Pharmaceutical Biology

ISSN: 1388-0209 (Print) 1744-5116 (Online) Journal homepage: informahealthcare.com/journals/iphb20

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**To cite this article:** Mehrdad Iranshahi, Gholam-Reza Amin, Hassan Jalalizadeh & Abbas Shafiee (2003) New Germacrane Derivative from Ferula persica, Pharmaceutical Biology, 41:6, 431-433, DOI: 10.1076/phbi.41.6.431.17834

**To link to this article:** https://doi.org/10.1076/phbi.41.6.431.17834

Pharmaceutical Biology
2003, Vol. 41, No. 6, pp. 431–433

1388-0209/03/4106-431$16.00


# New Germacrane Derivative from *Ferula persica*

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## Abstract

A new sesquiterpene (9-*O*-acetyl-8-*O*-tigloyltovarol,**1**) was isolated from aerial parts of *Ferula persica*. Also, umbelliprenin (**2**) as a sesquiterpene coumarin was isolated from roots of this plant. Their structures were determined by UV, IR, $^1$H-NMR, $13_C$-NMR, and mass spectra.

**Keywords:** Aerial parts, *Ferula persica*, roots, sesquiterpene, sesquiterpene coumarin, umbelliferae, umbelliprenin.

## Introduction

The roots of *Ferula persica* Willd (Umbelliferae) have been used in folk medicine to treat diabetes (Afifi & Abu-Irmaileh, 2000). Members of the genus *Ferula* are widespread throughout central Asia, specially in Iran. The chemistry of this genus has been studied by different groups, but only few compounds have been detected in *Ferula persica* (Bagirov et al., 1977; Stetskov et al., 1980). The present study was performed to examine, in detail, the structure of other compounds. As a result, in the aerial parts, in addition to the flavonoids reported previously (Stetskov et al., 1980), we found a new sesquiterpene with a germacrane structure. In the root, in addition to coumarins reported before (Bagirov et al., 1977), umbelliprenin was isolated for the first time.

## Materials and methods

Melting points were taken on a Reichert-Jung apparatus and are uncorrected. UV spectra were recorded on a Shimadzu 160A spectrometer. EIMS were determined on a Finnigan TSQ-MAT 70 at 70 eV. $^1$H-NMR and $^{13}$C-NMR spectra were measured in $CDCl_3$ as an internal standard using a Varian 400 Unity plus spectrometer. FTIR spectra were recorded on a Nicolet 550 spectrometer. $[\alpha]_D^{25}$ was measured on a Perkin Elmer 241 polarimeter. CC was conducted with silica gel (Kieselgel 60, 0.2–0.5 mm 35–70 mesh ASTM, Merck, Germany) and TLC with Merck silica gel 60 $F_{254}$ on glass plates. The structure of compound **1** was optimized with MOPAC using PM3 method (Stewart, 1991).

Aerial parts and roots of *F. Persica* var. *latisecta* Chamberlain were collected in May 2001 north of Tehran and identified by Dr. G. Amin, Dept. Pharmacognosy, Faculty of Pharmacy, Tehran University of Medical Sciences (TEH). A voucher speciment (6522) was deposited at the herbarium of the Faculty of Pharmacy.

Dried powdered aerial parts of the plant (300 g) were extracted with MeOH-$H_2O$ (4 : 1) at room temperature by maceration for 24 h. MeOH was evaporated *in vacuo* and after filtration was extracted with $CHCl_3$ (3 × 300 ml). The solvent was evaporated under reduced pressure, yielding 10.5 g viscous mass. The residue was chromatographed on silica gel column (4 cm × 60 cm), eluting with petroleum ether with increasing acetone. The fractions were monitored by TLC. Compound 1 was isolated and was purified by preparative layer chromatography on silica gel plates (hexane/EtOAc, 5 : 1, oil, 30 mg, $R_f = 0.5$).

Dried powdered roots (500 g) were extracted with MeOH (3.5 L) by maceration for 72 h. The solvent was evaporated and the residue was chromatographed on a silica gel column. Elution with petroleum ether-acetone (10 : 1) gave compound **2** which was further purified by PLC (petroleum ether/EtOAc, 3 : 1) to give white crystals after crystallization from MeOH (130 mg, $R_f = 0.63$).

Accepted: January 17, 2003

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## Results

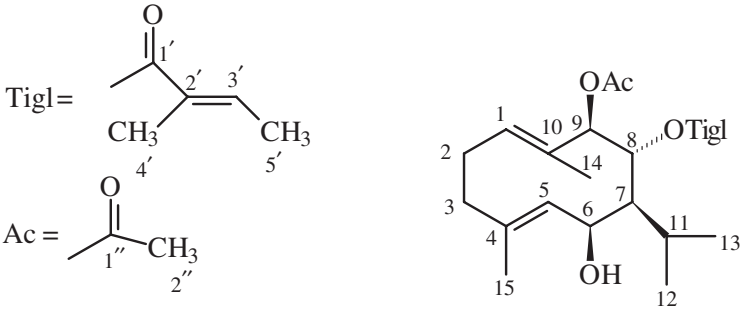
*Ferula persica* yielded a new sesquiterpene (**1**) and umbelliprenin (**2**). The structure of **1** was confirmed by chemical analysis and comparison of its $^{1}$H-NMR and $^{13}$C-NMR spectra with the reported values of other similar compounds; tovarol (De Pascual Teresa et al., 1985), 6-acetyl-8-benzoyl tovarol (Miski et al., 1990), 8-vanilloyltovarol (Miski et al., 1987), 8-*O*-Tigloyltovarol (Marco et al., 1991). The structure of umbelliprenin was confirmed by comparison of its $^{1}$H-NMR and $^{13}$C-NMR spectra with the reported values (Kutney et al., 1972; Greger et al., 1982, 1983). The results obtained for compounds **1** and **2** follow.

### Umbelliprenin (2)

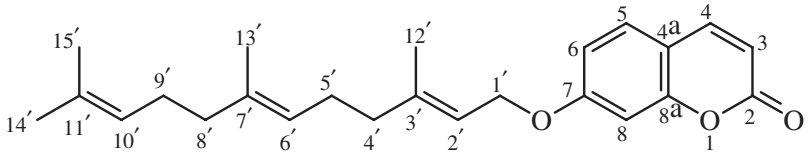
$C_{24}H_{30}O_3$; white powder; mp = 58 °C; EIMS: 366 ($M^+$, 5%), 309 (19), 204 (30), 163 (100), 134 (35), 93 (20), 81 (30), 69 (19). $^{1}$H-NMR: δ 7.63 (d, *J* = 9.6 Hz, H-4), 7.36 (d, *J* = 7.2 Hz, H-5), 6.84 (dd, *J* = 7.2 Hz, *J* = 2 Hz, H-6), 6.81 (d, *J* = 2 Hz, H-8), 6.22 (d, *J* = 9.6 Hz, H-3), 5.45 (t, *J* = 7 Hz, H-2′), 5.06 (q, *J* = 7 Hz, H-6′ and H-10′), 4.6 (d, *J* = 7 Hz, H-1′), 1.95–2.15 (m, H-4′, H-5′, H-8′, H-9′), 1.77 (s, H-12′), 1.67 (s, H-13′), 1.59, 1.6 (2s, H-14′, H-15′). $^{13}$C-NMR: 161.1 (C-2), 112.8 (C-3), 143.3 (C-4), 112.3 (C-4a), 128.6 (C-5), 118.4 (C-6), 162 (C-7), 101.5 (C-8), 155.7 (C-8a), 65.4 (C-1′), 113 (C-2′), 142.1 (C-3′), 39.4 (C-4′), 26 (C-5′), 124.2 (C-6′), 135.1 (C-7′), 39.5 (C-8′), 26.6 (C-9′), 123.4 (C-10′), 131.1 (C-11′), 16.6 (C-12′), 15.9 (C-13′), 25.7 (C-14′), 17.5 (C-15′).

### 9-*O*-Acetyl-8-*O*-tigloyltovarol (1)

$C_{22}H_{34}O_5$; oil $[\alpha]_D^{25}$-23° ($CHCl_3$ : MeOH, 1 : 1; c 0.43); UV$\lambda_{max}$ (MeOH) nm (log ε): 247 (2.16); IR$\nu_{max}$ (film) $cm^{-1}$: 3450 (OH), 1740 (acetate), 1690 (C═O ester), 1640 (C═C), 1440, 1020, 760; EIMS: 379 ($M^+$ + 1, 2%), 361 (379-$H_2O$, 80), 319 (20), 218 (60), 201 (100), 175 (40), 135 (45), 83 (tiglyl, 98). $^{1}$H-NMR: δ 6.9 (qq, 1H, *J* = 7.5 Hz, *J* = 1.5 Hz, H-3′), 5.37 (brd, 1H, *J* = 10.4 Hz, H-1), 5.3 (d, 1H, *J* = 8.4 Hz, H-5), 5.21 (dd, *J* = 9.6 Hz, *J* = 1.5 Hz, H-8), 5.09 (d, 1H, *J* = 9.6 Hz, H-9), 4.5 (dd, 1H, *J* = 8.4 Hz, *J* = 1.5 Hz, H-6), 2.1–2.4 (m, 4H, H-2, H-3), 1.95 (s, 3H, H-2″), 1.81 (dq, *J* = 7.5 Hz, *J* = 1.5 Hz, H-5′) and 1.84 (dq, *J* = 1.5 Hz, *J* = 1.5 Hz, H-4′), 1.8 (brs, 3H, H-14), 1.63 (m, 1H, H-11), 1.46 (s, 3H, H-15), 1.3 (dt, 1H, *J* = 10.5 Hz, *J* = 1.5 Hz, H-7), 1.04 and 1.1 (2d, 6H, *J* = 7.2 Hz, H-12, H-13). $^{13}$C-NMR: 170.2 (C-1″), 169.5 (C-1′), 139.1 (C-3′), 133.8 (C-5), 133.1 (C-1), 132.9 (C-10)[a], 131.4 (C-4)[a], 127.9 (C-2′), 77.6 (C-8), 75.2 (C-9), 67.5 (C-6), 53 (C-7), 38.2 (C-3), 26.2 (C-11), 24.3 (C-2), 23.3 (C-12), 21.1 (C-14), 21.0 (C-13), 19.1 (C-2″), 16.1 (C-15), 14.2 (C-5′), 11.9 (C-4′) ([a]signals may be interchanged).




**1**



**2**

*Figure 1.* The structure of compounds **1** and **2**.

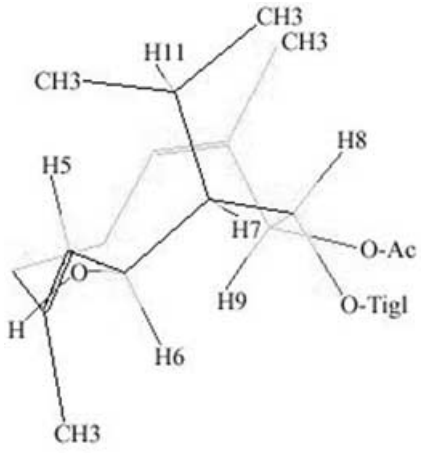



*Figure 2.* Three-dimensional structure of compound **1** (unimportant hydrogen atoms have not been shown).

*Table 1.* The observed and calculated coupling constants (*J*) of compound **1** hydrogen atoms.

| Hydrogen atoms | Dihyral angle[a] | $J_{calculated}$[b] (Hz) | $J_{observed}$ (Hz) |
|---|---|---|---|
| $H_5$-$H_6$ | 161.59° | 8.27 | 8.4 |
| $H_6$-$H_7$ | 64.72° | 1.27 | 1.5 |
| $H_8$-$H_9$ | 178.34° | 9.21 | 10.4 |
| $H_7$-$H_{11}$ | 169.69° | 8.92 | 10.5 |

[a] Dihydral angles were obtained from semi-empirical PM3 calculations.
[b] Calculated coupling constants (*J*) were calculated from Karplus equation.

## Discussion

Umbelliprenin (**2**) was identified on the basis of its melting point and spectroscopic data ($^1$H and $^{13}$C-NMR) in comparison with the reported values. The features of the $^1$H-NMR spectrum of **1** suggest a germacrane ring. The two doublets at δ 1.04 and δ 1.10 (*J* = 7.2 Hz) are assigned to six Me-protons of isopropyl. The two broadened doublets at δ 5.37 (*J* = 10.4 Hz) and δ 5.3 (*J* = 8.4 Hz) are assigned to H-1 and H-5 of the germacrane framework. H-6 and H-8 appeared as two double doublet (H-6: *J* = 8.4 Hz, 1.5 Hz and H-8: *J* = 9.6 Hz, 1.5 Hz).

The presence of a tigloyl residue follows from the signal at δ 6.9 (olefinic H, qq, *J* = 7.5 Hz, 1.5 Hz) and 1.81 (olefinic Me, dq, *J* = 7.5 Hz, 1.5 Hz). Other $^1$H-NMR data are given in results section.

The IR spectrum of compound 1 showed three strong absorptions at 3450, 1740 and 1690, which suggest the presence of hydroxyl, ester and conjugated ester functions, respectively. Also mass spectrum shows a molecular ion peak at *m/z* [$M^+$ + 1] 379, which agrees with the molecular formula $C_{22}H_{34}O_5$. Complete analysis of IR, UV and $^{13}$C-NMR spectra led to the proposal of structure **1**.

A doublet at δ 5.09 (*J* = 9.6 Hz) is assigned to H-9. β-Configuration of the acyl ester group at C-9 was deduced on the basis of the large coupling constant (*J* = 9.6 Hz). The geometry of compound **1** was optimized by semi-empirical $PM_3$ SCF-MO method (see Fig. 2). The predicted dihydral angles and $^3J_{HH}$ coupling constants for one of the optimized geometry are shown in Table 1, together with the observed coupling constants. The agreements between the calculated and observed values were generally good. Thus, we assign the β arrangement to the acetoxy group.

## Acknowledgements

This research was partially supported by the Tehran University of Medical Sciences research council. We would like to thank Dr. M. Amini for his technical help.

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