TẠP CHÍ KHOA HỌC
TRƯỜNG ĐẠI HỌC SƯ PHẠM TP HỒ CHÍ MINH
Tập 19, Số 3 (2022): 524-530
Website: http://journal.hcmue.edu.vn
ISSN: 2734-9918

HO CHI MINH CITY UNIVERSITY OF EDUCATION
JOURNAL OF SCIENCE
Vol. 19, No. 3 (2022): 524-530
https://doi.org/10.54607/hcmue.js.19.3.3392(2022)

Research Article

ANTHRAQUINONES AND PHENOLIC COMPOUNDS FROM *CISSUS MODECCOIDES*

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Received: March 16, 2022; Revised: March 19, 2022; Accepted: March 24, 2022

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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Cite this article as: Nguyen Ngoc Tin, Tran Huu Duy, Nguyen Thanh Binh, & Nguyen Thi Anh Tuyet (2022). Anthraquinones and phenolic compounds from *Cissus modeccoides. Ho Chi Minh City University of Education Journal of Science, 19*(3), 524-530.

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). ^{13}C NMR (CDCl$_3$) see Table 1.

***trans*-4-Hydroxymellein (5).** White needles**,** ^{1}H NMR (CDCl$_3$): δ_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-CH$_3$). ^{13}C NMR (CDCl$_3$) see Table 1.

3. Results and discussion

The ^{1}H–NMR spectrum of **1** showed signals of five aromatic protons at δ_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 (δ_H 2.46, 3H, *s*, 3-CH$_3$), and two chelate hydroxyl groups at δ_H 12.09, 11.98 (each *s*). Its ^{13}C and HSQC spectra revealed 15 carbons including two carbonyl carbons (δ_C 192.5, C-9; 182.0, C-10), and one aromatic methyl group (δ_C 22.3). The as-presented NMR data suggested that **1** was an anthraquinone. HMBC interactions (Figure 1) from two protons at δ_H 7.63 (H-4) and 7.80 (H-5) to one carbonyl carbon (δ_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 (δ_C 149.4), C-2 (δ_C 124.4), and C-4 (δ_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 (δ_C 163.5). In the HMBC analysis, the proton at δ_H 6.67 (*d*, J = 2.0 Hz) showed cross-peaks with C-1, C-4, the *meta* coupled proton at δ_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 δ_C 56.2, δ_H 3.94 (3H, *s*). This was supported by significant HMBC cross-peaks from the signals at δ_H 6.69 (*d*, J = 2.5 Hz, H-2), 3.94 (*s*, -OCH$_3$) to the same oxygenated aromatic carbon at δ_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}H-NMR spectrum of **4** showed signals of two *meta* coupled protons at δ_H 6.24 (*d*, J = 2.0 Hz) and 6.23 (*d*, J = 2.0 Hz), one oxymethine group (δ_H 5.28, *m*), one methoxyl group (δ_H 3.75, *s*), and one methyl group (δ_H 1.32, *d*, J = 6.0 Hz). The combination of ^{13}C, DEPT, and HSQC spectra of **4** showed the presence of 18 carbons, including a carbonyl carbon (δ_C 168.8, C-7), two oxygenated aromatic carbons (δ_C 158.0, 157.4), two aromatic methine carbons (δ_C 108.3, 97.0), two quaternary aromatic carbons (δ_C 143.1, 117.8), one oxymethine carbon (δ_C 72.3), one methoxyl group (δ_C 55.9), one methyl group (δ_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 (δ_H 2.67, 2.49) to C-11 (δ_C 143.1) and C-12 (δ_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 δ_H 3.75 to C-15 (δ_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°	**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_3/6-CH_3	22.3	22.1	22.3	19.5	17.9
3-OCH_3/15-OCH_3			56.2	55.9	

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

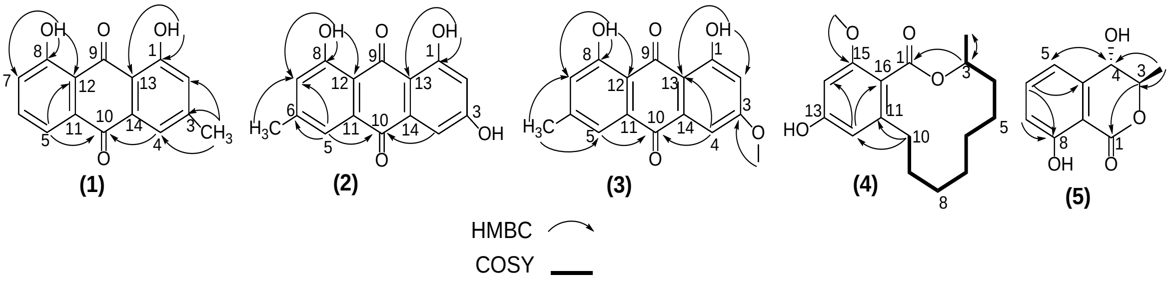

*Figure 1. Chemical structures and some key HMBC, COSY correlations of **1-5***

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

Ahmadu, A. A., Onanuga, A., & Aquino R. (2010). Flavonoid glycosides from leaves of *Cissus ibuensis* Hook (Vitaceae). *Afr. J. Trad. CAM*, *7*(3), 225-230.

Bafna, P. S., Patil, P. H., Maru, S. K., & Mutha, R. E. (2021). *Cissus quadrangularis* L: A comprehensive multidisciplinary review. *Journal of Ethnopharmacology, 279*, 114355.

Beltrame, F. L., Pessini, G. L., Doro, D. L., Dias Filho, B. P., Bazotte, R. B., & Cortez, D. A. G. (2002). Evaluation of the antidiabetic and antibacterial activity of *Cissus sicyoides. Brazilian Archives of Biology and Technology*, *45*(1), 21-25.

Bracher, F., & Schulte, B. (1996). Enantiodivergent synthesis of both enantiomers of the macrocyclic lactone lasiodiplodin. *Journal of the Chemical Society, Perkin Transactions 1, 21*, 2619.

Chang, C. W., Chang, W. T., Liao, J. C., Chiu, Y. J., Hsieh, M. T., Peng, W. H., & Lin, Y. C. (2012). Analgesic and anti-Inflammatory activities of methanol extract of *Cissus repens* in mice. *Evid. Based Complememt. Alternat. Med., 2012*, 1-10.

Danielsen, K., Aksnes, D. W., & Francis, G. W. (1992). NMR study of some anthraquinones from Rhubarb", *Magnetic Resonance in chemistry, 30*, 359-363, 1992.

Do, T. L. (2004). *Medicinal plants in Vietnam*. Medicinal Publishing House (Vietnam), 505-506.

Ferreira, M. de P., Nishijima, C. M., Seito, L. N., Dokkedal, A. L., Lopes-Ferreira, M., Di Stasi, L. C., … Hiruma-Lima, C. A. (2008). Gastroprotective effect of *Cissus sicyoides* (Vitaceae): Involvement of microcirculation, endogenous sulfhydryls and nitric oxide. *Journal of Ethnopharmacology, 117*(1), 170-174.

Ibrahim, H., Mdau, B. B., Ahmed, A., & Ilyas, M. (2011). Anthraquinones of *Cissus populnea* Guill & Perr (Amplidaceae). *African journal of traditional, complementary, and alternative medicines, 8*(2), 140-143.

Jainu, M., & Devi, C. S. (2005). *In vitro* and *In vivo* evaluation of free radical scavenging potential of *Cissus quadrangularis. Afr. J. Biomed Res*, *43*, 95-99.

Lin, C. F., Hwang, T. L., Lin, S. Y., & Huang, Y. L. (2012). Bioactive isocoumarin from *Cissus pteroclada, J Chin Med, 23*(1), 41-49.

Lombardi, J. A. (1996). Five New Species of Cissus (Vitaceae) from Northern Brazil. *Novon*, *6*(2), 195-200.

Montenegro, T. G. C., Rodrigues, F. A. R., Jimenez, P. C., Angelim, A. L., Melo, V. M. M., Rodrigues Filho, E., … Costa-Lotufo, L. V. (2012). Cytotoxic activity of fungal strains isolated from the *Ascidian eudistoma vannamei. Chemistry & Biodiversity, 9*(10), 2203-2209.

Panthong, A., Supraditaporn, W., Kanjanapothi, D., Taesotikul, T., & Reutrakul, V. (2007). Analgesic, anti-inflammatory and venotonic effects of *Cissus quadrangularis* Linn. *J. Ethnopharmacol*, *110*, 264-70.

Shah, U. (2011). *Cissus Quadrangularis* L.: Phytochemicals, traditional use and pharmacological activities – A review. *Int. J. Pharm. Pharm. Sci, 3*(4), 41-44.

Viana, G. S., Medeiros, A. C. C., Lacerda, A. M. R., Leal, L. K. A., Vale, T. G., & Matos, F. J. (2004). Hypoglycemic and anti-lipemic effects of the aqueous extract from *Cissus sicyoides*. *Bio. Med. Central Pharmacology*, *4*(1), 4-9.

Wang, Y.-H., Zhang, Z.-K., He, H.-P., Wang, J.-S., Zhou, H., Ding, M., & Hao, X.-J. (2007). Stilbene C-glucosides from *Cissus repens. Journal of Asian Natural Products Research, 9*(7), 631-636.

Xu, F., Matsuda, H., Hata, H., Sugawara, K., Nakamura, S., & Yoshikawa, M. (2009). Structures of new flavonoids and benzofuran-type stilbene and degranulation inhibitors of rat basophilic leukemia cells from the Brazilian Herbal Medicine *Cissus sicyoides. Chemical & Pharmaceutical Bulletin, 57*(10), 1089-1095.

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

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Ngày nhận bài: 16-3-2022; ngày nhận bài sửa: 19-3-2022; ngày duyệt đăng: 24-3-2022

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 kĩ 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 kĩ 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