Intermolecular Organization In Aqueous Mixtures Of Choline Lysinate Studied Via NMR And Molecular Dynamics / Quantum Mechanics

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Choline-aminoacid ionic liquids (ChoAA ILs) are classic example of 3rd generation ionic liquids – they not only melt at <100 °C temperatures, but are also biocompatible, biodegradable and therefore less toxic than more common and widely investigated ILs of 1st and 2nd generations. Diversity of aminoacid-based anions and a possibility to mix ionic liquids with water allow for fine-tuning of their physicochemical properties: density, viscosity, ion mobility etc. Thus ChoAA ILs have much potential in industrial and biomedical fields, especially because of their hydrotropy – ability to improve solubility of various drugs and macromolecules in aqueous media by a few orders of magnitude [1]. For instance, a small amount of choline tryptophanate enhance the solubility of antidiabetic drug glibenclamide by more than 130 times in aqueous medium [2]. Six ChoAA ILs, including choline lysinate (ChoLys, structural formula given in Fig. 1) were shown to effectively solubilize lignin in biomass [3]. This result provides promise to increase efficiency of biomass reusability for other biochemicals and biofuels.

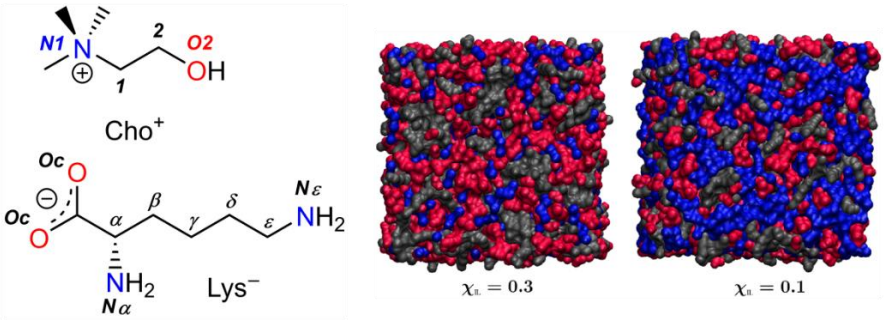

Figure 1 – Left: chemical structure and atomic labels of choline lysinate ionic liquid; right: still-images from molecular dynamics trajectories of choline lysinate-water systems with 0.3 and 0.1 ionic liquid molar fraction, colored by functional group polarity – non-polar moieties are grey, polar moieties are red, water molecules are blue.

While some targeted modelling studies on the effect of specific ionic liquid to a specific solute has been done [4-5], a more systematic study of ChoAA ILs and water mixtures intermolecular structure could lay a firmer foundation for investigating their mechanism of action and applicability for solubilization processes. To this day, most of the intermolecular structure studies of ChoAA ILs relies on X-ray or neutron scattering techniques. For example, it was shown that some ChoAA ILs exhibit nanoheterogeneity and they are comprised of varying size of domains of high-polarity and low-polarity, according to energy-dispersive X-ray diffraction measurements [1]. While X-ray or neutron scattering experiments provide information about domain size, they lack insight on chemical origin and substitution of those domains. For this purpose, nuclear magnetic resonance (NMR) is an advantageous technique since chemical shifts of each nuclei are to some extent sensitive to the solvating environment. Therefore, NMR chemical shifts can be used for detecting the local surroundings of ions and water and whether domain-like structure forms in ChoAA ILs and water mixtures or not.

In this study [6], we successfully utilized molecular dynamics (MD) simulations and quantum mechanics / molecular mechanics (QM/MM) calculations for 6 mixtures of ChoLys and water, ranging from 0.025% to 50% IL molar fraction (χ_{IL}). MD trajectories provided intermolecular structure data, including local coordination of

each species and the mesoscopic view of the system, i.e. what kind of aggregates or domains form in the investigated mixtures (see Fig. 1). Also, MD trajectories were used to calculate diffusion coefficients of water molecules and ions. QM/MM calculations are done by extracting 100 snapshots from MD trajectories to evaluate the nuclear shielding constants of a chosen particle and then averaging the values. This procedure accounts for different configurations of the solvation shell and the particles in it, depending on their proximity to the nuclei of consideration, are treated either quantum mechanically (QM level) or as simple point charges (MM level). Diffusion coefficients and nuclear shielding constants were compared with experimental ^{1}H NMR and NMR DOSY spectra to validate the computational results.

We characterized local coordination around N1 and O2 atoms of Cho^+ ion, Oc, Nα and Nε atoms of Lys^- ion and Ow atom of H_2O using radial distribution functions and calculating coordination numbers. We concluded that choline OH group, both amino (NH_2) groups and carboxylate group (COO^-) of lysinate, and H_2O participate in complex hydrogen bonding, with latter two being the most common H-bonding species in high IL content and low IL content, respectively. Positively charged NMe_3^+ group of choline disrupts the H-bond network and also attracts various functional groups (especially H_2O and COO^-) near itself.

From the mesoscopic point of view, we found that only small water clusters form when χ_{IL} is 30% or 50% and they are interspersed within network of ions (see Fig. 1). At χ_{IL} value of 10%, a percolation limit is reached and water clusters merges in a single network with ionic domains surrounded by it. This conclusion follows not only from the aggregate probability distributions, but also from the diffusion coefficients (D). D values exponentially decrease with respect to χ_{IL}, but the decrease of both calculated and experimental values slows down at around χ_{IL} = 11%, indicating a shift from one diffusional regime (water network) to another (IL network).

Lastly, shielding constants σ of H1, H2 (in Cho^+), Hα, Hε (in Lys^-) and Hw (in H_2O) were attained by performing QM/MM calculations. σ trend with respect to χ_{IL} was quantitavely and qualitatively similar to experimental data for Hα and Hw; only qualitatively comparable – for H1 and H2 protons. Hε shielding constant trend was somewhat inaccurate and it may be caused by usage of GAFF force field, since specific ChoAA ILs force fields were not derived at the time. We also showed that Hw is involved in fast proton exchange with NH_2 and OH groups. We deduced that because of mostly accurate NMR calculations and matching diffusion coefficient trends, our intermolecular data of ChoLys:water mixtures is accurate and this information, as well as our methodology, can be used to explain interactions in more complex ChoAA IL-water-solute systems.

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