(2017), Effect of ultrasonic-assisted extraction conditions on antioxidant activity of *Allium ascalonicum* extract, *Journal of Fisheries Science and Technology* (1), 91-98. **11.** Pham Thi Nguyet Hang, Tran Nguyen Hong, Nguyen Van Hiep, Phi Thi Xuyen, Dinh Thi Minh, Nguyen Huu Son, Do Thi Ha, Pham Thanh Huyen, Nguyen Minh Khoi, Nguyen Trong Tue, Nguyen Thi Lap (2020), Screening study on the effect of some medicinal extracts on an experimental autistic *Drosophila melanogaster* model, *Journal of Medicinal Materials-Hanoi*. 25(2), 67-74. **12.** Gutzeit D., Wray V., Winterhalter P., Jerz G. (2007), Preparative isolation and purification of flavonoids and protocatechuic acid from sea buckthorn juice concentrate (*Hippophaë rhamnoides* L. ssp. *rhamnodes*) by high-speed counter-current chromatography, *Chromatographia*. 65(1), 1-7. **13.** Al-Taweel A. M., Perveen S., El-Shafae A. M., Fawzy G. A., Malik A., Afza N., Iqbal L., Latif M. (2012), Bioactive phenolic amides from *Celtis africana*, *Molecules*. 17(3), 2675-2682. **14.** Sultana N., Armstrong J. A., Waterman P. G. (1999), Benzopyran derivatives from the aerial parts of *Eriostemon rhomboideus*, *Phytochemistry*. 52(5), 895-900. **15.** Zhang Y., Wang D., Yang L., Zhou D., Zhang J. (2014), Purification and characterization of flavonoids from the leaves of *Zanthoxylum bungeanum* and correlation between their structure and antioxidant activity, *PloS One*. 9(8), e105725. **16.** Fossen T., Pedersen A. T., Andersen Ø. M. (1998), Flavonoids from red onion (*Allium cepa*), *Phytochemistry* 47(2), 281-285. **17.** Cao X., Wei Y., Ito Y. (2008), Preparative isolation of isorhamnetin from *Stigma maydis* using high speed countercurrent chromatography, *Journal of Liquid Chromatography & Related Technologies*. 32(2), 273-280. **18.** Park Y. K., Lee C. Y. (1996), Identification of isorhamnetin 4'-glucoside in onions, *Journal of Agricultural and Food Chemistry*. 44(1), 34-36. **19.** Agrawal P. K. (2004), Dependence of ^{1}H NMR chemical shifts of geminal protons of glycosyloxy methylene (H2-26) on the orientation of the 27-methyl group of furostane-type steroidal saponins, *Magnetic Resonance in Chemistry*. 42(11), 990-993. **20.** Chen N., Zhang J., Liu J., Yu B. (2010), Highly efficient and regio-selective glucosylation of 25(*S*)-ruscogenin by *Gliocladium deliquescens* NRRL1086, *Chinese Journal of Chemistry*. 28(3), 439-442. **21.** Wang X., Wang M., Xu M., Wang Y., Tang H., Sun X. (2014), Cytotoxic oleanane-type triterpenoid saponins from the rhizomes of *Anemone rivularis* var. *flore-minore*, *Molecules*. 19(2), 2121-2134. **22.** Liu Y., Qiu P., Wang M., Lu Y., He H., Tang H., Zhang B. L. (2021), New steroidal saponins isolated from the rhizomes of *Paris mairei*, *Molecules*. 26(21), 6366.

Journal of Medicinal Materials, 2022, Vol. 27, No. 1 (pp. 9 - 14)

CHEMICAL CONSTITUENTS FROM THE ETHYL ACETATE EXTRACT OF *PAEDERIA SCANDENS* (LOUR.) MERR. COLLECTED IN VIETNAM

Tran Thanh Ha [1,*], Nguyen Thi Ha[1], Nguyen Tuan Hiep[1], Le Thi Huyen[2]

[1]*National Institute of Medicinal Materials, Hanoi, Vietnam;*

[2]*University of Natural Sciences - Vietnam National University, Hanoi*

*Corresponding author: thanhha.tran889@gmail.com

(Received December 21th, 2021)

Summary

Chemical Constituents from Ethyl Acetate Extract of *Paederia scandens* (Lour.) Merr. Collected in Vietnam

Phytochemical study on the ethyl acetate extract of the rhizomes of Paederia scandens (Lour.) Merr. resulted in the isolation of nine compounds: anthraquinone (**1**), 3,3′-dimethoxyellagic acid 4′-O-α-L-rhamnopyranoside (**2**), 3′,4′,7-trihydroxyflavanone (**3**), betulinic acid (**4**), kaempferol (**5**), linarin (**6**), paederoside (**7**), quercetin 3-O-α-L-rhamnosyl-(1→6)-β-D-glucopyranosyl-(1→3)-β-D-glucopyranoside (**8**), and kaempferol 3-O-β-D-glucopyranoside (**9**) on the basis of experimental spectral data. Compounds **1**, **2**, **3**, **6**, and **8** were reported from P. scandens for the first time.

Keywords: *Paederia scandens* (Lour.) Merr., *Rubiaceae quercetin glycoside.*

1. Introduction

Paederia scandens (Lour.) Merrill belonging to Rubiaceae, is used to treat aches, jaundice, dysentery, and dyspepsia as a folk medicine in the southern region of China, Vietnam, India, and Japan [1]. The roots, leaves, bark, and fruits of this plant have been used for the treatment of toothache, chest pain, inflammation, jaundice, and dysentery [2]. In 1969, Inouye et al. isolated four iridoid glycosides from this species for the first time [3]. From then on, more than 50 compounds have been obtained from *P. scandens*. Among these, iridoid glycosides, flavonoids, and volatile oils are the major constituents [4], which were mainly responsible for the anti-nociceptive, anti-inflammatory, and antitumor activities of *P. scandens* [5],[6],[7].

Quang et al. reported the isolation of anthraquinones and iridoid glycosides from the leaves of *P. scandens* in Vietnam as 1,3-dihydroxy-2,4-dimethoxy-9,10-anthraquinone, 2-hydroxy-1,4-dimethoxy-9,10-anthraquinone, 1-methoxy-2-methoxymethyl-3-hydroxy-9,10-anthraquinone, 1-hydroxy-2-hydroxymethyl-9,10-anthraquinone, paederoside, asperuloside, paederosidic acid, asperulosidic acid, and geniposide [8],[9]. This paper reports the isolation and structural elucidation of five known compounds from this plant, collected in Dong Nai province, Vietnam.

2. Experimental

2.1. Plant material

The rhizomes of *Paederia scandens* (Lour.) Merr. were collected in Dong Nai province,

Vietnam in March 2021 and botanically identified by MSc. Nguyen Van Hieu, Department of Botany, National Institute of Medicinal Materials (NIMM), Hanoi, Vietnam. A voucher specimen (ML-260321) was deposited at NIMM. After collection, the rhizomes were air-dried under the shade and dried at 45°C, then ground into fine powder.

2.2. General experimental procedures

^{1}H- and ^{13}C-NMR were measured in acetone-d_6, CD_3OD, $CDCl_3$, and DMSO-d_6 on a Bruker 500, 600 NMR spectrometer (500, 600 MHz for ^{1}H-NMR and 125, 150 MHz for ^{13}C-NMR). Chemical shifts were expressed in δ (ppm) with tetramethylsilane as an internal standard. Electrospray Ionization Mass Spectrometry (ESI-MS) spectra were recorded on Agilent 1200 series LC-MSD ion-trap spectrometer. *Silica gel* (Merck, Darmstadt, Germany), particle size 63-200 and 40-63 μm, were used for column chromatography. TLC was performed on precoated *silica gel* 60 F_{254} plates (Merck); spots were detected by UV radiation or by spraying with 10% aq. H_2SO_4 followed by heating or 5% $FeCl_3$/EtOH.

3. Extraction and isolation

Air-dried and pulverized rhizomes of *P. scandens* (7.0 kg) were extracted with 90% ethanol by maceration for four days. The extraction was repeated three times. The extracts were combined and evaporated at 50°C under low pressure to obtain an ethanol crude residue. The residue (330.53 g) was suspended in water and successively extracted with *n*-hexane, ethyl acetate, and *n*-butanol. Solvents were then evaporated *in vacuo* to obtain the corresponding *n*-hexane (91.86 g), ethyl acetate (93.57 g), and *n*-butanol extracts (71.43 g).

The ethyl acetate extract (50 g) was divided into fifteen fractions E1→E15 by a *silica gel* column chromatography (CC) eluting with gradient solvent of dichloromethane/methanol (100/1, 50/1, 9/1, 7/1, 5/1, 3/1, 1/1, v/v). Fraction E1 (1.15 g) was chromatographed on a *silica gel* CC and eluted with dichloromethane/acetone (100/1, 50/1, 20/1, 10/1, v/v) to give compound **1** (17 mg).

Fraction E2 (1.27 g) was decolorized by methanol and recrystallized in dichloromethane/acetone (1/1 to give compound **2** (15 mg). Fraction E3 (0.23 g) was removed the color by acetone to give compound **3** (11 mg). Fraction E4 (1.25 g) was washed-out by acetone to give two subfractions E4.1 and E4.2. Subfraction E4.1 was recrystallized in dichloromethane/methanol (1/1) solvent system to give compound **4** (15 mg). Subfraction E4.2 was subjected to a C-18 resin CC and eluted with MeOH/H_2O (7/3) to give compound **5** (17 mg). Fraction E8 (3.32 g) was separated over a *silica gel* CC and eluted with dichloromethane/methanol 5/1 to give compound **6** (15 mg). Fraction E9 (5.73 g) was submitted to a *silica gel* CC and eluted with gradient solvent of dichloromethane/methanol 20/1, 9/1, 7/1, 5/1 to give ten subfractions E9.1-E9.10. Subfraction E9.6 was decolorized by acetone and recrystallized in dichloromethane/methanol (1/1) to give compound **7** (50 mg). Fraction E10 (3.36 g) was separated over *silica gel* CC and eluted with ethyl acetate/methanol 3/1 to give compound **8** (33 mg). Fraction E12 (4.57 g) was decolorized by acetone to give compound **9** (45 mg).

Anthraquinone (1)

Pale-yellow amorphous powder, mp. 284-286 °C. ESI-MS *m/z*: 209 $[M+H]^+$. ^{1}H-NMR (600 MHz, $CDCl_3$), δ_H (ppm): 8.31 (4H, dd, J = 3.6; 6.0 Hz, H-1, H-4, H-5, H-8), 7.80 (4H, dd, J = 3.0; 5.4 Hz, H-2, H-3, H-6, H-7). ^{13}C-NMR (150 MHz, $CDCl_3$), δ_C (ppm): 183.2 (C-9, C-10), 134.1 (C-4a, C-8a, C-9a, C-10a), 133.6 (C-2, C-3, C-6, C-7), and 127.2 (C-1, C-4, C-5, C-8).

3,3′-Dimethoxyellagic acid 4′-*O*-α-L-rhamnopyranoside (2)

White amorphous powder, mp. 221-223 °C. ^{1}H-NMR (500 MHz, DMSO-d_6), δ_H (ppm): 7.42 (1H, s, H-5), 7.70 (1H, s, H-5'), 4.03 (3H, s, 3-OCH_3, 3′-OCH_3), 4.05 (3H, s, 3′-OCH_3); *α-rham*: 5.54 (1H, d, J = 1.0 Hz, H-1"), 3.97 (1H, br s, H-2"), 3.71 (1H, dd, J = 3.0; 9.0 Hz, H-3"), 3.36 (1H, m, H-4"), 3.52 (1H, m, H-5"), and 1.15 (1H, d, J = 6.0 Hz, H-6"). ^{13}C-NMR (125 MHz, DMSO-d_6), δ_C (ppm): 158.3 (C-7), 158.1 (C-7'), 152.8 (C-4), 150.3 (C-4'), 141.8 (C-3'), 141.4 (C-2'), 140.9 (C-2), 140.1 (C-3), 114.0 (C-1'), 112.4 (C-6'), 111.8 (C-6), 111.6 (C-5), 111.6 (C-5'), 110.8 (C-1), 60.9 (3-OCH_3), 61.5 (3'-OCH_3); *rham*: 99.9 (C-1"), 70.1 (C-2"), 75.0 (C-3"), 71.6 (C-4"), 70.3 (C-5"), and 17.9 (C-6'').

3′,4′,7-Trihydroxyflavanone (3)

Yellow amorphous powder. ^{1}H-NMR (500 MHz, CD_3OD), δ_H (ppm): 5.32 (1H, dd, J = 13.0; 3.0 Hz, H-2), 2.70 (1H, dd, J = 17.0; 3.0 Hz, H_a-3), 3.00 (1H, dd, J = 17.0; 13.0 Hz, H_b-3), 7.75 (1H, d, J = 9.0 Hz, H-5), 6.51 (1H, dd, J = 9.0; 2.0 Hz, H-6), 6.38 (1H, d, J = 2.0 Hz, H-8), 6.83 (1H, d, J = 2.0 Hz, H-2'), 6.95 (1H, d, J = 2.0 Hz, H-6'), and 6.83 (1H, dd, J = 2.0; 8.0 Hz, H-5'). ^{13}C-NMR (125 MHz, CD_3OD), δ_C (ppm): 81.0 (C-2), 44.9

(C-3), 193.5 (C-4), 114.9 (C-4a), 129.8 (C-5), 111.8 (C-6), 166.9 (C-7), 103.8 (C-8), 165.5 (C-8a), 132.0 (C-1'), 114.7 (C-2'), 146.8 (C-3'), 146.8 (C-4'), 116.3 (C-5'), and 119.2 (C-6').

Betulinic acid (4)

White crystal. mp. 316-318 °C. ^{1}H-NMR (600 MHz, $CDCl_3$), δ_H (ppm): 3.19 (1H, dd, J = 4.8; 12.0 Hz, H-3), 0.68 (1H, d, J = 9.6 Hz, H-5), 3.00 (1H, ddd, J = 7.2; 12.6 Hz, H-19), 0.98 (3H, s, H-23), 0.97 (3H, s, H-24), 0.82 (3H, s, H-25), 0.75 (3H, s, H-26), 1.03 (3H, s, H-27), 4.74 (1H, d, J = 1.8 Hz, H_a-29), 4.60 (1H, d, J = 1.8 Hz, H_b-29), 1.69 (3H, s, H-30). ^{13}C-NMR (150 MHz, $CDCl_3$), δ_C (ppm): 38.7 (C-1), 27.4 (C-2), 79.0 (C-3), 38.9 (C-4), 55.4 (C-5), 18.3 (C-6), 34.4 (C-7), 40.7 (C-8), 50.4 (C-9), 37.3 (C-10), 20.9 (C-11), 25.6 (C-12), 38.4 (C-13), 42.5 (C-14), 29.7 (C-15), 32.2 (C-16), 56.3 (C-17), 49.3 (C-18), 46.9 (C-19), 150.4 (C-20), 30.6 (C-21), 37.0 (C-22), 28.0 (C-23), 16.1 (C-24), 16.2 (C-25), 15.4 (C-26), 14.7 (C-27), 179.3 (C-28), 109.7 (C-29), 19.4 (C-30).

Kaempferol (5)

Yellow amorphous powder, mp. 276-278 °C. ^{1}H-NMR (500 MHz, CD_3OD), δ_H (ppm): 6.21 (1H, d, J = 1.5 Hz, H-6), 6.42 (1H, d, J = 1.5 Hz, H-8), 8.11 (2H, d, J = 9.0 Hz, H-2′, H-6′), 6.93 (2H, d, J = 9.0 Hz, H-3′, H-5′).

Linarin (6)

Pale yellow amorphous powder, mp. 258-260 °C. ^{1}H-NMR (500 MHz, DMSO-d_6), δ_H (ppm): 6.95 (1H, s, H-3), 6.46 (1H, d, J = 2.0 Hz, H-6), 6.80 (1H, d, J = 2.0 Hz, H-8), 8.05 (2H, d, J = 8.5 Hz, H-2', 6'), 7.17 (2H, d, J = 8.5 Hz, H-3', 5'), 3.87 (3H, s, 4'-OCH_3) ; *glc*: 5.07 (1H, d, J = 7.5 Hz, H-1"); *rham*: 4.56 (1H, m, H-1'"), 1.09 (3H, d, J = 6.0 Hz, H-6'"). ^{13}C-NMR (125 MHz, DMSO-d_6), δ_C (ppm): 164.5 (C-2), 104.3 (C-3), 182.5 (C-4), 161.6 (C-5), 100.4 (C-6), 163.4 (C-7), 95.3 (C-8), 157.5 (C-9), 105.9 (C-10), 123.2 (C-1'), 128.9 (C-2', 6'), 115.2 (C-3', 5'), 162.9 (C-4'), 56.1 (4'-OCH_3); *glc*: 100.4 (C-1"), 73. 6 (C-2"), 76.7 (C-3"), 70.1 (C-4"), 76.2 (C-5"), 66.6 (C-6"); *rham*: 101.0 (C-1'"), 70.8 (C-2'"), 71.2 (C-3'"), 72.5 (C-4'"), 68.8 (C-5'"), and 18.3 (C-6'").

Paederoside (7)

White solid, mp. 122-124°C. ^{1}H-NMR (600 MHz, CD_3OD): δ_H (ppm): 5.96 (1H, d, J = 1.8 Hz, H-1), 7.32 (1H, d, J = 2.4 Hz, H-3), 3.69 (1H, m, H-5), 5.58 (1H, br d, J = 6.6 Hz, H-6), 5.76 (1H, br s, H-7), 3.33 (1H, m, H-9), 4.92 (1H, dd, J = 14.4; 1.2 Hz, H_a-10), 4.86 (1H, d, J = 1.2 Hz, H_b-10), 4.70 (1H, d, J = 7.8 Hz, H-1′), 3.21 (1H, dd, J = 7.8; 9.0 Hz, H-2′), 3.41 (1H, t, J = 13.2 Hz, H-3′), 3.23 (1H, t, J = 7.8 Hz, H-4′), 3.37 (1H, m, H-5′), 3.94 (1H, dd, J = 11.4; 1.8 Hz, Ha-6′), 3.71 (1H, m, Hb-6′), 2.37 (3H, s, $COSCH_3$). ^{13}C NMR (150 MHz, CD_3OD): δ_C (ppm): 93.3 (C-1), 150.3 (C-3), 106.1 (C-4), 37.5 (C-5), 86.2 (C-6), 129.6 (C-7), 143.8 (C-8), 45.3 (C-9), 64.3 (C-10), 172.7 (C-11), 100.1 (C-1′), 74.7 (C-2′), 77.9 (C-3′), 71.6 (C-4′), 78.3 (C-5′), 62.8 (C-6′), 172.5 ($\underline{C}OSCH_3$), 13.6 ($COS\underline{C}H_3$).

Quercetin3-*O*-*α*-L-rhamnosyl-(1→6)-*β*-D-glucopyranosyl-(1→3)-*β*-D-glucopyranoside (8)

Yellow amorphous powder, mp. 191-193°C. ESI-MS *m/z*: 795,2 $[M+Na]^+$, $C_{33}H_{40}O_{21}$. ^{1}H-NMR (500 MHz, CD_3OD), δ_H (ppm): 6.23 (1H, d, J = 2.0 Hz, H-6), 6.41 (1H, d, J = 2.0 Hz, H-8), 7.68 (1H, d, J = 2.0 Hz, H-2'), 6.95 (1H, d, J = 8.5 Hz, H-5'), 7.56 (1H, dd, J = 8.5; 2.0 Hz, H-6'); *glc-1:* 5.30 (1H, d, J = 7.5 Hz, H-1"), 3.33 (1H, m, H-2"), 3.77 (1H, s, H-3"), 3.44 (1H, m, H-4"), 3.42 (1H, m, H-5"), 3.83 (1H, dd, J = 1.5; 2.0 Hz, Hb-6'"), 3.74 (1H, dd, J = 11.5; 5.0 Hz, Ha-6'"); *glc-2:* 4.78 (1H, d, J = 7.5 Hz, H-1'"), 3.42 (1H, m, H-2'"), 3.35 (1H, m, H-3'"), 3.33 (1H, m, H-4'"), 3.60 (1H, m, H-5'"), 3.37 (1H, s, Ha-6''), 3.80 (1H, m, Hb-6''); *α-rham*: 4.51(1H, d, J = 1.0 Hz, H-1''''), 3.50 (1H, dd, J = 9.5; 3.5 Hz, H-2''''), 3.60 (1H, m, H-3''''), 3.27 (1H, t, J = 9.5 Hz, H-4''''), 3.45 (1H, m, H-5''''), 1.11 (3H, d, J = 6.5 Hz, H-6''''). ^{13}C-NMR (125 MHz, CD_3OD), δ_C (ppm): 158.5 (C-2), 134.9 (C-3), 179.6 (C-4), 163.1 (C-5), 99.9 (C-6), 165.9 (C-7), 94.9 (C-8), 159.2 (C-9), 105.7 (C-10), 123.23 (C-1'), 116.2 (C-2'), 145.9 (C-3'), 149.8 (C-4'), 117.7 (C-5'), 123.17 (C-6'); *glc-1*: 101.2 (C-1"), 76.99 (C-2"), 82.6 (C-3"), 71.1 (C-4"), 77.9 (C-5"), 62.4 (C-6"), *glc-2*: 104.8 (C-1'"), 75.5 (C-2'"), 78.2 (C-3'"), 71.3 (C-4'"), 77.9 (C-5'"), 68.1 (C-6'"); *rham*: 102.2 (C-1''''), 72.3 (C-2''''), 72.1 (C-3''''), 73.9 (C-4''''), 69.7 (C-5''''), and 17.8 (C-6'''').

Kaempferol 3-*O*-*β*-D-galactopyranoside (9

^{1}H-NMR (600 MHz, CD_3OD), δ_H (ppm): 6.23 (1H, d, J = 2.4 Hz, H-6), 6.43 (1H, d, J = 2.4 Hz, H-8), 8.10 (2H, d, J = 9.0 Hz, H-2′, H-6′), 6.91 (2H, d, J = 9.0 Hz, H-3′, H-5′); *glc*: 5.15 (1H, d, J = 7.8 Hz, H-1″), 3.80 (1H, t, J = 7.8 Hz, H-2″), 3,54 (1H, m, H-3″), 3.84 (1H, d, J = 3.0 Hz, H-4″), 3.45 (1H, td, J = 0.6; 6.0 Hz, H-5″), 3.64 (1H, dd, J = 6.0; 11.4 Hz, H_a-6″), 3.55 (1H, dd, J = 7.8; 11.4 Hz, H_b-6″). ^{13}C-NMR (150 MHz, CD_3OD), δ_C (ppm): 158.5 (C-2), 135.6 (C-3), 179.7 (C-4), 163.0 (C-5), 100.0 (C-6), 166.2 (C-7), 94.8 (C-8), 159.1 (C-9), 105.7 (C-10), 122.7 (C-1′), 132.4 (C-2′, C-6′), 116.1 (C-3′, C-5′), 161.6 (C-4′); *gal*: 105.2 (C-1″), 73.0 (C-2″), 75.0 (C-3″), 70.0 (C-4″), 77.1 (C-5″), and 62.0 (C-6″).

3. Result and discussion

Compounds **1- 9** were known compounds, their NMR spectral data were in consistent with those reported [10-16, 18] and the structures were determined as anthraquinone (**1**) [10], 3,3′-dimethoxyellagic acid 4′-*O*-α-L-rhamnopyranoside (**2**) [11], betulinic acid (**4**) [12], kaempferol (**5**) [13], paederoside (**7**) [14], and kaempferol 3-*O*-*β*-D-galactopyranoside (**9**) [15].

An examination of its NMR data and a comparison with the literature [16] suggested that compound **3** was a flavanone. Thus, its ^{1}H-NMR spectrum revealed characteristic resonances of aromatic protons such as δ_H 7.75 (1H, d, J = 9.0 Hz, H-5), 6.51 (1H, dd, J = 9.0; 2.0 Hz, H-6), 6.38 (1H, d, J = 2.0 Hz, H-8) (A ring) and 6.83 (1H, d, J = 2.0 Hz, H-2'), 6.83 (1H, dd, J = 2.0; 8.0 Hz, H-5'), 6.95 (1H, d, J = 2.0 Hz, H-6') (B ring). The weak coupling constants of H-6 and H-8 were in agreement with the existence of the hydroxyl group at C-7 (δ_C 166.9). The presence of signals at δ_H 5.32 (1H, dd, J = 13.0, 3.0 Hz, H-2), 2.70 (1H, dd, J = 17.0, 3.0 Hz, H-3a), 3.00 (1H, dd, J = 17.0, 13.0 Hz, H-3b) in the ^{1}H-NMR spectrum was structural characterization of a flavanone. The chemical shift values of **3** were similar to those of 3′,4′,7-trihydroxyflavanone [17].

Compound **6** was isolated as a pale yellow amorphous powder. Analysis of NMR spectra suggested a flavonoid skeleton for compound **6**. The ^{1}H-NMR spectrum indicated a 5,7-dihydroxylated pattern for A ring (two *meta*-coupled doublets at δ_H 6.46 (1H, d, J = 2.0 Hz, H-6), and 6.80 (1H, d, J = 2.0 Hz, H-8) and a 4′-methoxylation pattern for B ring with resonance signals at δ_H 8.05 (2H, d, J = 8.5 Hz, H-2', 6'), 7.17 (2H, d, J = 8.5 Hz, H-3', 5'), 3.87 (3H, s, H-4'-OCH_3) allowing the aglycon to be recognized as acacetin [18].The ^{1}H-NMR spectrum of **6** also showed signals ascribable to sugar moieties. Two anomeric protons arising from the sugar moieties appeared at δ_H 5.07 (1H, d, J = 7.5 Hz, H-1") and 4.56 (1H, m, H-1'") which correlated respectively with signals at δ_C 100.4 (C-1") and 101.0 (C-1'") ppm in the HSQC spectrum. All the ^{1}H- and ^{13}C-NMR signals of **6** were assigned using HSQC and HMBC experiments. Complete assignments of proton and carbon chemical shifts of the sugar portion, based on chemical shifts and spin-spin coupling constants of the proton anomers allowed the identification of the sugar moieties as *β*-D-glucopyranosyl and *α*-L-rhamnopyranosyl units [19]. Unequivocal information could be obtained by 2D-NMR spectra; the HMBC experiment indicated correlations between δ_H 4.56 (H-1'") and δ_C 66.6 (C-6"), δ_H 5.07 (H-1") and δ_C 163.4 (C-7). Thus, the structure of **6** was determined as acacetin-7-*O*-*β*-D-rutinoside (linarin). The NMR spectral data were inconsistent with those reported [20].

Compound **8** was obtained as a yellow amorphous powder, mp. 191-193°C. The structure of compound **8** was established by EI-MS, 1D, and 2D-NMR spectra. This compound was assigned the molecular formula $C_{33}H_{40}O_{21}$ from the *positive* ESI-MS spectrum showing a $[M+Na]^+$ peak at *m/z* 795.2. The ^{1}H- and ^{13}C-NMR spectra showed the characteristic signals of a flavone 3-*O*-triglycoside. Quercetin (3,5,7,3',4'-pentahydroxyflavone) aglycone was indicated by two *meta*-coupled signals at δ_H 6.23 (1H, d, J = 2.0 Hz, H-6) and 6.41 (1H, d, J = 2.0 Hz, H-8) for the A ring and an ABX pattern system for the B ring: δ_H 7.68 (1H, d, J = 2.0 Hz, H-2'), 6.95 (1H, d, J = 8.5 Hz, H-5'), 7.56 (1H, dd, J = 8.5; 2.0 Hz, H-6').The structure of the triglycoside was determined by analysis of ^{1}H-, ^{13}C-NMR, and HMBC spectra. One rhamnosyl moiety was indicated by the anomeric proton at δ_H 4.51 (1H, d, J = 1.0 Hz, H-1'''), the anomeric carbon at δ_C 102.2 (C-1'''), and a methyl group at δ_C 17.8. The presence of two D-glucosyl moieties was apparent from two anomeric protons at δ_H 4.78 (1H, d, J = 7.5 Hz, H-1'") and 5.30 (1H, d, J = 7.5 Hz, H-1") and the corresponding carbon signals at δ_C 104.8 (C-1'") and 101.2 (C-1"). The two glucosyl moieties were deduced to be both *β*-config.d from the J values of the anomeric protons (J = 7.5 Hz) [21]. The rhamnosyl moiety was linked to the terminal of the outer glucosyl moiety from the significantly downfield shifted signal of C-6'" (δ_C 68.1) and HMBC correlations between H-1'" and C-6'". The glucosyl moiety substituted by the rhamnosyl moiety was attached to the hydroxyl group at C-3" of the inner glucosyl moiety, according to the downfield shifted signal of C-3" at δ_C 82.6 and HMBC correlations between H-1'" and C-3". Linkage of the inner glucosyl moiety to C-3 of the aglycone was determined from the C-3 signal at δ_C 134.9, which was significantly upfield shifted signal compared with the aglycone [22]. Furthermore, the correlation between H-1" (δ_H 5.30) and C-3 (δ_C 134.9) was observed in the HMBC spectrum (see Fig. 1). Thus, the structure of compound **8** was established as quercetin 3-*O*-*α*-L-rhamnopyranosyl-(1→ 6)-*β*-D-glucopyranosyl-(1→ 3)-*β*-D-glucopyranoside [23].

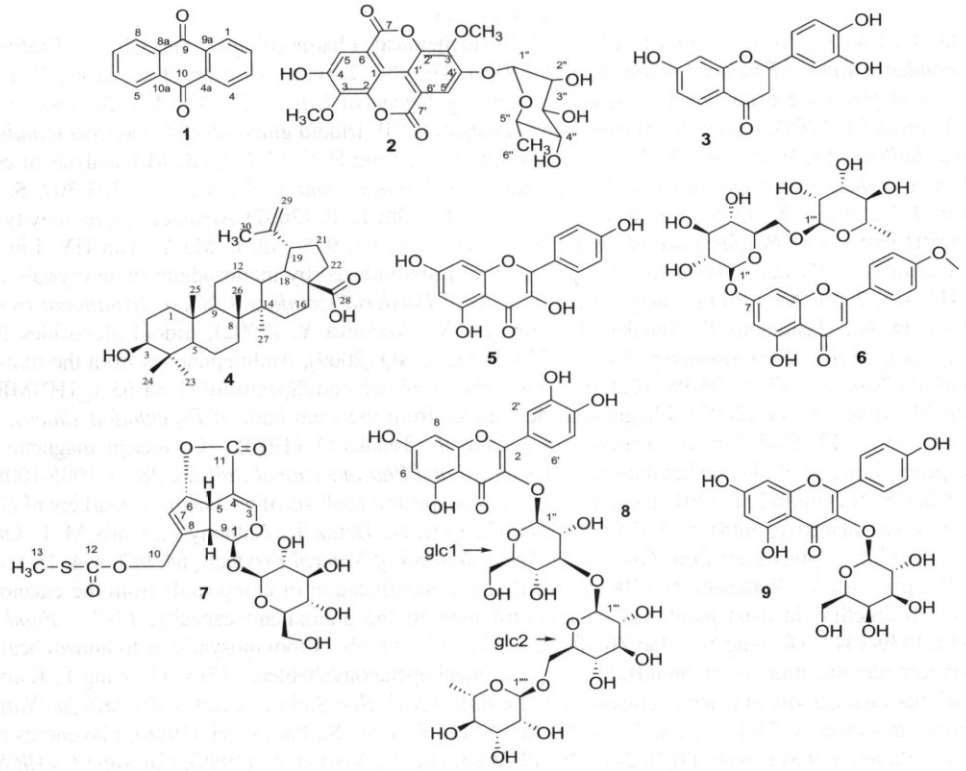

Fig. 1. Structure of compounds **1-8** from the ethyl acetate extract of *P. scandens*

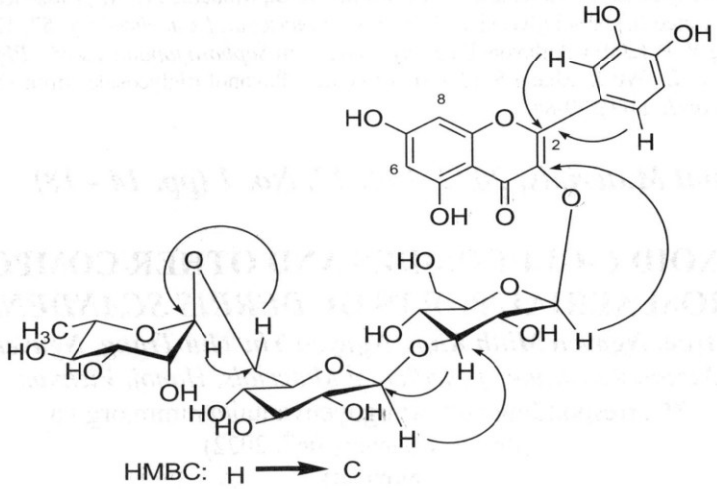

Fig. 2. HMBC correlation of compound **8**

4. Conclusion

Nine compounds were isolated from the rhizomes of *P. scandens* collected at Dong Nai, Vietnam. Their chemical structures were identified as anthraquinone (**1**), 3,3′-dimethoxyellagic acid 4′-*O*-*α*-L-rhamnopyranoside (**2**), 3′,4′,7-trihydroxyflavanone (**3**), betulinic acid (**4**), kaempferol (**5**), linarin (**6**), paederoside (**7**), quercetin3-*O*-*α*-L-rhamnosyl-(1→6)-*β*-D-glucopyranosyl-(1→3)-*β*-D-glucopyranoside (**8**), kaempferol 3-*O*-*β*-D-galactopyranoside (**9**) on the basis of 1D-, 2D-NMR spectral analysis and in comparison with the published NMR data. Of these, compounds **1**, **2**, **3**, **6**, **8** were isolated from this plant for the first time.

Acknowledgement: *This work was supported by National institute of Medicinal Materials under 2021 Scientific Research Fund for "Studying of chemical compositions in Paederia scandens". We are grateful to the Center for Applied Spectroscopy Methods-Institute of Chemistry-Vietnam Academy of Science and Technology for spectroscopic measurements.*

References

1. Wang L., Jiang Y., Han T., Zheng C., Qin L. (2014), A Phytochemical, Pharmacological and Clinical Profile of *Paederia foetida* and *P. scandens*, *Natural Product Communications*, 9 (6), 879-886. **2**. He D. H., Chen J. S., Wang X. L., Ding K. Y. (2010), A new iridoid glycoside from *Paederia scandens*, *Chinese Chemical Letters*, 21, 437-439. **3**. Inouye H, Inouye S, Shimokawa N, Okigawa M (1969), Studies on monoterpene glucosides. VII. Iridoid glucosides of *Paederia scandens*, *Chemical & Pharmaceutical Bulletin*, 17, 1942-1948. **4**. Yin G. H., Wang M. Y., Zeng H. C. (2009), GC-MS analysis of essential oil of leaves in *Paederia scandens* with supercritical CO_2 extraction, *Food Science and Technology*, 34, 303-307. **5**. Chen Y. F., Zhang H., Zhang Q. Y., Wu J. Z., Li N., Rahman K., Zheng H. C., Qin L. P. (2007) Antinociceptive activity of *n*-butanol fraction from MeOH extracts of *Paederia scandens* in mice, *Pharmazie*, 62, 943-948. **6**. Ma Y, Yan HY, Liu M, Zhou LL (2008), Effect of extracts of *Paederia scandens* on acute gouty arthritis induced by monosodium urate crystals in rats, *China Pharmacy*, 19, 411-414. **7**. Yu XY (2011), Chemical constituents of *Paederia scandens*, *Chinese Traditional Herb Drugs*, 42, 661-663. **8**. Quang D. N., Hashimoto T., Tanaka M., Dung N. X., Asakawa Y. (2002), Iridoid glucosides from roots of Vietnamese *Paederia scandens*, *Phytochemistry*, 60, 505-514. **9**. Dang NQ (2009), Anthraquinones from the roots of *Paederia scandens*, *Journal of Chemistry*, 47 (1), 95-98. **10**. https://www.chemicalbook.com/SpectrumEN_84-65-1_1HNMR.htm. **11**. Ye G., Peng H., Fan M., Huang C. G. (2007), Ellagic acid derivatives from the stem bark of *Dipentodon sinicus*, *Chemistry of Natural Compound*, 43, 2. **12**. Sholichin M., Yamasaki K., Kasai R., Tanaka O. (1980), ^{13}C Nuclear magnetic resonance of lupane-type triterpenes, lupeol, betulin and betulinic acid, *Chemical and Pharmaceutical Bulletin,* 28(3), 1006-1008. **13**. José G. N., David C. L., Chen S. N., Guido F. P. (2012), Complete ^{1}H NMR spectral analysis of ten chemical markers of *Ginkgo biloba*, *Magnetic Resonance in Chemistry*, 50(8), 569-575. **14**. Ihsan C., Jo¨rg H., Deniz T., Anthony L., Chris M. I., Otto S. (2001), Flavonoid, iridoid, and lignan glycosides from *Putoria calabrica*, *Journal of Natural Products*, 64, 961-964. **15**.Yang Z., Tu Y., Baldermann S., Dong F., Xu Y., Watanabe N. (2009), Isolation and identification of compounds from the ethanolic extract of flowers of the tea (Camellia sinensis) plant and their contribution to the antioxidant capacity, *LWT - Food Science and Technology*, 42(8), 1439-1443. **16**. Feng W., Hao Zh., Li M. (2017), Flavonoids - From biosynthesis to human health, chapter 2: Isolation and structure identification of flavonoids, https://www.intechopen.com/chapters/54713. **17**. Yang J., Kwon Y. S., Kim M. J. (2018), Antimicrobial activity and active compounds of a *Rhus verniciflua* Stokes extract, *Zeitschrift fur Naturforschung - Section C Journal of Biosciences*, 73(11-12), 457-463. **18**. Lee Y. H., Won W. S., Park C. H. (1988), Flavonoids of *Elscholtzia cristata, Archives of Pharmacal Research,* 11(3), 247-249. **19**. Breitmaier E., Voelter W. (1986), *Carbon-13 NMR Spectroscopy*, 3rd, Wiley-VCH, NewYork, 379-397. **20**. Zhang W. K., Xu J. K., Zhang L., Du G. H. (2012), Flavonoids from the bran of *Avena sativa*, *Chinese Journal of Natural Medicines*, 54. **21**. Kamel M. S., Mohamed K. M., Hassanean H. A., Ohtani K., Kasai R., Yamasaki K. (2001), Acylated flavonoid glycosides from *Bassia muricata*, *Phytochemistry*, 57, 1259-1262. **22**. Wang J. H., Lou F. C., Wang Y. L., Tang Y. P. (2003), A flavonol tetraglycoside from *Sophora japonica* seeds, *Phytochemistry*, 63, 463-465. **23**. Xu L. R., Zhou P., Zhi Y. E., Wu J., Zhang S. (2009), Three new flavonol triglycosides from *Derris trifoliate*, *Journal of Asian Natural Products Research*, 11(1), 79-84.

Journal of Medicinal Materials, 2022, Vol. 27, No. 1 (pp. 14 - 18)

FLAVONOID *C*-GLUCOSIDES AND OTHER COMPOUNDS FROM AERIAL PARTS OF *DERRIS SCANDENS*

Phung Nhu Hoa, Nguyen Minh Khoi, Nguyen Thi Thu Trang, Nguyen Van Tai*

National Institute of Medicinal Materials, Hanoi, Vietnam

*Corresponding author: nguyenvantai@nimm.org.vn

(Received January 06th, 2022)

Summary

Flavonoid *C*-glucosides and Other Compounds from Aerial Parts of *Derris scandens*

Six compounds were isolated and characterized from aerial parts of *Derris scandens*. Their structures were elucidated by spectroscopic techniques as heneicosan-1-ol (**1**), lupenone (**2**), behenic acid (**3**), rutin (**4**), 6-*C*-glucopyranosylquercertin (**5**), and 8-*C*-glucopyranosylquercertin (**6**). Except for rutin, other compounds were reported for the first time in the genus *Derris*.

Keywords: *Derris scandens, 6-C-glucopyranosylquercertin, 8-C-glucopyranosylquercertin, rutin.*

1. Introduction

Derris scandens (Roxb.) Benth. (Family Leguminosae) is distributed in Southeast Asia and Australia [1]. In India and Thailand, the stem was widely used in traditional medicine as an anti-tussive, diuretic, expectorant, anti-dysentery agent and for treatment of muscle pains, cough, and diarrhea [1],[2]. The powder and hydroalcoholic extract of *D. scandens* stem were recorded in the National List of Essential Medicines of Thailand for the treatment of muscle pain, low back pain, and knee osteoarthritis. *D. scandens* may be considered as an alternative for musculoskeletal pain reduction because of efficaciousness and safety [2]. Previous studies indicated the presence of coumarins, flavones, isoflavones, and their glycosides… as chemical constituents from *D. scandens* [1],[3]. To the best of our knowledge, there is no report on the chemical constituents