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...
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 $^1$H NMR and 125 MHz for $^{13}$C NMR, using TMS or residual solvent signal as internal reference (chloroform-$d$ δ$_H$ 7.260, δ$_C$ 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. $^1$H NMR (CDCl$_3$): δ$_H$ 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-CH$_3$). $^{13}$C NMR (CDCl$_3$) see Table 1.

**Emodin (2).** Orange needles, $^1$H NMR (CDCl$_3$): δ$_H$ 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-CH$_3$). $^{13}$C NMR (CDCl$_3$) see Table 1.

**Physcion (3).** Orange needles. $^1$H NMR (CDCl$_3$): δ$_H$ 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-OCH$_3$). $^{13}$C NMR (CDCl$_3$) see Table 1.

**Lasiodiplodin (4).** Colourless needles, $^1$H NMR (CDCl$_3$): δ$_H$ 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). 13C NMR (CDCl3) see Table 1.

**trans-4-Hydroxmellein (5).** White needles, 1H NMR (CDCl3): δH 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-CH3). 13C NMR (CDCl3) see Table 1.

3. Results and discussion

The 1H–NMR spectrum of 1 showed signals of five aromatic protons at δH 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 (δH 2.46, 3H, s, 3-CH3), and two chelate hydroxyl groups at δH 12.09, 11.98 (each s). Its 13C and HSQC spectra revealed 15 carbons including two carbonyl carbons (δC 192.5, C-9; 182.0, C-10), and one aromatic methyl group (δC 22.3). The as–presented NMR data suggested that 1 was an anthraquinone. HMBC interactions (Figure 1) from two protons at δH 7.63 (H-4) and 7.80 (H-5) to one carbonyl carbon (δC 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 (δC 149.4), C-2 (δC 124.4), and C-4 (δC 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 (δC 163.5). In the HMBC analysis, the proton at δH 6.67 (d, J = 2.0 Hz) showed cross-peaks with C-1, C-4, the meta coupled proton at δH 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 δC 56.2, δH 3.94 (3H, s). This was supported by significant HMBC cross-peaks from the signals at δH 6.69 (d, J = 2.5 Hz, H-2), 3.94 (s, -OCH3) to the same oxygenated aromatic carbon at δC 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 1H-NMR spectrum of 4 showed signals of two meta coupled protons at δH 6.24 (d, J = 2.0 Hz) and 6.23 (d, J = 2.0 Hz), one oxymethine group (δH 5.28, m), one methoxyl group (δH 3.75, s), and one methyl group (δH 1.32, d, J = 6.0 Hz). The combination of 13C, DEPT, and HSQC spectra of 4 showed the presence of 18 carbons, including a carbonyl carbon (δC 168.8, C-7), two oxygenated aromatic carbons (δC 158.0, 157.4), two aromatic methine carbons (δC 108.3, 97.0), two quaternary aromatic carbons (δC 143.1, 117.8), one
oxymethine carbon (δC 72.3), one methoxyl group (δC 55.9), one methyl group (δC 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 (δH 2.67, 2.49) to C-11 (δC 143.1) and C-12 (δC 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 δH 3.75 to C-15 (δC 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 13C NMR data of 1-5

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Compound 5 was obtained as white needles. Its ¹H NMR showed signals of a 1,2,3-trisubstituted benzene ring at δH 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 (δH 4.61, 2H, m), one methyl group (δH 1.52, 3H, d, J = 6.0 Hz), and one chelated hydroxyl group (δH 10.96). Its ¹³C and HSQC spectrum revealed 10 carbons, including one carboxyl (δC 168.5), one oxygenated aromatic carbon (162.0), three aromatic methine carbons (δC 136.9, 117.8, 116.3), two aromatic quaternary carbons (δC 141.2, 106.7), two oxymethine carbons (δC 80.0, 69.2), and one methyl group (δC 17.9). The HMBC correlations between the oxymethine protons (δH 4.61) and C-1 (δC 168.5), C-4a (δC 141.2), C-5 (δC 116.3), C-8a (δC 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 (δ_H 1.52) to oxymethine carbons C-3 (δ_C 80.0) and C-4 (δ_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.

![Chemical structures and some key HMBC, COSY correlations of 1-5](image)

**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.

REFERENCES


CÁC HỘP CHẤT ANTHRAQUINONE VÀ PHENOLIC TỪ LOÀI CISSUS MODECOIDES

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TÓM TÁT

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 kí. 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