FULL PAPER

Periplocain A, a New Naphthalene Derivative from *Periploca aphylla* Growing in Saudi Arabia

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Periplocain A (**2**), a new naphthalene derivative together with four known compounds: 2-ethylhexyl benzoate (**1**), quercetin-3-*O*-α-L-rhamnopyranoside (**3**), quercetin-3-*O*-β-D-glucopyranoside (**4**), and quercetin-3-(6-*O*-α-L-rhamnopyranosyl-β-D-glucopyranoside) (**5**) were isolated from the AcOEt fraction of the aerial parts of *Periploca aphylla* (Asclepiadaceae). Their structures were established by multiple spectroscopic methods in addition to HR-ESI-MS and by comparison with literature data.

Keywords: *Periploca aphylla*, Quercetin, Asclepiadaceae, Periplocain A, Naphthalene derivatives.

Introduction

The genus *Periploca* (family Asclepiadaceae) includes about 12 species. In Saudi Arabia, *P. somaliensis*, *P. aphylla*, *P. brevicoronata*, and *P. visciformis* are the most common species [1]. *Periploca aphylla* Dcne (suwwas) is an erect milky branched shrub, widely distributed in Najd and South Hijaz regions of Saudi Arabia [2]. It is used for treatment of urticaria, cerebral fever, tumors, and swellings [3 – 5]. The decoction of its bark is used against fever and constipation [6]. It possesses wide range of biological activities as cytotoxic, antioxidant [7], antibacterial [8][9], antiprotozoal, hepatoprotective [10], phytotoxic [11], α-glucosidase inhibitory [12], antidiarrheal, and laxative [1]. Earlier investigations of *P. aphylla* resulted in the isolation of norterpenoids, triterpenes, sterols [12 – 14], bisflavan-3-ols, xanthone, and lignans [13]. This study reports the isolation and structural elucidation of a new naphthalene derivative, periplocain A (**2**), along with four known compounds. Their structures were assigned by extensive spectroscopic methods as well as by comparison with the literature (*Fig. 1*).

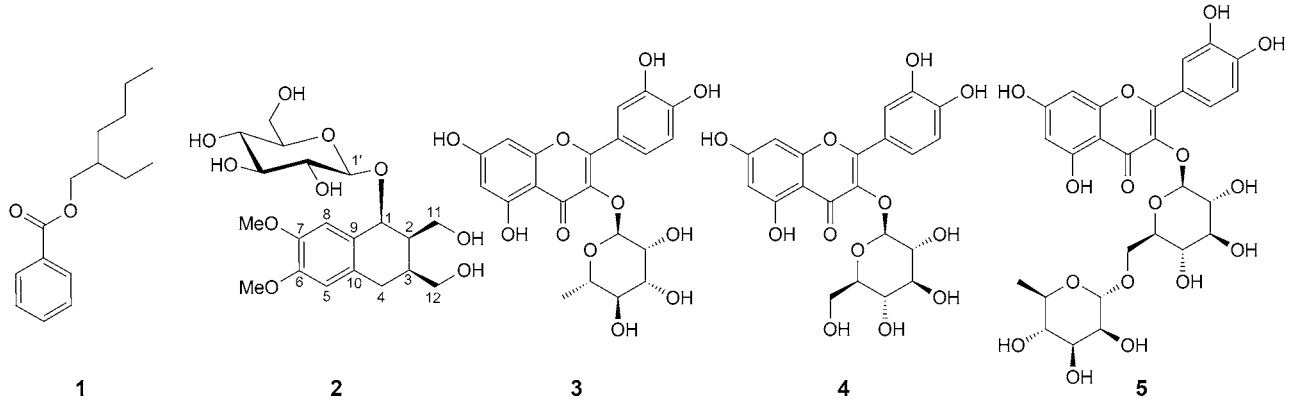

Fig. 1. Structure of isolated compounds **1** – **5**.

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Results and Discussion

Compound **2** was obtained as a white amorphous powder. Its molecular formula was deduced as $C_{20}H_{30}O_{10}$ by HR-ESI-MS pseudomolecular ion peak at *m/z* 431.1915 $[M+H]^+$ (calcd for $C_{20}H_{31}O_{10}$, 431.1917). It had UV absorptions at 242 and 281 nm. The IR spectrum showed absorptions for OH group (3415 cm^{-1}) and aromatic C–H (1595 and 1515 cm^{-1}) [15]. The ^{13}C-, DEPT-, and HSQC-NMR spectra of **2** (*Table*) revealed the presence of 20 C-atom signals representing two Me groups, four CH_2 groups, 10 CH groups, and four non-protonated C-atoms (aromatic ring 6,7,9,10-tetrasubstituted). Inspection of the ^{13}C-NMR and HSQC spectroscopic data for **2** allowed all H-atoms to be assigned to their respective C-atoms. The ^1H-NMR spectrum showed two aromatic H-atoms *singlet*s at δ(H) 6.52 H–C(5)and 6.55 H–C(8), an O-bearing CH group at δ(H) 4.66 (*d*, *J* = 5.5, H–C(1)), δ(H) 4.66 (*d*, *J* = 5.5, H–C(1)), two CH groups δ(H) 2.23 (*ddd*, *J* = 7.1, 6.5, 5.5, 3.4, H–C(2)) and 2.62 – 2.66 (*m*, H–C(3)), and a CH_2 group at δ(H) 2.87 (*dd, J* = 13.0, 5.3, H–C(4α)) and 2.46 (*dd*, *J* = 13.0, 3.9, H–C(4β)), correlated with the C-atom signals at δ(C) 106.7, 103.1, 81.9, 52.4, 41.6, and 32.8, respectively, in the HSQC spectrum indicating that **2** was 1,2,3,4-tetrahydronaphthalen-1-ol derivative. This was established by the observed $^1H,^1H$-COSY cross peaks and further confirmed by the HMBCs of H–C(1) to C(8), H–C(2) to C(3) and C(9), H–C(3) to C(1) and C(10), H–C(4) to C(5) and C(9), H–C(5) to C(4), C(6), and C(10), and H–C(8) to C(1), C(7), C(9), and C(10) (*Fig. 2*). Moreover, resonances for two MeO groups at δ(H) 3.75 (*s,* 6 H, 6, 7-MeO) were observed in the ^1H-NMR spectrum. They correlated with the C-atom signals at δ(C) 56.3 (6-MeO) and 55.9 (7-MeO) in the HSQC spectrum. Their connectivities at C(6) and C(7) were established by their HMBC cross peaks to the C-atoms at δ(C) 152.5 C (6) and 147.7 C(7). In addition, two oxymethylene groups at δ(H) 3.70 (*dd*, *J* = 11.9, 6.5, H_α–C(11)), 3.50 (*dd*, *J* = 11.9, 3.4, H_β–C(11)), 3.92 (*dd*, *J* = 12.3, 6.7, H_α–C(12)), and 3.60 (*dd*, *J* = 12.3, 2.8, H_β–C(12)), correlating with the C-atoms at δ(C) 58.6 C(11) and 71.8 C(12) in HSQC spectrum were observed. The $^1H,^1H$-COSY correlations of H–C(1) to H–C(11) and H–C(3) to H–C(12) and the HMBC cross peaks of H–C(1) to C(11), H–C(2) and H–C(3) to C(12), and H–C(11) to C(1), C(2), and C(3), and H–C(12) to C(2) and C(4) indicated the attachment of the O-bearing CH_2 groups at C(2) and C(3) of 1,2,3,4-tetrahydronaphthalen-1-ol moiety. Furthermore, an anomeric H-atom signal at δ(H) 4.85 (*d*, *J* = 7.5, 1 H, H–C(1′)) with a coupling constant characteristic of a β-configuration and additional sugar H-atoms at δ(H) 3.68 – 3.20 characteristic for a β-glucopyranose moiety were observed in ^1H-NMR spectrum. This was confirmed by the fragment ion peak at 268 $[M - Glu]^+$ in the ESI-MS spectrum. In the HMBC, the cross peaks of H–C(1′) to (C(1) (δ(C) 81.9) and H–C(1) to C(1′) established the attachment of the glucose moiety at C(1). The small *J* values of H–C(1) with H–C(2) and H–C(3) indicated α-orientation of these H-atoms. Furthermore, it was confirmed by the observed NOESY cross peaks of H–C(1) with H–C(2) and H–C(3). On the basis of the above evidences, the structure of **2** was unambiguously elucidated as depicted and named periplocain A.

Table. NMR spectral data of compound **2** ((D_6)DMSO, 700 and 176 MHz)

Position	δ(H) (mult., *J* [Hz])[a]	δ(C) (mult.)[a]	HMBC
1	4.66 (*d*, *J* = 5.5)	81.9 CH	1′, 8, 11
2	2.23 (*dddd*, *J* = 7.1, 6.5, 5.5, 3.4)	52.4 CH	3, 9, 12
3	2.62 – 2.66 (*m*)	41.6 CH	1, 4, 10, 12
4	2.87 (*dd*, *J* = 13.0, 5.3)	32.8 CH_2	5, 9, 12
	2.46 (*dd*, *J* = 13.0, 3.9)		
5	6.52 (*s*)	106.7 CH	4, 6, 10
6	–	152.5 C	–
7	–	147.7 C	–
8	6.55 (*s*)	103.1 CH	1, 7, 9, 10
9	–	133.7 C	–
10	–	136.1 C	–
11	3.70 (*dd*, *J* = 11.9, 6.5)	58.6 CH_2	1, 2, 3
	3.50 (*dd*, *J* = 11.9, 3.4)		
12	3.92 (*dd*, *J* = 12.3, 6.7)	71.8 CH_2	2, 4
	3.60 (*dd*, *J* = 12.3, 2.8)		
1′	4.85 (*d*, *J* = 7.5)	102.8 CH	1
2′	3.18 – 3.22 (*m*)	74.2 CH	
3′	3.25 – 3.28 (*m*)	76.4 CH	
4′	3.12 – 3.17 (*m*)	69.9 CH	
5′	3.02 – 3.05 (*m*)	77.1 CH	
6′	3.65 – 3.69 (*m*)	60.9 CH_2	
	3.45 – 3.48 (*m*)		
6-MeO	3.75 (*s*)	56.3 CH_3	6
7-MeO	3.75 (*s*)	55.9 CH_3	7
2′-OH	4.98 (br. *s*)	–	
3′, 4′-OH	4.92 (br. *s*)	–	
6′-OH	4.31 (*t*, *J* = 4.8)	6′	–
11-OH	4.74 (*t*, *J* = 3.9)	–	–

[a]) The assignments were based on $^1H,^1H$-COSY, HSQC, and HMBC experiments.

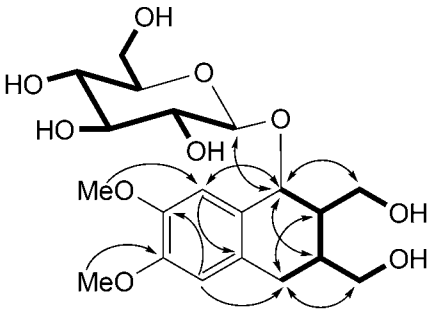

Fig. 2. Some Key $^1H,^1H$ COSY (—) and HMBC (H → C) correlations of **2**.

The known compounds were identified as 2-ethylhexyl benzoate (**1**) [16 – 18], quercetin-3-*O*-α-L-rhamnopyranoside (**3**) [19], quercetin-3-*O*-β-D-glucopyranoside (**4**) [20], and quercetin-3-(6-*O*-α-L-rhamnopyranosyl-β-D-glucopyranoside) (**5**) [19] by comparing their NMR spectral and physical data with the literature.

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Experimental Part

General

Vacuum liquid chromatography (VLC): silica gel *60* (SiO_2; 0.04 – 0.063 mm; 500 g; *Merck*, Darmstadt, Germany). Column chromatographic separations were performed on silica gel *60* (0.04 – 0.063 mm, *Merck*) and on *Sephadex LH-20* (*Merck*, Darmstadt, Germany). TLC analyses were conducted on precoated silica gel F_{254} aluminum sheets (*Merck*). Compounds were detected by spraying the sheets with *p*-anisaldehyde/H_2SO_4 reagent followed by heating at 110 °C for 1 – 2 min. Optical rotations: *PerkinElmer* Model *341 LC* polarimeter (*PerkinElmer*, Waltham, MA, USA). IR Spectra: *Shimadzu Infrared-400* spectrophotometer (*Shimadzu*, Kyoto, Japan). UV Spectra: in MeOH using a *PerkinElmer Lambda 25* UV/VIS spectrophotometer (*PerkinElmer*). ^{1}H- and ^{13}C-NMR spectra: *Bruker DRX 700* spectrometers (*Bruker*, Rheinstetten, Germany). ESI-MS: *Finnigan MAT TSQ-7000* triple stage quadrupole mass spectrometer (*ThermoFinnigan*, Bremen, Germany). HR-ESI-MS: *LTQ Orbitrap* mass spectrometer (*Thermo Fisher*, Waltham, MA, USA).

Plant Material

The aerial parts of *Periploca aphylla* were collected in March 2008 from Oyoun village located near Al-Baha, Saudi Arabia. The plant was identified by Dr. *Mohamed Yousef*, Prof. of Pharmacognosy, College of Pharmacy, King Saud University, Saudi Arabia. A voucher specimen (Pa-3-2008) was deposited at the herbarium of the Department.

Extraction and Isolation

The air-dried powdered aerial parts (1 kg) were extracted with MeOH (2 × 3 l, each) using *Soxhlet* apparatus (Cat. No: 80068-156, *Chemglass*) for 8 h at r.t. The combined extracts were concentrated under reduced pressure to afford a dark green residue (18.0 g) which was suspended in dist. H_2O (250 ml) then partitioned between hexane (3 × 500 ml), AcOEt (3 × 500 ml), and BuOH (3 × 500 ml), successively. Each fraction was concentrated to give hexane (2.3 g), AcOEt (4.9 g), BuOH (2.1 g), and aqueous (7.8 g). The AcOEt fraction (4.9 g) was subjected to VLC using $CHCl_3$/MeOH gradient, to afford six subfractions: *PE-1* to *PE-6*. Subfraction *PE-1* (0.61 g) was chromatographed over SiO_2 column (100 g × 50 × 2 cm) using hexane/AcOEt gradients to give **1** (10.3 mg, colorless oil). Subfraction *PE-2* (0.53 g) was similarly treated as subfraction *PE-1* to give **2** (4.1 mg, white amorphous powder). SiO_2 CC of subfraction *PE-4* (0.51 g; 100 g × 50 × 2 cm) using $CHCl_3$/MeOH gradients yielded **3** (11.8 mg, yellow amorphous powder) and **4** (9.6 mg, yellow amorphous powder). Subfraction *PE-5* (0.81 g) was chromatographed over *Sephadex LH-20* column (100 g × 50 × 3 cm) using MeOH as an eluent to give two subfractions: *PE-5A* (175 mg) and *PE-5B* (320 mg). Subfraction *PE-5B* was subjected to RP_{18} column (100 g × 50 × 2 cm) using MeOH/H_2O gradient to afford **5** (16 mg, yellow amorphous powder).

Periplocain A (= **(1*S*,2*R*,3*S*)-1,2,3,4-Tetrahydro-2,3-bis(hydroxymethyl)-6,7-dimethoxy-1-naphthalenyl *β*-D-Glucopyranoside**; **2**). White amorphous powder. $[\alpha]_D = -76.6$ (c = 0.5, MeOH). UV (MeOH): 242 (3.14), 276 (2.34). IR (KBr): 3415, 2978, 1595, 1515. NMR ((D$_6$)DMSO, 700 and 176 MHz): see *Table*. HR-ESI-MS: 431.1915 ($[M+H]^+$, $C_{20}H_{31}O_{10}^+$; calc. 431.1917).

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