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COMPUTATIONAL STUDIES OF POTENTIAL EBOLA VP40 INHIBITORS USING BIOACTIVE COMPOUNDS FROM MEDICINAL PLANTS OF MALAYSIA

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Abstract

Ebola virus (EBOV) belongs to Filoviridae family, a deadly virus that can cause severe viral haemorrhagic fevers (VHF) with a high fatality rate between 25 to 90 percent. Amongst EBOV proteins, the EBOV matrix protein VP40 is crucial in facilitating the transcription of the viral gene in the early stage of infection. To date, there is no cure for EBOV and available chemical drugs were known to cause severe side effects. It is known that bioactive compounds from natural products can potentially combat this viral disease with fewer side effects. Therefore, this study aims to screen 15 bioactive compounds of medicinal plants from Malaysia. These compounds were docked against the RNA active site (Phe125 and Arg134) on VP40 matrix protein using AutoDock Vina. The ADMET properties and the toxicity class of the compounds were predicted computationally, and the compounds with good oral bioavailability were chosen for docking simulations. The top three docked compounds namely apigenin, epiexcelsin and kaempferol have a binding affinity of-4.6,-4.4 and-4.3 kJ/mol respectively. Our MD simulation study showed that epiexcelsin is the best candidate among the three selected compounds. Binding free energy calculation via molecular-mechanics Poisson Boltzmann surface area (MM-PBSA) method showed that epiexcelsin has the lowest binding free energy of-56.503 kJ/mol compared to apigenin (-40.344 kJ/mol) and kaemferol (-27.329 kJ/mol). Our results suggest that epiexcelsin from local herbal plants can potentially be explored as a good candidate for further development of EBOV inhibitor targeting VP40.

Author Keywords

Apigenin; Bioactive compounds; EBOV; Epiexcelsin; Kaempferol; MM-PBSA; Molecular Dynamic Simulation

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