

*УДК 577.37***LANTHANIDE EFFECT ON PHYSICOCHEMICAL PROPERTIES OF LIPID BILAYER AS REVEALED BY INDICATOR DYE BROMOTHYMOL BLUE****A.V. Yudintsev¹, V.M. Trusova¹, G.P. Gorbenko¹, T. Deligeorgiev², A. Vasilev², N. Gadjev²**¹*V.N. Karazin Kharkov National University, 4 Svobody Sq., Kharkov, 61077*²*Department of Applied Organic Chemistry, Faculty of Chemistry, University of Sofia, Bulgaria*

Received 7 May, 2008

Development of new formulations of antineoplastic drugs currently represents extensively growing research area. Efficiency of existing anti-tumor drugs is frequently limited by their high general toxicity, metabolic instability in an organism and bad penetration into a cancer cell. Besides, insignificant direct influence on tumoral growth also limits the application of antineoplastic drugs in a free form. One efficient way of drug delivery is based on the use of lipid vesicles (liposomes). Liposomes are spherical, self-closed structures formed by one or several concentric lipid bilayers with an aqueous phase inside and between the lipid bilayers. The lipid bilayer favors solubilization of hydrophobic compounds, whereas internal aqueous phase of lipid vesicles is suitable for encapsulation of hydrophilic drugs. Design of liposomal carriers is heavily based on the evaluation of bilayer-modifying properties of the drug. This is important not only for achieving maximum payload without compromising liposome stability, but also for prediction of therapeutic and toxic effects of a certain compound, because membrane interactions may prove critical for drug absorption, distribution, metabolism and elimination in an organism. In the present work the effect of the two potential antineoplastic drugs – europium coordination complexes (LC) – on the physicochemical properties of phosphatidylcholine (PC) model membranes has been investigated using the environmentally-sensitive pH indicator dye bromothymol blue (BTB). This dye responds to the changes in environmental conditions by the shifts of its protolytic and partition equilibria. Incorporation of LC into the lipid vesicles was found to exert no influence on the effective electrostatic potential of model membranes, i.e. the mean potential at location of the dye prototropic moiety in the interfacial region. In contrast, BTB membrane partitioning markedly enhanced in the presence of drugs, indicating that europium coordination complexes can affect molecular organization of a lipid bilayer, presumably through generation of structural defects and altering the conformation of PC headgroups. High lipophilicity of Eu(III) coordination complexes together with their relatively weak membrane-modifying propensities create prerequisites for the development of liposomal formulations of these compounds.

KEY WORDS: lanthanide complexes, liposomes, bromothymol blue