A Comparison of the Solvation Thermodynamics of Amino Acid Analogs in Water, *N*-Octanol, and Imidazolium-Based Ionic Liquids by Molecular Simulation

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The use of ionic liquids as novel solvents for industrial processes has drawn considerable attention and research [1,2]. More recently, research has emerged suggesting the use of ionic liquids as solvents for biological systems, in particular to enhance the solubility and stability of proteins [3,4]. As emphasized in the literature, one can tailor ionic liquids for such applications. However, before an optimum choice of an ionic liquid can be made, a fundamental understanding of how the ionic liquid structure might influence solubility and stability of proteins must be known. Given the expanse of composition space that needs to be explored, such an undertaking represents a considerable investment of experimental effort. Thus, the ability to understand structure-property relations by molecular simulation is extremely beneficial; such calculations allow one to gain a deeper understanding of the system by studying the underlying driving forces of the process. In this talk, we report results of molecular simulations in which we compute the relative solvation free energy, enthalpy, and entropy of neutral amino acid analogs in water, *n*-octanol, and imidazolium-based ionic liquids. Based on the relative free energies of individual constituent amino acid analogs in various solvents, we can draw insight into the native structure and folding mechanisms of proteins in solution, as indicated in [5,6]. In particular, we examine the influence of varying the alkyl chain length of the methyl-alkyl-imidazolium cation, and the effect of several different anions on the free energy of solvation of these amino acid analogs. With reference calculations performed in water and *n*-octanol, we examine the role ionic liquid hydrophobicity plays on solvation thermodynamics. We expect that this work will lead to an improved understanding of the role of ionic liquid structure and composition on protein structure and stability. Ultimately, we expect studies of this nature to lead to the development of ionic liquids that can be used in pharmaceutical and other therapeutic applications.

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