ABSTRACT

Alzheimer's disease is a neurodegenerative disorder caused by amyloid beta plaque aggregation due to β-secretase activity, which disrupts brain signaling and leads to neuronal death. Inhibition of β-secretase is a crucial strategy for preventing aggregation. Gallagic acid and ellagic acid have been shown *in vitro* as β-secretase inhibitors with IC_{50} values of 1.29×10^{-6} M and 3.9×10^{-6} M, respectively. Hexahydroxydiphenic acid is predicted to have similar potential due to its structural similarities and shared biosynthetic pathway, punicalagin biosynthesis. This study aims to predict the interactions of these compounds with β-secretase using *in silico* molecular dynamics simulations at 300 K and 1 bar for 50 ns. The analysis includes conformational stability (RMSD) and interaction energies (van der Waals and electrostatic).The results suggest that gallagic acid exhibits strong and stable potential as a β-secretase inhibitor. Despite meeting only one of Lipinski's Rule of Five (LogP = 1.78), its favorable ADME profile supports good bioavailability and distribution. The stability of the BACE1–gallagic acid complex is attributed to optimal ligand positioning in active site, polarity compatibility, and the formation of hydrogen bonds that strengthen ligand–protein interactions.

Keywords: Alzheimer's, β-secretase, amyloid beta, gallagic acid, ellagic acid, hexahydroxydiphenic acid, molecular dynamics.