Junior Science Communications
Faculty of Applied Sciences, UiTM Shah Alam
https://journal.uitm.edu.my/ojs/index.php/JSC

E-ISSN 2637-0689
Vol 36 2024

Colloquium on Applied Sciences - CAS 2023
17-18 July 2023, Faculty of Applied Sciences, UiTM Shah Alam, Malaysia

Molecular Dynamics Simulation of Indoxyl 3-O-β-D-apiofuranosyl-(1 → 6)-β-D-glucopyranoside from *Wrightia* genus against wild-type and quadruple mutant *plasmodium falciparum* Dihydrofolate Reductase (*pf*DHFR).

Nurdiana Abdul Rahman [a], Syahrul Imran Abu Bakar [a*]

Structured Abstract

Background: Compound Indoxyl 3-O-β-D-apiofuranosyl-(1 →6)-β-D-glucopyranoside from *Wrightia* genus undergone molecular dynamic simulation in complex with quadruple mutant *pf*DHFR and wild-type *pf*DHFR to identify the most effective interaction to disrupt the DENV replication mechanism.

Methods: Firstly, compounds that will be subjected to molecular dynamics simulation were chosen based on previous molecular docking results of the *Wrightia* genus compound. Then, the protein-ligand complex will go through a pre-processing step in Maestro's protein preparation module. Hence, the system builder step module will be applied to the optimized and minimized protein complex. The protein complex will be solvated using the TIP3P water model in a cubic boundary condition with a minimized volume in this procedure. Next, the minimized system will be subjected to molecular dynamic simulation for 100 ns using periodic boundary conditions and particle-mesh Ewald (PME) for long-range electrostatics under NPT ensemble conditions at a constant pressure of 1.0 bar. Lastly, Molecular Mechanics Generalized Born Surface Area (MM-GBSA) analysis employing van der Waals (vdW) radii sets will be conducted using Thermal_MMGBSA.py script of Prime module v3.1 of the Schrödinger Suite 2018-4 to determine the binding free energy of the complexes.

Results: The findings result shows that indoxyl compounds form the greatest number of interactions with quadruple-mutant *pf*DHFR compared to wild-type mutant *pf*DHFR. The indoxyl ligand fits well in the binding site of the protein quadruple mutant *pf*DHFR through the simulation compared to wild-type *pf*DHFR. Indoxyl ligand in complex with quadruple mutant *pf*DHFR also interacts well with binding site residues Asp54, Gly44, Ser108, Thr107, Ser167, Ile164, and Phe58 for more than 30% of the simulation time.

Conclusion: The binding interaction of indoxyl and quadruple mutant *pf*DHFR in the complex could take place effectively to disrupt the DENV replication mechanism.

Keywords: Molecular dynamic simulation, wild-type *pf*DHFR, quadruple mutant *pf*DHFR.

*Correspondence: syahrulimran@uitm.edu.my
School of Chemistry and Environment, Faculty of Applied Sciences, Universiti Teknologi MARA, Shah Alam, Malaysia