

Title: Identification of natural compounds as potential antiviral drug candidates against Hepatitis E virus through molecular docking and dynamics simulations

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Abstract: Hepatitis E virus (HEV) is a single-stranded RNA virus, capable of infecting both humans and animals. This investigation targets ORF2 of HEV, as it plays an essential role in forming viral capsid. Inhibiting the capsid protein could prevent the virus from completing its life cycle and infecting new cells, making ORF2 an ideal target for new drug development, and the primary objective of this investigation is to identify the potential therapeutic candidate against HEV. The molecular docking analysis was conducted against the Hepatitis E virus ORF2 and out of the initially chosen 25 chemicals, eight demonstrated better binding affinities, particularly with Quercetin and Pinostrobin, which exhibited the most favorable binding energies. After that, theoretical ADMET analysis was analyzed to ensure the pharmacokinetics and safety profile of these therapeutic candidate. The stability of the maximum binding affinity containing compounds with the target protein was confirmed through molecular dynamics simulations over 100 ns timeframe. The finding of this investigation is highlighted as strong antiviral properties against the HEV, supported by in silico analysis, suggesting the urgent need for cost-effective and time-efficient strategies to discover potential therapeutic candidate against HEV. Further, laboratory experiments together with pre-clinical and clinical research are suggested to be carried out.

Keywords: Hepatitis E virus (HEV), ORF2 capsid protein, Molecular docking, Quercetin, Pinostrobin, Antiviral compounds, ADMET analysis

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