ABSTRACT

Influenza virus is a global threat that can cause disease in humans and many other animal species. Oseltamivir (Tamiflu) and rimantadine are potent and selective antiviral drugs employed to fight the flu virus in infected individuals by inhibiting neuraminidase (NA) and M2 proton channel respectively. However, drug resistance has become a critical problem. In particular, influenza strains with H274Y, N294S and R292K mutations in neuraminidase and S31N mutation in M2 proton are highly resistant to influenza treatment. Though the biological functions of the mutations have previously been characterized, the structural basis behind the reduced catalytic activity and reduced protein level is not clear. Hence, in our study, we have analyzed the impact of drug resistant mutations present in both neuraminidase and M2 proton channel targets of influenza virus using molecular docking and molecular dynamics approach. Furthermore Virtual screening procedures were carried out using PubChem, Traditional Chinese medicinal databases (TCMD) and DrugBank to identify novel class of lead molecules with potential inhibitory effects against the native and resistant targets. The lead molecules were analyzed with respect to the Lipinski rule of five, drug-likeness, toxicity profiles and other physico-chemical properties of drugs by suitable software program. The results indicated that these lead molecules can be more promising and effective in treating sensitive as well as drug resistant influenza virus strains.