In silico screening of therapeutic agents for COVID-19: A drug repurposing approach

Sadia Akter[1], Md. Riad Chowdhury[2]

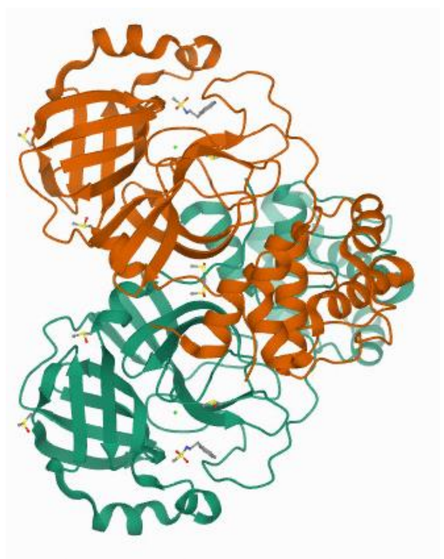
[1]Faculty of Medicine, Institute of Applied Health Sciences, Chittagong 4202, Bangladesh

[2]Department of Pharmacy, International Islamic University Chittagong, Chittagong 4318, Bangladesh

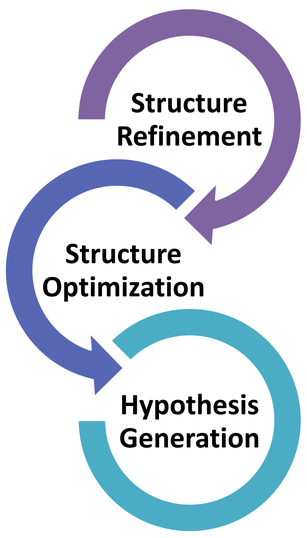
Abstract

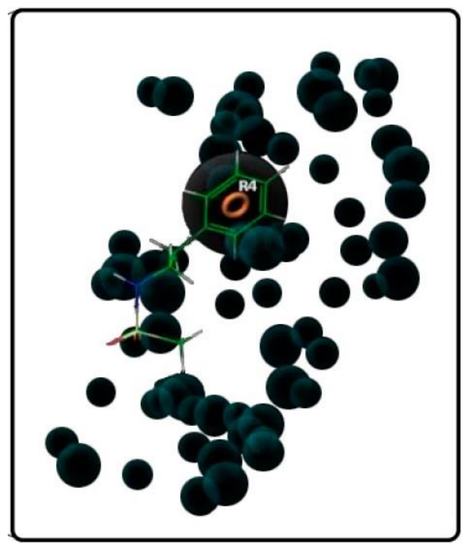
Since the end of December 2019, novel coronavirus has spread extensively throughout the world. Despite the introduction of different vaccines, a cure is still required to fight against the infection. Herein, we performed computational approaches including pharmacophore hypothesis, virtual screening and MM/GBSA analysis to identify a series of drugs that are suggested to be repurposed for the treatment of novel coronavirus disease. Targeting the viral receptor SARS-CoV-2 main protease, total of 16 drugs are shortlisted from a large database of approved and investigational drugs. Furthermore, MM/GBSA analysis revealed seven drugs specifically, ornidazole, sapanisertib, napabucasin, daniquidone, lenalidomide, salicylamide and indoximod, which inhibited the main protease with the highest binding scores. These drugs can feasibly be subjected to further *in vitro* and *in vivo* analysis to justify the mechanism against COVID-19.

Methodology

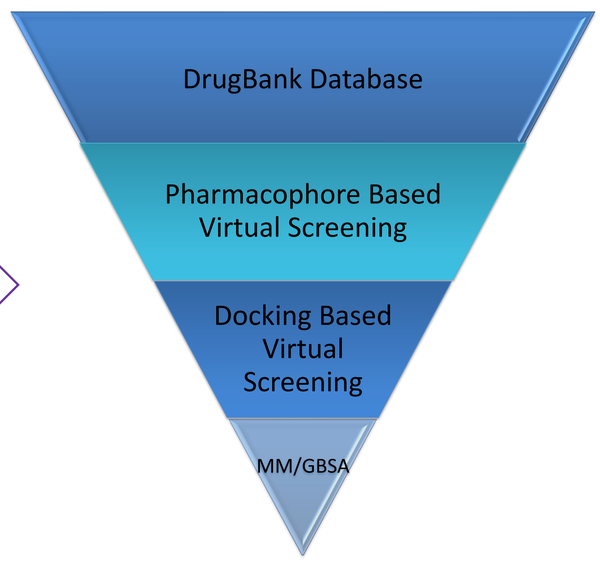


Crystal Structure of COVID-19 Main Protease





Pharmacophore Hypothesis



Results

Table-1: 16 potential drugs obtained through virtual screening.

Drug Name	Category	Docking score (kcal/mol)
Salicylamide	Analgesic	-7.10
Ornidazole	Antibiotic	-6.67
Eslicarbazepine	Anticonvulsants.	-6.56
2-(aminomethyl)phenol	Benzene Derivatives	-6.52
Fluindione	Anticoagulants	-6.34
Trioxsalen	Vitiligo	-6.34
Orotic acid	Pyrimidines	-6.29
Napabucasin	Anticancer	-6.25
Sapanisertib	Anticancer	-6.24
Daniquidone	Anticancer	-6.13
Norepinephrine bitartrate	Cardiovascular agent	-6.12
Aminophenazone	Analgesic	-6.10
Indoximod	Immunometabolic	-6.05
Taribavirin Hydrochloride	Antiviral	-6.03
lenalidomide	Anticancer	-5.99
Mercaptopurine monohydrate	Anticancer	-5.99

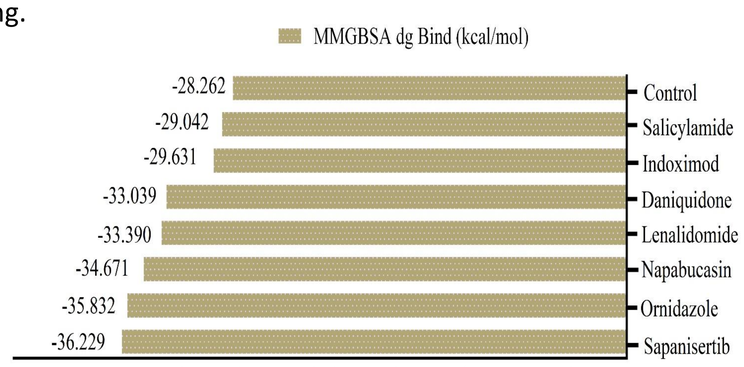


Figure-1: 7 Best hits obtained through MM/GBSA analysis

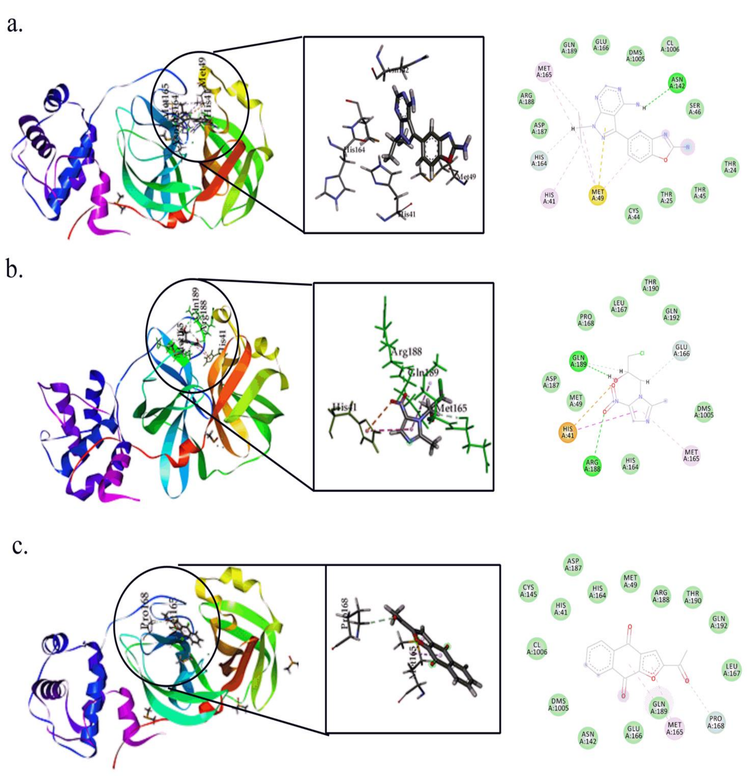


Figure-2: 3D and 2D interactions of **a.** Sapanisertib **b.** Ornidazole **c.** Napabucasin **d.** Lenalidomide **e.** Daniquidone**. f.** Indoximod **g.** Salicylamide with SARS-CoV-2 main protease.

Conclusion

In this study, structure based virtual screening identified several categories of drugs against SARS-CoV-2 main protease. Through docking based virtual screening, 16 drugs are found to form better interaction than the control. Among those, seven drugs namely ornidazole, sapanisertib, napabucasin, daniquidone, lenalidomide, salicylamide and indoximod exhibited promising MM/GBSA scores with the receptor active site. These drugs might be subjected to further analysis for repurposing against novel coronavirus disease.

References

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