Research article

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

Arief Hidayatullah1, Wira Eka Putra1,2,*, Sustiprijatno3, Galuh Wening Permatasari4, Wa Ode Salma5, Diana Widiastuti6, Hendra Susanto1,2, Bayyinatul Muchtaromah7, Dewi Ratih Tirto Sari8,9, Febby Nurdini Ningsih10, Muhammad Fikri Heikal1, Alyana Mahdavikia Rosyada Yusuf1, and Aliyya Suci Arizona1

1 Department of Biology, Faculty of Mathematics and Natural Sciences, Universitas Negeri Malang, East Java, Indonesia
2 Department of Biotechnology, Faculty of Mathematics and Natural Sciences, Universitas Negeri Malang, East Java, Indonesia
3 Indonesian Center for Agricultural Biotechnology and Genetic Resources Research and Development, West Java, Indonesia
4 Indonesian Research Institute for Biotechnology and Bioindustry, Bogor, West Java, Indonesia
5 Department of Nutrition, Faculty of Public Health, Haku Oleo University, Indonesia
6 Department of Chemistry, Faculty of Mathematics and Natural Science, Universitas Padjadjaran, West Java, Indonesia
7 Department of Biology, Faculty of Science and Technology, Universitas Islam Negeri Maulana Malik Ibrahim, East Java, Indonesia
8 Department of Biology, Faculty of Mathematics and Natural Sciences, Brawijaya University, Indonesia
9 Research center of Smart Molecule of Natural Genetics Resources, Brawijaya University, Indonesia
10 Center of Pharmaceutical and Medical Technology, Agency for the Assessment and Application of Technology (BPPT), Serpong, South Tangerang, Indonesia.

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 antiviral 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 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 Phe279 of 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

Funding: This study was funded by PNBP Universitas Negeri Malang (Wira Eka Putra).