Designing novel β-sheet breaker molecule and its interactions on βA(1-41) by Docking Studies

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Alzheimer disease is a neurodegenerative disease affecting the hippocampus region of the brain. It is characterized by intracellular plaques and neurofibrillary tangles. Plaques are formed due to the aggregation of amyloid beta protein by means of π-π stacking interactions. In this study, we have generated docking models for various beta sheet breaker (BSB) molecules reported in the literature and for many di- and tri-peptide model compounds. The NMR structure of the amyloid β peptide (PDB ID:2BEG) was used for docking of various model peptides. The 3D structures of the model peptides were generated using CHEMSKETCH followed by energy minimization using Adopted basis NIR and CHARM force field in Discovery Studio. AutoDock 4.0.1 program equipped with ADT was used for generating docking models. A total of 50 possible binding conformations were generated in each case and they were grouped into clusters based on a 2.0 Å cluster tolerance. The docking models were viewed and analyzed using PyMol. Based on the studies of model peptides, an efficient BSB molecule has been designed which has tendency to get self assembled. The experimental validity of the novel BSB molecule is under progress.