Effects of Ionic Liquids on the Interfacial Properties of Different Amino Acids and a Globular Protein

ABSTRACT

The primary objective of this thesis has been to investigate the microscopic effects of ionic liquids (ILs) in aqueous solutions on the conformational and interfacial properties of amino acids (AAs) of different types and that of the globular protein α-lactalbumin. We have carried out the investigations using state-of-the-art molecular dynamics (MD) simulations. The thesis consists of six chapters. **Chapter 1** provides a brief overview of the current status of research in this area and the methodologies employed in the thesis. Attempts have been made in **Chapter 2** to obtain a quantitative molecular level depiction of the structural arrangements of the cation-anion components of the IL 1-butyl-3-methyl imidazolium tetrafluoroborate ([BMIM][BF_4]) around different AAs and the interactions between them. Our calculations revealed distinctly nonuniform distribution of the IL components around different AAs. It is demonstrated that the $BMIM^+$ cations preferentially interact with the aromatic AAs through favorable stacking interactions between the cation imidazolium head groups and the aromatic AA side chains. The potential of mean force (PMF) calculations revealed that such favorable stacking interactions provide greater stability to the contact pairs (CPs) formed between the aromatic AAs and the IL cations as compared to the other AAs. In **Chapter 3**, we have investigated the effects of aqueous solutions containing [BMIM][BF_4] as the IL at different concentrations on the conformational properties of the protein α-lactalbumin and the distributions of the IL and water around it. The calculations revealed enhanced rigidity of the protein with reduced conformational fluctuations and increasingly correlated local motions in presence of the IL. It is demonstrated that exchange of water molecules by the IL around the protein results in rearrangement of hydrogen bond network at the interface with the breaking of a fraction of relatively weaker protein–water (PW) hydrogen bonds and formation of stronger protein–IL (PI) hydrogen bonds. It is further observed that the protein forms increased number of stronger salt bridges in presence of the IL. We believe that replacement of weaker PW hydrogen bonds by much stronger PI hydrogen bonds at the interface along with the formation of greater number of stronger salt bridges is the microscopic origin behind enhanced rigidity of the protein in presence of the IL. Detailed investigations on the influence of BMIM-based ILs with a series of different anions of varying hydrophobic/hydrophilic characters on the conformational and solvation properties of α-lactalbumin are presented in **Chapter 4**. It is found that ILs with hydrophobic anions make the protein more compact with reduced conformational fluctuations, while the protein tends to attain relatively more flexible expanded form in presence of ILs with hydrophilic anions. Most importantly, the results demonstrated enhanced propensity of hydrophilic ILs to replace the PW hydrogen bonds by PI hydrogen bonds at the protein surface as compared to the hydrophobic ILs. Such breaking of PW hydrogen bonds at a greater extent is the microscopic origin behind greater loss of water hydrating the protein in presence of hydrophilic ILs, thereby leading to its reduced stability. In **Chapter 5**, we have studied the effects of BMIM-based ILs with a series of Hofmeister anions on the heterogeneous dynamic environment at the interface of α-lactalbumin. The calculations revealed that the increasingly restricted diffusivity of the IL components and water around the protein is associated with a longer time scale for the onset of dynamic heterogeneity at the interface. Importantly, the time scale associated with the reorientations of the anions has been found to be anticorrelated with their translational diffusivity, the effect being more at the interface as compared to the bulk IL solutions. It is demonstrated that the nonuniform ability of the anions to form hydrogen bonds with water due to their differential shapes and hydrophilic characters is the origin behind such anticorrelation. Finally, the overall conclusions based on the results presented in the thesis have been summarized in **Chapter 6**.

Keywords: Molecular Simulation, α-Lactalbumin, Ionic Liquids, Hydrogen Bonds