سمینار هفتگی ماده چگال نرم

In silico exploration of novel protease inhibitors against coronavirus 2019 (COVID-19)

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Abstract

The spread of SARS-CoV-2 has affected human health globally. Hence, it is necessary to rapidly find the drug-candidates that could be used to treat the infection. Since the main protease (Mpro) is the key protein in the virus's life cycle, Mpro is served as one of the critical targets of antiviral treatment. We employed virtual screening tools to search for new inhibitors to accelerate the drug discovery process. The hit compounds were subsequently docked to the active site of SARS-CoV-2 main protease and ranked by their binding energy. Furthermore, in-silico ADME studies were performed to probe for adaption with the standard ranges. Finally, molecular dynamics simulations were applied to study the protein-drug complex's fluctuation over time in an aqueous medium. This study indicates that the interaction energy of the top ten retrieved compounds with COVID-19 main protease is much higher than the interaction energy of some currently in use protease drugs such as ML188, nelfinavir, lopinavir, ritonavir, and α-ketoamide. Among the discovered compounds, Pubchem44326934 showed the druglike properties and was further analyzed by MD and MM/PBSA approaches. Besides, the constant binding free energy over MD trajectories suggests a probable drug possessing antiviral properties. MD simulations demonstrate that GLU166 and GLN189 are the most important residues of Mpro which interact with inhibitors.

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