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Computational evaluation of influenza targets and target-based drug discovery using vasicine, vasicinone, and vasicine acetate

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The influenza virus has been there for centuries causing seasonal flu and pandemics resulting in deaths for millions of people. Influenza remains a significant global health concern, necessitating continuous exploration for novel therapeutic drugs. This study investigates the potential antiviral activity of vasicine and vasicinone, the isolated alkaloids of Justicia adhatoda, and vasicine acetate, a synthetic derivative of vasicine, against the influenza virus through computational analysis. In-silico methods were used to assess toxicities. The toxicity of a drug is assessed quantitatively through its LD50 value, which determines its classification. According to the predicted toxicity classifications, vasicine and vasicinone were categorized as Class 3, which indicates they are toxic if ingested, posing significant health risks upon exposure. In contrast, vasicine acetate was classified as Class 4, suggesting it is harmful if swallowed, representing a comparatively lower toxicity level but still requiring caution. An influenza protein database was created using influenza viral proteins via homology modeling. Molecular docking was carried out to explore the interaction between the above alkaloid compounds and viral proteins involved in the viral infection. Furthermore, molecular dynamics simulations were employed using CHARMM to assess the stability of the identified ligand-protein complexes, providing insights into the dynamic behavior of the interactions. Body functions occur under constant pressure and temperature to mirror accurate physiological conditions. Therefore, system equilibration was conducted to attain the preferred pressure and temperature using NAMD simulation software. The Langevin dynamics integrator was employed for integration, with a time step of 2 fs. Temperature control during equilibration was achieved using a Langevin thermostat, maintaining the system at 303.15 K with a damping coefficient of 1 ps-1 to simulate a heat bath. The RMSD analysis exhibited thermal stability and reached equilibrium at 303.15K throughout 5 nanoseconds. The alkaloids vasicine, vasicinone, and vasicine acetate show the highest binding affinity towards hemagglutinin spike protein. The results revealed promising interactions between the alkaloids and H1N1 hemagglutinin spike protein essential for the initial steps in the viral infection, suggesting potential inhibitory effects against the influenza virus. The extracted alkaloids exhibited the potential to inhibit the fusion process of the hemagglutinin spike protein. The extraction of these alkaloids was done following previous protocols. According to TLC studies, it was expected that the isolation of the compounds could be carried out via column chromatography using a solvent system with a low polarity, such as hexane-chloroform.

Keywords: Influenza, molecular docking, vasicine, vasicinone, vasicine acetate