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Interactions between the Pharmaceutical Active Ingredient Ionic Liquid and Small Biomolecules: A Mini Review

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Introduction

Due to many factors such as drug purity, thermodynamic stability, manufacturability, and ease of handling, until now the active pharmaceutical ingredients (APIs) in the pharmaceutical industry are mainly in solid or crystalline forms. However, these forms of APIs usually suffer from low solubility, low biological permeability, and polymorphic conversion, which lead to unsatisfactory bioavailability and low efficiency of drugs. Active pharmaceutical ionic liquids (API-ILs) are expected to solve these problems. Moreover, many investigations confirm that API-ILs can retain or result in increasing bioactivity of the involved active pharmaceutical ingredients (APIs) [1-3]. Considering the future application of API-ILs as pharmaceuticals, it is important and necessary to explore their action mechanism with biomolecules. Currently, the unique effect of API-ILs on the biomolecules in aqueous medium is only at the beginning of studies. Thus the physicochemical properties of aqueous individual small biomolecules with API-ILs will be necessary and useful to understand various interactions between API-ILs and biomacromolecules.

Results and Discussion

Shekaari and co-workers first carried out the research in this area. In 2016, they [4] synthesized a new API-IL 1-butyl-3-methylimidazolium ibuprofenate ([BMIM] [Ibu]) and studied the interactions between [BMIM][Ibu] and two amino acids (glycine and L-alanine) using conductivity, refractometric, volumetric, ultrasonic and viscometric methods [4,5]. The obtained volumetric and acoustic parameters indicate dominance of polar–polar and ion–polar interactions between (glycine, L-alanine) and [BMIM] [Ibu]. The more positive values of dB/dT for glycine and less negative values for L-alanine in aqueous [BMIM][Ibu] solutions suggest the promotion of structure-breaking ability in glycine and weakening of the structure-making ability in L-alanine. The limiting molar conductivities of [BMIM][Ibu] decrease with increase in the amino acid concentration and [BMIM][Ibu] is much easier to solvate in glycine solution.

In the same year, Shekaari et al. [6] synthesized 1-butyl-3-methylimidazolium salicylate ([BMIM][Sal]) as an active pharmaceutical ingredient ionic liquid and studied the thermodynamic properties of aqueous solutions of glycine and L-alanine with [BMIM][Sal] by volumetric, refractometric, ultrasonic, and viscometric properties at different temperatures. Results proclaim that presence of strong hydrophilic-hydrophilic and ion-hydrophilic interactions. The dehydration effect of studied API-IL on glycine and L-alanine was strengthened with the increased amount of API-IL. In 2017, our group [7] published the first report about the interactions of API-IL with small biomolecules (amino acids and glycyl dipeptides). The used API-IL is domiphen L-proline ([DOM][L-Pro]). The calculated volumetric parameters also indicate dominance of ion–hydrophilic and hydrophilic–hydrophilic interactions of the studied small biomolecules with [DOM][L-Pro] and the dehydration effect of [DOM][L-Pro] on amino acids/dipeptides. Both binding constant between amino acid/dipeptide and [DOM][L-Pro], and the volumetric result show that the extent of interaction increases with increasing alkyl chain length of amino acid/dipeptide and the concentration of [DOM][L-PRO].

In 2018, another API-IL [8] benzethonium L-proline ([BT] [Pro]) was synthesized by our group and a comparative study on the interactions of some small biomolecules with [BT][Pro] and its active drug benzethonium chloride [BTC] were carried out by conductivity, density, Uv-Vis and fluorescence spectroscopy methods. In the studied systems, hydrophilic-hydrophilic and ion-hydrophilic interactions between solute-solvent play the significant roles. The affinity between solute and co-solute depends on temperature, con-

centration and the alkyl chain length of small biomolecule. Addition of small biomolecule in water decreases the critical micelle concentration (cmc) and the aggregation number of [BTC]/[BT][Pro]. As compared with [BTC], [BT][Pro] shows stronger hydrophobicity, smaller cmc and weaker interactions with small biomolecules.

In recent years, the advantages of API-ILs have been highlighted [9,10]. Several studies have been focused mainly on the synthesis of novel API-ILs. There is a lack of information on API-IL-biomolecule interactions in physiological media. Therefore, the relative studies will be very attractive since it allows infinite new possibilities, opportunities and challenges.

References

1. Bica K, Rijksen C, Nieuwenhuyzen M, Rogers RD (2010) In Search of pure liquid salt forms of aspirin: Ionic liquid approaches with acetylsalicylic acid and salicylic acid. Phys Chem Chem Phys 12: 2011-2017.
2. Maddali K, Kumar V, Marchand C, Pommier Y, Malhotra SV (2011) Biological evaluation of imidazolium- and ammonium-based salts as HIV-1 integrase inhibitors. Med Chem Comm 2: 143-150.
3. Pernak J, Sobaszkiewicz K, Mirska I (2003) Anti-microbial activities of ionic liquids. Green Chem 5: 52-56.
4. Shekaari H, Zafarani-Moattar MT, Mirheydari SN (2016) Conductometric analysis of 1-butyl-3-methylimidazolium ibuprofenate as an active pharmaceutical ingredient ionic liquid (API-IL) in the aqueous amino acids solutions. J Chem Thermodyn 103: 165-175.
5. Shekaari H, Zafarani-Moattar MT, Mirheydari SN (2016) Effect of 1-butyl-3-methylimidazolium ibuprofenate as an active pharmaceutical ingredient ionic liquid (API-IL) on the thermodynamic properties of glycine and L-alanine in aqueous solutions at different temperatures. J Solution Chem 45: 624-663.
6. Shekaari H, Zafarani-Moattar MT, Mirheydari SN (2016) Thermodynamic properties of 1-butyl-3-methylimidazolium salicylate as an active pharmaceutical ingredient ionic liquid (API-IL) in aqueous solutions of glycine and L-alanine at T = (288.15-318.15) K. Thermochim Acta 637: 51-68.
7. Yan ZN, Chu WW, Shen SX, Ma LM (2017) Volumetric and UV absorption studies on interactions of an active pharmaceutical ingredient ionic liquid (API-IL) domiphen L-proline with amino acids and glycyl dipeptides in aqueous solution at T = (293.15–308.15) K. J Solution Chem 46: 1658-1679.
8. Yan ZN, Ma LM, Shen SX, Chu WW, Li JP (2018) Studies on the interactions of some small biomolecules with antibacterial drug benzethonium chloride and its active pharmaceutical ingredient ionic liquid (API-IL) benzethonium L-proline at varying temperatures. J Mol Liq 255: 530-540.
9. Pinto P, Ribeiro D, Azevedo A, Justina DV, Cunha E, et al. (2013) Active pharmaceutical ingredients based on salicylate ionic liquids: insights into the evaluation of pharmaceutical profiles. New J Chem 37: 4095-4102.
10. Stoimenovski J, MacFarlane DR, Bica K, Rogers RD (2010) Crystalline vs. ionic liquid salt forms of active pharmaceutical ingredients: A position paper. Pharm Res 27: 521-526.