DESCRIPTION FOR THE GENERAL PUBLIC

Cationic surfactants are the compounds of confirmed antibacterial activity as well as they are applied as carriers of DNA and drugs. In general these substances of characteristic amphiphatic structure and having a positive charge are potentially of great importance in wide range of medicinal, pharmaceutical and biotechnological applications as antibacterial agents, drug carriers and in gene therapy. However, their application is sometimes strongly limited due to occurrence of resistance in bacteria, not enough effectiveness and toxicity to mammalian cells. Therefore novel cationic amphiphiles of desirable properties are systematically synthesized and investigated. To this group of compounds belong triesters of phosphatidylcholine (P-O-ethylphosphatidylcholine; EPCs), which are called cationic lipoids. They were obtained from di-acyl-phosphatidylcholines(PCs) by phosphate ethylation of the polar head group and are the structural analogues of natural phosphatidylcholines. Since EPCs are derivatives of natural phospholipids they are of reduced toxicity than other cationic surfactants and they are well metabolized in the organism [1,2]. It was evidenced that these compounds are good candidates for the application in gene therapy and for the preparation of drug delivery systems [1-5]. Although the antibacterial properties of these compounds have never been investigated, it can be expected that, by the analogy to the other cationic amphiphiles, also these compounds may have antimicrobial potency. The antimicrobial effect of cationic lipoids as well as their application as drug/DNA carriers is directly connected with the interactions of these molecules with cellular membrane. The importance of lipid structures surrounding the cell in the activity of these compounds results also from the structural features of EPCs (amphiphilic nature and positive charge), which naturally determined the affinity of these compounds to lipid molecules.

On the other hand EPCs as a relatively new group of compounds have never been studied from the point of view of their effect on membranes. In literature only fragmentary information on the interactions of selected EPCs with only 3 membrane lipids can be found [6-8]. Therefore in this project we plan to perform systematic experiments on the interactions of structurally different EPCs (e.g. dipalmitoyl-*sn*-glycero-3-ethylphosphocholine (chloride salt) – EDPPC, 1-palmitoyl-2-oleoyl-*sn*-glycero-3-ethylphosphocholine (chloride salt) – EPOPC and dioleoyl-*sn*-glycero-3-ethylphosphocholine (chloride salt) EDOPC) with a large group of lipids (phosphatidylcholines, phosphatidylethanolamines, sphingomyelins, sterol, phosphatidylglicerols, cardiolipins and phosphatidylserines) typical for bacterial and mammalian membranes and with multicomponent membrane systems. The experiments will be done in artificial membranes that is Langmuir monolayers and bilayers, with the application of a large number of experimental techniques. This approach will allow one to describe in details the effect of EPCs on the condensation, permeability, morphology and molecular organization of the studied systems. The collected results will provide completely new information on the effect of EPCs on lipid systems, which in turn may be important to clarify various aspect of the activity of these compounds and determine their further medical applications. For example based on the results of these studies it will be possible to specify structural factors (of both EPCs and membrane lipids) responsible for the influence of cationic lipoids on membrane, to describe the relationship between the composition and morphology of membrane and the impact of EPCs as well as to compare the effect of EPCs on bacterial and animal membranes. All of these findings may help in planning the synthesis of novel, effective, less toxic cationic lipoids, verify the origin of toxicity of these compounds and select EPCs of potential antibacterial activity.

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