jection of peptide). Higher doses caused a decrease of enzyme activity in both fractions; the decrease was more marked, moreover, for the soluble enzyme. For instance, a dose of peptide of 500 μg/kg lowered ODC activity in the supernatant by 3.7 times, and in the homogenate by 1.7 times compared with the control. With a further increase in the dose of HPM, gradual weakening of the inhibitory effect of the peptpide on ODC activity, stimulated by hepatectomy, was observed. Thus the effect of HPM on ODC activity in the regenerating liver exhibits complicated dose-dependence: small doses stimulate the enzyme, somewhat larger doses inhibit activity induced by hepatectomy, and in even larger doses still, the inhibitory action disappears.

The results, in the writers' view, indicate that HPM may have a role in the regulation of anabolic processes and, in particular, of regenerative processes in mammals. This means that the physiological role of this peptide, or of compounds similar in structure to it, in higher animals may be the same as in invertebrates. The mechanism of action of HPM is not clear; however, the fact that some of its effects (for example, stimulation of ODC in the regenerating liver) are manifested in very small dose s indicates that it may act through specific mechanisms, including the presence of high-affinity receptors in target organs.

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INTERACTION OF α-TOCOPHEROL WITH FREE FATTY ACIDS AND STEREOCONFIGURATION OF THE COMPLEX

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It has recently been suggested that one of the molecular mechanisms of the action of vitamin E is by stabilization of biological membranes against the harmful action of free fatty acids (FFA) [1]. This hypothesis is based on the following facts: First, α-tocopherol (TP) can protect membranes of the sarcoplasmic reticulum against disturbances of structural and functional organization due to the action of FFA (inhibition of Ca^{++}-transporting function, lowering of the temperature resistance of Ca^{++}-dependent ATPase, lowering the temperature of thermotrophic phase transitions of Ca^{++}-dependent ATPase) [2, 3], and second, TP in solution can form complexes with FAA [1]. The formation of these complexes takes place through interactions of two types: 1) polar interaction of the OH-group of the chromane nucleus of TP with the C=O-group of fatty acids (FA); 2) nonpolar interaction of acyl chains of FA with methyl groups of the chromane nucleus of TP [4].

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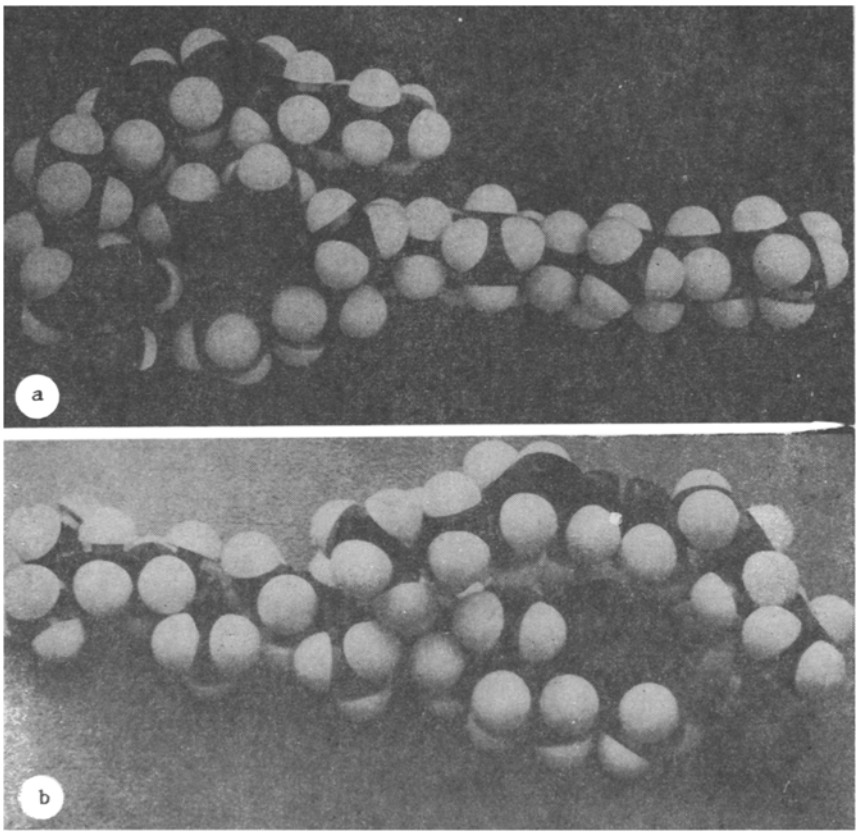

Fig. 1. Molecular models of two versions of stereoconfiguration of a complex of TP with linoleic acid: a) FA lies in plane of phenol ring of TP, bending it; b) FA lies above plane of phenol ring.

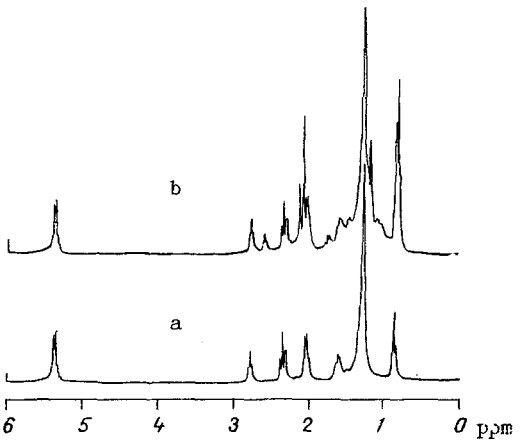

Fig. 2. ^{1}H-NMR spectrum of linoleic acid in $CDCl_3$ before (a) and after (b) addition of TP. Signals in spectrum a with values of δ of 5.36, 2.76, 2.34, 2.06, 1.62, 1.31, and 0.87 ppm belong to protons of CH=CH-, C=C-CH_2-C=C-, α-CM_2-, C=C-CH_2-, β-CH_2-, and $(CH_2)_n$-, and CH_3-groups. Signals with values of δ of 0.85, 1.22, 1.77, 2.10, and 2.57 ppm appearing in spectrum b belong to TP. The signal of the COOH group is not shown.

It was shown previously by methods of UV and NMR spectroscopy that the FA molecule in the complex is located in the region of the chromane nucleus of TP. In the present investigation, for which the method of high-resolution ^{1}H-NMR spectroscopy and the method of molecular models were used, the stereoconfiguration of these complexes was studied.

METHODS

TP was obtained from Serva (West Germany), linoleic acid from Sigma (USA), and deuterated chloroform ($CDCl_3$) from Merck (West Germany). NMR spectra were recorded on the WH-270 Fourier spectrometer.

RESULTS

For practical purposes elucidation of the stereochemical structure of the complex can be reduced to determination of the position of the acyl chain of FA relative to the plane of the chromane nucleus. Since the acyl chain of FA in the complex is in the immediate vicinity of the methyl groups of the chromane nucleus, there are two possible versions of mutual arrangement of the acyl chain of FA and the chromane nucleus of TP, which are clearly illustrated by molecular models (Fig. 1). In the first version the acyl chain of FA is located above the plane of the phenol ring. Under these circulstances interaction of electrons of π-orbitals of the C=C bonds of FA with electrons of conjugated π-orbitals of the phenol ring of the chromane nucleus may take place and the distance of the protons of the acyl chain of FA from the center of the phenol ring is 0.3-0.5 nm. In the second version the acyl chain of FA is located in the plane of the ring, which it bends. Under these circumstances interaction may take place on account of the fact that the cis-double bonds of FA form a structure complementary to the methyl groups of the chromane nucleus of TP. In this case the distance of the protons of the acyl chain of FA from the center of the phenol ring will be 0.7-1 nm.

The choice between the two possible stereochemical structures of the complex can be made on the basis of data of ^{1}H-NMR spectroscopy. In fact, if the first version of interaction of the acyl chain of FA and the chromane nucleus in the complex takes place, on addition of TP to a solution of FA changes ought to be observed in the magnitudes of the chemical shifts of the FA signals in the ^{1}H-NMR spectrum, for the FA will lie in the zone of action of the magnetic field of the nduced circular currents of the phenol ring of the chromane nucleus. In the second version of stereochemical structure, no such displacement should be observed, for FA in this case is some distance from the zone of action of the magnetic field of the circular currents.

Figure 2 shows the ^{1}H-NMR spectrum of a solution of linoleic acid in $CDCl_3$ before and after addition of TP to the solution (to a molar ratio of FA/TP of 2:1). It will be clear from Fig. 2 that no changes in the position of the signals in the ^{1}H-NMR spectrum took place for any of the groups of FA. This is evidence that the acyl chain of linoleic acid is located in the complex in the plane of the phenol ring of TP, which it bends, and that the 9th and 10th, and 12th and 13th cis-unsaturated bonds of linoleic acid form a structure complementary to the methyl groups of the phenol ring of TP, i.e., they demonstrate realization of the second version of the stereochemical structure of the complex of TP with linoleic acid.

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