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Molecular Docking and Dynamics of 2,5-Pyrrolidinedione Analogue Using the SARS-CoV-2 Main Protease as Target Protein

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ABSTRACT

Backgrounds: The goal of this study was to employ molecular docking and dynamics to investigate the interactions of twelve maleimide and succinimide derivatives (SD1-SD12) with the SARS-CoV-2 main protease (Mpro) (PDB ID:6LU7).

Materials & Methods: Molecular docking and molecular dynamics simulations were performed to study the interaction of twelve derivatives (SD1-SD12) of maleimide and succinimide with the SARS-CoV-2 main protease (Mpro) (PDB ID:6LU7). Four compounds (SD1, SD4, SD8, and SD12) were selected for further molecular docking analysis based on their binding energies (-7, -7.3, -7.3, and -7.2 kcal/mol, respectively), which were lower than the other compounds and close to the control crystal (-8.5 kcal/mol). Molecular docking was used to find the binding energy of non-bonding interactions between ligand and receptor in connection to the SARS-CoV-2 main protease (PDB code: 6LU7).

Findings: Molecular docking results showed binding energies ranging from -7.3 to -6.5 kcal/mol for the 2,5-pyrrolidinedione analog, the co-crystallized control ligand exhibited a binding energy of -8.5 kcal/mol. SD1 exhibited the best binding mode and drug-like properties to inhibit the SARS-CoV-2 main protease compared to the other ligands. Among the demonstrated interactions with the protein, RMSD (root mean square deviation) values decreased due to the improved and more stable states.

Conclusion: Overall, the current study proposed a strategy to combat COVID-19 using pharmaceuticals as prospective agents, which might also serve as a starting point for drug discovery. Additional studies on the target compounds are expected to yield substantial advances in the fight against COVID-19.

Keywords: Cyclic imides, Succinimide derivatives, Maleimide derivatives, Molecular docking, SARS-CoV-2 main protease (Mpro)

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