Pharmacophore-based virtual screening and *in-silico* study of natural products as potential DENV-2 RdRp inhibitors

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ABSTRACT

Dengue fever is a significant public health concern throughout the world, causing an estimated 500,000 hospitalizations and 20,000 deaths each year, despite the lack of effective therapies. The DENV-2 RdRp has been identified as a potential target for the development of new and effective dengue therapies. This research's primary objective was to discover an anti-DENV inhibitor using *in silico* ligand- and structure-based approaches. To begin, a ligand-based pharmacophore model was developed, and 130 distinct natural products (NPs) were screened. Docking of the pharmacophore-matched compounds were performed to the active site of DENV-2 RdRp protease . Eleven compounds were identified as potential DENV-2 RdRp inhibitors based on docking energy and binding interactions. ADMET and drug-likeness were done to predict their pharmacologic, pharmacokinetic, and drug-likeproperties . Compounds ranked highest in terms of pharmacokinetics and drug-like

appearances were then subjected to additional toxicity testing to determine the leading compound. Additionally, MD simulation of the lead compound was performed to confirm the docked complex's stability and the binding site determined by docking. As a result, the lead compound (compound-108) demonstrated an excellent match to the pharmacophore, a strong binding contact and affinity for the RdRp enzyme, favourable pharmacokinetics, and drug-like characteristics. In summary, the lead compound identified in this study could be a possible DENV-2 RdRp inhibitor that may be further studied on in vitro and in vivo models to develop as a drug candidate.

KEYWORDS

Anti-dengue; natural products; pharmacophore; virtual screening; molecular docking; molecular dynamic simulation

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