

Name of the Scholar: Sania Bashir

Name of the Supervisor: Dr. Asimul Islam

Name of the Centre: Centre for Interdisciplinary Research in Basic Sciences

Topic of Research: The effect of osmolytes on protein fibrillation and their therapeutic application

Finding

“The effect of osmolytes on protein fibrillation and their therapeutic application” is concerned with investigating two proteins, alpha-lactalbumin (α -LA) and recombinant human insulin (rHI). Many neurodegenerative diseases are caused due to protein aggregation such as Alzheimer's, Parkinson's diseases, type 2. This work investigated on α -LA protein, which was thermally induced to aggregate at high concentrations from with a temperature range from 25-80 °C. The aggregation was prevented by employing chosen sugar osmolytes that can protect protein against severe, harsh conditions. Thus insulin kinetics has been performed at physiological pH and temperature in visualizing the effect of these sugars. According to these investigations, rHI is adversely affected in the presence of sugar, with the maximum reported in 1.0 M trehalose. Aggregation was inhibited comparatively at very low concentrations to trehalose using a combination of trehalose and co-solutes such as Arginine/CTAB/MSG, which decreased aggregation to that of the native protein. The co-solutes are expected to form bonding complex with the trehalose. Aggregation may be prevented for one protein while enhancing the aggregation of another. Trehalose inhibits α -LA aggregation while increasing insulin aggregation propensity. Mixtures of insulin with incubated trehalose and co-solutes as CTAB/MSG/Arginine need a more in-depth study on the mechanism of action of these solutes on protein fibril imbibition. The main motive to carry this work is to maintain the structural integrity of recombinant human insulin (rHI) to be feasible carrier vials for diabetic patients; secondly, a worrisome solution for insulin injection. The research presented has the potential to create a trend and become a keystone of the long-term goal of comprehensively understanding aggregation and its preventative actions. These observations have significant biological implications, since insulin fibrillation is known to cause injection amyloidosis and our data may help in designing lead drug molecules and development of potential therapeutic strategies.