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In-Silico Prediction of Anti COVID-19 Therapeutics Maximum Binding Affinity with *Homo sapiens* Acrosomal Protein SP-10

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Abstract

Infectious virus diseases have significant impacts on public health and emerge at an unprecedented rate. Compare to all viral diseases, combating COVID-19, that is caused by the SARS-CoV-2 virus was a big challenge to the researchers. Among all the therapeutics, antiviral drugs, corticosteroids, and Disease-Modifying Anti-Rheumatic Drugs (DMARDs) occupy a prominent position in declining the COVID-19 mortality rate. With the advent of science and technology, recent clinical studies extended towards the assessment of Multi-Drug Therapy (MDT) impact on invading the pathogen and adverse effects on cellular metabolism. Recent studies showed that MDT also affects major cellular functions such as fertility, however, the interactions of Anti COVID-19 Therapeutics (ACTs) with the fertility-related biomolecules are not yet clear. In the current study, I show the interaction of ACTs such as Dexamethasone, Remdesivir, and Baricitinib with the *Homo sapiens* acrosomal protein SP-10 using molecular docking studies. Among all the drug interactions with the SP-10 protein structure, Dexamethasone showed the highest binding affinity -5.9, followed by Remdesivir -5.3 and Baricitinib -5.0 kcal/mol. The interaction between ACTs and human SP-10 might help to unveil the fertility issues that arise in males during COVID-19 disease management.

Keywords: Anti COVID-19 Therapeutics, *Homo sapiens* acrosomal protein SP-10, molecular docking studies, fertility.

INTRODUCTION

The major challenge associated with unsustainable population growth is exacerbating health and disease management strategies [1]. The steep rise in the global population evoked the attention of researchers, chiefly to explore various technologies to fulfil the essential needs in the health sector. Compare to all the microbial diseases, Coronavirus disease (COVID-19) that was caused by the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) virus, management is very difficult with the limited drug resources [2]. With the advent of science and technology, researchers are exploring millions of naturally derived and synthetic compounds for the betterment of human life [3]. To combat COVID-19 effectively and decline the mortality rate globally, FDA authorized the Multi-Drug Therapeutics (MDT) in the combination of Dexamethasone, Remdesivir, and Baricitinib because of their immense advantage on the invading pathogen [4,5]. However, prescribing more than one drug together may cause serious side effects including headache, fever, dizziness, skin rashes, nausea, vomiting, diarrhea, and drowsiness to the patients [6,7].

Remdesivir is a carboxylic ester-derived broad-spectrum antiviral prodrug of adenosine triphosphate (ATP) analog, used in the disease management of RNA viruses such as Ebola, Middle East respiratory syndrome coronavirus (MERS-CoV), and COVID-19 that was caused by SARS-CoV2. *In-vivo* activated Remdesivir competes with the adenosine triphosphate for integration into RNA and inhibits the mechanism of action of viral RNA dependent RNA polymerase to terminate the RNA transcription, this fails in viral RNA production [8].

Dexamethasone is a synthetic fluorinated adrenal corticosteroidal compound with potent anti-inflammatory properties used to treat COVID-19, respiratory, hematologic, rheumatic, collagen, endocrine, dermatological, allergic, ophthalmic, gastrointestinal, neoplastic, edematous disease conditions. The FDA-approved Dexamethasone was prescribed in the combination with Remdesivir to reduce the mortality rate of COVID-19 patients [9].

Baricitinib is a potential disease-modifying antirheumatic drug (DMARD), that acts as an anti-

inflammatory, immunomodulating and antineoplastic agent, by showing a potent inhibition effect against Janus kinase 1 (JAK1) and 2 (JAK2). Because of its positive benefits in COVID-19 therapy and specific mechanism of activity, FDA authorized to use of Baricitinib in combination with Remdesivir on 19 November 2020 for the treatment of COVID-19 in severe emergency conditions to decrease the death rate and various other complications [10].

However, a few clinical reviews and case studies support the side effects of antiviral drugs, corticosteroids, and DMARDs, but the interactions of these medicines with fertility-related biomolecules are not clearly understood [11]. To investigate the possible interaction of ACTs like Dexamethasone, Remdesivir, and Baricitinib with the acrosomal protein, in the current study *in-silico* binding affinity analysis was carried out with the *Homo sapiens* acrosomal protein SP-10, that play an essential role in fertilization [12-14].

MATERIALS AND METHODS

Preparation of Protein

Before molecular docking, the *Homo sapiens* acrosomal protein SP-10 protein sequence with the accession number AAB28238.2 was retrieved from National Centre for Biotechnology Information (NCBI). Three-dimensional structure was predicted for the obtained sequence by template-based modeling using the GalaxyTBM server [14, 15]. The protein was prepared for molecular docking studies by using BIOVIA Discovery Studio software and PyRx Virtual Screening software [16].

Preparation of Ligand

The chemical structures of anti COVID-19 therapeutics such as Dexamethasone (5743), Remdesivir (121304016), and Baricitinib (44205240) were retrieved from PubChem database site in .sdf format and energy minimization was done for the selected ligands by using PyRx Virtual Screening software [16]. The prepared ligands were saved in the PDBQT (Protein Data Bank, Partial Charge(Q), & Atom Type (T)) formats that are essential for finding binding affinity in docking [16].

Molecular Docking

Molecular docking studies were conducted to obtain the maximum binding affinity of ACTs such as Dexamethasone, Remdesivir, and Baricitinib with SP-10 protein using Autodock vina of PyRx Virtual Screening software [16]. By using the BIOVIA Discovery Studio SP-10 protein amino acids residues interactions with the ligands were visualized [17].

RESULTS AND DISCUSSION

Preparation of Protein

To assess the binding efficiency of ACTs with *Homo sapiens* acrosomal protein SP-10, the protein was initially screened in BIOVIA Discovery Studio software to remove the heteroatoms (HETATM) and water molecules that are responsible for the unwanted interactions while docking. The protein structure predicted using the GalaxyTBM server, did not have HETATMs and water molecules. To prepare the SP-10 for the docking, polar hydrogens were added and the prepared structure was primarily saved as .pdb and converted to Pdbqt with the AutoDoc interphase of PyRx.

Ligand Preparation

Before molecular docking, Energy Minimization (EM) was done to decrease the overall energy potential of Dexamethasone, Remdesivir, and Baricitinib ligands and SP-10 using AutoDock interphase of PyRx. After EM, the prepared protein was saved in pdbqt format, which is essential for molecular docking studies.

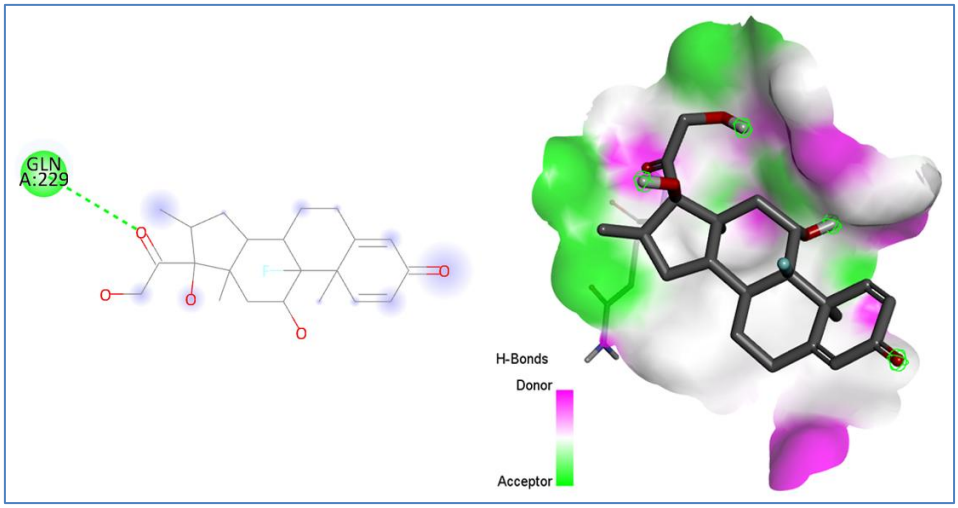
Molecular docking analysis

To investigate the binding affinity and possible interaction of Anti COVID-19 Therapeutics such as Dexamethasone, Remdesivir, and Baricitinib against *Homo sapiens* acrosomal protein SP-10 structure, the Grid parameters (X, Y, and Z attributes); Center: X:181.6634, Y: 12.5753 and Z: 96.2337 and Dimensions: X: 70.1273, Y: 55.1820 and Z: 62.6558 Angstroms that are essential for molecular docking were obtained from PyRx. The results of binding affinity, rmsds, and amino acid residues involved in H bond formation between the ligands and SP-10 protein were curated in Table-1 and Figure 1.

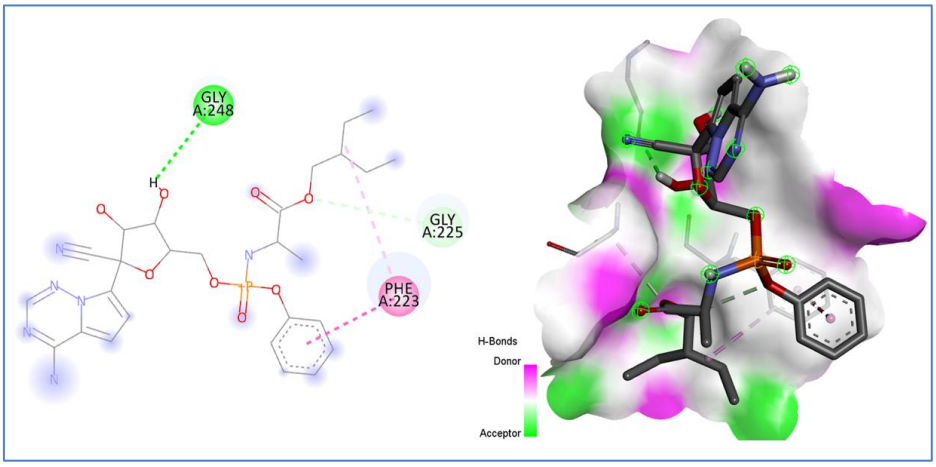
Table-1: Binding affinity and the amino acid residues involved in H bond formation between the ligands and SP-10 protein structure

Ligands	Homo sapiens acrosomal protein SP-10			
	Binding affinity (kcal/mol)	RMSD/UB	RMSD/LB	Amino acid Residues involved in H bond formation
Dexamethasone	-5.9	0	0	Gln-229
Remdesivir	-5.3	0	0	Gly-248
Baricitinib	-5	0	0	Thr-182, Glu-206 and Ser-260

A. Dexamethasone



B. Remdesivir



C. Baricitinib

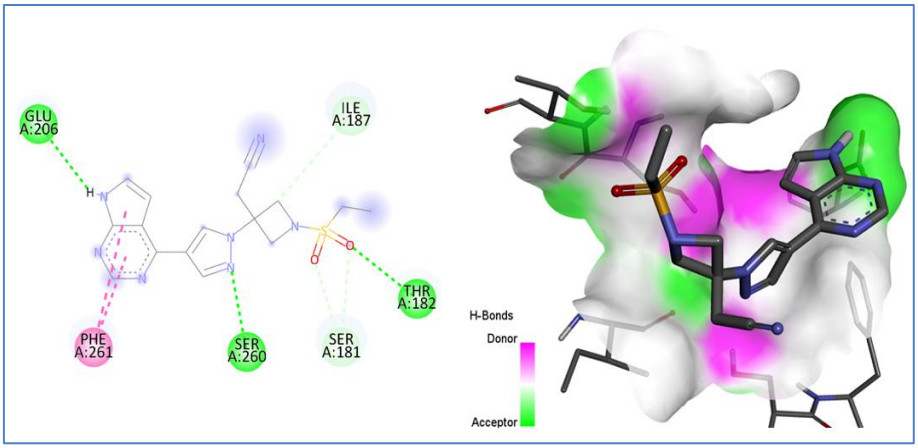


Fig-1: 2D interaction profile of amino acid residues involved in hydrogen bond with the ligands (A. Dexamethasone, B. Remdesivir, C. Baricitinib): Green color denotes the H bond interaction between amino acid residues and ligand.

CONCLUSION

Through the *in-silico* analysis, Dexamethasone showed the highest binding affinity -5.9, followed by Remdesivir -5.3 and Baricitinib -5.0 kcal/mol. The hydrogen bond interaction of SP-10 amino acid residues with the ligands is as follows Gln-229 with Dexamethasone, Gly-248 with Remdesivir, and Thr-182, Glu-206, and Ser-260 with Baricitinib. Among the

three drugs, Dexamethasone exhibited the maximum binding affinity with SP-10 protein, which indicates Dexamethasone might be responsible to assess the functionality of the SP-10 protein that plays a major role in fertility. The reported docking results provide leads to perform *in-vitro* and *in-vivo* studies to address the male fertility apprehensions.

AUTHOR CONTRIBUTION

The author made substantial contributions to the design of the work, analysis, interpretation of data, drafting the work, and revising critically for important intellectual content. The author agreed to submit the research paper to the current journal.

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CONFLICTS OF INTEREST

The author declares no conflict of interest.

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