MOLECULAR DOCKING AND DYNAMIC STUDIES TOWARDS THE BINDING OF MULTIPOTENT PHYTOCHEMICAL WITH THE MAJOR TARGETS OF ALZHEIMER’S DISEASE

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Introduction: The Neuropathology of Alzheimer’s disease (AD) is multifactorial involving several targets and pathways contribute to its pathogenesis. A multi-functional phytochemical might modify the course of disease with greater efficacy and better utility as potential neuroprotective disease-modifying drugs.

Aim: To identify a multipotent phytochemical that is able to alter multiple targets involved in the pathology of AD and investigate the stability of binding and interaction.

Methods: The present study analysed the conformational orientation and binding affinity of 410 multipharmacological neuroprotective phytochemicals screened against potent molecular targets of AD. The docking calculations were performed with the Schrödinger’s maestro module using Glide combined with Induced Fit Docking which uses full flexibility to the docked ligands and active site residues. In order to gain some insight on the mode of binding and inhibition mechanism, molecular dynamics studies on Ligand-protein complex were carried out on the basis of molecular docking results using Gromacs software.

Results and discussion: The docking analysis ranked several phytochemicals that have high theoretical scores to bind to the proteins. The binding mode of the phytochemical that bound to all the target proteins with high affinity was studied. The simulations demonstrated that the protein-ligand complex stabilized by multiple hydrogen bonds was preferentially formed at the catalytic site.

Conclusions: The results highlighted in this study reveals the phytochemical capable of binding efficiently to more than two major molecular targets of AD could be a promising candidate for the development multi-target directed drug discovery for AD.