RS21-016: OP7

Anti-Covid 19 Drug Candidates from Sri Lankan Natural Products: In-Silico Approach to Identify Inhibitors of SARS COV 2

S.M. Abdulla[1,3], G.A.S. Premakumara[2#], P. Ranasinghe[3], C. Udawatte[4]

[1]Department of Chemistry, Faculty of Science, University of Colombo
[2]Department of Basic Sciences and Social Sciences, Faculty of Nursing, University of Colombo
[3]Herbal Technology Section, Industrial Technology Institute, Sri Lanka
[4]College of Chemical Sciences, Institute of Chemistry Ceylon

[#]sirimal@dss.cmb.ac.lk

Introduction: The development of potent antiviral drugs against COVID-19 is of utmost importance. In this context, computational pharmacology may play a lead role. This study aimed on in-silico screening of Sri Lankan natural products by molecular docking (MD) and molecular dynamics studies against SARS-CoV-2 main protease Mpro responsible for multiplication.

Objective: To identify plant-derived compounds of Sri Lankan flora as antiviral agents with protease inhibitory potential against SARS-CoV-2 pandemic.

Methods: Four hundred & eighty molecules isolated from Sri Lankan natural resources were virtually screened for anti-viral activities against SARS-CoV-2 main protease Mpro. Binding energies were calculated using Auto Dock Vina and the active site of SARS-CoV-2 was defined using data from literature studies. The results were compared with that of a synthetic construct of N3, a peptidomimetic inhibitor of coronavirus main protease. The complexes with favorable binding interactions were filtered and subjected to molecular dynamic studies using AMBER with GPU acceleration where the dynamic behavior of protein-ligand complex at different time scales was determined. Visual Molecular Dynamic (VMD, version 1.9.4) was used to study the atom trajectories and the Root Mean Square Deviation (RMSD) of each of the protein ligand complex. The RMSD of the SARS-CoV-2 and drug complex was analyzed through a 100ns trajectory and results were compared with that of N3. Further, the ADME parameters, pharmacokinetic properties and the druglike nature of identified compounds were studied.

Results: One of the natural products, SLNP_012, showed favorable interactions with the binding pocket of Mpro as compared to that of N3. SLNP_012 showed up to 5 possible H-bond with the active site residues. It also showed favorable physiochemical properties for oral bio availability with a very high gastrointestinal absorption and blood brain barrier permeation.

Conclusions: Sri Lankan plant derive natural product SLNP_012 could be a potential anti-viral agent for SARS-CoV-2 infection.

Keywords: SARS-CoV-2, Molecular docking, Molecular dynamics, Sri Lankan Natural Products.