



## Research Article

# ANTHRAQUINONES AND PHENOLIC COMPOUNDS FROM *CISSUS MODECCOIDES*

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## ABSTRACT

The aerial of *Cissus modeccoides* was collected in Binh Duong province, Vietnam. The ethanolic extract from this aerial was prepared by maceration. By liquid-liquid extraction, three extracts, *n*-hexane, ethyl acetate, and methanol were obtained. Three known anthraquinones 1-3 and two phenolic compounds 4-5 were isolated from the ethyl acetate extract by chromatography technique. Their structures were elucidated as chrysophanol (1), emodin (2), physcion (3), lasiodiplodin (4), and trans-4-hydroxymellein (5) based on NMR spectra analysis. All of these compounds were isolated from this plant for the first time.

**Keywords:** anthraquinone; *Cissus modeccoides*; phenolic compounds

## 1. Introduction

*Cissus* is the largest genus in the Vitaceae family with about 350 species (Lombardi, 1996) that are distributed in the tropical and subtropical regions. The previously pharmacological studies from some species showed anti-inflammatory (Panthong et al., 2007; Chang et al., 2012), antioxidant (Jainu & Devi, 2005), anti-diabetic, anti-lipemic (Beltrame et al., 2002; Viana et al., 2004), and gastroprotective action (Ferreira et al., 2008). The investigation of phytochemistry has been reported including anthraquinones (Ibrahim et al., 2011), flavonoids (Xu et al., 2009; Ahmadu et al., 2010), stilbenes (Xu et al., 2009; Shah, 2011; Wang et al., 2007), coumarins (Lin, 2012), and terpenoids (Bafna et al., 2021). In folk medicine of Vietnam, *Cissus modeccoides* was used to treat headaches, rheumatism bone, and joint pain (Do, 2004). The phytochemical study of this plant has not been reported. In our investigation of the constituents of this plant, three anthraquinones and two phenolic compounds were obtained from this plant for the first time. Herein, in this paper, the isolation

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and structural elucidation of five compounds from this plant collected in Vietnam were demonstrated

## 2. Experiment

### 2.1. General experimental procedures

NMR spectra were recorded on a Bruker Avance III spectrometer, at 500 MHz for  $^1\text{H}$  NMR and 125 MHz for  $^{13}\text{C}$  NMR, using TMS or residual solvent signal as internal reference (chloroform- $d$   $\delta_{\text{H}}$  7.260,  $\delta_{\text{C}}$  77.16).

### 2.2. Plant material

The aerial of *Cissus modeccoides* was collected in Binh Duong, Vietnam in October 2017 and authenticated by Dr. Dang Van Son from the Institute of Tropical Biology, Vietnam Academy Science and Technology, Vietnam.

### 2.3. Extraction and Isolation

The 10.5 kg dried powder of the aerial was macerated with ethanol at room temperature (4x15 L), evaporated solvent to give an ethanolic extract (417.0 g). This extract was partitioned into *n*-hexane (96.2 g), ethyl acetate (167.6 g) and methanolic (97.4 g) extracts by liquid-liquid extraction. The ethyl acetate extract was applied to a silica gel column chromatography (CC), eluted with *n*-hexane – ethyl acetate (0–100% ethyl acetate), ethyl acetate – methanol (0–50% methanol) to give six fractions (EA1–EA6).

Fraction EA1 (60.7 g) was chromatographed and eluted with *n*-hexane – ethyl acetate (0–100% ethyl acetate) to give 12 fractions (EA1.1–EA1.12). Further fractionation of EA1.2 on silica column eluted with *n*-hexane- acetone (0–20% acetone) yielded compounds **1** (15.3 mg), **2** (6.5 mg) and **4** (3.5 mg). Subfraction EA1.6 was subjected to a silica gel CC, eluted with *n*-hexane-chloroform (0–100% chloroform), obtained compounds **3** (7.1 mg) and **5** (11.2 mg).

**Chrysophanol (1).** Yellow needles.  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ):  $\delta_{\text{H}}$  12.09 (1H, *s*, 8-OH), 11.98, (1H, *s*, 1-OH). 7.80 (1H, *dd*,  $J = 7.5/1.0$  Hz, H-5), 7.65 (1H, *dd*,  $J = 8.5/7.5$  Hz, H-6), 7.63 (1H, *d*,  $J = 1.5$  Hz, H-4), 7.27 (1H, *dd*,  $J = 9.5/1.0$  Hz, H-7), 7.08 (1H, *dd*,  $J = 1.0/0.5$  Hz, H-2), 2.46 (3H, *s*, 3- $\text{CH}_3$ ).  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ ) see Table 1.

**Emodin (2).** Orange needles,  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ):  $\delta_{\text{H}}$  12.27 (1H, *s*, 1-OH), 12.01 (1H, *s*, 8-OH), 7.63 (1H, *brs*, H-5), 7.29 (1H, *d*,  $J = 2.0$  Hz, H-4), 7.09 (1H, *brs*, H-7), 6.67 (1H, *d*,  $J = 1.5$  Hz, H-2), 2.45 (3H, *s*, 6- $\text{CH}_3$ ).  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ ) see Table 1.

**Physcion (3).** Orange needles.  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ):  $\delta_{\text{H}}$  12.31 (1H, *s*, 1-OH) và 12.12 (1H, *s*, 8-OH), 7.63 (1H, *d*,  $J = 1.0$  Hz, H-5), 7.37 (1H, *d*,  $J = 2.5$  Hz, H-4), 7.08 (1H, *d*,  $J = 0.5$  Hz, H-7), 6.69 (1H, *d*,  $J = 2.5$  Hz, H-2), 3.94 (3H, *s*, 3-  $\text{OCH}_3$ ).  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ ) see Table 1.

**Lasiodiplodin (4).** Colourless needles,  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ):  $\delta_{\text{H}}$  6.24 (1H, *d*,  $J = 2.0$  Hz, H-14), 6.23 (1H, *d*,  $J = 2.0$  Hz, H-12). 5.28 (*m*, H-3) 3.75 (*s*, 15-OMe). 2.67 (*dt*,  $J = 13.5/9.0$ ,

H-10a), 2.49 (*dt*,  $J = 13.5/6.5$ , H-10b), 1.93 (*m*, H-4a), 1.63 (*m*, H-4b).  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ ) see Table 1.

***trans*-4-Hydroxymellein (5).** White needles,  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ):  $\delta_{\text{H}}$  10.96 (1H, *s*, 8-OH), 7.54 (1H, *dd*,  $J = 8.0/8.0$  Hz, H-6), 7.03 (1H, *d*,  $J = 7.5$  Hz, H-5), 6.99 (1H, *d*,  $J = 8.5$  Hz, H-7), 4.61 (2H, *m*, H-3, H-4), 1.52 (3H, *d*,  $J = 6.0$  Hz, 3- $\text{CH}_3$ ).  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ ) see Table 1.

### 3. Results and discussion

The  $^1\text{H}$ -NMR spectrum of **1** showed signals of five aromatic protons at  $\delta_{\text{H}}$  7.80 (1H, *dd*,  $J = 7.5/1.0$  Hz, H-5), 7.65 (1H, *dd*,  $J = 8.5/7.5$  Hz, H-6), 7.63 (1H, *d*,  $J = 1.5$  Hz, H-4), 7.27 (1H, *dd*,  $J = 9.5/1.0$  Hz, H-7), 7.08 (1H, *dd*,  $J = 1.0/0.5$  Hz, H-2), one aromatic methyl group ( $\delta_{\text{H}}$  2.46, 3H, *s*, 3- $\text{CH}_3$ ), and two chelate hydroxyl groups at  $\delta_{\text{H}}$  12.09, 11.98 (each *s*). Its  $^{13}\text{C}$  and HSQC spectra revealed 15 carbons including two carbonyl carbons ( $\delta_{\text{C}}$  192.5, C-9; 182.0, C-10), and one aromatic methyl group ( $\delta_{\text{C}}$  22.3). The as-presented NMR data suggested that **1** was an anthraquinone. HMBC interactions (Figure 1) from two protons at  $\delta_{\text{H}}$  7.63 (H-4) and 7.80 (H-5) to one carbonyl carbon ( $\delta_{\text{C}}$  182.0) suggested that these aromatic protons attached at C-4 and C-5 respectively, and two hydroxyl groups located at C-1 and C-8. The methyl group could attach to C-3 based on HMBC correlations from these protons to C-3 ( $\delta_{\text{C}}$  149.4), C-2 ( $\delta_{\text{C}}$  124.4), and C-4 ( $\delta_{\text{C}}$  121.4). Along with the observation of spectroscopic data, the comparison with analogs reported in the literature (Danielsen et al., 1992) indicated that **1** was chrysophanol.

The spectroscopic data of **2** and **1** were similar, except for the presence of one more oxygenated aromatic carbon ( $\delta_{\text{C}}$  163.5). In the HMBC analysis, the proton at  $\delta_{\text{H}}$  6.67 (*d*,  $J = 2.0$  Hz) showed cross-peaks with C-1, C-4, the *meta* coupled proton at  $\delta_{\text{H}}$  7.29 (*d*,  $J = 2.0$  Hz) showed correlations to C-2, C-10. This supports that the third hydroxyl group could be located at C-3. The comparison of NMR data of **2** to those of the reported ones in the literature (Danielsen et al., 1992) indicated that **2** was emodin.

The NMR spectra of **3** were similar to those of **1** and **2**. The difference was that the hydroxyl group at C-3 in **2** was replaced by a methoxyl group at  $\delta_{\text{C}}$  56.2,  $\delta_{\text{H}}$  3.94 (3H, *s*). This was supported by significant HMBC cross-peaks from the signals at  $\delta_{\text{H}}$  6.69 (*d*,  $J = 2.5$  Hz, H-2), 3.94 (*s*, - $\text{OCH}_3$ ) to the same oxygenated aromatic carbon at  $\delta_{\text{C}}$  166.7 (C-3). The structure of **3** was determined as physcion because its NMR data were compatible with those in the literature (Danielsen et al., 1992).

The  $^1\text{H}$ -NMR spectrum of **4** showed signals of two *meta* coupled protons at  $\delta_{\text{H}}$  6.24 (*d*,  $J = 2.0$  Hz) and 6.23 (*d*,  $J = 2.0$  Hz), one oxymethine group ( $\delta_{\text{H}}$  5.28, *m*), one methoxyl group ( $\delta_{\text{H}}$  3.75, *s*), and one methyl group ( $\delta_{\text{H}}$  1.32, *d*,  $J = 6.0$  Hz). The combination of  $^{13}\text{C}$ , DEPT, and HSQC spectra of **4** showed the presence of 18 carbons, including a carbonyl carbon ( $\delta_{\text{C}}$  168.8, C-7), two oxygenated aromatic carbons ( $\delta_{\text{C}}$  158.0, 157.4), two aromatic methine carbons ( $\delta_{\text{C}}$  108.3, 97.0), two quaternary aromatic carbons ( $\delta_{\text{C}}$  143.1, 117.8), one

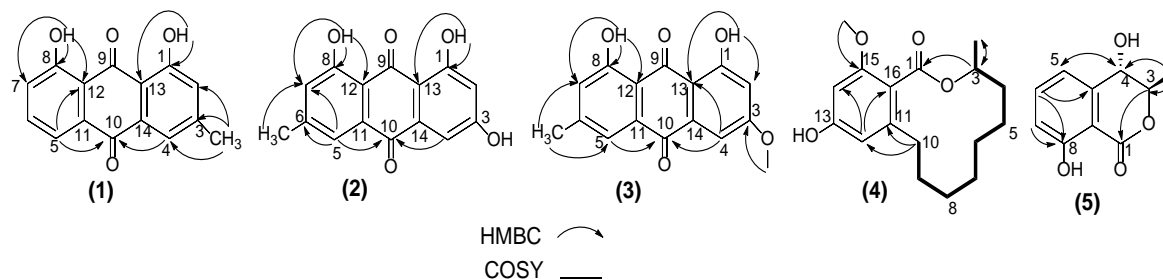
oxymethine carbon ( $\delta_C$  72.3), one methoxyl group ( $\delta_C$  55.9), one methyl group ( $\delta_C$  19.5), and seven methylene groups. The COSY spectrum showed the correlations of H-17/H-3/H-4, H-4/H-5/H-6/H-7/H-8/H-9/H-10, indicating connectivity in the macrolide system. The HMBC correlations from H-10 ( $\delta_H$  2.67, 2.49 ) to C-11 ( $\delta_C$  143.1) and C-12 ( $\delta_C$  108.3) defined that the aliphatic ring and benzene ring were connected via C-11 and C-16. The location of the methoxy group was corroborated by significant HMBC cross-peaks from the signal at  $\delta_H$  3.75 to C-15 ( $\delta_C$  158.0). By comparing these data to those in the literature (Bracher & Schulte, 1996), the structure of **4** was defined as lasiodiplodin.

**Table 1.** The  $^{13}C$  NMR data of 1-5

N <sup>o</sup>	1	2	3	4	5
1	162.7	165.5	165.4	168.8	168.5
2	124.4	108.9	107.0	-	-
3	149.4	163.5	166.7	72.3	80.0
4	121.4	108.9	108.4	32.4	69.2
5	119.9	121.3	121.5	21.3	116.3
6	136.9	148.6	148.6	26.5	136.9
7	124.6	124.6	124.7	24.2	117.8
8	162.4	162.8	162.7	25.5	162.0
9	192.3	191.1	191.0	30.1	106.7
10	182.0	182.0	182.2	30.4	141.2
11	133.7	133.5	133.4	143.1	
12	115.9	113.9	113.9	108.3	
13	113.8	101.3	110.5	157.4	
14	133.3	136.0	135.5	97.0	
15				158.0	
16				117.8	
3-CH <sub>3</sub> /6-CH <sub>3</sub>	22.3	22.1	22.3	19.5	17.9
3-OCH <sub>3</sub> /15-OCH <sub>3</sub>			56.2	55.9	

Compound **5** was obtained as white needles. Its  $^1H$  NMR showed signals of a 1,2,3-trisubstituted benzene ring at  $\delta_H$  7.54 (1H, *dd*,  $J$  = 8.0/8.0 Hz), 7.03 (1H, *d*,  $J$  = 7.5 Hz) and 6.99 (1H, *d*,  $J$  = 8.5 Hz), two oxymethine protons ( $\delta_H$  4.61, 2H, *m*), one methyl group ( $\delta_H$  1.52, 3H, *d*,  $J$  = 6.0 Hz), and one chelated hydroxyl group ( $\delta_H$  10.96). Its  $^{13}C$  and HSQC spectrum revealed 10 carbons, including one carboxyl ( $\delta_C$  168.5), one oxygenated aromatic carbon (162.0), three aromatic methine carbons ( $\delta_C$  136.9, 117.8, 116.3), two aromatic quaternary carbons ( $\delta_C$  141.2, 106.7), two oxymethine carbons ( $\delta_C$  80.0, 69.2), and one methyl group ( $\delta_C$  17.9). The HMBC correlations between the oxymethine protons ( $\delta_H$  4.61) and C-1 ( $\delta_C$  168.5), C-4a ( $\delta_C$  141.2), C-5 ( $\delta_C$  116.3), C-8a ( $\delta_C$  103) suggested that **5** was an isocoumarin derivative. The position of a methyl group at C-3 could be determined thanks

to HMBC cross-peaks between methyl protons ( $\delta_H$  1.52) to oxymethine carbons C-3 ( $\delta_C$  80.0) and C-4 ( $\delta_C$  69.2). These spectroscopic data were in line with the published ones (Montenegro et al., 2012). Therefore, **5** was defined as *trans*-4-hydroxymellein.



**Figure 1.** Chemical structures and some key HMBC, COSY correlations of **1-5**

#### 4. Conclusions

From the ethyl acetate extract of *Cissus modeccoides*, five compounds chrysophanol (**1**), emodin (**2**), physcion (**3**), lasiodiplodin (**4**), and *trans*-4-hydroxymellein (**5**) were isolated. Although these compounds were already known in other species, this is the first time they were found in *Cissus modeccoides*.

❖ **Conflict of Interest:** Authors have no conflict of interest to declare.

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**CÁC HỢP CHẤT ANTHRAQUINONE VÀ PHENOLIC  
TỪ LOÀI *CISSUS MODECCOIDES***

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**TÓM TẮT**

*Cây Chìa vôi (Cissus modeccoides) được thu hái tại tỉnh Bình Dương, Việt Nam. Cao chiết ethanol được điều chế từ phần trên mặt đất của cây này bằng phương pháp ngâm ở nhiệt độ phòng. Thực hiện kỹ thuật chiết lỏng-lỏng, từ cao ethanol, ba cao n-hexane, ethyl acetate và methanol cũng được điều chế. Từ cao chiết ethyl acetate, ba hợp chất anthraquinone đã biết và hai hợp chất phenolic đã được phân lập bằng kỹ thuật sắc ký. Cấu trúc của những hợp chất này được xác định là chrysophanol (1), emodin (2), physcion (3), lasiodiplodin (4) và trans-4-hydroxymellein (5) bằng phương pháp phổ NMR. Lần đầu tiên, các hợp chất này được phát hiện có trong cây Chìa vôi.*

**Từ khóa:** anthraquinone; *Cissus modeccoides*; phenolic compounds