Chapter-07

DETERMINATION OF POTENTIAL DRUG CANDIDATES FOR SARS-COV-2: PART 1

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INTRODUCTION

Since December 2019, a significant part of the world has endured from the episode of Coronavirus disease 2019 (COVID-19), the infection brought about by a novel human coronavirus, serious acute respiratory syndrome coronavirus 2 (SARS-CoV-2)(Zhou P, 2020). Since 2019-nCoV is profoundly homologous with SARS-CoV, it is viewed as a nearby relative of SARS-CoV. The International Virus Classification Commission (ICTV) grouped 2019-nCoV as Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) on February 11, 2020. Simultaneously, WHO named the disease brought about by 2019-nCoV as COVID-19. Normal side effects of an individual contaminated with COVID-19 incorporate respiratory manifestations, fever, cough, shortness of breath, and dyspnea. In more serious cases, disease can cause pneumonia, extreme intense respiratory condition, kidney failure, and even death. There is at present no particular medication or treatment for illnesses brought about by SARS-CoV-2(Huang C., 2020).

Coronavirus pandemic takes us back in the set of experiences reminding to 1918 influenza pandemic brought about by the H1N1 infection which contaminated around 500 million and caused significant deaths of around 50 million individuals. Viral pandemic greatly affects individuals from contamination, morbidity, mortality and dread of economic precariousness. In December 2019, individuals contaminated from this infection announced having side effects like that of pneumonia. The coronaviruses comprise of club-like projections that cause colds and intense upper respiratory trouble, additionally at times mellow pneumonia and intense gastroenteritis. They perpetrate various disorders in a wide scope of mammals and well evolved creatures and are contagious in human beings too(Gupta MK, 2020). Despite the fact that SARS-CoV-2 has a lower mutation rate than most RNA infections, transformations absolutely amass and result in genomic variety both between and inside individual infected patients. Hereditary heterogeneity empowers viral variation to various hosts and various conditions inside hosts and is regularly connected with progression of disease, drug resistance and treatment result(Franziska Hufsky, 2020).

The spread of this lethal infection must be directed by forcing curfew, lockdown, isolate, seclusion and social distancing alongside upgrade of immunity. Currently, because of unavailability of authorized antibodies or medications, the cure is confined to steady mind with not many repurposed drugs.

CONCLUSION

The COVID-19 continues to spread across the world with a very fast pace. In India, out of the 3 approved vaccines, Covishield based on Serum Institute of India and
Covaxin based on Bharat Biotech have been dispatched from their respective facilities to different locations across India. To conclude our study, we had focused on three target proteins, replicase polyprotein, nucleocapsid and envelope protein and followed in silico approach to carry out virtual screening (molecular docking) and find potential drug candidates against them to our best potential. Our docking studies revealed the following drug ligands as the best drug candidates for the following target proteins:

1. Replicase polyprotein: Ritonavir (-6.9 kcal/mol) showing interactions such as hydrogen bonding with ASN 55, carbon-hydrogen interactions with PRO 7, Pi-alkyl with ALA 10, and Pi-sigma interactions with LYS 249.

2. Nucleocapsid: Lopinavir (-7.6 kcal/mol) showing interactions such as hydrogen bonding with TRP 132 residues. It fits in the cavity of the protein and inhibits its activity. Lopinavir ligand has pi sigma interaction with ILE 131 and LYS 65 and ALA 134 whereas Ifenprodil has interactions with three residues – ILE 131 and ARG 68.

3. Envelope: Rutin (-6.5 kcal/mol) shows hydrogen bond different with other with TYR42 and LEU51 but it shows hydrophobic interaction, pi-pi stacked with TYR59, and pi-alkyl with VAL58 and VAL62.

REFERENCES


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