

**IMPACT OF ORGANIC CATIONS  
ON THE THERMAL STABILITY OF ALBUMIN**

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Maintaining protein structural stability is essential for their biological functions. Proteins fold into native conformations via noncovalent interactions, which are highly sensitive to the changes in temperature, pH, ionic strength, or the presence of cosolvents. These changes often lead to protein unfolding and loss of function, however, in some cases, the conformational stability increases.

The well-known Hofmeister series ranks inorganic ions by how they affect the solubility and stability of proteins: from stabilizing and salting-out kosmotropes to denaturing and salting-in chaotropes. At the same time, the effects of organic cations on protein stability are poorly studied, despite the widespread interest to the behavior of proteins in the presence of ionic liquids (ILs). Most common ILs contain alkyimidazolium or alkylammonium cations. Unlike metal ions, they can engage in many different types of interactions with proteins such as salt bridges, hydrogen bonding, hydrophobic and  $\pi$ - $\pi$  stacking interactions, which makes it difficult to predict their effect on protein denaturation and aggregation.

In this work, the thermal stability of bovine serum albumin (BSA) in the presence of various organic thiocyanates was studied. The thermograms of BSA denaturation in the presence of different concentrations of thiocyanates were obtained using capillary DSC, and the temperatures of phase transition were determined. The cations were ranked by their destabilizing effect according to these temperatures. Guanidinium thiocyanate has shown the strongest destabilizing effect, while ethylenediammonium thiocyanate has led to the smallest decrease in denaturation temperature.

In addition, we performed molecular dynamics simulations of native and unfolded BSA in aqueous solutions of organic thiocyanates, which provided the information on the composition of BSA solvation shells. The difference in Kirkwood-Buff integrals of the solvent components can be interpreted as the preferential binding of one of the components. An increase in the preferential binding of organic salt upon BSA denaturation was shown to correlate with its denaturing effect.

*The work was supported by RSF project №24-13-00062.*