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DRUG REPURPOSING: IN SILICO MODELING OF COVID-19

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ABSTRACT: By and by the world is in a battle with the novel Covid and with no prompt medicines accessible the scourge brought about by the SARS-CoV-2 is expanding step by step. A ton of researchers are continuing for the potential medication up-and-comer that could help the medical care framework in this battle. We present a docking-based screening using a quantum mechanical scoring of a library built from approved drugs and compounds that are Remdesivir, Hydroxy-chloroquine, Curcumin, Moroxydine, Artesunate Sulphate, Quercetin, Amantadine, Zanamivir, Umifenovir, Tipranavir, Indinavir with SARS-CoV-2 Mpro Proteins with PDB id's 6LU7, 6WTT, 7BQY. could display antiviral activity against SARS-CoV-2. Clearly, these compounds should be further evaluated in experimental assays and clinical trials to confirm their actual activity against the disease. We hope that these findings may contribute to the rational drug design against COVID-19.

Keywords: COVID-19, Drug Repurposing, Synthetic modeling, Curcumin, Bioinformatics.

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1. INTRODUCTION

Covid malady (COVID-19) has become a significant public issue over the globe since December 2019. As of twelfth of April 2020, more than 1.79 million cases have been accounted for in 210 nations and domains. [3] It influences individuals worldwide and there is no

immunization yet for this infection. Specific kinds of pneumonia are embroiled in the new Covid, which is viewed as a major danger to worldwide general wellbeing. There is a pressing need to create an intense enemy of COVID-19 specialists for the avoidance of the flare-up and stop viral contaminations. Repurposing of realized little particles is by all accounts an exceptionally productive path so as to create strong medications to battle Covid in this brief timeframe period. As of late, various endeavors were made to plan novel inhibitors or utilize drug repurposing ways to deal with recognize hostile to COVID-19 medications, which can go about as promising inhibitors against Covid protease. [2,30]

Proteins:

PDB Id- 6LU7

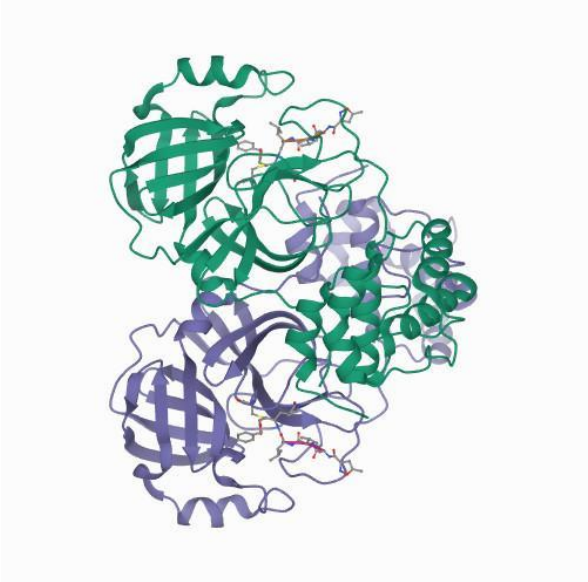


Fig 1: 6LU7 with its native ligand.

6lu7 is the major protease (Mpro) in COVID-19. The Mpro in coronavirus is very important for proteolytic maturation of the virus. 6lu7 is a multifunctional protein that is involved in transcription and replication of viral RNAs. It contains the proteases responsible for the cleavage of the polyprotein. Moreover, it inhibits host translation by interacting with the 40S ribosomal subunit. The main protease is the molecule at chain A of 6lu7. 6lu7 chain A, has been identified as a member of the main protease domain (Mpro) and has been reported to be a target, in favor of designing new inhibitors throughout the entire coronaviridae family. The two-third region of 5' in the coronavirus genome consists of the open reading frame I. This encodes two large polypeptides of the replicase machinery: pp1a, and through ribosomal frameshift, pp1ab1. Two proteases encoded in the 5' region of ORF1: papain like proteases (PLP) and 3C-like proteases (3CL or Nsp5) translationally cleaves the two polypeptides into mature nonstructural proteins (NSPs). The 3 CL protease is more commonly known as the Mpro as it has a dominant

role in the post translational processing of the replicase protein. In different human and animal CoVs significant homology of Mpros in primary amino acid sequence and 3D architecture has been reported. Moreover, they have a similar substrate binding pocket with a requirement for glutamine at P1 position and also a preference for leucine/methionine at P2 position. This strong structural basis provides an opportunity to design a wide- spectrum anti CoV inhibitors. [23,24,26,28,29]

PDB Id- 6WTT

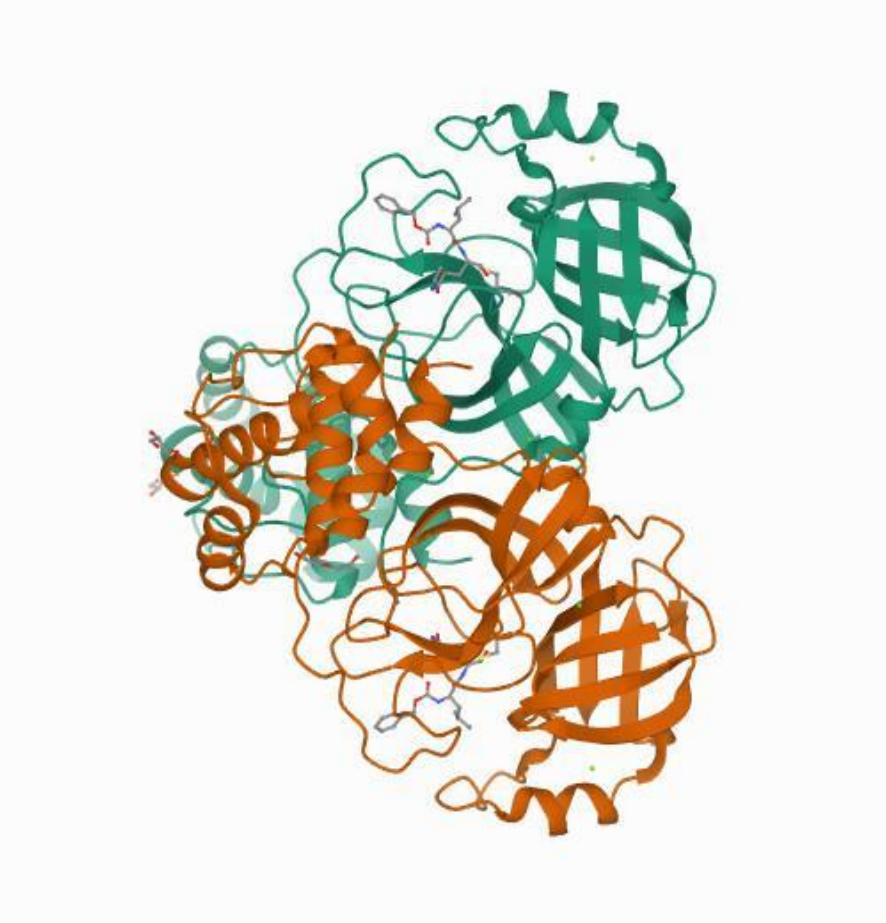


Fig 2: 6WTT with its native ligand.

6wtt is a multifunctional protein involved in the transcription and replication of viral RNAs. It further consists of proteinases responsible for the cleavages of polyprotein. It also inhibits host translation by interacting with the 40s ribosomal subunit. 3C like protease of chains A, B and C of 6wtt has been chosen as a drug target by me. The 3C like protease (3CLpro), which hydrolyzes the polyprotein to produce functional proteins. It is essential for coronavirus replication and considered an important therapeutic target for diseases caused by coronaviruses, including coronavirus disease 2019 (COVID-19). The 3CLpro is a cysteine protease that hydrolyzes the polyproteins pp1a and pp1b to produce functional proteins during coronavirus replication. 3CLpro has been validated as a potential target for the development of drugs to

treat SARS, MARS, and COVID-19 because of its highly conserved sequence and essential functional properties. [27]

PDB Id- 7BQY

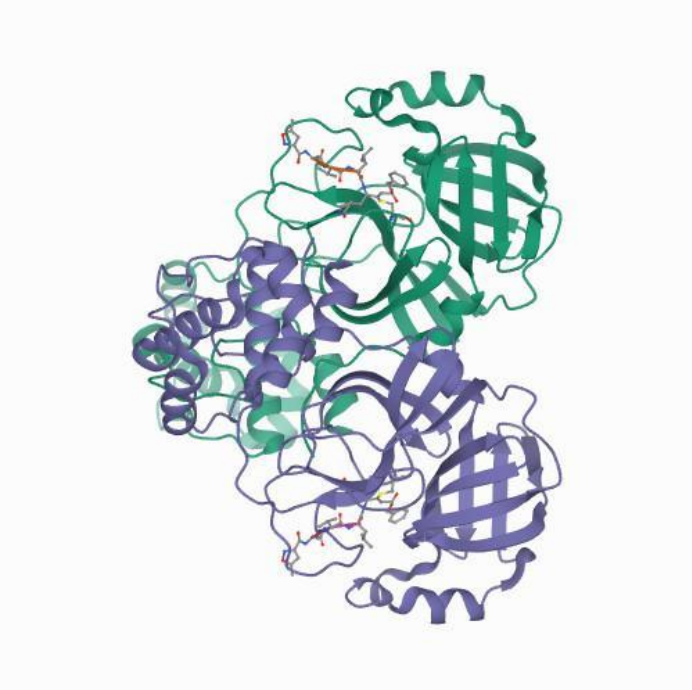


Fig 3: 7BQY with its native ligand

7bqy is a multifunctional protein involved in the transcription and replication of viral RNAs. It contains the proteinases responsible for the cleavages of the polyprotein. Moreover, it also inhibits host translation by interacting with the 40s ribosomal subunit. The main protease consists of generally the three: Mpro, 3Clpro, nsp5. The main protease Mpro exclusively cleaves polypeptide sequences after a glutamine residue. Thus, it positions the main protease as an ideal drug target because till now no human host-cell proteases are known with this substrate specificity. The SARS-CoV-2 Mpro proteolytically cleaves the overlapping pp1a and pp1ab polyproteins to functional proteins. This is a critical step during viral replication. Replication essential enzymes such as the RdRp or nsp13 cannot fully function without prior proteolytic release, positioning Mpro as a key enzyme in the viral replication cycle. Consequently, its inhibition can stall the production of infectious and thus alleviate disease symptoms. Therefore, the main protease Mpro is one of the most attractive viral targets for antiviral drug discovery against SARS-CoV-2. [23,24,26,28,29]

Ligands

Remdesivir

Remdesivir is also known as GS-5734. It is an adenosine triphosphate analog which belongs to a class of compounds known as alpha amino esters. It has been previously used as a potential treatment for Ebola. Recently Remdesivir was granted an FDA Emergency Use Authorization

on 1st May 2020. It is now used in adults and children with suspected or confirmed Covid-19 in hospital with an SpO2 less than equals to 94%.

Hydroxychloroquine [10]

Hydroxychloroquine belongs to a class of organic compounds known as 4-aminoquinolines containing an amino group attached to the 4-position of a quinolone ring system. Hydroxychloroquine consists of a racemic mixture of R and S enantiomer and is commonly prescribed in the treatment of uncomplicated malaria, rheumatoid arthritis, chronic discoid lupus erythematosus, and systemic lupus erythematosus. Furthermore, it is also used for the prophylaxis of malaria. The FDA emergency use authorization for hydroxychloroquine in the treatment of COVID-19 was revoked on 15th June 2020.

Curcumin [14]

Curcumin is also known as diferuloylmethane. It is an active component in the golden spice turmeric (Curcuma longa) and in Curcuma xanthuria oil. Curcumin belongs to the class of organic compounds known as curcuminoids which are aromatic compounds containing a curcumin moiety and is further composed of two aryl buten-2-one (feruloyl) chromophores joined by a methylene group. Moreover, it is a highly pleiotropic molecule that exhibits antibacterial, anti-inflammatory, hypoglycemic, antioxidant, wound-healing, and antimicrobial activities

Moroxydine

This compound belongs to the class of organic compounds known as biguanides which are basically compounds containing two N-linked guanidine's.

Artesunate [9]

Artesunate belongs to the class of organic compounds known as artemisinin's which are generally sesquiterpenoids. These are originally isolated from the herb Artemisia annua. Their structure is based on artemisinin. Artemisinin is a tetracyclic compound that contains a 1,2-dioxepane fused to a tetrahydro benzofuran moiety. Basically, the internal peroxide bridge is believed to be a key to the mode of action of artemisinin. Artesunate is mainly indicated for the initial treatment of severe malaria in adult and pediatric patients.

Quercetin [11]

Quercetin belongs to the class of organic compounds known as flavonoids which are compounds containing a flavone (2-phenyl-1-benzopyran-4-one) and with backbone carrying a hydroxyl group at the 3-position. Quercetin is basically a flavanol widely distributed in plants and acts as an antioxidant.

Zanamivir [8,12]

Zanamivir belongs to the class of organic compounds known as acetamides which are organic

compounds with the general formula RNC(=O) CH3, where R=organyl group. Zanamivir is basically an antiviral drug as well as a guanidino-neuraminic acid that is used to inhibit neuraminidase and hence is indicated for treatment of uncomplicated acute illness due to influenza A and B virus.

Umifenovir

Umifenovir belongs to the class of organic compounds known as indole carboxylic acids and derivatives which are compounds containing a carboxylic acid group or its derivatives linked to an indole. Umifenovir is a hydrophobic, dual-acting direct antiviral/host targeting agent used for the treatment and prophylaxis of influenza and other respiratory infections. Umifenovir is currently being investigated as a potential treatment for COVID-19 caused by SARS-CoV2 infections in combination with both currently available and investigational HIV therapies.

Tipranavir [4,5]

Tipranavir belongs to the class of organic compounds known as linear diarylheptanoids which are diaryl heptanoids with an open heptane chain. The two aromatic rings are linked by the heptane chain. Tipranavir is a sulfonamide-containing dihydropyrrole as well as a non-peptide protease inhibitor. It generally targets the HIV protease.

Indinavir [5,6]

Indinavir belongs to the class of organic compounds known as alpha amino acid amides. These compounds are basically amide derivatives of alpha amino acids. It is an antiretroviral drug for the treatment of HIV infection.

Amantadine [7]

Amantadine belongs to the class of organic compounds known as mono alkyl amines. These are basically compounds containing a primary aliphatic amine group. Amantadine is an antiviral drug that is generally used in the prophylactic or symptomatic treatment of influenza A and is also used as an antiparkinsonian agent, to treat extrapyramidal reactions, and for post therapeutic neuralgia.

2. MATERIALS AND METHODS

1. Ligand Screening

For the initial Ligand screening purposes, a web-based tool named SwissADME [22] was used to eliminate a few compounds according to Lipinski's rule of five parameters. For a compound to qualify as ligand it should Have < 500 Da molecular weight, a high lipophilicity i.e., value of Log P being less than 5, hydrogen bond acceptors being less than 10 and H-bond donors less than 5. Any compound with more than 2 violations was ruled out for further study.

2. Protein Preparation and Active Site Determination

Required protein in pdb format was downloaded from the website **rcsb.org**, commonly known

as the **Protein Data Bank**. **[20,21]** 3D conformers of the ligand were downloaded from PubChem.

Using **PyMOL (Version 2.4.1) [16]** software water molecules as well as native ligands from the protein were removed, defined as cleaning/purification of the protein for further application.

Using a web server called DeepSite [18] Active Pockets of the proteins were calculated. The results calculated by web server was in the form of different ids, centers and scores.

Scoring in deep site was using neural networking based on following instructions using DCNN architecture. Center values for the grid were selected keeping score greater than 0.98.

UCSF Chimera (Version 1.14) [19] was used to prepare the receptor using DockPrep function.

Dock Prep prepared structures for Docking using these functions:

- deleting water molecules
- repairing truncated sidechains
- adding hydrogens
- assigning partial charges
- writing files in Mol2 format

3. In silico Docking Using Auto Dock Vina

Auto dock Vina (Version 1.1.2) [1,17] along with UCSF Chimera (Version 1.14) [18] was used for molecular **Docking Studies**. Center values and size of the grid of different scores were used from **DEEPSITE [17]** calculations done above.

Following Parameters were set in auto dock vina.

Receptor options –

- **Add hydrogens in Chimera** (**true**/false) – whether to add hydrogens in Chimera before calling the script. The receptor prep script will check for hydrogens and add them if they are missing. AutoDock Vina needs the polar (potentially H-bonding) hydrogens to identify atom types for scoring purposes.
- **Merge charges and remove non-polar hydrogens** (**true**/false) – note AutoDock Vina does not use charges or nonpolar hydrogens, so this setting is not expected to affect results except for the presence or absence of nonpolar hydrogens in the processed receptor
- **Merge charges and remove lone pairs** (**true**/false) – note AutoDock Vina does not use charges or lone pairs, so this setting is not expected to affect results except for the presence or absence of lone pairs in the processed receptor (and there may not have been any lone pairs to start with)
- **Ignore waters** (**true**/false)

- **Ignore chains of non-standard residues** (**true**/false) – ignore chains composed entirely of residues other than the 20 standard amino acids.
- **Ignore all non-standard residues** (true/**false**) – ignore all residues other than the 20 standard amino acids.

For Ligands

- **Merge charges and remove non-polar hydrogens** (**true**/false) – note Auto Dock Vina does not use charges or nonpolar hydrogens, so this setting is not expected to affect results except for the presence or absence of nonpolar hydrogens in the ligand output files
- **Merge charges and remove lone pairs** (**true**/false) – note AutoDock Vina does not use charges or lone pairs, so this setting is not expected to affect results except for the presence or absence of lone pairs in the ligand output files (and there may not have been any lone pairs to start with)

Docking parameters

- **Number of binding modes** (1-10, **10**) – maximum number of binding modes to generate
- **Exhaustiveness of search** (1-8, **8**) – thoroughness of search, roughly proportional to time
- **Maximum energy difference (kcal/mol)** (1-3,**3**) – maximum score range; binding modes with scores not within this range of the best score will be discarded.

The docking results were calculated by Auto dock vina using its Scoring function and results were displayed in the form of Scores and RMSD values. Docking results with the highest value score accompanied by negative sign and least RMSD values were chosen for further studies.

4. Residue Analysis

PyMOL [16] was used for visualization of interactions of the docked structure at the ligand sites. **Discovery Studio 2020 [15]** was used to study the ligand interactions and total number of residues. It was also used to plot the 2D structure of the interactions and residues.

5. Statistical Analysis

Descriptive, estimation and Hypothesis testing with confidence interval of 95% was applied to data using formula 1 given below.

$$CI = \bar{x} \pm z\frac{s}{\sqrt{n}}$$

CI = confidence interval

$\bar{x}$ = sample mean

z = confidence level value

s = sample standard deviation

n = sample size

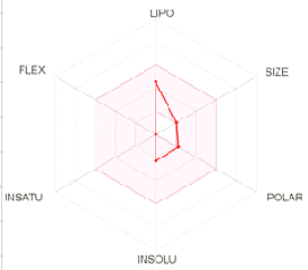
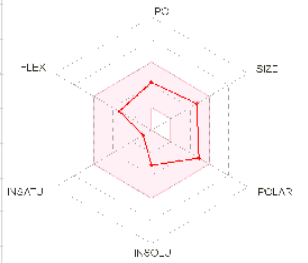
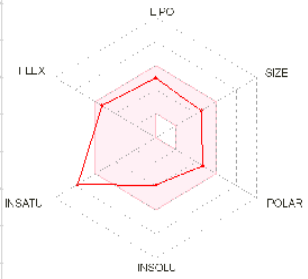
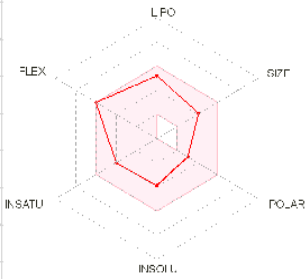
Formula 1 used for calculation of confidence interval

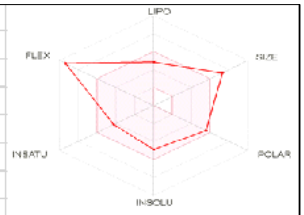
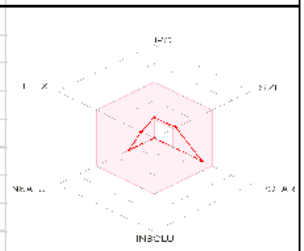
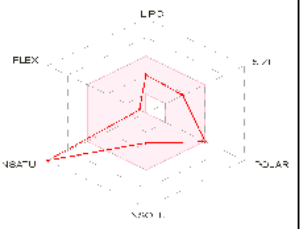
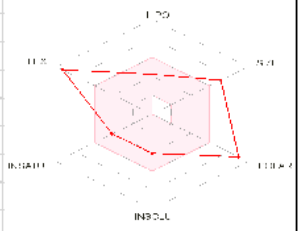
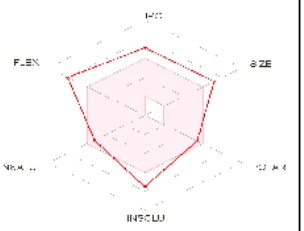
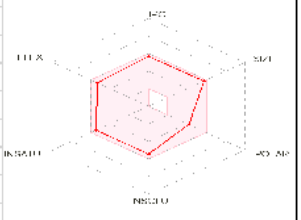
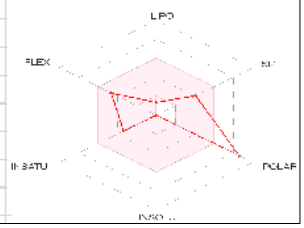
3. RESULTS AND DISCUSSION

Bioavailability Radar

Further analysis included four selected ligands viz. Remdesivir, Hydroxy-chloroquine, Curcumin, Moroxydine, Artesunate Sulphate, Quercetin, Amantadine, Zanamivir, Umifenovir, Tipranavir, Indinavir, a more illustrated and comprehensive study was done using bio-availability radar. Bioavailability radar is descriptive tool to investigate the drug-likeness of the ligands based on six physicochemical properties. The radar that fits the shaded area are Orally Bioavailable **Table 1**.

Table 1: Bioavailability radar charts of selected ligands

Ligands	Log P	Bioavailability Score	Lipinski violation	Images
AMANTADINE	2.18	0.55	0	
Not Orally available				
ARTESUNATE	2.18	0.56	0	
Orally available				
CURCUMIN	3.03	0.55	0	
Orally available				
HCQ	3.29	0.55	0	
Orally available				

INDINAVIR	2.78	0.55	1	
Not Orally available				
MOROXYDINE	-1	0.55	0	
Not Orally available				
QUERCETIN	1.23	0.55	0	
Orally available				
REMDESIVIR	1.53	0.17	2	
Not Orally available				
TIPRANAVIR	6.06	0.56	1	
Not Orally available				
UMIFENOVIR	4.26	0.55	0	
Orally available				
ZANAMAVIR	-2.59	0.17	2	
Not Orally available				

Molecular Docking

The docking result was obtained from AutoDock vina in the form of Dock score for all the three proteins docked with above mentioned ligands, average docking Score of each ligand aggregated to average dock score of three proteins were taken Fig 4. Standard deviation and Confidence interval was calculated, based on the confidence interval minimum value of dock score for each ligand was calculated Table 1. All the dock scores above the minimum score were considered for further evaluations.

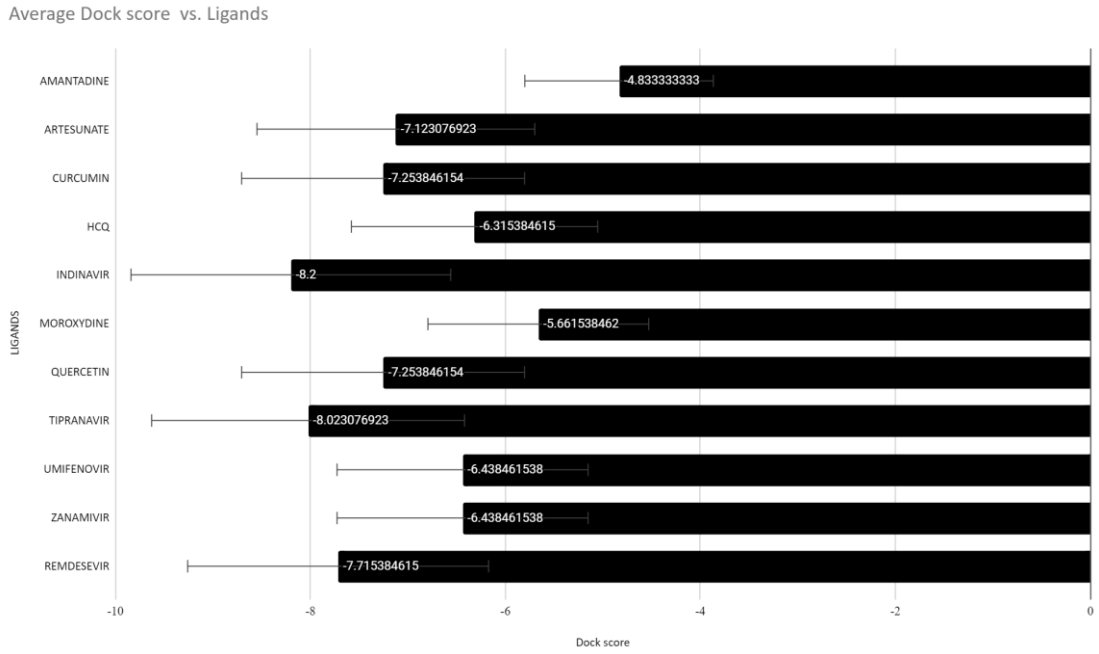


Fig 4: Average aggregate dock score for 3 proteins with respective ligands.

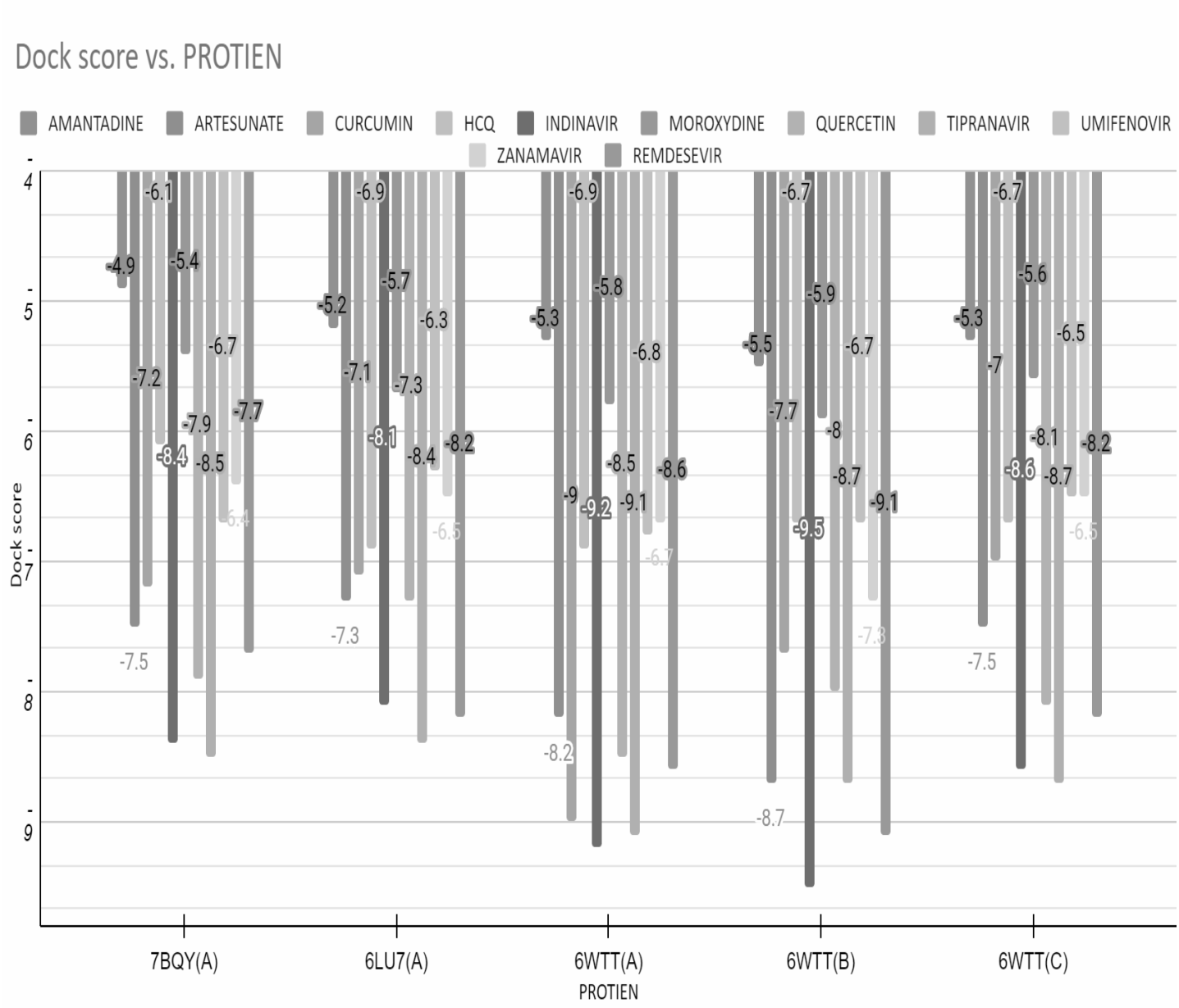
Table 2: Standard deviation, confidence interval at 95% with minimum dock score.

Table 2

LIGANDS	Average	Standard Deviation Sample	Sample Size	Confidence Interval 95%	Min Score in 95% Confidence
REMDESEVIR	-7.876923077	0.5717718749	13	0.345518286	-7.531404791
AMANTADINE	-4.8	0.4672615256	13	0.282363314	-4.517636686
ARTESUNATE	-7.338461538	0.6292038111	13	0.3802240577	-6.958237481
CURCUMIN	-7.176923077	0.8115354235	13	0.4904059483	-6.68651713
HYDROXYCHLOROQUINE	-6.338461538	0.3927222546	13	0.2373196833	-6.101141855
INDINAVIR	-8.330769231	0.7028330947	13	0.4247177884	-7.906051443

MOROXYDINE	-5.4	0.3674234614	13	0.2220317756	-5.177968224
QUERCETIN	-7.392307692	0.6701511502	13	0.404968287	-6.987339405
TIPRANAVIR	-8.184615385	0.5505242257	13	0.3326784601	-7.851936925
UMIFENOVIR	-6.261538462	0.4839739345	13	0.2924625216	-5.96907594
ZANAMIVIR	-6.4	0.3763863264	13	0.2274479807	-6.172552019

Fig 5: Selected max docking score with -ve sign of all the ligands with all the proteins



Docking Results

Table 3: Interactions and max docking score with -ve sign of Amantadine and Artesunate with all proteins used in study.

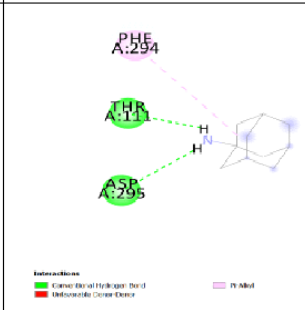
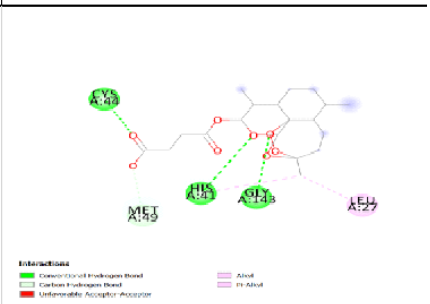
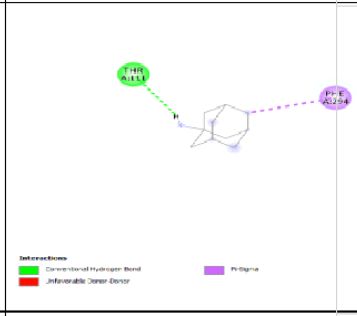
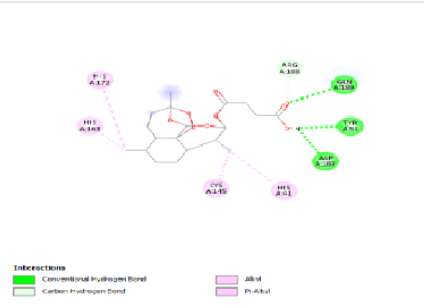
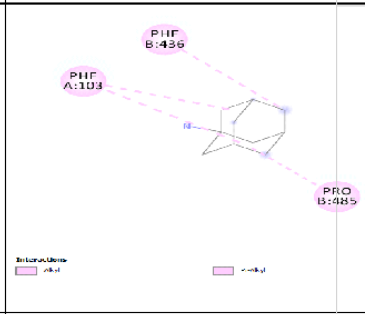
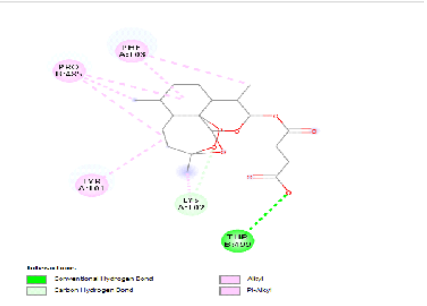
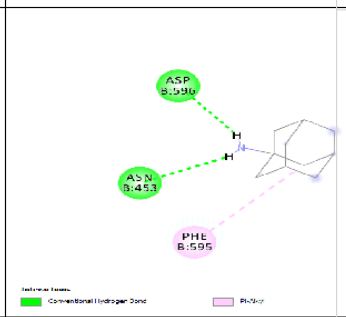
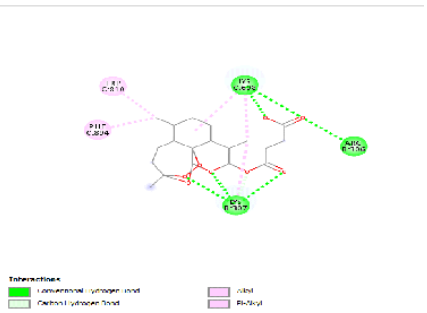
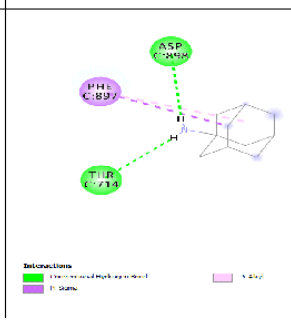
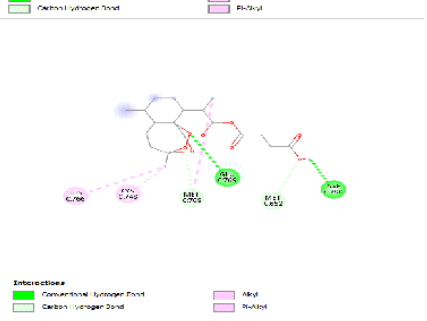
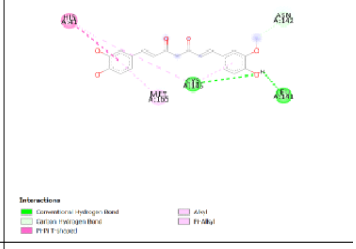
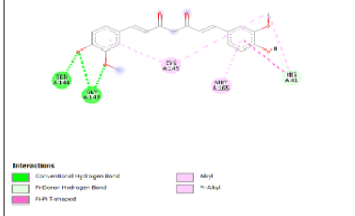
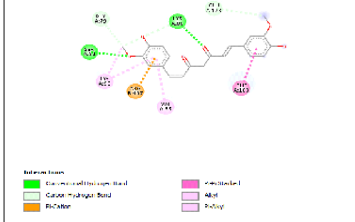
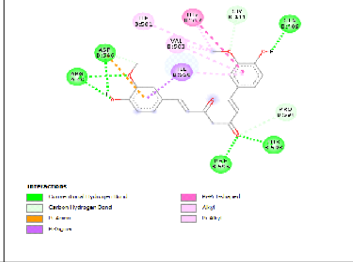
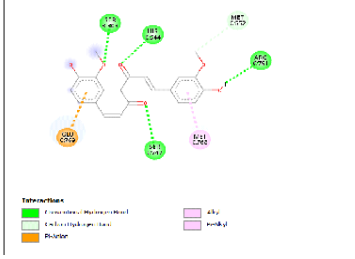
Dock score	Proteins	Ligands	Intercations	Dock score	Proteins	Ligands	Intercations
-4.9	7BQY(A)	AMANTADINE		-7.5	7BQY(A)	ARTESUNATE	
-5.2	6LU7(A)	AMANTADINE		-7.3	6LU7(A)	ARTESUNATE	
-5.3	6WTT(A)	AMANTADINE		-8.2	6WTT(A)	ARTESUNATE	
-5.5	6WTT(B)	AMANTADINE		-8.7	6WTT(B)	ARTESUNATE	
-5.3	6WTT(C)	AMANTADINE		-7.5	6WTT(C)	ARTESUNATE	

Table 4: Interactions and max docking score with -ve sign of Curcumin and Hydroxychloroquine (HCQ) with all proteins used in study.

Dock score	Proteins	Ligands	Intercations
-7.2	7BQY(A)	CURCUMIN	
-7.1	6LU7(A)	CURCUMIN	
-9	6WTT(A)	CURCUMIN	
-7.7	6WTT(B)	CURCUMIN	
-7	6WTT(C)	CURCUMIN	

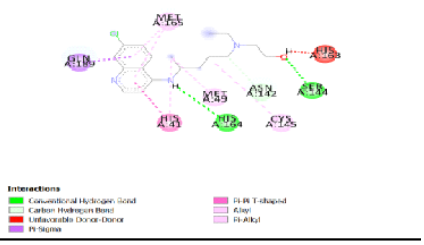
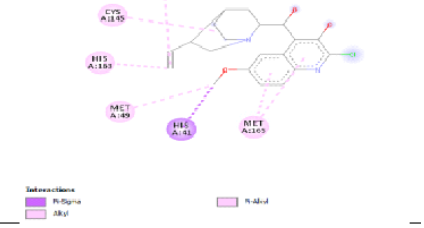
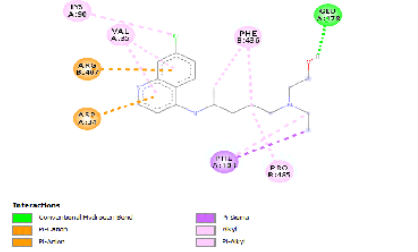
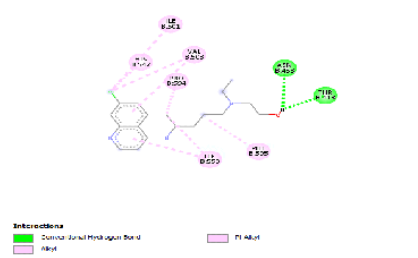
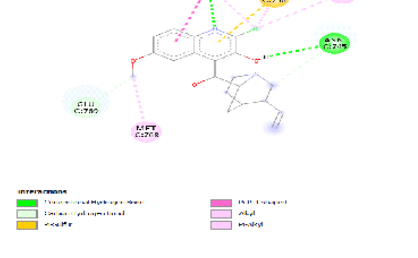
Dock score	Proteins	Ligands	Intercations
-6.1	7BQY(A)	HCQ	
-6.9	6LU7(A)	HCQ	
-6.9	6WTT(A)	HCQ	
-6.7	6WTT(B)	HCQ	
-6.7	6WTT(C)	HCQ	

Table 5: Interactions and max docking score with -ve sign of Indinavir and Moroxydine with all proteins used in study.

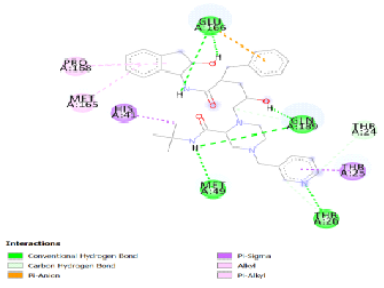
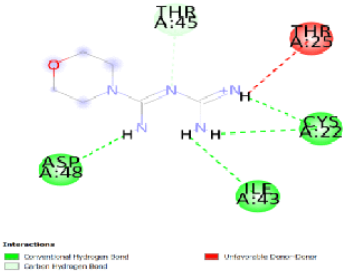
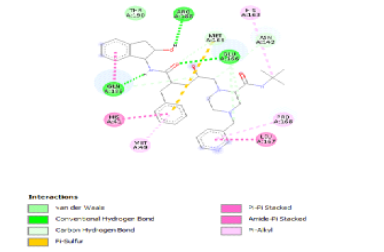
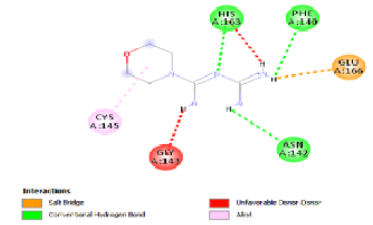
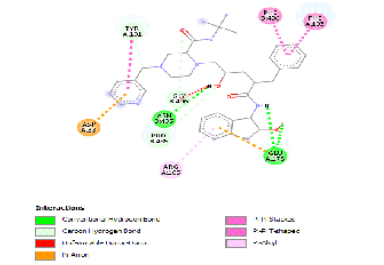
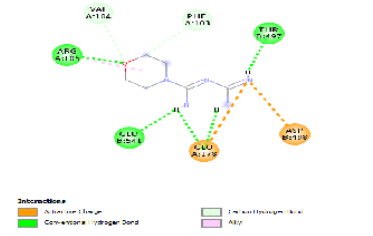
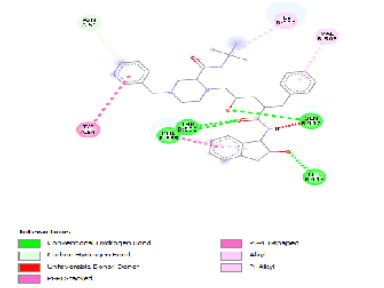
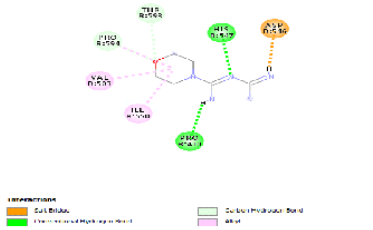
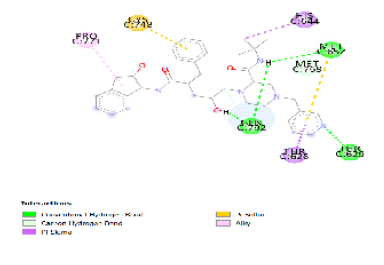
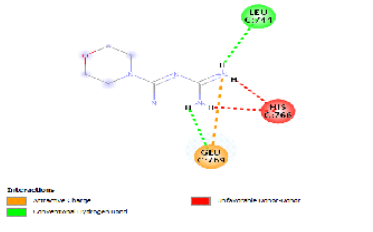
Dock score	Proteins	Ligands	Intercations	Dock score	Proteins	Ligands	Intercations
-8.4	7BQY(A)	INDINAVIR		-5.4	7BQY(A)	MOROXYDINE	
-8.1	6LU7(A)	INDINAVIR		-5.7	6LU7(A)	MOROXYDINE	
-9.2	6WTT(A)	INDINAVIR		-5.8	6WTT(A)	MOROXYDINE	
-9.5	6WTT(B)	INDINAVIR		-5.9	6WTT(B)	MOROXYDINE	
-8.6	6WTT(C)	INDINAVIR		-5.6	6WTT(C)	MOROXYDINE	

Table 6: Interactions and max docking score with -ve sign of Quercetin and Tipranavir with all proteins used in study.

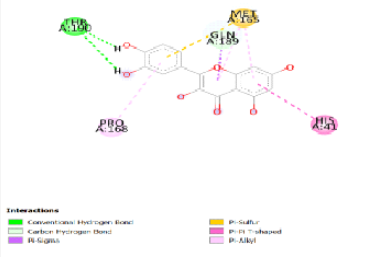
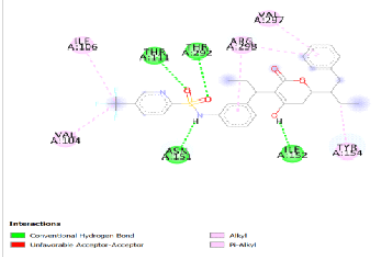
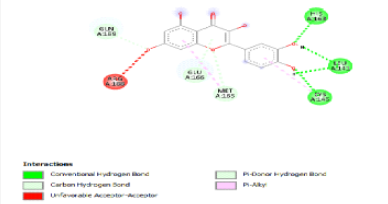
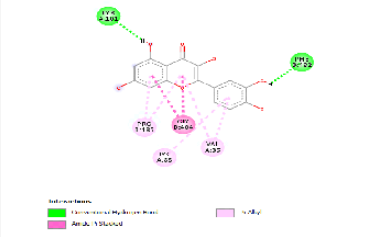
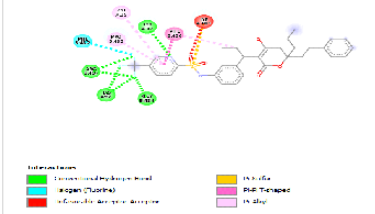
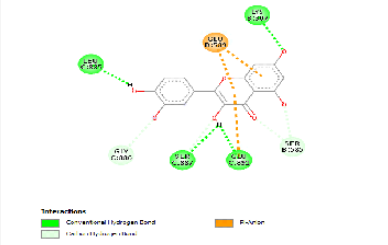
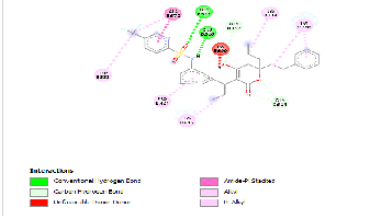
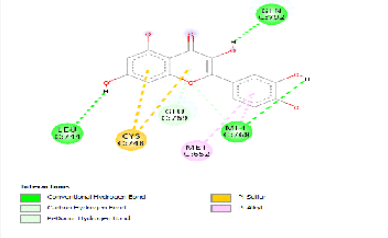
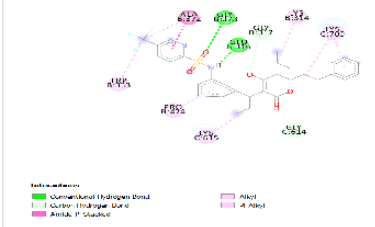
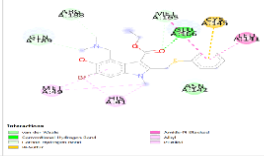
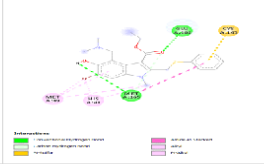
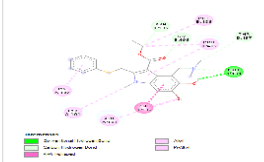
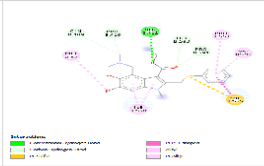
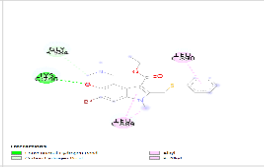
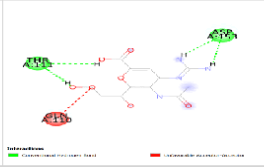
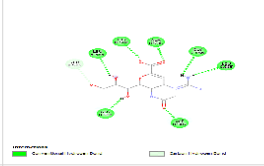
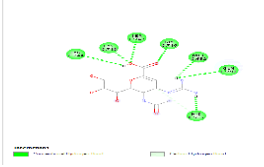
Dock score	Proteins	Ligands	Intercations	Dock score	Proteins	Ligands	Intercations
-7.9	7BQY(A)	QUERCETIN		-8.5	7BQY(A)	TIPRANAVIR	
-7.3	6LU7(A)	QUERCETIN		-8.4	6lu7(A)	TIPRANAVIR	
-8.5	6WTT(A)	QUERCETIN		-9.1	6WTT(A)	TIPRANAVIR	
-8	6WTT(B)	QUERCETIN		-8.7	6WTT(B)	TIPRANAVIR	
-8.1	6WTT(C)	QUERCETIN		-8.7	6WTT(C)	TIPRANAVIR	

Table 7: Max docking score with -ve sign of Remdesivir, Umifenovir, Zanamivir

Dock score	Proteins	Ligands	Intercations
-6.7	7BQY(A)	UMIFENOVIR	
-6.3	6LU7(A)	UMIFENOVIR	
-6.8	6WTT(A)	UMIFENOVIR	
-6.7	6WTT(B)	UMIFENOVIR	
-6.5	6WTT(C)	UMIFENOVIR	
-6.4	7BQY(A)	ZANAMIVIR	
-6.5	6LU7(A)	ZANAMIVIR	
-6.7	6WTT(A)	ZANAMIVIR	
-7.3	6WTT(B)	ZANAMIVIR	
-6.5	6WTT(C)	ZANAMIVIR	

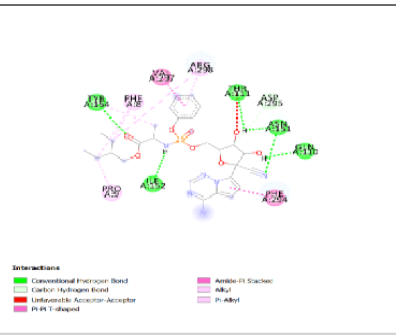
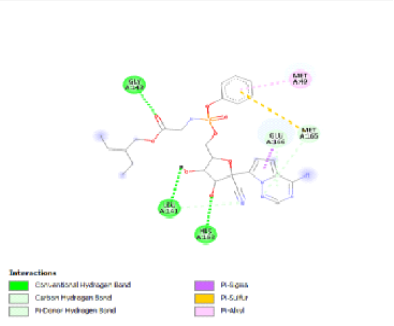
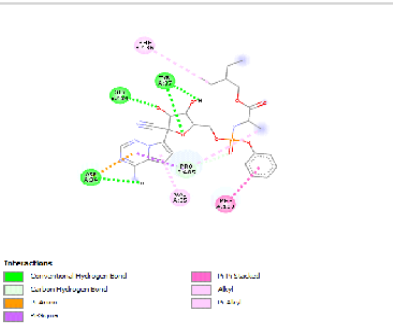
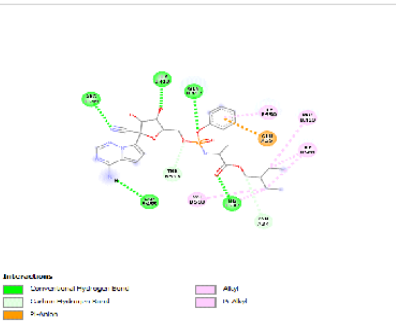
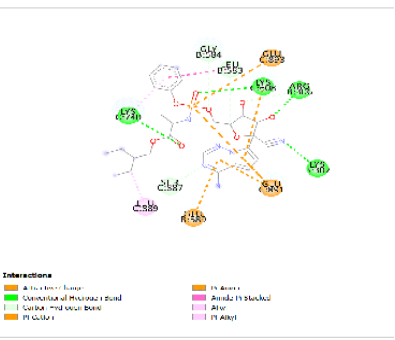
Dock score	Proteins	Ligands	Intercations
-7.7	7BQY(A)	REMDESEVIR	
-8.2	6LU7(A)	REMDESEVIR	
-8.6	6WTT(A)	REMDESEVIR	
-9.1	6WTT(B)	REMDESEVIR	
-8.2	6WTT(C)	REMDESEVIR	

Table 8: Collective and comparative result of the docking and inhibition shown by ligands to selected proteins based on the above data table and interactions.

Ligands	6LU7	7BQY	6WTT (A)	6WTT (B)	6WTT (C)	Remark
REMDESEVIR	YES	YES	YES	YES	YES	HIGH POTENTIAL
AMANTADINE	NO	NO	NO	NO	NO	NO POTENTIAL
ARTESUNATE	YES	YES	YES	YES	YES	HIGH POTENTIAL
CURCUMIN	YES	YES	YES	YES	YES	HIGH POTENTIAL
HYDROXYCHLOROQUINE	YES	NO	YES	YES	YES	POTENTIAL
INDINAVIR	YES	YES	YES	YES	YES	HIGH POTENTIAL
MOROXYDINE	NO	NO	NO	NO	NO	NO POTENTIAL
QUERCETIN	YES	YES	YES	YES	YES	HIGH POTENTIAL
TIPRANAVIR	YES	YES	YES	YES	YES	HIGH POTENTIAL
UMIFENOVIR	YES	YES	YES	YES	YES	HIGH POTENTIAL
ZANAMIVIR	YES	YES	YES	YES	YES	HIGH POTENTIAL

4. CONCLUSION

All eleven ligands were studied using bioavailability radar. Our results proposed Remdesivir, Hydroxy-chloroquine, Curcumin, Artesunate Sulphate, Quercetin, Zanamivir, Umifenovir, Tipranavir, Indinavir showed best docking result SARS-CoV-2 Mpro Proteins with PDB id's 6LU7, 6WTT, 7BQ whereas Amantadine and Moroxydine didn't show a good docking result. To find the effectiveness and to propose the exact mechanism in-vitro studies can be encouraged on Remdesivir, Hydroxy-chloroquine, Curcumin, Artesunate Sulphate, Quercetin, Zanamivir, Umifenovir, Tipranavir, Indinavir to find a potent cure for the COVID-19.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Not applicable.

HUMAN AND ANIMAL RIGHTS

No Animals/Humans were used for studies that are base of this research.

CONSENT FOR PUBLICATION

Not applicable.

AVAILABILITY OF DATA AND MATERIALS

The author confirms that the data supporting the findings of this research are available within the article.

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CONFLICT OF INTEREST

The authors whose names are listed immediately above certify that they have NO affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

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