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A New Coumarin from *Ferula persica*

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Abstract

From the roots of *Ferula persica* Willd., four known coumarins (farnesiferol A, B, badrakemone, gummosin) and a new coumarin, farnesiferone A, have been isolated. From the aerial parts, badrakemone, farnesiferone A, and farnesiferol A were also isolated. Their structures were elucidated by spectroscopic methods.

Keywords: Aerial parts, coumarins, farnesiferol, farnesiferone A, *Ferula persica*, roots, umbelliferae.

Introduction

Members of the genus *Ferula* are widespread throughout central Asia, especially in Iran. The roots of *F. persica* Willd. var. *Persica* Chamberlain (Apiaceae) have been used in folk medicine to treat diabetes (Afifi & Abu-Irmaileh, 2000). The chemistry of *F. persica* has previously been studied. Coumarins (Bagirov et al., 1977; Iranshahi et al., 2003b), flavonoids (Stetskov et al., 1980), sulfur-containing compounds (Iranshahi et al., 2003a), and a germacrane-type sesquiterpene (Iranshahi et al., 2003b) have been isolated from the plant. The roots of *Ferula* species contain large amounts of sesquiterpene coumarin ethers.

In this study, we report the isolation and structural elucidation of a new coumarin, **1** (Fig. 1), which was isolated for the first time from this plant, in addition to four coumarins (**2**–**5**) that were previously reported (Pinar & Rodriguez, 1977; Nabiev et al., 1982; Appendino et al., 1992; Buckingham et al., 1994).

Materials and Methods

Melting points were taken on a Reichert-Jung apparatus (Vienna, Austria). Ultraviolet spectra were recorded on a Shimadzu 160A spectrometer (Kyoto, Japan). Electron Iomization Mass Spectra (EIMS) were determined on a Finnigan TSQ-MAT 70 (California, USA) at 70 eV. ^{1}H NMR and ^{13}C NMR spectra were measured in $CDCl_3$ with tetramethysilane (TMS) as an internal standard using a Varian 400 Unity *plus* spectrometer. Fourier-transform infrared (FTIR) spectra were recorded on a Nicolet 550 spectrometer (Madison, WI, USA). Optical rotation was measured on a Perkin Elmer 241 polarimeter (Buckinghamshire, UK). Column chromatography (CC) was conducted with silica gel (Kieselgel 60, 60–100 mesh ASTM; Merck, Darnstalt, Germany) and thin-layer chromatography (TLC) with Merck silica gel 60 F_{254} on glass plates.

The plant material was collected in May 2002 from north of Tehran. The plant was identified by the Department of Pharmacognosy, Faculty of Pharmacy, Tehran University of Medical Sciences (TEH). A voucher specimen (no. 6523) has been deposited at the Herbarium of the Faculty of Pharmacy.

Dried powdered roots (300 g) of the plant were extracted with chloroform (9 l) by maceration for 72 h. The solvent was evaporated, and the residue (14.25 g) was chromatographed on PLC (petroleum ether/EtOAc, 2 : 1) and gave 5 coumarin fractions (R_{f1} = 0.71, R_{f2} = 0.5, R_{f3} = 0.43, R_{f4} = 0.37, R_{f5} = 0.25).

The first fraction was previously reported as umbelliprenin (37 mg) (Iranshahi et al., 2003b). R_{f2} and R_{f3} were identified as compounds **1** (184 mg) and **2** (147 mg), respectively. R_{f4} was further purified by Preparative Layer Chromatography (PLC) (petroleum ether/EtOAc, 1 : 1) to yield compound **5** (R_f = 0.43, 369 mg). R_{f5} was also further purified by PLC (petroleum ether/EtOAc, 5 : 2) to give two fractions [R_f = 0.25, R_f = 0.21 for compounds **4** (25 mg) and **3** (300 mg), respectively].

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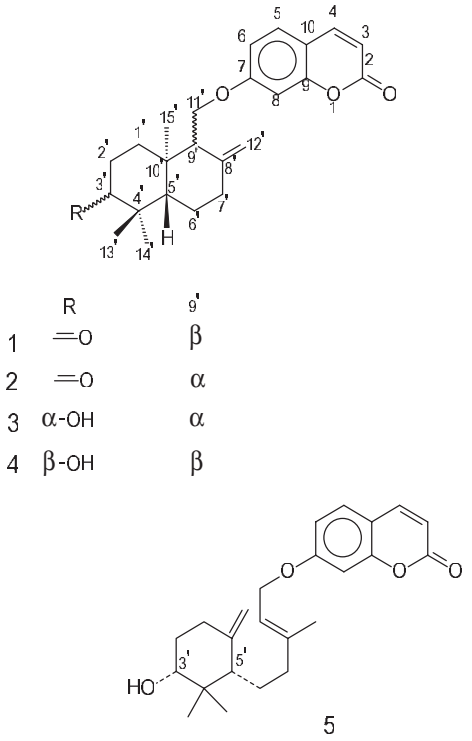

Figure 1. The structures of compounds **1**–**5**.

Table 1. ^{1}H NMR data obtained with compound **1** (400 MHz, $CDCl_3$, δ values).

Protons	Compound **1** (*J*)	Compound **2** (*J*)
H-3	6.23*d* (9.6)	6.24*d* (9.6)
H-4	7.61*d* (9.6)	7.62*d* (9.6)
H-5	7.34*d* (8)	7.35*d* (8.8)
H-6	6.79*d* (8)	6.83*dd* (8.8, 2.8)
H-8	6.77*s*	6.81*d* (2.8)
H-1′	1.69*bd* (15)	1.71*ddd*[a]
	1.92*ddd* (15, 15, 4)	1.82*ddd* (12.4, 12.4, 5)
H-2′	2.37*ddd*[a]	2.42*ddd* (15, 6, 3)
	2.76*ddd* (15, 15, 5.6)	2.69*ddd* (15, 12.4, 6)
H-5′	1.78*dd* (12, 1.6)	1.67*dd*[a] (12, 1.6)
H-6′	1.57*m*	1.58*m*
H-7′	2.1*m*	2.11*m*
	2.4*m*[a]	2.5*m*
H-9′	2.37*t*[a]	2.3*t* (6)
H-11′	4.0*dd* (9.6, 5.6)	4.23*d* (6)
	4.27*dd* (9.6, 5.6)	
H-12′	4.81*s*	4.6*s*
	4.89*s*	4.98*s*
H-13′,14′,15′	1.05*s*, 1.14*s*, 1.2*s*	1.04*s*, 1.06*s*, 1.12*s*

[a] Overlapped by the other signals.

In addition, dried aerial parts (350 g) of the plant were extracted with chloroform (5 l) by maceration for 6 days. The extract was concentrated under reduced pressure to leave a residue (10.68 g), which was chromatographed on a silica gel column (66 × 5 cm). Elution was started by petroleum ether-acetone (95 : 5) and increasing slightly the polarity with acetone. The fractions were compared by TLC (silica gel using petroleum ether/EtOAc as solvent), and those giving similar coumarin spots were combined and further purified on PLC to give compounds **1** (5 mg), **2** (4 mg), and **3** (23 mg).

Results

From the roots of *F. persica* Willd. var. *persica* Chamberlain, a new sesquiterpene coumarin, farnesiferone A (**1**) in addition to known coumarines badrakemone (**2**) (Appendino et al., 1992), farnesiferol A (**3**), (Pinar & Rodriguez, 1977), gummosin (**4**) (Buckingham et al., 1994), and farnesiferol B (**5**) (Nabiev et al., 1982; Buckingham et al., 1994) were isolated. From the aerial parts, farnesiferone A, farnesiferol A, and badrakemone were also isolated. The results obtained for compound **1** follow.

Farnesiferone A (**1**): White crystals, m.p. 126–128 °C (ethanol-water); $[\alpha]^{25}_D$: –4 ° ($CHCl_3$, c 0.43); UV (CH_3OH): λ_{max} = 322, 251, 224 nm; IR ν_{max} (film) cm^{-1}: 3015, 2921, 2825, 1706, 1609, 1460, 1236, 1122, 759; EIMS: *m/z* (%) = 380 (M^+, 68), 219 (70), 201 (38), 177 (42), 163 (100), 162

Table 2. ^{13}C NMR data obtained with compounds **1** and **2** (100.45 MHz, $CDCl_3$, δ values).

Carbons	Compound **1**	Compound **2**
C-2	161.7*s*	161.8*s*
C-3	113.2*d*	113.0*d*
C-4	143.2*d*	143.2*d*
C-5	128.7*d*	128.6*d*
C-6	112.9*d*	112.9*d*
C-7	161.0*s*	160.9*s*
C-8	101.6*d*	101.2*d*
C-9	155.8*s*	155.8*s*
C-10	112.6*s*	112.5*s*
C-1′	35.5*t*	37.5*t*
C-2′	32.1*t*	34.4*t*
C-3′	215.5*s*	215.6*s*
C-4′	47.8*s*	47.7*s*
C-5′	47.7*d*	54.0*d*
C-6′	23.9*t*	24.4*t*
C-7′	35.0*t*	37.0*t*
C-8′	146.1*s*	145.8*s*
C-9′	56.1*d*	55.0*d*
C-10′	37.4*s*	38.6*s*
C-11′	68.0*t*	65.6*t*
C-12′	112.1*t*	108.4*t*
C-13′	25.8*q*	25.8*q*
C-14′	21.1*q*	21.7*q*
C-15′	22.3*q*	14.6*q*

(90), 133 (20); ^{1}H NMR and ^{13}C NMR are shown in Tables 1 and 2.

Discussion

The structure of compound **2** was deduced from its mass spectrum, ^{1}H and ^{13}C spectral data. The EI mass spectrum showed a $[M]^+$ at *m/z* 380, in accordance with $C_{24}H_{28}O_4$. Comparison of ^{1}H NMR and ^{13}C NMR data with those of badrakemone, which has been reported from *Heptaptera anisoptera* (DC.) Tutin (Appendino et al., 1992), suggested the two compounds were identical.

The ^{1}H NMR (Table 1) and ^{13}C NMR (Table 2) data of compound **1** were very similar to those of **2**. The structure of **1** differs from badrakemone in the stereochemistry on C-9′. Thus, the only differences between the ^{1}H NMR spectra of **1** and **2** appeared in the signals due to protons on C-11′, the exocylic methylene (C-12′) and C-Me groups. In **2**, the signal for the C-11′ protons appears at δ 4.23 as a doublet (J = 6.0 Hz) and those for the exocyclic methylene as two singlets at δ 4.6 and 4.98. In **1**, C-11′ protons appear as an AB part of an ABX system (δ_A 4.27, δ_B 4.0, J_{AB} = 9.6 Hz, J_{Ax} = J_{Bx} = 5.6 Hz), and C-12′ protons show two singlets at 4.81 and 4.89. The ^{1}H NMR data indicate that the compound is epimeric at C-9′, which was also confirmed by the fact that singlets for C-Me protons appear at δ 1.04, 1.06, and 1.12 in compound **2** and at δ 1.05, 1.14, and 1.2 in compound **1**.

The structures of compounds **3** and **4** were assigned as farnesiferol A and gummosin, respectively, by comparison of their spectral data with those of references (Pinar & Rodriguez, et al., 1977; Dawidar et al., 1979). The ^{1}H NMR spectra of both **3** and **4** displayed identical signals at δ 4.1 and 4.4 (*dd*, J = 5.6 Hz, J = 6.4 Hz) and two distinct triplets (J = 1.5 Hz) at δ 4.7 and 4.8 due to protons of C-11′ and C-12′, respectively. However, H-3′ of compounds **3** and **4** was different. In **3**, the signal of H-3′ appeared as pseudo-broad singlet at δ 3.47 and that of **4** as quartet (J = 10 Hz, J = 6 Hz) at δ 3.38. This difference was assigned to dissimilar stereochemistry of OH at C-3′. Melting points of two compounds were very different and confirmed the structures (Buckingham et al., 1994).

The structure of farnesiferol B (**5**) was deduced from its mass spectrum, ^{1}H NMR and ^{13}C NMR spectral data and optical rotation. The EI mass spectrum showed a $[M]^+$ at *m/z* 382, in accordance with $C_{24}H_{30}O_4$. Other spectral data of compound **5** were identical to that of farnesiferol B (Nabiev et al., 1982; Buckingham et al., 1994).

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