Theoretical investigation on insulin dimer - b - cyclodextrin interactions using docking and molecular dynamics simulation

ABSTRACT

In our study, molecular docking and molecular dynamics (MD) simulations were performed in order to explore the interactions between human insulin and β-cyclodextrin (β-CD). Molecular docking study was performed using the Autodock v4.2 program to determine the number of β-CD molecules that adhere to the binding sites of insulin. A random structure docking approach using an initial ratio of 1:1 insulin-β-CD was conducted and from these, additional β-CDs were added. Molecular docking results revealed that a maximum of four β-CDs are able to bind to the insulin structure with the 1:3 insulin-β-CD ratio producing the lowest binding free energy. The docked conformations showed that hydrophobic interactions played a crucial role in insulin-β-CD conformational stability in addition to the formation of hydrogen bonds. A 50 ns MD simulation was further conducted using an NPT ensemble to verify the results obtained by molecular docking. The analysis of the MD simulation results of the 1:3 insulin-β-CD formation system conclude that a good interaction exists between insulin and β-CDs and the RMSD value obtained was 4.00 ± 0.50 Å. The RMSF profiles of insulin in the 1:3 insulin-β-CD formation also show reduced amino acid residues flexibility as compared to the free insulin system. The theoretical results indicated the presence of significant interactions between insulin and β-CD which could provide interesting insights into an insulin formulation.

Keyword: Insulin; b-Cyclodextrin; Molecular docking; Molecular dynamics simulation