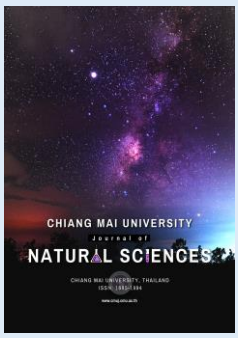

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Research article

In Silico Targeting DENV2's Prefusion Envelope Protein by Several Natural Products' Bioactive Compounds

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Abstract Dengue caused by the dengue virus (DENV) is a severe health problem in tropical regions such as Southeast Asia, especially Indonesia. Indonesian have used rhizome as traditional medicine for 1300 years. This study investigated the compounds from *Kaempferia galanga, Curcuma longa, Zingiber officinale, Curcuma aeruginosa, Curcuma zanthorrhiza, Alpinia galanga*, and *Allium sativum* as antivirals agents, explicitly targeting the DENV envelope protein to inhibit viral fusion. This study involved 121 bioactive compounds and DENV2's prefusion envelope protein. The virtual screening and molecular docking were done through occupied the Lipinski rule of five checker (http://www.scfbio-iitd.res.in/software/drugdesign/lipinski.jsp) and AutoDock Vina (https://pyrx.sourceforge.io/) respectively. The top nine compounds with the strongest binding affinity were galangin, kampferide, demetoxy curcumin, bisdemethoxycurcumin, β-selinene, 6-(hydroxymethyl)-1,4,4-trimethylbicyclo[3.1.0]hexan-2-ol, piperine, estra-1,3,5(10)-trien-17β-ol, and curcumin. These compounds' affinity values were significantly lower, around 45-62%, than chloroquine. Most of them interact with the kl hairpin and hydrophobic pocket formed by residues Val130, Leu135, Phe193, Leu198, and Phe279of critical domains that can interfere with the conformational change and rearrangement of protein dimer in the post-fusion stage. This study suggested that the galangin, demethoxycurcumin, and bisdemethoxycurcumin are considered the most potential compounds to be developed as anti-prefusion E DENV2 low-affinity and intense interaction with those.

Keywords: DENV2, envelope protein, in silico, viral fusion, viral infection

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