THE STRUCTURE OF XEROFERIN

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Continuing an investigation of esters of the plant *Ferula xeromorpha* Eug. Kor. (xeromorphic giantfennel), by chromatographing a methanolic extract of the roots we have isolated a new ester with the composition $C_{23}H_{32}O_5$, which we have called xeroferin (I). The substance is readily soluble in chloroform, ether, and alcohols, sparingly soluble in petroleum ether, and insoluble in water. The UV spectrum of (I) has the maxima of a 3,4-dihydroxy-substituted benzoyl group at 267 and 297 nm (log ε 4.03 and 3.97) and its IR spectrum has absorption bands at (cm^{-1}) 1250, 1700, (ester group), 3200-2600 (hydroxy group), and 1520, 1600 (aromatic ring). The mass spectrum of xeroferin showed the peaks of ions with m/e 370 $(M - H_2O)^+$, 202 $(M - 168 - 18)^+$, 187 $(M - 168 - 18 - 15)^+$, and 168 $(C_8H_8O_4)^+$, which are characteristic for esters of sesquiterpene alcohols and aromatic acids [1].

On alkaline hydrolysis of the substance, from the neutral fraction we isolated a sesquiterpene alcohol with the composition $C_{15}H_{26}O_2$ (M^+ 238) with mp 142-144°C, which has been called xeroferol (II). From the acid fraction of the hydrolyzate we obtained an acid with the composition $C_8H_8O_4$, mp 245-247°C, identified from its IR spectrum and a mixed-melting point as isovanillic acid [2].

The oxidation of xeroferol with chromium trioxide in pyridine led to a monoketone with the composition $C_{15}H_{24}O_2$ (III), in the IR spectrum of which, in addition to the absorption band of a carbonyl group (1700 cm^{-1}), there was the absorption band of a hydroxy group (3200-3600 cm^{-1}). This shows that two oxygen atoms in xeroferol are present in the form of secondary and tertiary hydroxy groups. In the PMR spectrum of (II) signals from methyl groups appear at 1.69, 1.19, 0.87, and 0.95 ppm, the two latter being due to tertiary methyl groups on a quaternary carbon atom. This is also confirmed by the fact that in the spectrum of xeroferin, xeroferol, and its ketone the difference between the signals of the tertiary methyl groups changes.

On the basis of the empirical composition, $C_{15}H_{26}O_2$, and the presence of one double bond and four $C-CH_3$ groups, and taking into account the rule for calculating the number of double bonds and rings [3], it was found that xeroferol is a bicyclic compound, and nine skeletons are possible for it — the eudesmane, carotane, amorphane, pseudoguaiane, guaiane, eremophilane, widdrane, caryophyllane, and himachalane skeletons [4]. The first six of them are excluded because of the nature of the signals of the methyl groups in the PMR spectra.

On the basis of the results of a comparison of the CSs and SSCCs of the signals of the protons in the PMR spectra of xeroferin, xeroferol, and ketone (II) with those of himacholol (IV) [5] (Table 1) we chose the himachalane skeleton as the only possible one.

The positions of the hydroxy groups and of the double bond in xeroferol were determined from the following chemical and spectral characteristics. As mentioned above (see Table 1) the double bond has a secondary–tertiary nature. In the himachalane skeleton three variants are possible that satisfy this condition: C_2-C_3, C_3-C_4, and C_7-C_8. The last two are excluded because of the multiplicity of the signal of the olefinic proton in the PMR spectra of xeroferol and its derivatives, and the only possible position remaining for the bond is that at C_2-C_3.

The position of the tertiary hydroxy group follows from the multiplicity and the CS of the signal of the methyl group at 1.19 ppm in the spectrum of (II); i.e., it occupies the C_7 position. The secondary hydroxy group may be present in one of five possible positions: C_4, C_5, C_8, C_9, or C_{10}. The UV spectrum of the ketone of xeroferol (III) shows a characteristic maximum for an α,β-unsaturated carbonyl at 245 nm (log ε 3.70), and in its PMR spectrum the

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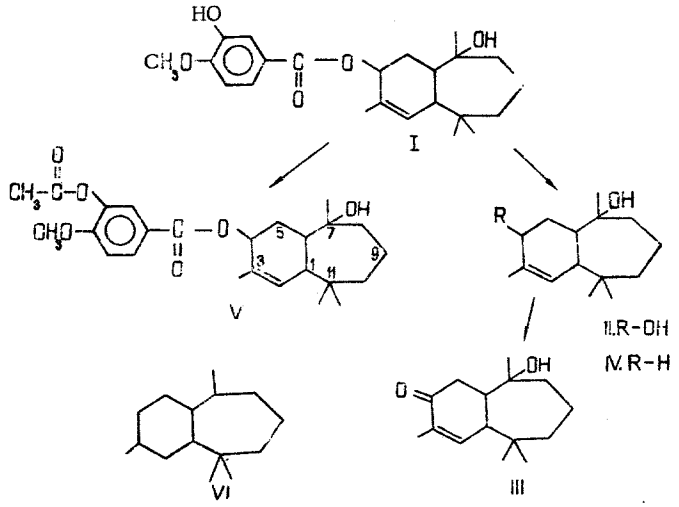
TABLE 1. Chemical Shifts (ppm), SSCCs, Integral Intensities, and Multiplicities of the Signals of the Proton of Xeroferol Derivatives

Substance	C_4–H	C_1–H	C_3–CH_3	C_1–H	C_7–CH_3	C_{11}–$2CH_3$	$COOCH_3$
Xeroferin (I)	5,77 d J=7,5 Hz	2,2 br. m 1 H	1,65 s 3 H	5,49 t $J_1=J_2=9$ Hz	1,23 s 3 H	s, 0,94; 0,98 each 3 H	
Xeroferol (II)	5,57 d J=7,5 Hz	2,25 br. m 1 H	1,69 s 3 H	4,00 t	1,19 s 3 H	0,87; 0,95 s each 3 H	
Himacholol (IV)	5,5 d J=6 Hz	2,2 br. m 1 H	1,65 s 3H	–	1,20 s 3 H	0,83; 0,98 s 3 H	
Acetate of (I) (V)	5,78 d J=7,5 Hz	—	1,75 s 3 H	5,41 $J_1=J_2=9$ Hz	1,22 s 3 H	0,99; 0,95 s 3 H	2,21 s 3 H
Ketone of (II) (III)	6,86 d J=6 Hz	— —	1,82 s 3 H	—	1,18 s 3 H	0,85; 1,06 s 3 H	—

Note. s) singlet; d) doublet; t) triplet; br. m) broadened multiplet.

signal of the olefinic proton has undergone a paramagnetic shift of 2.29 ppm in comparison with the initial substance. These results unambiguously show that the secondary hydroxy group in (II) is located at C_4. Consequently, xeroferol has structure (II). The downfield shift of the C_4–H signal in the PMR spectrum of xeroferin as compared with xeroferol shows that the isovanillic acid esterifies the secondary hydroxy group.



On the basis of the facts given, the most probable structure (I) is proposed for xeroferin. It was observed previously in the proof of the structure of juniferin and juniferinin [6] that esterification of an allyl hydroxy group led to a paramagnetic shift of the signal of the olefinic proton by 0.18 ppm. The same relationship is observed in the PMR spectra of xeroferin and xeroferol, which confirms the proposed structure.

Thus, we have isolated for the first time from a plant of the genus *Ferula* an ester forming a himachalane derivative.

EXPERIMENTAL

The conditions for recording the spectra and for chromatography have been described previously [7].

Isolation of Xeroferin. The combined esters of *Ferula xeromorpha* [7] (30 g) were deposited on a column (6.5 × 145 cm) of KSK silica gel. Elution was carried out with hexane–ethyl acetate (4:1) with a subsequent increase in the concentration of ethyl acetate, 300-ml fractions being collected. Fractions 81-89 were combined, the solvent was distilled off to dryness, and the residue was dissolved in a mixture of hexane and ethyl acetate (1:1), giving 0.22 g of xeroferin, $C_{23}H_{32}O_5$ (M^+ 388), mp 118-120°C (hexane–ethyl acetate). Yield 0.026% of the weight of the dry raw material.

Alkaline Hydrolysis of Xeroferin. A solution of 0.26 g of the substance in 5 ml of 10% aqueous ethanolic caustic soda was heated on a boiling-water bath for 7 h. After the end of the reaction, the hydrolyzate was diluted with two volumes of water and was treated with ether (5 × 50 ml). The ethereal solution was washed with water and dried with anhydrous sodium sulfate and the solvent was distilled off. The oily residue (0.113 g) was purified on a column (1 × 30 cm) of KSK silica gel with elution by chloroform—ethyl acetate (9:1). This gave 0.081 g of xeroferol (II) with mp 142-144°C.

After the treatment with ether, the hydrolyzate was acidified with 5% sulfuric acid and was again treated with ether. The resulting extracts were washed with water and dried, and the solvent was distilled off. This gave 0.102 g of isovanillic acid, mp 245-247°C.

Acetylation of Xeroferin. A solution of 0.13 g of the substance in 5 ml of pyridine was treated with 4.5 ml of acetic anhydride and the mixture was heated on a water bath for 6 h. The acetyl derivative was isolated by the usual method. Composition $C_{25}H_{34}O_6$. PMR spectra: singlet at 2.21 ppm (CH_3COO—).

Oxidation of Xeroferol. A solution of 0.126 g of chromium trioxide in 6 ml of acetone was added dropwise to a solution of 0.1014 g of the substance in 5 ml of acetone. The mixture was left at room temperature for 2 h. Then it was diluted with water and extracted with ether. The ethereal extracts were washed with water and dried, and the solvent was distilled off. This gave a mixture of two substances (0.063 g), which were separated on a column (0.5 × 25 cm) of KSK silica gel. Elution was performed with hexane—ether (3:1). This gave 0.048 g of the ketone of xeroferol, with the composition $C_{15}H_{24}O_2$.

SUMMARY

From the roots of *Ferula xeromorpha* Eug. Kor. (xeromorphic giantfennel) an ester of undescribed alcohol — himachal-2-ene-4,7-diol — and isovanillic acid has been isolated.

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