



Preferential and competitive role of hydrophilic/hydrophobic interactions quantifying amino acid-based ILs for papain stabilization

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ARTICLE INFO

Article history:

Received 18 May 2022

Revised 20 June 2022

Accepted 21 July 2022

Available online 25 July 2022

Keywords:

Cholinium amino acid ionic liquids

Papain

Molecular interactions

Proteolytic activity

ABSTRACT

A plethora of amino acid based ionic liquid (AAIL) has been synthesized recently in order to thermally and structurally stabilize the proteins, however, critical impact of AAIL cations and anions hydrophilicity has been significantly ignored and subsided. Herein, the pivotal role of cations competitive hydrophilicity has been envisaged by investigating the proteolytic activity, structural stability, and alteration in microenvironment of papain in the presence of varying concentration of cholinium tryptophan ionic liquids [CHO][Trp]IL and tetraethylammonium tryptophan ionic liquids [TEA][Trp]IL. The proteolytic activity of papain in increasing concentration of [CHO][Trp]IL and [TEA][Trp]IL shows that at lower concentration of [CHO][Trp]IL more hydrophilic cholinium cation enhanced the papain activity from 100 to 131 %, however detrimental effects on the activity have been observed at lower concentration of [TEA][Trp]IL due to less hydrophilic nature of tetraethylammonium anions. Moreover, the highly interactive nature of [TEA][Trp]IL can be concluded by Fourier transmission infrared spectroscopy (FTIR). The UV-vis, steady state fluorescence and circular dichroism results also concluded the prowess of AAILs hydrophilic cation for stabilization nature. However, at higher concentration detrimental effects have been observed even for AAILs which are having hydrophilic cations. Thus, the study highlighted that [CHO][Trp]IL can enhance the activity and structure stability of papain more significantly while maintaining its surrounding microenvironment due to more hydrophilic nature of cholinium cation in contrast to [TEA][Trp]IL which consists of less hydrophilic tetraethylammonium cation. Moreover, with increase in the concentration of both AAILs, detrimental effects on the proteolytic activity and structural stability of papain have been observed. To differentiate further between the polar and non-polar interactions, protein-ligand molecular docking studies of papain and cations of both AAILs, have been performed using AutoDock Vina and AutoDock tools 1.5.7. The evaluated results corroborated the data obtained by FTIR, spectroscopic studies and enzymatic activity. From docking, activity and spectroscopic studies, it can be observed that at cholinium cation vehemently prefers polar interaction by forming hydrogen bonding with Arg-64 and Asp-158, however, tetraethylammonium cation longs for the polar interactions by forming van der Waals interactions with Ala-162, Val-133 and Val-207. Moreover, at the higher concentration of AAILs no extraordinary distinction between hydrophilic/hydrophobic natures has been observed and both AAILs denatured the papain at higher concentration irrespective of hydrophilic/hydrophobic nature of cation.

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1. Introduction

Ionic liquids (ILs) have proved to be efficient greener solvent as well as reaction media eventually for protein stability and drug delivery which substantially overthrow the classical organic solvent owing to their low volatility, low inflammability, surface tension, less toxicity, miscibility with water, tunable viscosity, high

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