

Antiviral Activity of *Syzygium aromaticum* Leaf Extract Against Experimental Infections with Dengue Virus-1, -2, -3 and -4

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Dengue is a global public health issue. To date, there are no antiviral treatments to combat dengue. Plant-based products have become a primary source in the development of antiviral drugs. *Syzygium aromaticum* has been used in traditional medicine in most tropical countries. The objective of this study was to determine the anti-dengue viral activity of *S. aromaticum* leaf extract against experimental (dengue virus) DENV-1, DENV-2, DENV-3 and DENV-4 infections. Leaf extract was prepared in two-fold dilutions from neat to 1/1024 in normal saline. First, the cytotoxic effects were determined to select the minimum toxic concentration of leaf extract in both Vero cells and C6/36 cells. Then, plaque assay was done to determine the anti-viral activity of *S. aromaticum* leaf extract against experimental DENV infection. Based on the plaque assay results, plaque reduction was observed against DENV-1 at concentrations $>1/16$, DENV-2 at concentrations $>1/64$, DENV-3 at concentrations $>1/32$ and DENV-4 at concentrations $>1/16$. Based on the cytotoxicity assay results, concentrations higher than 1/64 and 1/32 were toxic to C6/36 cells after 5 and 24 h post-treatment, respectively whereas the concentrations higher than 1/32 and 1/4 were toxic to Vero cells after 5 and 24 h post-treatment, respectively. Water-based *S. aromaticum* leaf extract demonstrated anti-DENV activity against all four DENV serotypes in a dose-dependent manner while inhibiting the replication of DENV. Concentrations that are toxic to C6/36 cells and Vero cells were identified. These findings are the early steps in producing scientific evidence for the anti-viral activity of *S. aromaticum* leaf extracts against all four DENV infections. It is necessary to isolate and identify leaf chemical compositions and proper concentrations for further appropriate intake of leaf extract. More experiments will be conducted on the anti-viral activity of *S. aromaticum* leaf extracts on experimental DENV infections in Vero cells prior to clinical trials.

Keywords: Antiviral activity, Cytotoxicity, DENV, *Syzygium aromaticum* leaf extract.

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