Breaking the cytokine storm: An *in-silico* study of bamboo shoot sterols as natural TNF-α brakes in severe Dengue

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Severe dengue is primarily driven by cytokine storm and increased vascular permeability. Tumor necrosis factor-alpha (TNF-α), a key proinflammatory cytokine plays a central role in this process by promoting endothelial dysfunction and amplifying the cytokine storm. TNF-α activates downstream signaling by binding three receptor molecules. Currently, dengue has no approved antiviral treatments, with clinical care limited to supportive measures. Therefore, modulating TNF-α activity presents a promising therapeutic strategy for severe dengue intervention. Recent advances have demonstrated the potential of small molecules, such as A7A, to inhibit TNF-α by stabilizing an asymmetric conformation of the trimer. This conformation restricts receptor recruitment to two subunits, thereby impairing TNF-α signaling. Traditional Sri Lankan medicine advocates the use of juice of juvenile shoots of *Bambusa vulgaris* as a treatment for dengue. This study explores the inhibitory potential of phytochemicals from *Bambusa vulgaris* to modulate TNF-α function. A total of 22 phytochemicals from juvenile *Bambusa vulgaris* shoots were identified through literature and subjected to *in silico* ADMET screening using SwissADME and pkCSM. Compounds compliant with Lipinski's rule of five were selected for further analysis. The crystal structure of TNF-α in its asymmetric, ligand-stabilized form (PDB ID: 6OP0) was subjected to 1000 ns molecular dynamics (MD) simulations using CHARMM36m forcefield in GROMACS (version 2024.1) to obtain a stable protein conformation for docking studies. Molecular docking studies were conducted using AutoDock Vina (Version v1.2.5). Several sterols—ergosterol, β-sitosterol, campesterol, stigmasterol, and stigmastanol—demonstrated strong binding affinities ranging from –12.4 to –12.9 kcal/mol, surpassing that of the positive control A7A. These hits were further validated via 1000 ns MD simulations. This study underscores the potential of *Bambusa vulgaris* phytochemicals, particularly sterols, as natural TNF-α inhibitors. The findings provide a foundation for the development of novel, dietary interventions targeting TNF-α in the management of severe dengue. Although the binding affinities observed are promising, further experimental studies are required to confirm the inhibitory potential of these sterols against TNF-α.

Keywords: *TNF-α, Bambusa vulgaris, Cytokine storm, Molecular docking, Molecular dynamics*