

The *in vitro* effect of *Andrographis paniculata* on the viability and morphological changes induced by Vascular Endothelial Growth Factor on endothelial cells

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Vascular leakage, a hallmark of dengue hemorrhagic fever, is attributed to complex interactions between dengue viral (DENV) factors and the host immune response. Significantly elevated levels of Vascular Endothelial Growth Factor (VEGF) have been continuously reported in dengue hemorrhagic fever (DHF) patients, rendering it a potential biomarker of severity. Further, VEGF is known to drive the endothelial hyperpermeability, resulting in vascular leakage. *Andrographis paniculata* is a widely used medicinal plant in Sri Lankan traditional medicine, demonstrating promising antiviral activities against dengue. In this study, we examined its ability to modify the viability and morphological changes of the VEGF-induced EA.hy926 cells (EC). The effects of selected VEGF concentrations (50-2000 pg/mL) on EC were assessed using the Sulforhodamine B (SRB) assay, which were then compared with the results obtained after *A. paniculata* post-treatment. EC viability was >80% across all VEGF concentrations tested, indicating that VEGF was not toxic across all concentrations. Morphological observations revealed a prominent gap formation in the EC monolayer at high VEGF concentrations (>500 pg/mL), marking a 30-60% cell reduction in 50% of the observable view under the inverted light microscope at 20X magnification. The *A. paniculata* treatment of the VEGF-induced EC monolayer yielded over 80% EC viability at all VEGF concentrations (similar to that of VEGF-only). Further, the morphological observations revealed that VEGF-induced EC treated with *A. paniculata* maintained a tight monolayer with a 5-20% increase in the number of cells observed under the microscope than at high VEGF. These results show that *A. paniculata* post-treatment had effectively reversed the VEGF-induced morphological changes of the EC monolayer, highlighting its potential therapeutic use in DHF.

Keywords: *Dengue, VEGF, Andrographis paniculata, Endothelial hyperpermeability, Vascular leakage*

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