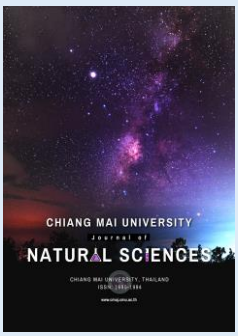

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Research article

Discovery of Drug Candidate from Various Natural Products as Potential Novel Dengue Virus Nonstructural Protein 5 (NS5) Inhibitor

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Abstract Dengue is a severe health problem, especially in under-developing countries like Indonesia. The government and the community have made various efforts. However, the current programs are focusing on controlling disease vector. Medical treatment so far only treats the symptoms. On the other hand, the development of antiviral compounds has been dominated by synthetic compounds which may have serious side effects. The potential of natural compounds in Asia is still largely unexplored. Dengue virus nonstructural protein 5 (NS5) is highly conserved in all serotypes. This study aims to screen several potential natural compounds to be developed as specific antiviral compounds targeting DENV NS5. This research conducted by using in silico approaches including data mining, molecular docking, and 2D-3D visualization. About 170 compounds from 88 organisms analyzed to get the top nine compounds with the highest affinity against NS5 protein. The top nine compounds are from the halichondramide, trigocherriolide, quinadoline, tryptoquivaline, and zingiberene groups. The docking results showed that these potential compounds have an affinity of about 67-100% higher than ribavirin. The visualization results show that these compounds are grouped into three different binding sites. They are RdRP, MTase, and the junction. Compounds that bind in RdRP are thought to interfere with the process of RNA viral synthesis, compounds that bind to MTase are thought to disrupt the viral RNA capping process, while compounds that bind between the two domains are thought to interfere NS5 structural integrity. The compound with the highest affinity is halishigamide A. Halishigamide A is known to have antimicrobial properties, but the action mechanism is still unknown. Compared to the control drug, the halishigamide A tends to have more dynamic movement and interaction to the target protein's binding site due to its residues' chemicals motive. Together, these results showed the potency of natural products as specific antiviral compounds targeting DENV NS5.

Keywords: Antiviral compounds, Bioinformatics, DENV-2 NS5, Halishigamide A, Ribavirin

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