Abstract

Dengue fever is caused by a flavivirus that infect 50-100 million people each year and is among the significant emerging infectious diseases worldwide, mostly in tropical areas. The virus has prominent mutational capacity being the main reason that currently, no specific drugs or vaccine is available. Studies have been conducted to design inhibiters by focusing entry and replication of virus within human cell. Mannose and NS5 methyltransferase (Mtase) have crucial roles in trafficking of virus within human cell. In this study activities of these two molecules were focused to develop inhibitors against these molecules. Mannose is present as glycan on E protein of DENV and binds with DC-SIGN receptor to initiate endocytosis. As DENV replicates within human cell, S-adenosyl-L-methionine (SAM) is transferred by methyltransferase (Mtase) to RNA cap where it donates methyl group for its 2-O' and N-7 methylation. The inhibition of mannose binding and activity of Mtase is expected to prevent entry and propagation of dengue virus. Structural conformation of mannose and SAM were used as a base either to design inhibitors or to screen databases to find suitable ligand through the use of bioinformatics tools. Collectively 34 inhibitors were designed as ligands for Mtase. For mannose, 14 molecules were designed computationally while 18 were screened from Pubchem. Each ligand was docked with respective receptor i.e. Mtase and DC-SIDN utilizing Hex web Server. Results were analyzed on basis of energy of docking complex, count of hydrogen bond from ligplot generated by PDBsum for each docking complex and drug-likeness score calculated using molsoft. The results showed that heptulose was the best inhibitor of mannose binding with DC-SIGN posscssing an estimated energy range of -1.575675e+02 to -1.287312e+02, showing maximum hydrogen binding with mannose-binding amino acid residues and having estimated drug score 1.15. Similarly SAMphos was found to be the best inhibitor for methyltransferase with estimated energy range of -2.631696e+02 to 2.406720e+02, showed maximum hydrogen binding with SAM-binding residue and had a drug score of 1.19. Hence it is likely to expect that heptulose and SAMphos may be used as drug candidates exhibiting antidengue potential through inhibition of entry and replication of DENV.