, cytotoxicity, HepG2

INTRODUCTION

Aglia is the largest genus of the Meliaceae family and consists of approximately 250 species[1]. *Aglaia lawii* (Wight) Fald. ex Raman[2] or *A. lawii* (Wight) C.J. Saldanha (synonyms: *Aglaia andamanica*, *Amoora tsangii*)[3] is found mainly in India, Bhutan, China, and Southeast Asia, including Vietnam, Myanmar, Thailand, Indonesia, Malaysia, the Philippines, and Laos[1]. In folk medicine, the leaves are used for the treatment of headache[2], and the stem bark is used as a vermicide[4]. Previous phytochemical investigations of this species have revealed the significant existence of limonoids[4–6], triterpenoids[7,8], sesquiterpenoids[5,9], and steroids[10], which exhibit diverse pharmacological activities, such as cytotoxic[7], anti-inflammatory[9–11], antiallergic[11], and anti-HIV-1[12] properties. In this work, we report the isolation and structural characterization of six phenolic compounds (**1–6**) from the ethyl acetate of the bark of *Aglaia lawii*. Furthermore, the in vitro cytotoxic activity of the isolated compounds against HepG2 human liver cancer cells was evaluated via the MTT assay to identify active compounds with therapeutic effects on liver cancer.

MATERIALS AND METHODS

General experimental procedures

Optical rotation was measured via a P8000 polarimeter manufactured by A. Krüss Optronic, whereas HR-ESI-MS data were recorded via an Agilent 6500 series Q-TOF mass spectrometer. IR spectra were recorded with KBr using a JASCO FT/IR-6600 spectrometer. NMR spectra were obtained on a Bruker AV 500 (500 MHz for ^{1}H and 125 MHz for ^{13}C) with $CDCl_3$, acetone-d_6 or methanol-d_4 as the solvent and calibrated on the basis of the chemical shifts of the corresponding deuterated solvents[13]. Column chromatography (CC) was run on silica gel (Merck, 40–63 mm)- or RP-18 (Merck, 40–63 mm)-bonded phases. For gel permeation chromatography (GPC), Sephadex LH-20 (GE Healthcare) was used. TLC was carried out on TLC silica gel (Merck, 250 mm)- or RP-18 (Merck, 200 mm)-precoated aluminum plates. The TLC plates were visualized via UV light, sprayed with ethanolic

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ferric chloride or vanillin-H_2SO_4 in EtOH, and then heated at approximately 120 °C for several minutes. Fetal bovine serum (FBS), minimal essential medium with Eagle salt (MEME), and ellipticine were purchased from Sigma. HepG2 cells (HB-8065^{TM}) were obtained from the American Type Culture Collection. Cytotoxic activity was determined in Costar 96-well plates.

Plant material

The bark of *A. lawii* was collected at the Center for Experimental Forest Research in Eastern South Vietnam (formerly known as Trang Bom Plant Collection Garden), Dong Nai Province, in November 2019. According to the document kept at the Center, the plant has been cultivated at Lot H with Code Number 83, Vietnamese name: Gội bốn cánh.

Extraction and isolation

The dried, ground bark (10 kg) was extracted with EtOAc and MeOH, respectively, via a Soxhlet extractor. Removing the solvents via a rotary evaporator produced an EtOAc extract (110 g) and a MeOH extract (138 g). The CC of the EtOAc extract with silica gel (*n*-hexane-EtOAc 0–100%) furnished 10 fractions (F1–10). Fraction F6 (9.5 g) was separated via CC on silica gel (*n*-hexane-EtOAc 0-50%) to afford 8 fractions (F6.1–8). Further separation of fraction F6.2 (1.22 g) via CC on silica gel (*n*-hexane-$CHCl_3$ 30–100%) afforded eight fractions (F6.2.1–8). Fraction F6.2.5 (30.5 mg) was purified via CC on RP-18 (70–100% MeOH in H_2O) to give **2** (5.4 mg). Fraction F6.3 (835 mg) was separated via repeated CC on silica gel (*n*-hexane-EtOAc 0–70%) to obtain **1** (24.5 mg). F6.4 (600 mg) was subjected to Sephadex LH-20 ($CHCl_3$-MeOH 1:1) and then purified via CC on silica gel (*n*-hexane-EtOAc 0–40%) to produce **3** (12.6 mg) and **4** (3.5 mg). F6.6 (1.64 g) was subjected to CC on silica gel (*n*-hexane-acetone 0–40%) to furnish five fractions (F6.6.1–5). The purification of fraction F6.6.2 (83.0 mg) via Sephadex LH-20 ($CHCl_3$-MeOH 1:1) yielded **5** (7.2 mg). The CC of fraction F6.6.4 (55.0 mg) on silica gel (*n*-hexane-EtOAc, 0–40%) led to the isolation of **6** (4.4 mg).

Cytotoxicity assay

The MTT (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium) assay was carried out via the method described by Mosmann[14], with ellipticine used as the positive control (n = 3). The cells were cultured in MEME supplemented with 10% FBS at 37°C in a humidified atmosphere with 5% CO_2. Ellipticine was dissolved in DMSO at a concentration of 0.01 mM. Briefly, HepG2 cells were separated with trypsin, seeded in each well at 3×10^4 cells/mL, treated with the test compounds at concentrations of 256, 64, 16, 4 and 1 μg/ml for 72 hours under standard conditions, and then stained with 10 μl of MTT (5 mg/ml) for 4 hours. The formazan crystals were dissolved in 100 μl of DMSO after the environmental solutions were removed. Optical density (OD) values were measured at a wavelength of 540 nm via a 96-well microtiter plate reader (Synergy HT, Biotek Instruments). The percentage of growth inhibition (I%) was calculated according to the formula:

$$I\% = \frac{|OD_c - OD_t|}{OD_c} \times 100$$

OD_t: Optical density values of the tested sample
OD_c: Optical density values of the control sample.
The IC_{50} values were calculated via nonlinear regression via RawData software (Gen5 2.07.17).

RESULTS

From the ethyl acetate extract of the bark of *A. lawii*, six compounds (**1**–**6**) were isolated via chromatographic methods. Their structures are shown in Figure 1.

Palmarumycin JC2 (1): yellow needles. $[\alpha]_D^{25}$+142.4 (*c* 7 mg in 1 ml $CHCl_3$); IR (KBr) ν_{max}: 3452, 3059, 2924, 1643, 1612, 1554, 1269, 814, 756 cm^{-1}. HR-ESI-MS: *m/z* 333.0758 $[M–H]^-$ (calculated for $C_{20}H_{13}O_5$ 333.0768). ^{1}H-NMR ($CDCl_3$, 500 MHz): δ_H 13.84 (1H, s, 9-OH), 7.55 (3H, m, H-7, H-1', H-9'), 7.49 (1H, t, 8.0 Hz, H-2'), 7.44 (1H, t, 7.9 Hz, H-8'), 7.33 (1H, dd, 7.6, 1.0 Hz, H-6), 7.08 (1H, d, 8.3 Hz, H-8), 7.08 (1H, d, 8.3 Hz, H-3'), 6.92 (1H, d, 7.5 Hz, H-7'), 4.60 (1H, t, 3.7 Hz, H-3), 3.24 (1H, dd, 17.8, 3.4 Hz, H-2a), 2.95 (1H, dd, 17.8, 4.0 Hz, H-2b); ^{13}C-NMR ($CDCl_3$, 125 MHz): δ_C 201.1 (C-1), 162.3 (C-9), 147.3 (C-6'), 146.5 (C-4'), 138.1 (C-5), 134.3 (C-10'), 137.2 (C-7), 127.9 (C-2'), 127.8 (C-8'), 121.3 (C-9'), 121.6 (C-1'), 120.0 (C-8), 118.1 (C-6), 115.5 (C-10), 113.3 (C-5'), 109.7 (C-3'), 109.0 (C-7'), 98.9 (C-4), 67.4 (C-3), 41.4 (C-2) (^{1}H- and ^{13}C-NMR assignments were performed using HSQC, HMBC and COSY techniques).

5-Hydroxy-4',7-dimethoxyflavone (2): yellow needles. ^{1}H-NMR ($CDCl_3$, 500 MHz): δ_H 12.80 (1H, s, 5-OH), 7.84 (2H, d, 8.9 Hz, H-2'/H-6'), 7.01 (2H, d, 8.9 Hz, H-3'/H-5'), 6.57 (1H, s, H-3), 6.48 (1H, d, 2.2 Hz, H-8), 6.36 (1H, d, 2.2 Hz, H-6), 3.89 (3H, s, 7-OCH_3), 3.88 (3H, s, 4'-OCH_3); ^{13}C-NMR ($CDCl_3$, 125 MHz): δ_C 182.6 (C-4), 165.6 (C-7), 164.2 (C-2), 162.8 (C-4'), 162.4 (C-5), 157.9 (C-9), 123.8 (C-1'), 128.2 (C-2'/C-6'), 114.7 (C-3'/C-5'), 105.8 (C-10),

104.5 (C-3), 98.2 (C-6), 92.8 (C-8), 55.9 (4'-OCH_3), 55.7 (7-OCH_3).

Coniferaldehyde (3): yellowish needles. ^{1}H-NMR ($CDCl_3$, 500 MHz): δ_H 9.65 (1H, d, 7.7 Hz, H-9), 7.40 (1H, d, 15.8 Hz, H-7), 7.12 (1H, dd, 8.2, 1.9 Hz, H-6), 7.07 (1H, d, 1.9 Hz, H-2), 6.96 (1H, d, 8.2 Hz, H-5), 6.60 (1H, dd, 15.8, 7.7 Hz, H-8), 3.95 (3H, s, 3-OCH_3); ^{13}C-NMR ($CDCl_3$, 125 MHz): δ_C 193.9 (C-9), 153.4 (C-7), 149.3 (C-3), 147.4 (C-4), 127.1 (C-1), 126.9 (C-8), 124.5 (C-6), 115.3 (C-5), 109.9 (C-2), 56.4 (3-OCH_3).

3-Hydoxy-1-(4'-hydroxy-3'-methoxyphenyl)propan-1-one (4): White crystals. ^{1}H-NMR ($CDCl_3$, 500 MHz): δ_H 7.55 (2H, m, H-2', H-6'), 6.96 (1H, d, 8.0 Hz, H-5'), 4.02 (1H, t, 5.3 Hz, H-3), 3.96 (3H, s, 3'-OCH_3), 3.18 (1H, t, 5.3 Hz, H-2); ^{13}C-NMR ($CDCl_3$, 125 MHz): δ_C 199.2 (C-1), 151.0 (C-4'), 146.9 (C-3'), 129.9 (C-1'), 123.8 (C-6'), 114.1 (C-5'), 109.8 (C-2'), 58.5 (C-3), 56.3 (3'-OCH_3), 40.0 (C-2).

***p*-Hydroxybenzaldehyde (5):** white crystals. ^{1}H-NMR (acetone-d_6, 500 MHz): δ_H 9.85 (1H, s, H-7), 7.80 (2H, d, 8.5 Hz, H-2, H-6), 7.00 (2H, d, 8.5 Hz, H-3, H-5);^{13}C-NMR (acetone-d_6, 125 MHz): δ_C 191.0 (C-7), 164.0 (C-4), 132.8 (C-2, C-6), 130.5 (C-1), 116.7 (C-3, C-5).

Vanillin (6): white needles. ^{1}H-NMR (methanol-d_4, 500 MHz): δ_H 9.74 (1H, s, H-7), 7.44-7.41 (2H, m, H-2, H-6), 6.93 (1H, d, 6.6 Hz, H-5), 3.91 (3H, s, 3-OCH_3); ^{13}C-NMR (methanol-d_4, 125 MHz): δ_C 191.5 (C-7), 153.4 (C-3), 148.3 (C-4), 129.3 (C-6), 126.5 (C-1), 114.9 (C-5), 109.9 (C-2), 55.0 (3-OCH_3).

Cytotoxicity of compounds **1–3** against HepG2 cells

Palmarumycin JC2 (**1**): IC_{50} = 36.09 ± 3.79 μg/ml; 5-Hydroxy-4',7-dimethoxyflavone (**2**): IC_{50} > 256 μg/ml; Coniferaldehyde (**3**): IC_{50} = 53.20 ± 4.37 μg/ml; Ellipticine (positive control): IC_{50} = 0.45 ± 0.04 μg/ml.

DISCUSSION

Compound **1** was obtained as yellow needles, $[\alpha]_D^{25}$+142.4 (c = 0.7, $CHCl_3$). Its molecular formula was determined to be $C_{20}H_{14}O_5$ by HR-ESI-MS ($[M–H]^-$ m/z 333.0758, calculated for $C_{20}H_{13}O_5$ 333.0763), indicating that **1** had fourteen degrees of unsaturation. The ^{1}H-NMR spectrum showed resonances for the presence of a chelated hydroxy proton [δ_H 13.84 (s, 9-OH)], a 1,8-disubstituted naphthalene moiety [δ_H 7.55 (2H, m, H-1', H-9'), 7.49 (1H, t, 8.0 Hz, H-2'), 7.44 (1H, t, 7.9 Hz, H-8'), 7.08 (1H, d, 8.3 Hz, H-3'), 6.92 (1H, d, 7.5 Hz, H-7')], three aromatic protons of a 1,2,3-trisubstituted benzene ring [δ_H 7.55 (1H, m, H-7), 7.33 (1H, dd, 7.6, 1.0 Hz, H-6), 7.08 (1H, d, 8.6 Hz, H-8)], an oxymethine proton of a secondary alcohol [δ_H 4.60 (1H, t, 3.7 Hz, H-3), two protons of a methylene group lying between two electron-withdrawing groups [δ_H 3.24 (1H, dd, 17.8, 3.4 Hz, H-2a), 2.95 (1H, dd, 17.8, 4.0 Hz, H-2b)]. The ^{13}C-NMR spectrum had signals due to 20 carbons, comprising a 1,8-disubstituted naphthalene moiety carrying two oxygenated carbons [δ_C 147.3 (C-6'), 146.5 (C-4')], a trisubstituted benzene ring carrying an oxygenated carbon [δ_C 162.3 (C-9)], a conjugated carbonyl carbon [δ_C 201.1 (C-1)], a spiroketal carbon [δ_C 98.9 (C-4)], an oxymethine carbon [δ_C 67.4 (C-3)], and a methylene group [δ_C 41.4 (C-2)]. The planar structure of **1** was elucidated by analysis of its HSQC, HMBC, and COSY spectra. In the COSY spectrum, correlations between H_2-2 and H-3 revealed a bond between C-2 and C-3. In the HMBC spectrum, proton H-2 correlated with C-1, C-3, C-4 and C-10, whereas proton H-3 presented cross-peaks at C-1, C-4 and C-5, indicating a 1-tetralone subunit that carried a secondary alcohol at C-2 and a spiroketal carbon at C-4. Other HMBC and COSY correlations revealed the presence of a 1,2,3-trisubstituted benzene ring of the 1-tetralone subunit and a 1,8-dioxygenated naphthalene moiety in the molecule (Figure 2). The spectral data, along with the lack of one degree of unsaturation, indicated that the 1-tetralone fragment was bonded to the 1,8-dioxygenated naphthalene moiety via the spiroketal carbon [δ_C 98.9 (C-4)]. On the basis of the spectral analysis and comparison of the data with the published article,[15,16] compound **1** could be (3*S*)- almarumycin JC2 ($[\alpha]_D^{25}$+131.9 (c = 0.5, $CHCl_3$)[15] or the enantiomer (3*R*)- almarumycin BG1 ($[\alpha]_D^{25}$–151.0 (c = 0.5, $CHCl_3$)[16]. Since the optical rotation of compound **1** was $[\alpha]_D^{25}$+142.4 (c = 0.7, $CHCl_3$), it was identified as almarumycin JC2, which was previously isolated from *Jatropha curcas*.[15]

Compound **2** was isolated as a yellow needle. The ^{1}H-NMR spectrum showed resonances for the presence of a chelated hydroxy proton [δ_H 12.80 (1H, *s*, 5-OH)], an isolated olefinic proton [δ_H 6.57 (*s*, H-3)], two *meta*-coupled protons [δ_H 6.48 (1H, *d*, 2.2 Hz, H-8) and 6.26 (1H, *d*, 2.2 Hz, H-6)], four aromatic protons of a 1,4-disubstituted benzene ring [δ_H 7.84 (2H, *m*, H-2' and H-6') and 7.01 (2H, *m*, H-3' and H-5')] and two methoxy groups [δ_H 3.89 and 3.88 (3H each, *s*, 7-OCH_3 and 4'-OCH_3)]. The ^{13}C-NMR spectrum revealed 17 carbon signals corresponding to a conjugated carbonyl carbon [δ_C 182.6 (C-4)], fourteen olefinic/aromatic carbons with five oxygenated carbons (δ_C 165.6, 164.2, 162.8, 162.4,

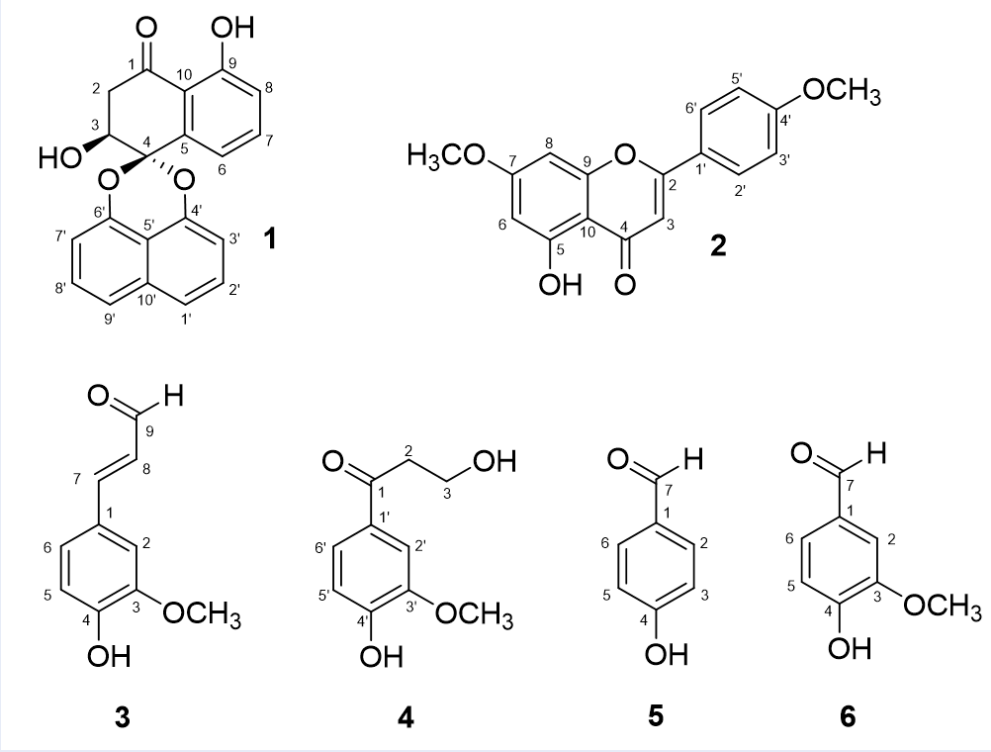

Figure 1: Structures of compounds **1**-**6**

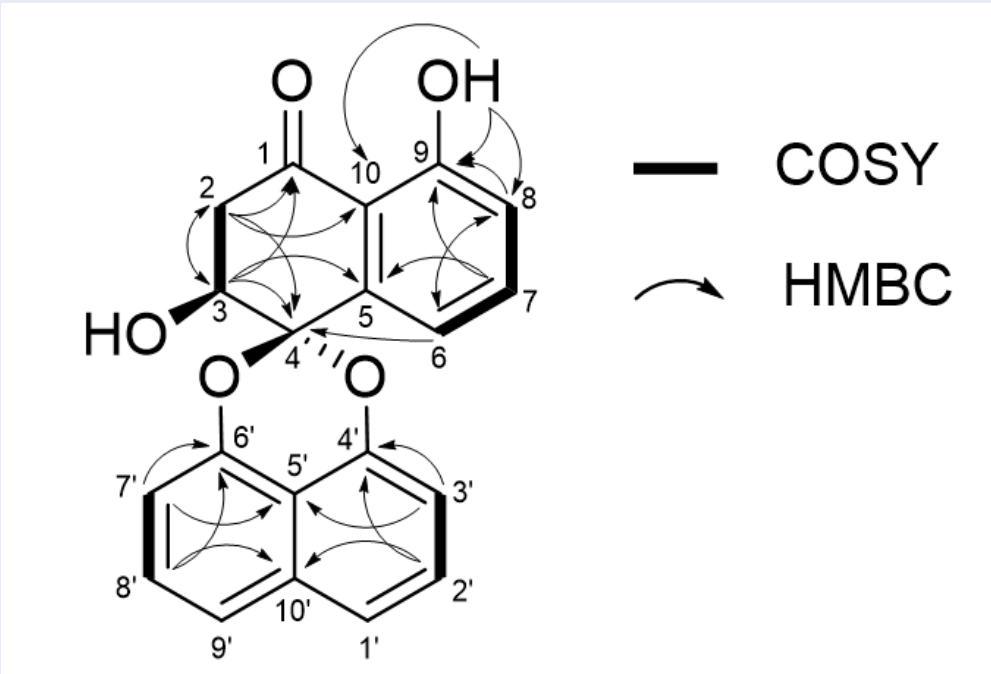

Figure 2: ^{1}H-^{1}H COSY and selected HMBC correlations of **1**

157.9), seven protonated carbons (δ_C 128.2, 114.7, 104.5, 98.2, 92.8), two fully substituted carbons (δ_C 123.8, 105.8) and two methoxy groups [δ_C 55.9 and 55.7 (7-OCH_3 and 4'-OCH_3)]. The spectral data suggested a flavone carrying a chelated hydroxy group at C-5 and two methoxy groups attached to C-7 and C-4'. A comparison of the NMR data of **2** with those of the reference[17] suggested that **2** was 5-hydroxy-4',7-dimethoxyflavone, which was previously reported in *Combretum zeyheri*.

Compound **3** was obtained as yellow needles. The ^{1}H-NMR spectrum had resonances for an aldehyde proton [δ_H 9.65 (1H, d, 7.8 Hz, H-9)], two trans-coupled protons [δ_H 7.40 (1H, d, 15.8 Hz, H-7), 6.60 (1H, dd, 15.8, 7.8 Hz, H-8)], three aromatic protons of a 1,2,4- trisubstituted benzene ring [δ_H 7.12 (1H, dd, 8.2, 1.9 Hz, H-6), 7.07 (1H, d, 1.9 Hz, H-2), 6.96 (1H, d, 8.2 Hz, H-5)], and a methoxy group (δ_H 3.95 (3H, s, 3-OCH_3)). The ^{13}C-NMR spectrum showed resonances for 10 carbons, comprising an aldehyde carbonyl carbon [δ_C 193.9 (C-9)], two olefinic carbons [δ_C 153.4 (C-7), 126.9 (C-8)], a benzene ring and a methoxy group [δ_C 56.4 (3-$OCH_{3)}$]. The benzene ring consists of three protonated carbons [δ_C 124.5 (C-6), 115.4 (C-5), 109.9 (C-2)] and three substituted carbons, two of which are oxygenated [δ_C 149.3 (C-3), 147.4 (C-4), 127.1 (C-1)]. The above spectral data revealed that the compound had a benzene ring with a conjugated aldehyde, a methoxy group and a hydroxy group. The compound was determined to be 4-hydroxy-3-methoxycinnamaldehyde or coniferaldehyde (**3**) by comparison of the NMR spectral data with those published in the literature[18].

Compound **4** was isolated as white crystals. The ^{1}H- and ^{13}C-NMR spectra closely resembled those of **3**. There were resonances for a 1,3,4-trisubstituted benzene ring carrying two oxygenated carbons [δ_H 7.55 (2H, m, H-2' and H-6'), 6.96 (1H, d, 8.0 Hz, H-5'); δ_C 151.0 (C-4'), 146.9 (C-3'), 129.9 (C-1').123.8 (C-6'), 114.1 (C-5'), 109.8 (C-2')], and a methoxy group [δ_H 3.96 (3H, s, 3'-OCH_3); δ_C 56.3 (3'-OCH_3)]. The three carbons of the conjugated aldehyde in **3** were replaced by a carbonyl carbon of a ketone [δ_C 199.2 (C-1)], an oxymethylene group [δ_H 4.02 (1H, t, 5.3 Hz, H-3); δ_C 50.5 (C-3)] and a methylene group [δ_H 3.18 (1H, t, 5.3 Hz, H-2)]; δ_C 40.0 (C-2)]. The spectral data were consistent with those previously reported[19], suggesting that compound **4** was 3-hydroxy-1-(4'-hydroxy-3'-methoxyphenyl)propan-1-one or β-hydroxypropiovanillone, which was previously isolated from *Cassia laevigata*.

Compound **5** was obtained as white crystals. The ^{1}H-NMR spectrum had resonances for the aldehyde proton [δ_H 9.85 (1H, s, H-7)] and four aromatic protons of a 1,4-trisubstituted benzene ring [δ_H 7.80 (2H, d, 8.5 Hz, H-2 and H-6), 7.00 (2H, d, 8.5 Hz, H-3 and H-5)]. The ^{13}C-NMR spectrum showed resonances for a conjugated carbonyl carbon [δ_C 191.0 (C-7)], six aromatic carbons consisting of two pairs of protonated symmetrical carbons [δ_C 132.8 (C-2, C-6), 116.7 (C-3, C-5)], and two substituted carbons, one of which were oxygenated [δ_C 164.0 (C-4)]. The compound was therefore determined to be *p*-hydroxybenzaldehyde (**5**)[20].

Compound **6** was isolated as white needles. The ^{1}H- and ^{13}C-NMR spectra of 3 were very similar to those of compound **3**. There were signals for an aldehyde [δ_H 9.74 (1H, s, H-7); δ_C 191.5 (C-7)], a 1,3,4-trisubstituted benzene ring carrying two oxygenated carbons [δ_H 7.43-7.41 (2H, m, H-2, H-6), 7.04 (1H, d, 6.6 Hz, H-5); δ_C 153.4 (C-3), 148.3 (C-4), 129.3 (C-6), 126.5 (C-1), 114.9 (C-5), 109.9 (C-2)], and a methoxy group [δ_H 3.91 (3H, s, 3-OCH_3); δ_C 55.0 (3-OCH_3)]. The only difference was that the signals for a carbon–carbon double bond disappeared. A comparison of the NMR data with those in the literature[21] suggested that compound **6** was vanillin (**6**).

Compounds **1**–**3** were evaluated for their in vitro cytotoxicity against HepG2 cells via the MTT assay, with ellipticine used as the positive control. The two polyphenol derivatives, palmarumycin JC2 (**1**) and coniferaldehyde (**3**), had very weak effects, with IC_{50} values of 36.09 and 53.20 μg/ml, respectively (ellipticine, IC_{50} = 0.45 μg/ml), whereas 5-hydroxy-4',7-dimethoxyflavone (**2**) was inactive (IC_{50} > 256 μg/ml). Previously, palmarumycin JC2 (**1**) was reported to exhibit weak or no activity against the NCI-H187, BC, KB, and Vero cell lines[22]. The low cytotoxicity of the compound is consistent with our findings. This is the first report on the cytotoxicity of compounds **2** and **3**.

CONCLUSION

Six phenolic compounds, palmarumycin JC2 (**1**), 5-hydroxy-4',7-dimethoxyflavone (**2**), coniferaldehyde (**3**), 3-hydoxy-1-(4'-hydroxy-3'-methoxyphenyl)propan-1-one (**4**), *p*-hydroxybenzaldehyde (**5**) and vanillin (**6**), were isolated from the ethyl acetate of the bark of A. lawii. This is the first time that six compounds have been found in *A. lawii*. The in vitro cytotoxicity of compounds **1**–**3** toward HepG2 cells was evaluated via the MTT assay. Nevertheless, the compounds exhibited very weak effects or no activity.

Table 1: Cytotoxicity of compounds 1-3 against HepG2 cells

Compound	IC_{50} (μg/ml)	IC_{50} (μM)
Palmarumycin JC2 (1)	36.09 ± 3.79	108.03 ± 11.35
5-Hydroxy-4',7-dimethoxyflavone (2)	> 256	> 859
Coniferaldehyde (3)	53.20 ± 4.37	298.88 ± 24.55
Ellipticine [a]	0.45 ± 0.04	1.83 ± 0.16

IC50 values are expressed as the mean ± standard deviation (n=3).
[a] Positive control

ABBREVIATIONS

NMR Nuclear magnetic resonance
CC Column Chromatography
COSY Correlation Spectroscopy
d Doublet
dd Doublet of doublet
GPC Gel Permeation Chromatography
HMBC Heteronuclear Multiple Bond Coherence
HSQC Heteronuclear Single Quantum Correlation
HR-ESI-MS High Resolution Electron Spray Ionization Mass Spectroscopy
IC_{50} The Half maximal inhibitory concentration
IR Infrared
J Coupling Constant
m Multiplet
q Quartet
RP Reversed-phase
s Singlet
t Triplet
TLC Thin Layer Chromatography

COMPETING INTEREST

The authors declare that they have no conflicts of interest.

AUTHORS' CONTRIBUTION

Pham Hoang Quan, Ngo Trang Nhu Ngoc, Nguyen Dieu Lien Hoa: research ideas and project plans; Pham Hoang Quan, Nguyen Thi Thao Ly, Trinh Thi Dieu Binh, and Ngo Trang Nhu Ngoc: sample collection, extraction, isolation; structure elucidation; Pham Hoang Quan, Nguyen Dieu Lien Hoa: writing the article.

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