Molecular Docking suggests repurposing of Brincidofovir as a potential drug targeting SARS-CoV-2 "COVID-19" ACE2 receptor and main protease

Mostafa A. Hussien (maabdulaal@kau.edu.sa)
King abdulaziz university https://orcid.org/0000-0002-4803-167X
Ahmed E.M. Abdelaziz
University of Calgary

Research Article

Keywords: Novel Coronavirus; SARS-CoV-2; Molecular Docking; ACE2 Receptor; 3C-like Protease; Brincidofovir; COVID-19

Posted Date: June 18th, 2020

DOI: https://doi.org/10.21203/rs.3.rs-35787/v1

Abstract

The current outbreak of the highly transmittable and life-threatening treme intense respiratory disorder coronavirus 2 (SARS-CoV-2) has advanced rapidly and posed a global health emergency. Many clinical trials are now being conducted to test possible therapies. To assist, the molecular docking was applied on some selected FDA-approved drugs, previously used in epidemics, and the top ten compounds were selected. These ten well-characterized drugs, previously used to treat Malaria and Ebola infections, were screened based on their interactions with the SARS-CoV-2 ACE2 Receptor and 3C-like Protease. Compared to the other nine medicines, Brincidofovir, an ether lipid ester analog of cidofovir with potent antiviral activity, showed the highest docking scores and binding interactions. Therefore, Brincidofovir worth further investigations and clinical trials as a possible therapeutic agent for the COVID-19 disease .

1. Introduction

Humankind has previously witnessed the outbreak of many life-threatening pathogens including Ebola, Zika, the Middle East respiratory syndrome (MERS) coronavirus, Severe Acute respiratory syndrome (SARS) coronavirus and nowadays, the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) [1-5]. The novel coronavirus has initially spread from china and propagated rapidly throughout the globe and has received worldwide attention due to its alarming levels of transmission and aggressive behavior in causing acute respiratory disease. The virus was then officially declared pandemic by the World Health Organization (WHO).

Researchers throughout the globe are working around the clock to develop potential vaccines and drugs to fight SARS-CoV-2 the causative agent of the COVID-19 disease. However, developing a new drug or vaccine usually takes a long time as it should be intensively tested and confirmed safe through clinical trials before they can be approved for human use [6]. Therefore, repurposing FDA-approved drugs seems to be a quicker way to treat patients who otherwise have no option. The SARS-CoV-2 is a single-stranded positive-sense RNA virus that relies on its spike (S) protein to attach and enter the target cells [7, 8]. The virus S protein binds to the host cell angiotensin-converting enzyme 2 (ACE2) receptor allowing the virus particles to enter the cells [7, 9]. Thus, blocking the ACE2 receptor reveals a effective therapeutic target for drug discovery to prevent the SARS-CoV-2 transmissibility. Besides, the two coronavirus proteases, designated 3-chymotrypsin-like protease (3CLpro) and a papain-like protease (PLpro) were previously considered vital targets to combat the SARS and MERS Coronavirus epidemics [8]. These two proteases were shown to be highly conserved with the novel SARS-CoV-2, especially in the functional regions [8]. Viruses use their proteases to breakdown its viral peptides into functional units essential for its replication and packaging inside the host cells, thus considered anti-viral drug targets.

Molecular docking is a popular bioinformatic modeling tool broadly used in structure-based drug design [10]. It is an efficient way to predict the type of interaction, binding affinity and the appropriate target binding sites between the drug and corresponding receptor using, for instance, scoring functions [10, 11].

Elucidating the binding behavior has an important role in the rational drugs-design as well as to explicate fundamental biochemical processes [10, 11].

In this study, molecular docking was performed on dozens of FDA-approved drugs and the top ten hits, previously used in the treatment of malarial, fungal/bacterial and Ebola infections and FDA-approved/fast-tracked for human treatment, were selected. The selected drugs used in this study were performed by the MOE modeling program to predict the binding sites and their docking score.

2. Materials And Methods

2.1. Molecular docking Method

2.1.1. Software and machinery used

All docking studies calculated and characterized by the MOE program. Drug Preparation was done by changing the two-dimensional structure of the drugs into a three-dimensional structure. Three-dimensional structure optimization of compounds was done by geometry optimization. Geometry optimization was a process to minimize total energy so that the structure of the most stable test compound was obtained, characterized by a decrease in the overall energy value of the structure of the test drugs. In geometry optimization results a shift in the structure of compounds into the most stable structure, so that there was a decreasing energy value of the structure of the test compound.

2.1.2. SARS-CoV-2 protease and receptor structure.

Generation of the protein structures and the crystal structure of the new COVID-19 Protease (PDB code = 1Q2W) and ACE2 Receptor (PDB code = 6M0J) were retrieved from the Protein Data Bank (http://www.rcsb.org/pdb/welcome.do) [12]. All bound solvent, ligands and metal ions removed from the proteins and then we added hydrogen atoms for optimization.

2.1.3. Molecular docking procedure

The docking protocol was done against the SARS-CoV-2 ACE2 receptor (PDB code = 6M0J), the SARS-CoV-2 3CL protease (PDB code = 1Q2W) and its four active sites. The active sites were isolated and used as dummies atoms. The docking strategy was performed by using MMFF94x force field [13]. The Dock scoring in MOE software was done through the London dG scoring function. flexiable rotatable bonds were allowed for all Drugs, and the best five binding poses were used for analysis to get the best score. We used the database browsers to compare the docking poses to the drug inside the reciptore structure and to obtain RMSD of the docking pose. To rank the binding affinity of all drugs toward the protein molecule, the binding free energy and hydrogen bonds between the compounds and amino acid in the receptor have been calculated [14]. Also, the RMSD of the drug position compared to the docking pose was used in the ranking. RMSD, as well as the docking score of the native drug within the corresponding receptor, were used [13-16].

3. Results And Discussions

Molecular docking and other computer-related methods are efficient tools broadly used to understand the molecular aspects of protein-ligand interactions during drug discovery against many of previous emerging and fatal diseases including SARS coronavirus [10, 11]. In this study, virtual screening of several FDA-approved/fast-tracked drugs were performed against the SARS-CoV-2 ACE2 host receptor (PDB code = 6M0J), the SARS-CoV-2 3CL protease (PDB code = 1Q2W) and its four active sites, in order to find the most predicated drug-ligand interactions. The presented parameters include the docking scores, ligand binding efficiency and hydrogen bonding interactions. The top ten ranked compounds were selected and presented in Table 1-6 and Figure 1-4. These ten drugs include four antivirals (*Favipiravir, Ribavirin, Brincidofovir, and Galidesivir)*, four anti-malarial (*Chloroquine, Mefloquine, Primaquine, and Tafenoquine)* and two antimicrobial agents (*Doxycycline and Atovaquone)*. Whether we docked against the ACE2 receptor (PDB code = 6M0J), the SARS-CoV-2 3CL protease (PDB code = 1Q2W) or the four main active sites within the SARS-CoV-2 3CL protease, the docking scores of the 10XC19 drug)*Brincidofovir* or BCV) shown to be the top hit (ranked #1) compared to the other nine drugs. The docking scores for the BCV were -10.83, -8.30 and -9.02 towards the SARS-CoV-2 3CL protease active site 1 (PDB code = 1Q2W), the SARS-CoV-2 3CL whole protease (PDB code = 1Q2W) (Tables 1-2 and Figure 1-2) and the ACE2 receptor (PDB code = 6M0J) (Tables 3-4 and Figure 3-4), respectively. The antimalarial drug *Tafenoquine* comes second in the rank where it scored -8.15 and -7.76 with the AC2 receptor and the SARS-CoV-2 3CL protease active site 1, respectively (Table 1 and 3).

Tab. 1 Docking score and energy of the Malaria and Ebola drugs and 1Q2W of COVID-19 with site 1 of COVID-19 Protease (PDB code = 1Q2W)

Drug name	Score	rmsd_refine	E_conf	E_place	E_score1	E_refine	E_score2	Log P	Log P
Atovaquone	-6.34	2.92	60.20	-69.94	-10.85	-32.69	-6.34	6.48	6.48
Chloroquine	-6.98	1.88	-42.83	-64.37	-9.70	-22.01	-6.98	3.98	3.98
Doxycycline	-7.16	0.94	46.19	-126.91	-14.26	-38.51	-7.16	0.46	0.46
Mefloquine	-6.89	0.90	119.56	-74.76	-10.09	-33.12	-6.89	3.91	3.91
Primaquine	-6.15	1.19	2.88	-70.02	-9.23	-32.80	-6.15	2.21	2.21
tafenoquine	-7.76	2.04	53.55	-57.83	-9.67	-37.11	-7.76	5.08	5.08
favipiravir	-5.29	1.27	51.65	-63.25	-9.80	-26.76	-5.29	-0.21	-0.21
Ribavirin	-5.91	1.45	150.55	-77.89	-9.55	-28.37	-5.91	-2.27	-2.27
Galidesivir	-5.69	1.18	18.61	-74.21	-10.14	-27.67	-5.69	-2.34	-2.34
Brincidovir	-10.83	2.88	-58.15	-51.62	-11.43	-58.84	-10.83	5.54	5.54

Tab. 2 : interaction table between Malaria and Ebola drugs and 1Q2W of COVID-19 with site 1 of COVID-19 Protease (PDB code = 1Q2W)

z	Ligand	Receptor	Interaction	Distance	E (kcal/mol)
Atovaquone	6-ring	CD PRO 122 (B)	pi-H	4.11	-0.5
Chloroquine	O 5	NZ LYS 5 (A)	H-acceptor	3.34	-0.9
	6-ring	CB LYS 137 (A)	pi-H	4.16	-0.6
	6-ring	CA GLY 2 (B)	pi-H	3.49	-0.5
Doxycycline	N 6	N GLN 127 (A)	H-acceptor	3.27	-3.2
Mefloquine	O 41	OG1 THR 285 (A)	H-donor	3.09	-0.9
Primaquine	F 1	N GLN 127 (B)	H-acceptor	3.05	-0.6
	6-ring	CG LYS 5 (B)	pi-H	3.72	-0.8
tafenoquine	N 27	NH1 ARG 4 (B)	H-acceptor	3.58	-1.6
	6-ring	CD LYS 5 (A)	pi-H	4.49	-0.7
favipiravir	N 13	O LYS 5 (A)	H-donor	3.16	-1.6
	N 9	N GLN 127 (B)	H-acceptor	3.32	-2.3
Ribavirin	O 1	O PHE 3 (B)	H-donor	2.98	-0.8
	O 15	NZ LYS 5 (A)	H-acceptor	3.26	-1.2
	O 26	N GLN 127 (B)	H-acceptor	3.14	-3.2
	N 27	N GLN 127 (A)	H-acceptor	3.32	-2.1
	5-ring	CB LYS 5 (B)	pi-H	3.99	-0.7
Galidesivir	O 33	O PHE 3 (B)	H-donor	3.00	-1.2
	N 9	NH1 ARG 4 (B)	H-acceptor	3.25	-4.0
	N 12	N GLN 127 (A)	H-acceptor	3.59	-1.0
	6-ring	CD LYS 5 (A)	pi-H	4.39	-0.7
Brincidovir	O 63	O GLN 127 (B)	H-donor	3.02	-2.9
	O 68	NH1 ARG 4 (A)	H-acceptor	2.95	-2.4

Tab. 3 Docking score and energy of the Malaria and Ebola drugs with ACE-2 Receptor (PDB code = 6M0J)

).	Drug name	Score	rmsd_refine	E_conf	E_place	E_score1	E_refine	E_score2	Log P
	Atovaquone	-6.65	1.64	64.11	-76.16	-10.05	-28.61	-6.65	6.48
	Chloroquine	-6.55	1.58	-38.85	-81.75	-8.86	-30.65	-6.55	3.98
	Doxycycline	-7.11	3.84	47.57	-117.63	-11.62	-44.11	-7.11	0.46
	Mefloquine	-6.38	1.95	120.39	-78.94	-12.26	-28.38	-6.38	3.91
	Primaquine	-6.10	1.44	5.46	-77.03	-9.45	-30.29	-6.10	2.21
	tafenoquine	-8.15	1.57	52.07	-101.66	-9.88	-44.36	-8.15	5.08
	favipiravir	-4.63	1.17	49.20	-63.61	-9.14	-21.46	-4.63	-0.21
	Ribavirin	-5.55	1.04	148.09	-80.63	-9.69	-27.83	-5.55	-2.27
	Galidesivir	-5.78	1.35	18.31	-73.22	-11.53	-25.24	-5.78	-2.34
)	Brincidovir	-9.02	2.19	-52.46	-57.61	-8.93	-49.64	-9.02	5.54

Tab. 4 : interaction table between Malaria and Ebola drugs with ACE-2 Receptor (PDB code = 6M0J)

Drug	Ligand	Receptor	Interaction	Distance	E (kcal/mol)
Atovaquone	6-ring	CA VAL 209 (A)	pi-H	3.90	-1.0
Chloroquine	N 17	O GLU 208 (A)	H-donor	3.16	-0.6
	CL 1	NZ LYS 94 (A)	H-acceptor	3.45	-0.9
	6-ring	CA VAL 209 (A)	pi-H	4.40	-0.5
	6-ring	CG1 VAL 209 (A)	pi-H	4.14	-0.6
	6-ring	N ASN 210 (A)	pi-H	3.62	-0.6
Doxycycline	O 24	OE1 GLU 208 (A)	H-donor	3.01	-1.8
	6-ring	CG2 VAL 209 (A)	pi-H	4.28	-0.7
Mefloquine	N 29	O ASN 210 (A)	H-donor	2.91	-0.7
	N 29	N ASN 210 (A)	H-acceptor	3.33	-0.5
	6-ring	CB GLU 208 (A)	pi-H	4.42	-0.5
	6-ring	CG2 VAL 209 (A)	pi-H	4.46	-0.6
Primaquine	6-ring	CG1 VAL 209 (A)	pi-H	4.24	-0.7
	6-ring	CG1 VAL 209 (A)	pi-H	4.52	-0.7
tafenoquine	No measured interaction				
favipiravir	O 12	NZ LYS 94 (A)	H-acceptor	3.12	-3.5
Ribavirin	O 15	NZ LYS 562 (A)	H-acceptor	3.03	-3.6
Galidesivir	N 14	O ASN 210 (A)	H-donor	3.05	-1.0
	O 29	CE LYS 562 (A)	H-acceptor	3.16	-0.7
	5-ring	CA VAL 209 (A)	pi-H	3.79	-2.1
	6-ring	CA VAL 209 (A)	pi-H	4.40	-0.5
	5-ring	N ASN 210 (A)	pi-H	4.25	-2.7
	6-ring	ND2 ASN 210 (A)	pi-H	4.58	-1.3
Brincidovir	O 63	OE2 GLU 208 (A)	H-donor	2.79	-6.4
	O 74	NE2 GLN 98 (A)	H-acceptor	3.01	-1.2

Brincidofovir (BCV) is an orally bioavailable, long-acting, nucleotide analog broad-spectrum antiviral developed by Chimerix Inc. of Durham, North Carolina, USA for the treatment of double-stranded DNA (dsDNA) viruses [17]. BCV is less toxic with an enhanced cellular penetration prodrug of cidofovir wherein the cidofovir acyclic nucleoside monophosphate conjugated through its phosphonate group to a lipid, 3-(Hexadecyloxy)-1-propanol [18]. Being linked to a lipid particle, the compound ensures better and higher intracellular releases of cidofovir and lower plasma concentrations of the active drug, effectively increasing its antiviral activity. When intracellular, the released free cidofovir from the BCV is phosphorylated to its active metabolite cidofovir diphosphate which due to its structural similarity to the deoxycytidine triphosphate (dCTP) nucleotides it gets incorporated into the growing viral DNA strands [19]. Once incorporated, it prevents further DNA polymerization and disrupts DNA replication of viruses. The drug received FDA Fast Track Designation and has been evaluated in healthy individuals in Phase I and Phase II/III clinical trials and revealed to be well-tolerated and highly efficacious against adenoviruses, BK virus, herpes simplex viruses, and smallpox but eventually somehow failed for cytomegalovirus [20, 21]. Preliminary *in vitro* tests have also shown the drug potential for Ebola virus disease treatment, despite that Ebola is an RNA virus, albeit trials eventually discontinued [22]. Being acted on the Ebola RNA virus before, it is encouraging to act as well on the novel RNA SARS-CoV-2 today. And in addition to its intracellular therapeutic strategy of arresting the viral replication and packaging, our

study shows here that it also interferes efficiently with the SARS-CoV-2 ACE2 receptor revealing a different therapeutic mode of action through potentially blocking or inhibiting the virus entry to the host cell, thereby slowing the progression of the infection.

The second top-ranked drug is *Tafenoquine* which is an orally-active 8-aminoquinoline, a long-acting analog of primaquine, anti-malarial medicine developed by GlaxoSmithKline and 60 Degrees Pharmaceuticals [23, 24]. The drug was FDA-approved for the radical cure of *Plasmodium vivax* (*P. vivax*) malaria and the prophylaxis of malaria in 2018. The drug is active against pre-erythrocytic, erythrocytic forms and the gametocytes of Plasmodium species that include *P. falciparum* and *P. vivax* [23, 24]. Clinical trials for this drug may be also recommended. Chloroquine, which is an anti-malaria and immunosuppressive drug, recently shown to improve the outcomes in patients with the novel coronavirus pneumonia which made the FDA issue an Emergency Use Authorization to be tested as a treatment for COVID-19, ranked at the fourth position in this study [25].

Lastly, while we were working in this research, an Australian study showed that *Ivermectin*, an anti-parasitic drug, to be effective against the COVID-19 disease although, further clinical trials are underway to confirm this effectiveness [26]. We decided to do some investigations using molecular docking to check the binding interaction between Ivermectin and the SARS-CoV-2 protease and receptor. We got comparable data to the antiviral *Brincidofovir* where the docking scores were -10.31 and -8.84 with the SARS-CoV-2 protease and ACE2 receptor, respectively. But overall, Brincidofovir is superiorly recommended because for its high lipophilicity “5.54” where Ivermectin “2.01”.

Tab. 5 Docking score and energy of Ivermectin drug and 1Q2W of COVID-19 with site 1 of COVID-19 Protease (PDB code = 1Q2W)

Lvermectin	S	rmsd_refine	E_conf	E_place	E_score1	E_refine	E_score2	Log P
B1a	-10.90	1.73	85.45	-72.26	-8.53	-57.13	-10.90	2.10
B1B	-10.31	1.29	89.61	-102.28	-9.56	-53.44	-10.31	1.59

Tab. 6 Docking score and energy of Ivermectin drug with ACE-2 Receptor (PDB code = 6M0J)

Lvermectin	S	rmsd_refine	E_conf	E_place	E_score1	E_refine	E_score2	Log p
B1a	-8.84	2.25	34.89	-62.74	-7.46	-52.54	-8.84	2.10
B1B	-8.62	3.56	60.89	2.73	-7.05	-47.16	-8.62	1.59

In conclusion, molecular modeling tools were used to screen for potential anti- SARS-CoV-2 therapeutic agents. After a virtual screening against SARS-CoV-2 protease and ACE2 receptor, a set of antivirals, antimalarials, and antimicrobials drugs showed a potent binding interaction, wherein Biocidofovir showed to be the top hit. Therefore, repurposing of Biocidofovir against the COVID-19 disease is suggested.

Declarations

Competing Ineterest

The authors declare no competing interest.

Acknowledgments

King Abdulaziz University, Jeddah is highly acknowledged for scientific facilitation.

Funding source

The authors declare no funding grant used in this article.

References

1. Sikka, V., et al., *The emergence of Zika virus as a global health security threat: a review and a consensus statement of the INDUSEM Joint Working Group (JWG).* Journal of global infectious diseases, 2016. **8**(1): p. 3.
2. Zhu, N., et al., *A novel coronavirus from patients with pneumonia in China, 2019.* New England Journal of Medicine, 2020.
3. Organization, W.H., *Ebola virus disease. Fact sheet N 103. Updated September 2014. Fecha de consulta: 18 de octubre de 2014*.
4. Memish, Z.A., et al., *Middle East respiratory syndrome coronavirus in bats, Saudi Arabia.* Emerging infectious diseases, 2013. **19**(11): p. 1819.
5. Su, S., et al., *Epidemiology, genetic recombination, and pathogenesis of coronaviruses.* Trends in microbiology, 2016. **24**(6): p. 490-502.
6. Control, C.f.D. and Prevention, *Vaccine Testing and the Approval Process*. 2014, Webpage. Updated: May.
7. Hoffmann, M., et al., *SARS-CoV-2 cell entry depends on ACE2 and TMPRSS2 and is blocked by a clinically proven protease inhibitor.* Cell, 2020.
8. Wu, C., et al., *Analysis of therapeutic targets for SARS-CoV-2 and discovery of potential drugs by computational methods.* Acta Pharmaceutica Sinica B, 2020.
9. Wan, Y., et al., *Receptor recognition by the novel coronavirus from Wuhan: an analysis based on decade-long structural studies of SARS coronavirus.* Journal of virology, 2020. **94**(7).
10. Kitchen, D.B., et al., *Docking and scoring in virtual screening for drug discovery: methods and applications.* Nature reviews Drug discovery, 2004. **3**(11): p. 935-949.
11. Lengauer, T. and M. Rarey, *Computational methods for biomolecular docking.* Current opinion in structural biology, 1996. **6**(3): p. 402-406.
12. Bonanno, J., et al., *X-ray crystal structure of the SARS Coronavirus main protease*. 2003.

13. Abdel-Rhman, M.H., et al., *Synthesis, characterization, molecular docking and cytotoxicity studies on N-benzyl-2-isonicotinoylhydrazine-1-carbothioamide and its metal complexes.* Journal of Molecular Structure, 2019. **1196**: p. 417-428.
14. Abdellattif, M.H., M.A. Hussien, and E. Alzahrani, *New approaches of 4-aryl-2-hydrazinothiazole derivatives synthesis, molecular docking, and biological evaluations.* INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES AND RESEARCH, 2018. **9**(12): p. 5060-5078.
15. Mashat, K.H., et al., *Synthesis, structures, DNA-binding and anticancer activities of some copper (I)-phosphine complexes.* Polyhedron, 2019. **158**: p. 164-172.
16. Althagafi, I., N.M. El-Metwaly, and T. Farghaly, *Characterization of new Pt (IV)–thiazole complexes: Analytical, spectral, molecular modeling and molecular docking studies and applications in two opposing pathways.* Applied Organometallic Chemistry, 2019. **33**(9): p. e5099.
17. Lanier, R., et al., *Development of CMX001 for the treatment of poxvirus infections.* Viruses, 2010. **2**(12): p. 2740-2762.
18. Florescu, D.F. and M.A. Keck, *Development of CMX001 (Brincidofovir) for the treatment of serious diseases or conditions caused by dsDNA viruses.* Expert review of anti-infective therapy, 2014. **12**(10): p. 1171-1178.
19. Parker, S., et al., *Efficacy of therapeutic intervention with an oral ether–lipid analogue of cidofovir (CMX001) in a lethal mousepox model.* Antiviral research, 2008. **77**(1): p. 39-49.
20. Chittick, G., et al., *Short-term clinical safety profile of brincidofovir: A favorable benefit–risk proposition in the treatment of smallpox.* Antiviral research, 2017. **143**: p. 269-277.
21. Schepers, J., *Chimerix announces emergency investigational new drug applications for brincidofovir authorized by FDA for patients with Ebola virus disease*.
22. Dunning, J., et al., *Experimental treatment of Ebola virus disease with brincidofovir.* PloS one, 2016. **11**(9).
23. Baird, J.K., *Tafenoquine for travelers' malaria: evidence, rationale and recommendations.* Journal of travel medicine, 2018. **25**(1): p. tay110.
24. Frampton, J.E., *Tafenoquine: first global approval.* Drugs, 2018. **78**(14): p. 1517-1523.
25. Gao, J., Z. Tian, and X. Yang, *Breakthrough: Chloroquine phosphate has shown apparent efficacy in treatment of COVID-19 associated pneumonia in clinical studies.* Bioscience trends, 2020.
26. Caly, L., et al., *The FDA-approved Drug Ivermectin inhibits the replication of SARS-CoV-2 in vitro.* Antiviral Research, 2020: p. 104787.

Figures

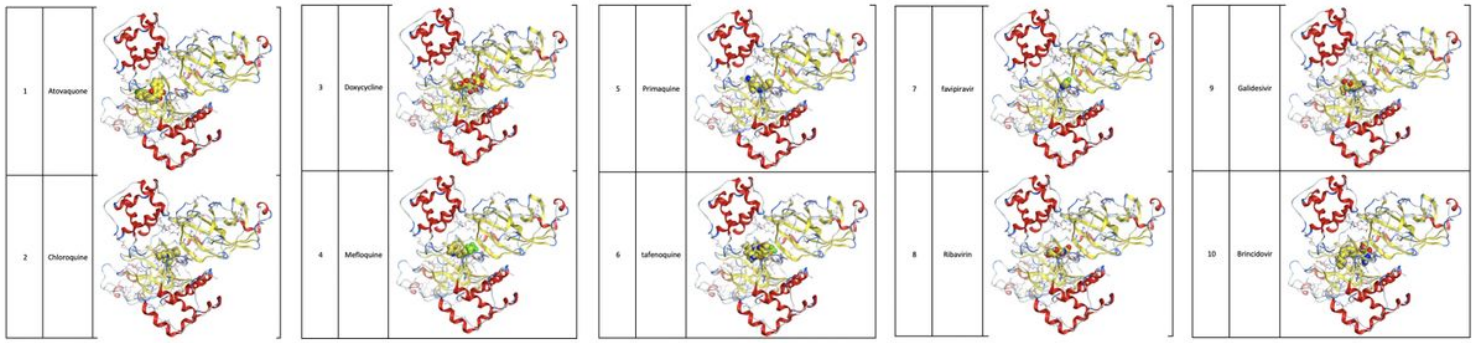

Figure 1

3d Docking of Malaria and Ebola drugs and 1Q2W of COVID-19 with site 1 of COVID-19 Protease (PDB code = 1Q2W)

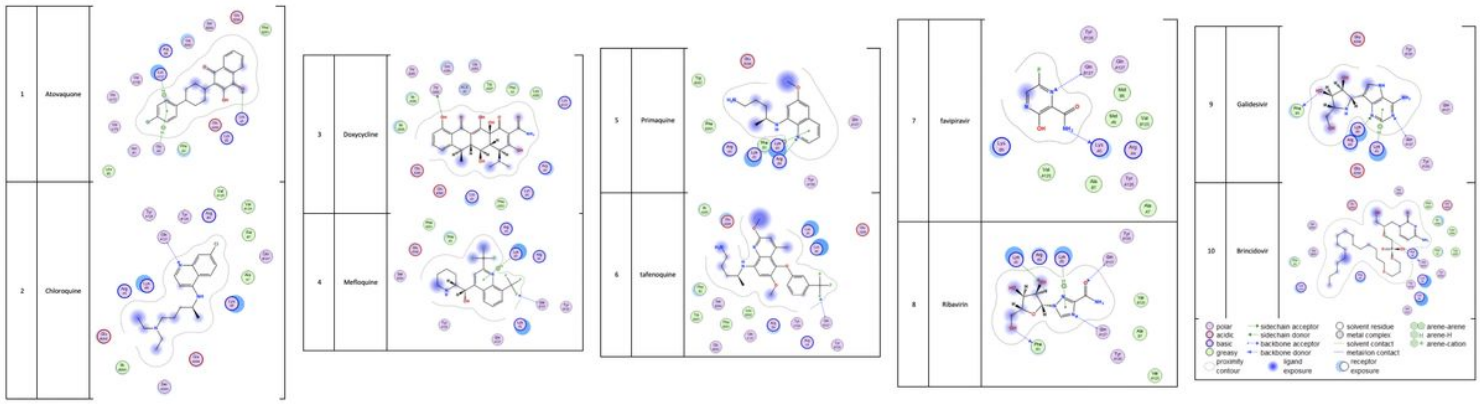

Figure 2

2d Docking of Malaria and Ebola drugs and 1Q2W of COVID-19 with fixing the active site 1 of of COVID-19 Protease (PDB code = 1Q2W)

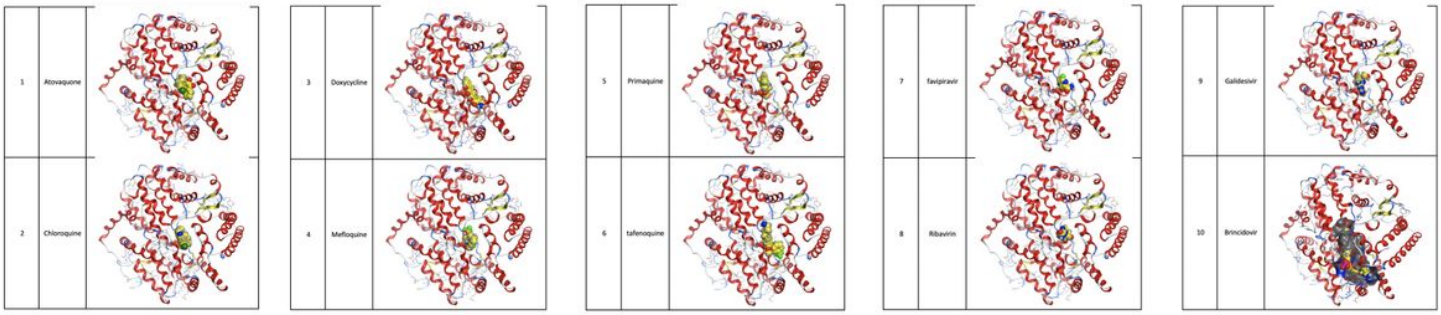

Figure 3

3d Docking of Malaria and Ebola drugs with ACE-2 Receptor (PDB code = 6M0J)

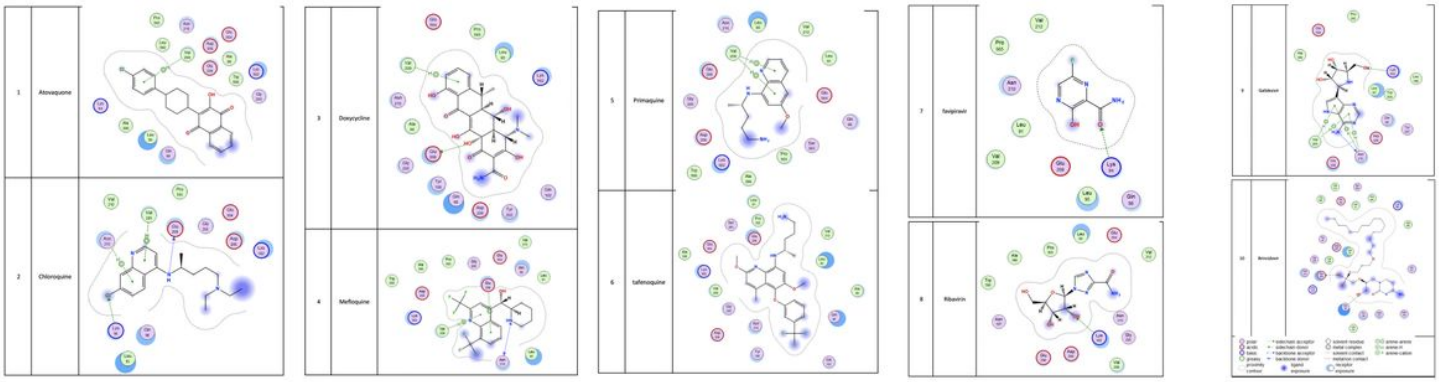

Figure 4

2d Docking of Malaria and Ebola drugs with ACE-2 Receptor (PDB code = 6M0J)