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FERCOPEROL, AN UNUSUAL CYCLIC-ENDOPEROXYNEROLIDOL DERIVATIVE FROM *FERULA COMMUNIS* SUBSP. *COMMUNIS*

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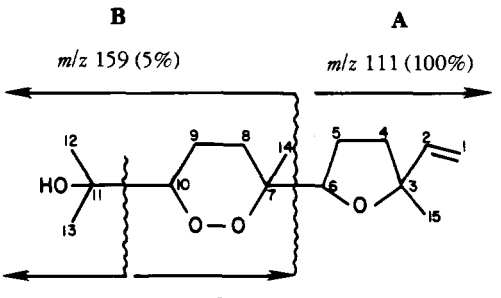
We have previously reported several daucane aromatic esters and a daucane-γ-lactone from the roots of *Ferula communis* L. subsp. *communis* (Apiaceae) (1,2), and we now describe from the same extract an unusual minor component fercoperol (**1**).

F. communis is a well-known ancient medicinal plant that has been used, for example, as an antidysenteric agent (3). Fercoperol (**1**) with its polyoxygenated endoperoxy moiety might have amoebicidal activity inasmuchas other endoperoxy-type sesquiterpenes, such as qinghaosu and yingzhaosu A, have antiparasitic activity (4,5). Notably, qinghaosu and its derivatives are used for the succesful treatment of different types of malaria. Strong antimicrobial effects have also been observed for cyclic-nerolidol derivatives (6).

To date cyclic-nerolidol derivatives are known only from species of the Compositae family, especially *Artemisia* (7-10), *Tanacetum* (6,11), and *Osmanthus* (12).

Fercoperol (**1**) did not exhibit a molecular ion in the eims; however, in its cims a molecular ion was observed at *m/z* 271 $[M+H]^+$ ($C_{15}H_{26}O_4$), which is in accord with a sesquiterpene skeleton. The ir spectrum of **1** showed absorption bands for a tertiary hydroxyl (3440 cm^{-1}, sharp) and a terminal vinyl (1645, 923 cm^{-1}).

The ^{1}H-nmr spectrum of **1** exhibited doublets of doublets for three vinylic proton at δ 5.87 (1H, J=10.6 and 17.2 Hz, H-2), 5.18 (1H, J=1.5 and 17.2 Hz, H-1), and 5.02 (1H, J=1.5 and 10.6 Hz, H-1′); double resonance experiments indicated that these three protons belonged to an isolated terminal vinylic group. The ^{1}H nmr also showed signals for two protons geminal to oxygen at δ 4.5 (1H, brt, J=6.3 Hz, H-6) and 3.88 (1H, dd, J=3.2 and 10.2 Hz, H-10), as well as a ddd signal at δ 2.28



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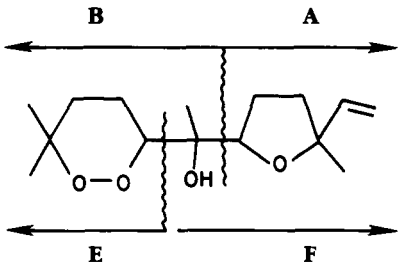
(1H, J=4.6, 5.8 and 14.3 Hz, H-8), four tertiary methyl signals at δ 1.31, 1.22, 1.17, 1.07 (each 3H, s, H-15, H-13, H-12, and H-14), and the remaining signals for two complex multiplets at δ 1.93 (3H) and 1.62 (4H). Double resonance experiments starting from protons geminal to oxygen indicated the presence of two isolated -O-CH-CH_2-CH_2-moieties.

Under mild conditions, **1** was not acetylated; consequently, no primary or secondary hydroxyl function is present. Also, the absence of carbonyl absorptions in the ir spectrum of **1** eliminated the presence of lactone and/or ester moieties. The ^{1}H-nmr spectrum showing two protons geminal to oxygen and a downfield tertiary methyl group confirmed the presence of two endocyclic ether groups in **1**.

Fercoperol (**1**) developed a rust-red color with acidic ammonium thiocyanate-ferrous ammonium sulfate (13) on tlc as expected for the presence of peroxy functional group(s). The lack of a hydroperoxy proton signal in its ^{1}H-nmr spectrum (14,15) and specific fragmentations in its eims indicated that one of the endocyclic ethers should be an endoperoxy group (16). The eims of **1**, together with ^{1}H-nmr data, indicated that the other endocyclic ether group should be part of a terminal 5-methyl-5-vinyltetrahydrofuran moiety; this moiety is the source of the fragment at *m/z* 111.

On the basis of the above spectral data, two structures, **1** and **2**, could be assigned to fercoperol. The presence of an abundant *m/z* 59 (98%), as well as the absence of **E**, **E**-H_2O, and **F** fragments in its ei- or cims (17,18) strongly suggest that the structure of fercoperol is **1** (no stereochemical assignments).



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EXPERIMENTAL

The roots of *F. communis* were collected in June 1983, near Istanbul, Turkey (ISTE 50856). A voucher specimen is deposited in the Herbarium of the Faculty of Pharmacy, University of Istanbul, Turkey. The air-dried root material (1.5 kg) was coarsely powdered, extracted, and worked up as previously described (1). For the isolation of fercoperol (**1**), a portion of the fraction eluted from the silica gel column with CH_2Cl_2-EtOAc (7:3) was rechromatographed on silica gel plates (1.5-mm thickness) using cyclohexane-EtOAc (8:2, double development) to yield 7 mg of **1**.

FERCOPEROL (**1**).—Compound **1** $C_{15}H_{26}O_4$, is a gum; ir ν max $CHCl_3$ cm^{-1} 3440 (OH), 1645, 1125, 923 (-CH=CH_2); ^{1}H nmr (200 MHz, $CDCl_3$, TMS), see text; eims (probe, 70 eV) *m/z* (rel. int.) 253 [M-OH]$^+$ (0.8), 211 [M-**D**]$^+$ (1.4), 159 [**B**]$^+$ (5), 141 [**B**-H_2O]$^+$ (14), 123 [**B**-2XH_2O]$^+$ (13), 111 [**A**]$^+$ (100), 101 [**C**+H]$^+$ (38), 93 [**A**-H_2O]$^+$ (90), 83 [**C**-H_2O+H]$^+$ (70), 59 [**D**]$^+$ (98), 55 (95); cims (iso-C_4H_{10}) *m/z* (rel. int.) 271 [M+H]$^+$ (38), 253 [271-H_2O]$^+$ (12), 111 [**A**]$^+$ (100), 143 [253-**A**+H]$^+$ (20).

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