

Title: Quercetin derivatives as potential inhibitors of Nipah virus phosphoprotein through *in silico* drug design approaches

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Abstract: The [Nipah virus](#) (NiV) is a pathogenic infection presenting a substantial risk to both human and animal communities. Despite its virulence, there are currently no available drugs or vaccines for NiV. To fight against this challenge, we applied a multi-step *in silico* [drug design](#) strategy, including PASS prediction, [molecular docking](#), absorption, distribution, metabolism and excretion (ADMET) analysis, molecular dynamics simulations, frontier [molecular orbitals](#) calculations, dynamic cross-correlation matrix (DCCM), and [principal component analysis](#) (PCA). To find out the potential drug candidate against NiV target protein, more than 100 derivatives were taken from the PubChem database. After that, the Pa (probability “to be active”), and Pi (probability “to be inactive”) calculation was conducted. Based on the maximum probability “to be active score (Pa), the top nine compounds were studied against NiV. Our findings suggest that the [quercetin](#) derivatives exhibit promising [binding affinities](#) with the [Nipah virus phosphoprotein](#), particularly compounds 03 (−7.8 kcal/mol), 22 (−6.9 kcal/mol), and 89 (−7.3 kcal/mol). The molecular dynamics simulations over the 100 ns had confirmed excellent stability and ADMET profiles has reported that all the mentioned ligands are free from Hepatotoxicity, and AMES toxicity, suggesting them as promising candidates for anti-NiV drugs. Based on the results of molecular dynamics simulations, it was observed that the reported drug candidates 03, 22, and 89 exhibited a high degree of stability in forming protein-ligand complexes. These complexes showed only minor fluctuations in RMSF over the 100 ns simulation period. The utilization of frontier [molecular orbitals](#) aided in the understanding of the electronic structure behavior, providing strong evidence for their suitability. The study indicates that certain [quercetin derivatives](#), such as 03, 22, and 89, show promise as potentially effective antiviral drug candidates against NiV. Future research should focus on experimental testing of these compounds to develop new antiviral drugs against NiV.

Key words: Nipah virus (NiV) In silico drug design Quercetin derivatives Molecular docking ADMET analysis

<https://doi.org/10.1016/j.jics.2024.101196>

<https://www.sciencedirect.com/science/article/abs/pii/S0019452224000761>