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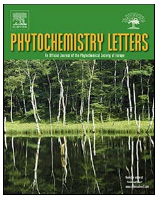

Short communication

A new lignan and a new terpenoid from *Achillea millefolium* L

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ABSTRACT

A phytochemical investigation from methanol extract of *Achillea millefolium*, (Asteraceae) resulted in the isolation of one new lignan, (+)-lyoniresinol 4-*O*-α-L −arabinofuranoside (**1**) and one new terpenoid, achiterpenoside A (**2**), together with four other known compounds, named as Achillinin A (**3**), (+)-lyoniresinol (**4**), luteolin (**5**), camazulene (**6**). The structures of **1** and **2** were elucidated based on various spectroscopic data, including IR, HR-EI-MS, ^{1}H NMR, ^{13}C NMR, DEPT, COSY, HMBC and HSQC, and compared with previous literature.

1. Introduction

The genus *Achillea* (family Asteraceae) comprises over 130 species, which were distributed across the world, from Europe to Asia (Si et al., 2006). *Achillea millefolium* L., one of the most widespread species, was used as folk medicine for a long time (Radusiene and Gudaityte, 2005), such as spasmolytic, antiinflammatory, analgesic, antidiabetic, cholagogue, antitumor, haemostatic, antioxidant. Previous studies have revealed that *Achillea millefolium* contains numerous natural compounds, like essential oils, sesquiterpenes, phenolic compounds etc (Karamenderes and Apaydin, 2003; Stojanovic et al., 2005; Cavalcanti et al., 2006; Si et al., 2006; Tajik et al., 2008; Lazarevic et al., 2010; Fierascu et al., 2015).

In this study, two new isolates (**1** and **2**), together with four known compounds were isolated from the methanol extract of *Achillea millefolium*. Various spectrometric analyses, including 2D NMR and HR-ESI–MS spectra, were used to characterize the structure of the compounds. Literature was used to analyze the known compounds.

2. Results and discussion

Compound **1** was obtained as a brown powder, $[\alpha]_D^{24}$ + 18.1 (c 0.32, MeOH), and its molecular formula was determined as $C_{27}H_{36}O_{12}$ by positive HR-ESI–MS (*m/z* 575.2121 $[M + Na]^+$, calcd for 575.2105). The IR spectrum revealed the absorptions for hydroxyl group (3463 cm^{-1}), benzene ring (1614 cm^{-1}、1573 cm^{-1}), and carbonyl group (1664 cm^{-1}). The ^{1}H NMR spectrum (Table 1) of **1** exhibited signals characteristic for four methoxyl groups at δ_H 3.71 (3H, s), 3.37 (3H, s), and 3.61 (6H, s). In addition, one single aromatic proton at δ_H 6.54 (1H, s), suggested that compound **1** possessed a 1, 2, 3, 4, 5-pentasubstituted benzene ring. A total 27 carbon signals were observed in the ^{13}C NMR spectrum (Table 1), in which six carbons (δ_C 107.5, 75.1, 69.5, 73.4, 62.1) suggested the presence of a L–arabinofuranosyl, which was confirmed by TLC and GC analysis, and the rest 21 carbons were assigned to the aglycone. Comparison of the ^{1}H and ^{13}C NMR spectroscopic data of **1** (Table 1) with those of (+)-lyoniresinol (Tanaka et al., 2001) allowed the identification of the aglycone of **1** as (+)-lyoniresinol. Furthermore, the configuration of the aglycone of **1** was confirmed by the key NOESY correlations of H-9′/H-7′, and H-9′/H-8. In the HSQC spectrum (Fig. 2), the anomeric protons at δ_H 4.66 (br s, H″-1) showed correlations with the signal at δ_C 107.5, which suggested the anomeric carbon signal at δ_C 107.5. In addition, the α configuration of the anomeric center was deduced by the singlet resonance at 4.66, br s (Idaka et al., 1991; Wen et al., 2015). The linkage points of the sugar units to each other and to C-4 of the aglycone were established from the HMBC correlations. The arabinose was connected to C-4 via an oxygen bond, as evidence by the HMBC (Fig. 2) correlations from H-1″ (δ_H 4.66, br s) to C-4 (δ_C 137.6). Based on the above information, the structure of compound **1** was elucidated as (+)-lyoniresinol 4-*O*-α-L–arabinofuranoside (Fig. 1).

Compound **2** was obtained as a colorless oil. Its molecular formula was established as $C_{25}H_{36}O_5$ by HRESIMS (*m/z* 417.2634 $[M + H]^+$, calcd for 417.2563), corresponding to 8 ° of unsaturation. The IR spectrum indicated the presence of hydroxyl (3427 cm^{-1}) and double bond (1616 and 1519 cm^{-1}) groups, whereas ^{13}C NMR and DEPT spectra displayed 25 carbon signals including two carbonyl, six quaternary carbons (two sp^2 and four aliphatic), four methine (one olefinic, one oxygenated, and two aliphatic), and nine methylene (one olefinic,

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Table 1
^{1}H (600 MHz) and^{13}C (150 MHz) NMR spectroscopic data of compound **1** in CD_3OD.

Position	δ_H (*J* Hz)	δ_C	HMBC (H-C)
1		134.3	
2		125.3	
3		151.6	
4		137.6	
5		151.5	
6	6.54, 1H, s	107.5	
7a	2.91, 1H, m	32.6	C-1, C-2, C-8, C-8′, C-9
7b	2.63, 1H, m		
8	1.83, 1H, m	40.4	C-1, C-7, C-7′, C-9
9a	3.47, 1H, m	64.4	C-7, C-8, C-8′
9b	3.37, 1H, m		
1′		133.3	
2′/6′	7.18, 2H, d, 1.8	106.1	C-1′, C-3′, C-4′, C-5′
3′		147.6	
4′		136.1	
5′		150.9	
7′	4.53, 1H, d, 4.5	40.1	C-1′, C-2, C-8′, C-1, C-8, C-9′
8′	2.42, 1H, m	45.8	C-2, C-7, C-7′, C-8, C-9′
9′a	4.21, 1H, m	69.5	C-7′, C-8, C-8′
9′b	4.52, 1H, m		
3-OCH_3	3.71, 3H, s	59.8	C-3
5-OCH_3	3.37, 3H, s	56.1	C-6
3′/5′-OCH_3	3.61, 6H, s	56.1	C-3′, C-5′
1″	4.66, 1H, br s	107.5	C-2″, C-3″, C-4
2″	3.36, 1H, m	75.1	C-1″, C-3″
3″	3.18, 1H, m	69.5	C-2″, C-5″
4″	3.52, 1H, m	73.4	C-3″, C-5″
5″a	3.70, 1H, m	62.1	C-3″, C-4″
5″b	3.24, 1H, m		

and eight aliphatic), four methyl groups. One aliphatic quaternary carbon (δ_C 75.9) was ascribed to that attached to oxygen atom.

The ^{1}H NMR spectrum of **2** showed signals for four methyl groups at δ_H 1.14 (3H, s, CH_3-7′), 1.13 (3H, s, CH_3-8′), 0.86 (3H, d, $J = 6.6$ Hz, CH_3-16), and 0.92 (3H, d, $J = 6.6$ Hz, CH_3-17), and one ABX system at δ_H 2.08 (1H, dd, $J = 9.6$, 15.0 Hz, H-4′β), 1.54 (1H, dd, $J = 1.8$, 15.0 Hz, H-4′α), and 3.28 (1H, d, $J = 1.8$, 9.6 Hz, H-5′). Both the methyl signals (CH_3-7′ and CH_3-8′) showed three-bond correlations with C-5′ in the HMBC spectrum; therefore, the dimethylcarbinol group was bonded to C-5′ and gave rise to a 2, 3-dihydroxy-3-methylbutyl group as a C_5 unit (C4′-C8′). Moreover, in the HMBC spectrum, long-range correlations of H_2-4′/C-1 (C=O), H_2-4′/C-6, H_2-4′/C-5, and H-5′/C-6 indicated that the 2,3-dihydroxy-3-methylbutyl group was linked to C-6. The ^{13}C NMR spectrum showed two carbonyl groups at δ_C 192.5 (C-4), and 201.8 (C-1), and four olefinic carbon atoms at δ_C 123.2 (C-2), 156.5 (C-3), 132.6 (C-2′), and 119.6 (C-3′). Additionally, the NMR spectroscopic data indicated the presence of one allyl group (C-1′-C-3′), which was confirmed by the correlations from H-2′ to C-1′ and C-3′ via HMBC analysis. In the HMBC spectrum Fig. 2 of **2**, long-range correlations from H-14 to C-9 and C-11, and from H-10 to C-13 and C-12 confirmed that **2** possessed a cyclohexane ring (C-9-C-14), and HMBC correlations from H-16 and H-17 to C-12 suggested that the isopropyl group was connected to C-12. In addition, the correlations from H-15 to C-11 , C-13 and C-14 confirmed that C-12 was connected to C-13, which formed a cyclopropane (C-12-C-14).

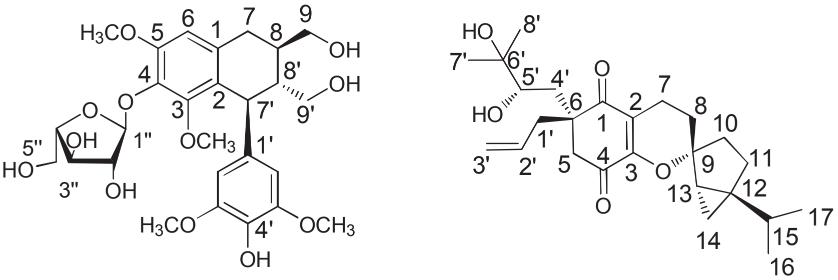
The correlations from H_2-7 to C-1, C-2, and C-3, from H_2-5 to C-1, C-3, C-4, and C-6 indicated the presence of cyclohex-2-ene-1,4-dione (C6 unit, C1-C6) in **2**, and HMBC correlations from H-1′ to C-6 and from H-2′ to C-6 confirmed that the allyl group (C-1′–C-3′) was located at C-6. In the ^{1}H-^{1}H COSY spectrum, correlations between δ 1.75 (2H, m, H-8) and 2.38 (2H, t, $J = 6.6$ Hz, H-7) indicated the presence of C(7)- H_2-C(8)- H_2 in **2**. In conjunction with HMBC spectrum, correlations from H-7 to C-2, C-9, and C-3, from H-8 to C-9 and C-2 confirmed involvement of a C_5 unit in a 2*H*-pyran ring. NOESY correlations (Fig. 3) were observed between H-4′β, H-5 and H-1′; between H-1′ and H-8, between H-8 and H-13; and between H-13 and H-15. Thus, the structure of compound **2** was elucidated as achiterpenoside A Fig. 1.

Four known compounds were also isolated; achillinin A (**3**) (Li et al., 2011), (+)-lyoniresinol (**4**) (Assoumatine et al., 2004), luteolin (**5**) (Csupor-Löffler et al., 2009), camazulene (**6**) (Zahara et al., 2014). The structures of these compounds were determined through spectral analysis and comparison of data with those reported in the literature.

3. Methods

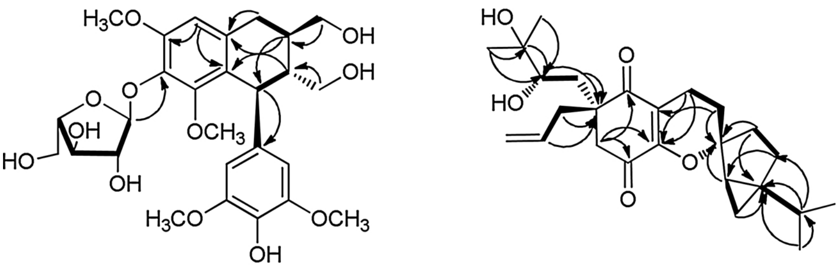
3.1. General experimental procedures

Optical rotations were measured on a PerkinElmer polarimeter. IR spectra were measured on FTIR 6700 Infrared spectrometer with KBr pellets. The ^{1}H NMR (600 MHz), ^{13}C NMR (150 MHz) and 2D NMR



1   **2**

Fig. 1. Compounds **1-2** isolated from *A. millefolium*.



1   **2**

Fig. 2. ^{1}H-^{1}H COSY () and key HMBC (HC) correlations of compound **1** and compound **2**.