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Study of Capah Membranotropic Action on the Artificial Biomembranes

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Study of Capah Membranotropic Action on the Artificial Biomembranes

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The drugs neurotropic effects are known to be connected with their ability to change the physicochemical parameters of membrane organisation. Having been investigated last time, phosphorylacetate hydrazides $R(R')P(O)CH_2C(O)NHNH_2$ display neuroprotective, memory enhancing and antidepressive activities^[1]. The lead representative of these series is CAPAH (I) ($R=4-Me_2NC_6H_4$; $R'=ClC_2H_4O$). We have now studied these compounds influence on the organization of model phospholipid membranes from egg yolk phosphatidylcholine (PC). ³¹P NMR technique was applied as particularly useful analytical tool for the study of the polymorphic phase behavior of hydrated phospholipids. The main feature of the CAPAH effect on ³¹P NMR spectra consists of an appearance of narrow symmetrical signal indicating effectively isotropic motion of the phospholipid molecules. PHOSENAZID (II) ($R=R'=C_6H_5$) renders the similar action on the membranes. It is confirmed by earlier obtained Infrared spectroscopy data that showed the formation of intermolecular hydrogen bond between carbonyl group of phospholipid molecule and hydrazide fragment of CAPAH^[2]. N-acyl derivative of CAPAH (III) did not affect the PC liposomes. Using of CAPAH and PHOSENAZID hydrochloride salts (IV, V) causes more drastic changes in the bilayer structure of liposomes apparently in the consequence of the additional interaction of salt anion with positive charged PC choline fragment. The results obtained are in an agreement with the preliminary studies of antioxidant effect of these compounds in vitro. Thus, the hydrochloride salts (IV, V) possess more marked influence on lipid peroxidation process in membranes of rat brain, and all tested hydrazides form the line increasing antioxidant activity (III)→(II)→(I)=(V)→(VI).

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