ANTIOXIDANT ACTIVITY OF ALANTOLACTONE AND ISOALANTOLACTONE

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Interest in the lipids of biological tissues is rising in connection with their significance as structural elements of cell membranes and regulators of the most important metabolic processes of the cell in the norm and in pathogeny. On the other hand, lipids readily undergo oxidative deterioration. This relates in the first place to processes in which an interaction of active forms of oxygen with the unsaturated acyl residues of phospholipids takes place, since an accumulation of peroxide groupings leads to various pathological states [1]. In view of this, the search for new antioxidants normalizing the level of lipid peroxides in the organism is acquiring ever greater urgency.

Our aim was to study the antioxidant activity (AOA) of the lipids of the mouse liver on a model — thermal hyperoxia [2] — after the separate administration of two sesquiterpene lactones: alantolactone and isoalantolactone, which have been isolated from the roots of *Inula helenium*. The roots of *Inula helenium* were collected in the environs of the villages of Chukhuryut and Astrakhanovka in the Shemakaha region of the Azerbaidzhan SSR in July, 1984. The isolation and identification of the lactones was performed as in [3]. The lipids were extracted from the liver homogenate by Folch's method [4]. The amounts of lipid hydroperoxides formed were judged from the decoloration of chloroform solutions of iodine by iodometric titration [5]. Table 1 gives the mean values obtained for three groups, each of which consisted of 60 mice.

The AOA of the lipids was evaluated with the oxidation of methyl oleate as a model [6]. The experiments showed that the intraperitoneal administration of the sesquiterpene lactones in doses of 100-200 mg/kg led to a rise in the AOA of the lipids; for alantolactone the AOA averaged 7500 h·ml/g and for isoalantolactone 8500 h·ml/g, while in the control group (pure methyl oleate) it was 1000 h·ml/g; in the case of the well-known natural antioxidants α-tocopherol and ubiquinone the AOA averages 1200 and 100 h·ml/g, respectively [7, 8].

The experiments performed showed that alantolactone and isoalantolactone increase the AOA of lipids. Apparently, the inhibiting action of sesquiterpene lactones is due to the detachment of a highly mobile hydrogen atom present in the reactive exocyclic methylene group by a peroxide radical, as a result of which the radical chain reaction is terminated.

TABLE 1.

Amounts of lipid hydroperoxides in the livers of random-bred mice, mole/g of lipids

hyperoxia		methyl oleate M±m. $\times 10^{-3}$	methyl oleate + alantolactone M ± m, $\times 10^{-3}$	methyl oleate + isoalantolactone M ± m, $\times 10^{-3}$
After	12 h.	0,21±0,01	0,05±0,001	0,04±0,003
		P<0,001	P<0,001	P<0,001
	24 h.	0,18±0,02	0,08±0,001	0,05±0,001
		P<0,001	P<0,001	P<0,001
	48 h.	0,30±0,01	0,15±0,06	0,12±0,01
		P<0,001	P<0,001	P<0,001
	68 h.	0,59±0,03	0,30±0,01	0,25±0,02
		P<0,001	P<0,001	P<0,001
	84 h.	0,70±0,09	0,32±0,03	0,26±0,04
		P<0,001	P<0,001	P<0,001

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ELLAGIC ACID DERIVATIVES FROM *Euphorbia ferganensis*

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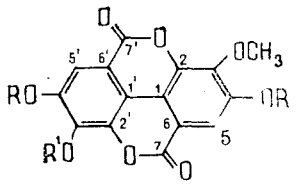
Scopoletin and ethyl gallate have been isolated previously from the roots of *Euphorbia ferganensis* B. Fedtsch. [1]. Continuing the investigation of this plant, from the ethyl extract fraction of an ethanolic extract of the roots we have isolated two more compounds of phenolic character by chromatography on a column of silica gel in the benzene–ethanol (7:3) solvent system.

Compound (I) has the composition $C_{15}H_8O_8$, mp 303-305°C, ν_{max}^{KBr} (cm^{-1}); 3450-3030 (OH), 1725-1707 (C=O), 1615, 1590, 1510 (C=C bond). Its UV spectrum had maxima at 254, 358* (inflection), and 372 nm (log ε 3.58, 3.91, 3.96) and was similar to the spectrum of 3,3'-di-O-methylellagic acid [2]. The PMR spectrum of (I) (C_5D_5N, δ, ppm. 0 – HMDS) showed a three-proton singlet at 4.08 ppm ($Ar-OCH_3$), two one-proton singlets at 7.88 and 7.94 ppm (H-5 and H-5'), and a broadened signal at 7.52-8.06 ppm apparently due to the protons of phenolic hydroxy groups. In actual fact, when the spectrum was taken with the addition of trifluoroacetic acid (TFA) the signs of these protons, exchanging with the OH protons of the TFA, shifted downfield and appeared in the form of a broadened singlet at 8.4 ppm.

In the mass spectrum of compound (I) in addition to the 100% peak of the molecular ions with m/z 316 there were the peaks of ions with m/z 301 $(M - CH_3)^+$, 287 $(M - CHO)^+$, 273 $(M - CH_3 - CO)^+$, 259, 231, and others.

The acetylation of substance I gave a triacetyl derivative (Ia) with mp 251-252°C (2.20 ppm, 9H, s) while methylation with diazomethane led to the trimethyl derivative, (Ib), $C_{18}H_{14}O_8$, mp 343-344°C (decomp.), M^+ 358; ν_{max}^{KBr} 1741, 1616, 1577, 1497 cm^{-1}. In its physical and spectral properties, substance (Ib) was identical with the tetramethyl derivative of ellagic acid [3]. Consequently, the compound (I) was a monomethyl derivative of ellagic acid.



I. R=R'=H
Ia. R=R'=$COCH_3$
Ib R=R'=CH_3
II. R=H, R'=CH_3

As mentioned above, the UV spectrum of (I) was close to that of 3,3'-di-O-methylellagic acid and differed considerably from that of 4,4'-di-O-methylellagic acid. Furthermore, the signal of the carbon atoms of the $Ar-OCH_3$ group appeared in the ^{13}C NMR spectra of (I) at 60.8 ppm, which is characteristic for a sterically hindered methoxy group in a benzene ring [4]. This corresponds to the C-3 and C-3' positions of ellagic acid, but in biew of the symmetry of the molecule the above-mentioned positions are equivalent. Thus, compound (I) was the 3-O-methyl derivative of ellagic acid. This substance has not been described in the literature.

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