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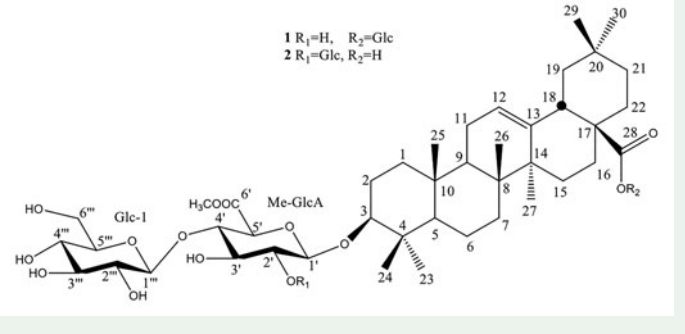
Polysciosides J and K, two new oleanane-type triterpenoid saponins from the leaves of *Polyscias fruticosa* (L.) harms. cultivating in An Giang Province, Viet Nam

Van Mai Do[a,b], Cong Luan Tran[a] and Tan Phat Nguyen[c,d]

[a]Nursery and Pharmaceutical Faculty, Tay Do University, Can Tho City, Viet Nam; [b]Faculty of Pharmacy, University of Medicine and Pharmacy, Ho Chi Minh City, Viet Nam; [c]Graduate University of Science and Technology Vietnam Academy of Science and Technology, Hanoi, Viet Nam; [d]Institute of Chemical Technology, Vietnam Academy of Science and Technology, Ho Chi Minh City, Viet Nam

ABSTRACT

For the first time, the phytochemical constituents of the leaves of *Polyscias fruticosa* (L.) Harms. cultivating in An Giang Province, Viet Nam were investigated and led to purify two new oleanane-type triterpenoid saponins, named polyscioside J (**1**) and polyscioside K (**2**) together with two known saponins, ladyginoside A (**3**) and chikusetsusaponin IVa (**4**) using variously chromatographic methods. Saponin (**4**) was reported for the first time from this species. Their structures were verified by IR, UV, HR-ESI-MS, NMR 1D and 2D experiments and compared with previous literatures.



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1. Introduction

Polyscias is the second largest genus in the family Araliaceae, with 159 species and is distributed from tropical Africa to the islands of the eastern Pacific Ocean (Bean 2015), which 7 species and 1 variety are found in Vietnam (La et al. 2013). *Polyscias fruticosa*

CONTACT Tan Phat Nguyen ntphat@ict.vast.vn

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has been used traditionally in Vietnam for the treatment of ischemia, inflammation and increase blood in the brain (Do 2004; Vo 2012). Pharmacological investigation of extracts from *P. fruticosa* possessed anti-asthmatic, anti-inflammatory (Bernard et al. 1998; Koffuor et al. 2014, 2016); anti-histaminic, mast cell stabilization effect (Koffuor et al. 2016); anti-pyretic, anagesic, molluscicidal properties (Bernard et al. 1998), diuretic effect (Varadharajan and Rajalingam, 2011), anti-diabetic activity (Divakar and Bensita, 1998; Hanh et al. 2016). Phytochemical study of *P. fruticosa* illustrated triterpenoid saponins (Chaboud et al. 1995; Proliac et al. 1996; Hanh et al. 2016), and polyacetylens (Lutomski et al. 1992) as the main ingredients. Moreover, steroids (Tram et al. 2017) and sesquiterpenoids (Brophy et al. 1990) were reported. Continuing a study of the bioactive triterpenoids (Nguyen et al. 2015, 2016; Ngo et al. 2017, 2018), this paper concentrates the isolation and structural elucidation of two new oleanane-type triterpenoid saponins (**1, 2**) and two known saponins from the leaves of *P. fruticosa* cultivating in An Giang Province, Viet Nam.

2. Results and discussion

The *n*-butanol extract from the leaves of *P. fruticosa* cultivating in An Giang Province, Viet Nam was subjected to column chromatography over silica gel normal-phase and reversed-phase RP-18 to give two new oleanane-type triterpenoid saponins, polyscioside J (**1**) (3-*O*-[β-D-glucopyranosyl-(1→4)]-β-D-(6-*O*-methyl)glucuronopyranosyl oleanolic acid 28-*O*-β-D-glucopyranosyl ester) and polyscioside K (**2**) (3-*O*-[β-D-glucopyranosyl-(1→4), β-D-glucopyranosyl-(1→2)]-β-D-(6-*O*-methyl)glucuronopyranosyl oleanolic acid) together with two known saponins, ladyginoside A (3-*O*-[β-D-glucopyranosyl-(1→4)]-β-D-glucuronopyranosyl oleanolic acid) (**3**) (Huan et al. 1998) and chikusetsusaponin IVa (3-*O*-β-*D*-glucuronopyranosyl oleanolic acid 28-*O*-β-D-glucopyranosyl ester) (**4**) (Nguyen et al. 2015) (Figure 1).

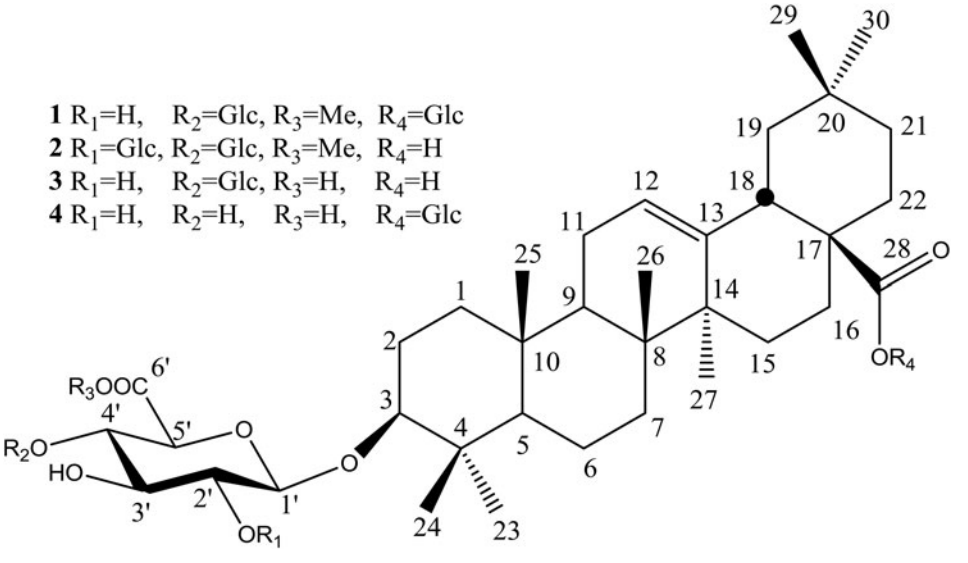

Figure 1. Chemical structures of compounds **1**–**4**.

Compound (**1**) was obtained as a white amorphous powder. The molecular formula was established as $C_{49}H_{78}O_{19}$ by HR-ESI-MS data ($[M-H]^-$ *m/z* 969.5011, calcd. 969.5059). The IR spectrum of **1** showed absorptions of hydroxyl group (3316 cm^{-1}) and the C–O stretching (1023 cm^{-1}). The ^{13}C-NMR and DEPT spectrum of **1** (Table S1) showed forty-nine carbons including: two carbonyl carbons, two olefinic carbons, three anomeric carbons, thirteen oxygenated methine carbons, two oxygenated methylene carbons, one oxygenated methyl carbon, six quaternary carbons, three methine carbons, ten methylene carbons, seven methyl carbons. The presences of seven tertiary methyl groups at δ_C 15.5–33.1, one oxygenated methine carbon at δ_C 89.3 (C-3) corresponding to proton at δ_H 3.28 (*dd*, 4.0 and 11.5, H-3), two olefinic carbons at δ_C 144.5 (C-13) and 122.0 (C-12) corresponding to proton at δ_H 5.40 (*brs*, H-12), and one carbonyl carbon at δ_C 176.5 (C-28) were confirmed a bidesmosidic saponin of oleanolic acid in ^{13}C and ^{1}H-NMR (Nguyen et al. 2015, 2016; Ghislain et al. 2018). Moreover, the ^{13}C and ^{1}H-NMR of **1** revealed three anomeric carbons at δ_C 106.8 (C-1′), 105.0 (C-1″) and 95.7 (C-1‴) corresponded to three anomeric protons at δ_H 4.94 (*d*, 8.0, H-1′), 4.96 (overlap, H-1″) and 6.28 (*d*, 8.0, H-1‴), respectively; one carbonyl carbon at δ_C 170.0 (C-6′), one oxygenated methyl carbon at δ_C 52.4 (-OMe); two oxygenated methylene carbons at δ_C 62.5 (C-6″) and 62.2 (C-6‴) were assigned to methyl β-D-glucuronate (Me-GlcA), β-D-glucose (Glc-1) and β-D-glucose (Glc-2), respectively (Nguyen et al. 2015, 2016). Moreover, acidic hydrolysis and TLC comparision of the hydrolysate with authentic sugar verified sugar moiety as D-glucose (*Rf* 0.40). The HMBC spectrum of **1** (Figure S1) showed correlations between oxygenated methyl protons at δ_H 3.85 (*s*) and carbon carbonyl of glucuronic unit at δ_C 170.0, which identified a methyl β-D-glucuronate moiety (Me-GlcA). On the orther hands, three anomeric protons at δ_H 4.94 (H-1′) of Me-GlcA, 4.96 (H-1″) of Glc-1 and 6.28 (H-1‴) of Glc-2 corresponded to carbons at δ_C 89.3 (C-3) of aglycone, 82.7 (C-4′) of Me-GlcA and 176.5 (C-28) of aglycone, respectively. Based on data of HR-ESI-MS, 1D, 2D-NMR and compared with previous published data (Huan et al. 1998); the structure of **1** was evidenced as 3-*O*-[β-D-glucopyranosyl-(1→4)]-β-D-(6-*O*-methyl)glucuronopyranosyl oleanolic acid 28-*O*-β-D-glucopyranosyl ester, named Polyscioside J.

Compound (**2**) was obtained as a white amorphous powder. The molecular formula was established as $C_{49}H_{78}O_{19}$ by HR-ESI-MS data ($[M-H]^-$ *m/z* 969.5013, calcd. 969.5059). The ^{1}H and ^{13}C-NMR data (Table S1) demonstrated that **2** has the same aglycone and sugar moieties as **1**, except for the down field shift of carbon due to C-2′ of Me-GlcA (δ_C 80.2), indicating one β-D-glucose moiety (Glc-2) linked at this carbon. Further, the HMBC spectrum of **2** (Figure S1) showed correlations between three anomeric protons at δ_H 4.88 (*d*, 7.5, H-1′) of Me-GlcA, 4.90 (*d*, 8.0, H-1″) of Glc-1, 5.37 (*d*, 7.5, H-1‴) of Glc-2 and carbons at δ_C 89.5 (C-3) of aglycone, 81.7 (C-4′) of Me-GlcA, 80.2 (C-2′) of Me-GlcA, respectively. Thus, the structure of **2** was recognized as 3-*O*-[β-D-glucopyranosyl-(1→4), β-D-glucopyranosyl-(1→2)]-β-D-(6-*O*-methyl)glucuronopyranosyl oleanolic acid, named Polyscioside K.

The genus *Polyscias* were acknowledged as a rich source of triterpenoid saponins which revealed mainly oleanane-type aglycones. Oleanolic acid framework was described from *P. scutellaria* (Paphassarang et al. 1988; 1989a, 1989b, 1990; Mitaine-Offer et al. 2004). Whereas, hederagenin genin was reported from *P. dichroostachya*

(Gopalsamy et al. 1990) and *P. scutellaria* (Mitaine-Offer et al. 2004). Moreover, some rare skeletones, such as echinocystic acid and collinsogenin were detailed from *P. scutellaria* (Mitaine-Offer et al. 2004), 12-oxo-3β,16β,20(S)-trihydroxydammar-24-ene was illustrated from *P. fulva* (Bedir et al. 2001). In our study, four oleanane-type triterpenoid saponins were indicated as well as the previous investigations (Chaboud et al. 1995, 1996; Proliac et al. 1996; Huan et al. 1998; Hanh et al. 2016). However, it is the first time that the methyl glucuronate saponins were characterized from the species *P. fruticosa*.

3. Experimental

3.1. General experimental procedures

The optical rotations were determined on a Krüss-optronic GmbH polarimeter equipped with a sodium lamp (589 nm) (Hamburg, Germany). The IR spectra were recorded with a Bruker Tensor 27 FT-IR Spectrometer (Bremen, Germany). The UV spectra were performed with Agilent 1260 HPLC-UV (*Waldbronn*, *Germany)*. The high resolution electrospray ionisation mass spectroscopy (HR-ESI-MS) was recorded on a LC-X500R QTOF spectrometer (Sciex, USA). The ^{1}H-NMR (500 MHz), ^{13}C-NMR (125 MHz), DEPT, COSY, HSQC and HMBC spectra were recorded on a Bruker AM500 FT-NMR spectrometer using tetramethylsilane (TMS) as internal standard (MA, USA). Column chromatography was carried out using Merck Silica gel normal-phase (230–240 mesh) and reversed-phase C_{18} Merck (Darmstadt, Germany). Analytical TLC was carried out in silica gel plates Merck DC-Alufolien 60 F_{254} (Darmstadt, Germany). Compounds were visualized by spraying with aqueous 10% H_2SO_4 and heating for 3–5 min. Camptothecin was purchased from Calbiochem.

3.2. Plant material

The leaves of *Polyscias fruticosa* were cultivated in An Giang Province, Viet Nam and identified by Prof. Dr. C.L. Tran, Nursing Pharmaceutical Sciences, Tay Do University. A voucher specimen (No. Mai-PF-2016) was deposited in Nursing Pharmaceutical Sciences, Tay Do University.

3.3 Extraction and isolation

Dried powder of leaves *P. fruticosa* (859 g) were extracted with 96° EtOH for three time (3 × 10 L) at room temperature, residue was filtered, solvents were removed under low pressure and the crude extract was obtained. The crude extract (156 g) was applied to liquid-liquid extraction procedures and successively partitioned into diethyl ether, ethyl acetate, *n*-butanol and aqueous partition. The *n*-butanol extract (50 g) was eluted by Diaion HP-20 column with H_2O, 50% MeOH, 80% MeOH, 100% MeOH and 100% Me_2CO to give five major fractions (I–V), respectively. Fraction III (11 g) was subjected to silica gel normal-phase column chromatography with mobile phase $CHCl_3$–MeOH gradient (0–100%) to get five subfractions (III.1–III.5).

Fraction III.1 (3,0 g) was classified on silica gel column chromatography with eluted solvent $CHCl_3$–MeOH–H_2O (95:5:0 → 80:20:1, v/v) and reseparated by RP-18 using mixtures of MeOH–H_2O (60:40, v/v) to obtain **3** (13 mg) and **4** (10 mg). Fraction III.2 (2,5 g) was chromatographed on silica gel normal-phase with solvent $CHCl_3$–MeOH–H_2O (90:10:0 → 80:20:1, v/v) and further purified by RP-18 using mixtures of MeOH–H_2O (50:50, v/v) to afford **1** (12 mg). Fraction III.3 (2,0 g) was fractioned on silica gel column with solvent $CHCl_3$–MeOH–H_2O (88:12:0 → 75:25:2, v/v) and segregated by RP-18 using mixtures of MeOH–H_2O (50:50, v/v) to yield **2** (15 mg).

Polyscioside J (1): Amorphous powder (MeOH); IR (KBr) υ_{max}: 3316, 2943, 2831, 1449, 1416, 1023 cm^{-1}; UV (MeOH) λ_{max}: 207 nm; HR-ESI-MS m/z 969.5011 $[M-H]^-$ (calcd for $C_{49}H_{78}O_{19}$, 969.5059); ^1H and ^{13}C-NMR data (pyridine-d_5), see Table S1.

Polyscioside K (2): Amorphous powder (MeOH); IR (KBr) υ_{max}: 3262, 2942, 2915, 2831, 1022 cm^{-1}; UV (MeOH) λ_{max}: 204 nm; HR-ESI-MS *m/z* 969.5013 $[M-H]^-$ (calcd for $C_{49}H_{78}O_{19}$, 969.5059); ^1H and ^{13}C-NMR data (pyridine-d_5), see Table S1.

3.4. Acid hydrolysis

Two new saponins **1, 2** (2 mg) was refluxed with 2N aq. CH_3COOH (5 mL) for 2 h at 100 °C. After extraction with $CHCl_3$ (3x5 mL), the aqueous layer was repeatedly evaporated to dryness with MeOH until neutral, and then analyzed by TLC over silica gel (MeCOEt–isoPrOH–Me_2CO–H_2O 20:10:7:6) by comparison with authentic sugar of D-glucose *Rf* 0.40 according to Nguyen et al. (2015, 2016, 2017a, 2017b).

Disclosure statement

No potential conflict of interest was reported by the author(s).

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