ABSTRACT

The aim of the study is to synthesize grafted knottin-based inhibitor, which will be directed against the Human islet amyloid polypeptide. Cystine-knot mini-proteins, termed as knottin, contains a conserved core which imparts extraordinary thermal, proteolytic stability and has a potential to refold correctly, due to three tightly wounded disulfide bonds making it a promising biomolecular tool for protein expression and purification. The grafted knottin-based inhibitor protein has been expressed with intein tag using cloned in a pTXB1 vector and expressed in BL21 (DE3), and further purified through CHITIN - Column Affinity chromatography. The motive to perform this study is to understand the role of hIAPP (Human Islet Amyloid Polypeptide), which is secreted from β-pancreatic cells along with insulin. The hIAPP aggregates and deposits on β-cells and inhibit its functions, causing Type-2 Diabetes. In Type-2 Diabetic, the pancreas produces enough insulin but due to hIAPP aggregation and deposition, dysfunction pancreatic beta cell and insulin receptor malfunction inside the target cell. The cell, as a result, become irresponsive to insulin, hence cannot import glucose, which stays in the bloodstream increasing blood glucose level. To carry on this study first objective is to synthesize the peptides of hIAPP by using Fmoc protected solid phase peptide synthesis, further grafted knottin mini-protein was used as an inhibitor against Human islet amyloid polypeptide to explore the effect of grafted knottin on hIAPP.

Keywords: Alzheimer's, Tau protein, Type-2 Diabetes, hIAPP, Knottin- Cysteine mini-protein, Amyloids, Aggregation, Peptide,