Ebola Virus Glycoprotein Inhibitors from Natural Compounds: Computer-Aided Drug Design

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Abstract : The Ebola virus is a highly contagious and deadly pathogen that causes Ebola virus disease. Ebola outbreaks are characterized by high mortality rates, reaching up to 90%. The Ebola virus glycoprotein (EBOV-GP) is a key factor in viral entry into host cells, making it a critical target for therapeutic intervention. Using a combination of computational approaches, this study focuses on the identification of natural compounds that could serve as potent inhibitors of EBOV-GP. The 3D structure of EBOV-GP was selected, with missing residues modeled, and this structure was minimized and equilibrated. Two large natural compound databases, COCONUT and NPASS, were chosen and filtered based on toxicity risks and Lipinski's Rule of Five to ensure drug-likeness. A pharmacophore model, built from 22 reported active inhibitors, was used to further refine the compound selection. Virtual screening through molecular docking identified ten promising compounds: five from each database. These compounds were then subjected to molecular dynamics simulations to assess their interaction with EBOV-GP. The top three compounds from each database were further analyzed through ADMET profiling, revealing favorable binding affinities, stability, and pharmacokinetic properties. These results suggest that the selected compounds have the potential to inhibit EBOV-GP, offering new avenues for antiviral drug development against the Ebola virus.

Keywords : EBOV-GP, ebola virus glycoprotein, high-throughput drug screening, molecular docking, molecular dynamics, natural compounds, pharmacophore modeling, virtual screening
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