Structure and mobility of the lipid system in water-ionic liquid mixtures: magnetic resonance measurements and molecular dynamics simulations

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Introduction

An ionic liquid (IL) is a salt in the liquid state. They usually consist of an organic cation and an organic or inorganic anion. They have unique properties such as thermal and chemical resistance, good solubility, high ionic conductivity, etc. Recently, the interaction of these liquids with phospholipids and their use in transdermal and oral drug delivery has been actively researched [1]. The options for interaction between ILs and biological membranes are different. ILs with long hydrocarbon tails self-organize into micelles, which are then absorbed on the surface of the cell membrane. Short-tailed ILs are more mobile and can integrate into the membrane spontaneously [2]. They can be used as permeability enhancers for transdermal delivery of drugs. Research into the interaction between these liquids and phospholipids is important for understanding their potential toxicity to cells and the environment. In this work, we discuss the features of the structure, phase behavior and molecular mobility of the system consisting of lecithin and water-ethylammonium nitrate (EAN) mixtures studied by nuclear magnetic resonance (NMR) and molecular dynamics methods.

NMR measurements

The ^{31}P NMR line shape analysis revealed two lipid phases in the systems: lamellar and isotropic phases. The ^{31}P NMR spectrum for lecithin in pure D_2O has a “bilayer” shape. With the addition ionic liquid to water-ionic liquid mixtures, the fraction of the ^{31}P NMR spectrum with a “bilayer” line shape decreases, while the spectral intensity of the “isotropic” component increases. And the ^{31}P NMR spectrum of lecithin in pure EAN only has an “isotropic” component.

Diffusion NMR experiments were carried out using the pulsed-field gradient method. The self-diffusion coefficient (SDC) value related to lipids in pure EAN can be associated with lipids which undergo isotropic motion observed by ^{31}P NMR. The hydrodynamic radius calculated using the Stokes-Einstein equation corresponds to micellar size of lipid particles. The SDC related to lipids in pure D_2O may be associated with the movement of lipids with bilayer arrangements observed in the ^{31}P NMR spectrums. The hydrodynamic radius corresponds to the vesicular size of lipid particles. As the portion of D_2O in the D_2O-EAN solvent mixture increases, the self-diffusion coefficients related to the ionic liquid and lipids increase, i.e. the system becomes more mobile, which may be due to a decrease in viscosity.

According to NMR relaxometry data, the transverse magnetization decay for the lipids in D_2O-EAN mixtures (in the ratios from 80/20 to 20/80), are due to the sum of contributions from three components. This indicates the presence in the system of components with different molecular mobility: “liquid-phase” components and components associated with fast movement of diffusing lipids and with slow movement of lipids.

Computer modeling methods

The method of molecular dynamics shows that lecithin molecules assemble into a micelle in water. This micelle remains stable and compact during the entire calculated time (30 ns). Water molecules are mainly concentrated on the surface of the micelle, with the majority of hydrogen bonds formed with the phosphate group. In a mixture of IL and water, the micelle becomes cylindrical during the first 10 ns. At the same time, an increase in the average area per phospholipid was observed. Within the next 20 ns, this phospholipid structure remains unchanged. The analysis reveals that the cation penetrates deep into the micelle along with water. The changes in structure can be explained by the weakening of the interaction between lecithin molecules due to the presence of ILs molecules. When lecithin interacts only with EAN molecules, the micelle disintegrates. The disintegration of the structure may be due to Coulomb interactions between the cation of EAN and the phosphate part of phospholipid, and between the anion of EAN and choline.

Self-diffusion coefficients (SDCs) for lecithin molecules were calculated in the investigated systems. The comparative analysis of the SDCs revealed a correlation between values obtained by molecular dynamics and NMR methods [3].

References

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