Electronic Supplementary Information

A Combined DFT and MD Simulation Studies of Protein Stability on Imidazolium-Water Clusters (ImH$^+$W$_n$) with Aromatic Amino Acids

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Percentage of reduction BEs, noncovalent index (NCI) plots of AAs-ImH$^+$W$_n$ (n = 1 – 3) clusters, SDF and potential energy plots of Protein-L with AAs are obtained from MD simulations provided in this supporting information.
The overall reduction percentages of BEs are 50%, 66%, and 75% for the Phe-ImH\(^+\)W\(_4\), Trp-ImH\(^+\)W\(_4\) and Tyr-ImH\(^+\)W\(_4\), respectively. The percentage of reduction in the BE plot is displayed in Fig. S1. From that, water molecules considerably decrease the interaction affinity of hydrophobic AAs (i.e., Phe) when compare with the Trp and Tyr. A very less reduction of BEs observed in Trp and Tyr, because of the formation of \(\pi\) stacking with water-mediated H-bonds. The water-mediated H-bonded networks are playing a main driving force for the stability of \(\pi\)-stacking complexes.

![Graph showing percentage of reduction of BEs](image)

**Fig. S1** The percentage of reduction of BEs during the stepwise addition of water molecules with AAs (Phe, Trp, and Tyr). W1, W2, W3, and W4 are denoted as AAs-ImH\(^+\) with water monomer, dimer, trimer, and tetramer, respectively.
(a) Phe-ImH$^+$$w_1$
Trp-ImH$^+$$w_1$
Tyr-ImH$^+$$w_1$

(b) Phe-ImH$^+$$w_2$
Trp-ImH$^+$$w_2$
Tyr-ImH$^+$$w_2$

(c) Phe-ImH$^+$$w_3$
Trp-ImH$^+$$w_3$
Tyr-ImH$^+$$w_3$
**Fig. S2** Noncovalent Index (NCI) plots of most stable geometries were obtained from DFT calculations (a) AAs-ImH\(^+\)W\(_1\) (b) AAs-ImH\(^+\)W\(_2\) (c) AAs-ImH\(^+\)W\(_3\). The green and cyan color indicates the strong and weak interactions between the AAs and ImH\(^+\)W\(_n\) clusters.

![Phe Trp Tyr](image)

**Fig. S3** The SDF of ImH\(^+\) (blue) and water (red) molecules around the AA models are shown.

**Fig. S4** The kinetic, potential, and total energies of Protein-L and Protein-L-ImH\(^+\) with corresponding to time are displayed.