

Virtual screening of clinical trial compounds for COVID-19 against the SARS-CoV-2 main protease

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Abstract—The COVID-19 outbreak occurred in 2019 that has been resulted in the global crisis. The discovery of effective compounds to contain the virus is a positive step to complete annihilation alongside other strategies. Since the design and discovery of a new drug requires a lot of cost and time, the use of virtual screening of small compounds against SARS-CoV-2 proteins can help to identify the potential treatments. The main protease (M^{PRO}) of SARS-CoV-2 plays a very important role in the viral life cycle and is considered one of the most promising targets for drug discovery against SARS-CoV-2. In this study, we have used and screened 1266 compounds from the NCBI PubChem database, all of which are in clinical trials against COVID-19. structures of all compounds were geometry optimized using Open Babel. The M^{PRO} structure (PDB Code = 6LU7) was retrieved from the RCSB protein database. Enzyme was prepared for docking screening and finally convert to PDBQT File. All of molecular docking screening related to 1266 compounds were performed using AutoDock Vina, and the possible candidate lead compounds were selected based on their binding energy. The binding energies (E_b) were obtained in the range of -3.3 to -10.2 kcal / mol. For better analysis and comparison of the achieved data, the anti- M^{PRO} compound from Pfizer's protease inhibitor, PF-07321332, has been docked and evaluated against enzyme ($E_b = -8.5$). The number of 37 compounds were achieved with higher binding energies compared to Pfizer's inhibitor. Finally, top compounds (PubChem CID: 155803731, 46215462, 155803730) are suggested to inhibit the main protease of SARS-CoV-2 virus. The results of this research are available to provide suggestions for prioritization in subsequent research of compounds that will have the ability to strongly inhibit the virus.

Keywords—SARS-CoV-2, M^{PRO} , Virtual screening, COVID-19, Docking

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