ISSN No:-2456-2165

Molecular Docking Studies of Synthetic and Natural Anti-Viral Agents Against Sars Covid 19 Main Protease

Abirami.G*, Shanmugavel[1].R Jayavani.S[2], Kaviya.K[3], Nandiga.D[4]
*1, 2, 3, 4 Department of Pharmaceutical Chemistry,Adhiparasakthi College of Pharmacy,
The Tamil Nadu Dr.M.G.R.Medical University, Chennai-28, Melmaruvathur- 603319, Tamilnadu, India.

For Correspondence*:- Dr .G.ABIRAMI, M.Pharm, Ph.D., Assistant Professor,Department of Pharmaceutical Chemistry,Adhiparasakthi College of Pharmacy, Melmaruvathur 603319. Tamilnadu, India.

Abstract:- The first coronaviruses that were discovered to infect humans were known as 229E and OC43, but they only produced extremely minor infections that were comparable to the common cold. The potential for dangerous human infections was not realised until the epidemics of SARS (severe acute respiratory syndrome) and then MERS (Middle Eastern Respiratory Syndrome or camel flu). It is believed that those two illnesses originated in bats and travelled to civet cats and camels. The history of publications regarding coronaviruses shows how interest in them has fluctuated throughout time. The number of publications on corona-viruses gradually increased since their discovery in 1968, reaching two maxima after two epidemics: the SARS corona-virus outbreak in 2003–2004 and a porcine epidemic diarrhoea outbreak in North America in 2013. The discovery of the first cases of MERS in Saudi Arabia in 2012—a disease similarly brought on by the coronavirus—may have played a role. While there will be more than 4 million COVID-19 patients by May 16, 2020, the World Health Organization (WHO) has listed cancer as one of the top 10 major causes of mortality. This work deals with 4 different proteins that docked with various antiviral medicines derived from natural and synthetic sources, utilising Auto dock Vina 4.2.6. Molecular docking helps to find compounds such as antiviral medications with possible inhibitory activity. A number of studies have demonstrated that the surface area at the interface directly correlates with binding affinity and that the hydrophobicity of the interacting protein molecule increases the selectivity of the binding domain.

***Keywords*:-** *Drug Repurposing, Inhibitory Action, Molecular Docking, SARS-COV-2 Nucleocapsid, Htra-Type Protease Algw withTri-Peptide, COVID-19.*

I. INTRODUCTION

The current COVID-19 pandemic has had an impact on all of us. However, depending on our status as individuals and as members of society, the pandemic's effects and repercussions are felt in different ways. While some people try to adjust to working online, homeschooling their kids, and using Instacart to get groceries, others are forced to be exposed to the virus in order to maintain society. The term "corona virus" comes from the Latin word corona, which means "crown" or "wreath" and is itself a derivation from the Greek v-korn, which means "garland, wreath." The corona virus 2 (SARS-CoV-2) that is the infectious disease known as corona virus disease (COVID-19) was first discovered in Wuhan, China, in December 2019. The rapid spread of this highly contagious and pathogenic virus led to the declaration of the pandemic by the World Health Organization (WHO) on 11 March 2020.The scientific community around the world is concerned with finding an effective treatment for the new corona virus. Short-term efforts are focused on developing vaccines such as **covishield and covaxin** or inhibitors that act as protection against infection with the new corona virus. To develop new drugs with antiviral activity, the concern of many research groups is focused on **the repositioning/repurposing of already approved drugs**. The fastest way is to find potential drugs by molecular docking studies using auto dock vina.

➢ *A Look Back to COVID Era*

- Dec-2019- first case of covid 19
- Jan 2020- The outbreak was deemed a global public health emergency by the WHO.
- Feb 2020 - naming of covid 19
- Mar 2020 -The US proclaimed a state of emergency after there were 1 lakh cases of covid 19, and the first human trials for a modern mRNA vaccine for covid 19 were conducted.
- Apr 2020 -1 million covid 19 cases, WHO release guidance on mask wearing
- Sep 2020 - 19 incidents of million covid deaths
- Nov 2020 - 90% effectiveness was demonstrated in Pfizer and Bio N Tech vaccination trials, and contemporary vaccine effectiveness was also demonstrated.

- Dec 2020 - WHO issues its first emergency use validation for covid 10 vaccination, delta variants was discovered first.
- Apr 2021 - 1 billion covid 19 vaccine dose administered

II. MOLECULAR DOCKING

The preferred orientation of one molecule to another when they are bonded together to create a stable structure is predicted using a technique called docking. Knowing the preferred orientation allows one to estimate the degree of association or burning affinity between two molecules.

Signal transmission is heavily dependent on the interactions between biologically important components such proteins, nucleic acids, carbohydrates, and lipids. Additionally, the type of signal generated may vary depending on the relative direction of the two interacting partners (e.g., agonism vs antagonism). Docking is therefore helpful for forecasting the signal's kind and strength.[3]

Due to its capacity to anticipate the binding-conformation of sn cule ligands to the proper target binding site, molecular docking is one of the most widely employed techniques in structure-based drug design. Characterizing the binding behaviour is crucial for the rational design of medications and for illuminating basic biological mechanisms. [4]

➢ *Protein-Ligand Docking*

Using protein structure is referred to as "using structure" in the structure-based drug design (SBDD) approach. Computer technique that simulates the interaction of a ligand with a protein Given. Site of protein binding Complex Ligand. Predicts. the molecule's position within the binding site The strength of the binding, measured by the binding affinity, or a score.

➢ *Molecular Docking*

In structural molecular biology and computer assisted drug design, molecular docking is a crucial technology. Predicting the dominant binding mode(s) of a ligand with a protein having a known three-dimensional structure is the aim of ligand-protein docking. The term "docking" mostly refers to interactions between protein molecules. The binding energy, free energy, and stability of complexes can be suggested using the information gleaned through the docking procedure. At the moment, the tentative binding characteristics of the ligand receptor complex are predicted using docking approach. [5]

Obtaining a ligand-receptor complex with an optimal shape and the idea of having less binding free energy is the main goal of molecular docking. The hydrogen bond (AGMbond), electrostatic (AGelec), torsional free energy (AGior), dispersion and repulsion (AGvdw), desolvation (AGdesolv), total internal energy (AG101al), and unbound system's energy are some of the characteristics used to show the net anticipated binding free energy (AG bind) (AG unb). **[Agarwal S et al., (2015)].**

- *There are Various Kinds of Molecular Docking for Interactions between Proteins:*

✓ A protein-ligand interaction occurs when two molecules interact.
✓ Whenever one protein interacts with another: the interaction between proteins
✓ Protein-DNA interaction occurs when a protein binds to DNA.

➢ *Advantages*

- Determining the target spot.
- Choosing the "best" medication (based on scoring function)
- Mechanisms of enzymes.
- The actions of proteins.
- Virtual compound screening, etc.

➢ *Steps Involved In Molecular Docking:*

- Preparation of ligand
- Preparation of protein
- Setup ligand protein docking calculations
- Evaluation of results

➢ *Applications of Molecular Docking*

- *Lead Optimization*

Molecular docking is able to foretell the best way for a ligand to interact with its target. It can foretell several ligand binding mechanisms in the groove of the target molecule. This can be utilised to create medication candidates that are more powerful, selective, and effective.[6]

- *Hit Identifications*

Large datasets can be evaluated using docking in conjunction with a scoring algorithm to uncover powerful drug candidates that can target the target molecule in silico. **[7]**

- *Drug-DNA Interaction*

When predicting how a medication will initially attach to nucleic acid, molecular docking is crucial. The relationship between a drug's molecular structure and cytotoxicity is established using this information. [8]

- *Bioremediation*

It is also possible to forecast which contaminants can be broken down by enzymes using protein ligand docking. To develop and create the medications, in silico strategies and models were used. These investigations heavily rely on various software. **[9]**

ISSN No:-2456-2165

III. MATERIALS AND METHODS

With the reference of literatures the drugs and proteins were aken from the drug bank online and protein data bank.

A. *Protein Information:* [21]

➢ *6WZQ:*

Structure of SARS-CoV-2 Nucleocapsid dimerization domain, P21 form

- DOI : 10.2210/pdb6WZQ/pdb
- Classification : VIRAL PROTEIN
- Organism(s) : Severe acute respiratory syndrome coronavirus 2
- Expression System : Escherichia coli
- Mutation(s) : No
- Deposited : 2020-05-14 Released: 2020 -05-27
- Deposition Author(s) : Ye, Q., Corbett, K.D.

➢ *6WZO:*Structure of SARS-CoV-2 Nucleocapsid dimerization domain, P1 form

- DOI : 10.2210/pdb6WZO/pdb
- Classification : VIRAL PROTEIN
- Organism(s) : Severe acute respiratory syndrome coronavirus 2
- Expression System : Escherichia coli
- Mutation(s) : No
- Deposited : 2020-05-14 Released: 2020-05-27
- Deposition Author(s) : Ye, Q., Corbett, K.D.

➢ *7CO2:* HtrA-type protease AlgW with tripeptide

- DOI : 10.2210/pdb7CO2/pdb
- Classification : PEPTIDE BINDING PROTEIN
- Organism(s) : synthetic construct, Pseudomonas aeruginosa PAO1
- Expression System : Escherichia coli BL21 (DE3)
- Mutation(s) : No
- Deposited : 2020-08-03 Released: 2021-03-10
- Deposition Author(s) : Li, T., Song, Y.J., Bao, R.

➢ *6XCA:*

Crystal structure of an anti-SARS-CoV-2 human neutralizing antibody Fab fragment, C105.

- DOI : 10.2210/pdb6XCA/pdb
- Classification : IMMUNE SYSTEM
- Organism(s) : Homo sapiens
- Expression System : Homo sapiens
- Mutation(s) : No
- Deposited : 2020-06-08 Released: 2020-07-01
- Deposition Author(s) : Sharaf, N.G., Barnes, C.O., Bjorkman, P.J.
- Funding Organization(s) : National Institutes of Health/National Institute Of Allergy and Infectious Diseases (NIH/NIAID).

➢ *Protein Preparation*

Significant proteins were chosen based on prior in vitro experiments that were conducted on them, and Protein Data Base was used to gather the structural information of the proteins (PDB). The protein was downloaded in PDB format and saved as a brand-new, pre-existing file.

- *Import the Protein File and the Steps as to be Followed,*

✓ Delete the extra chains if the protein has more than one chain (mostly A chain is active)
✓ Remove the water molecules
✓ Add the hydrogen molecules
✓ Click the calculation tools and select energy optimization and followed by geometry optimizations
✓ Click the active site and select “make a group from this residue” and save the protein.

- *Ligand Preparation:*

✓ ligand was downloaded from the pub chem or drug bank online and saved in the mol.2000 or SDF form
✓ click the calculation tools and select energy optimizaation and followed by geometry optimization.
✓ Click the active site and select “make a ligand from this group residue”
✓ Set up a docking database and run docking calculation.

- *Active Site Prediction*

Finding the ligand-binding sites on a protein is the most important step in molecular docking. The innovative energy-based approach Q-Site Finder created by Jackson, which analyses the interaction energies of a methyl probe with a protein, is used to discover the protein-ligand binding sites. **(Laurie and Jackson, 2005**).

The software was used to find the poisons' likely active binding locations. For this investigation, more flexible binding sites were favoured.

- *Protein Ligand Docking:*

Following the screening of the compounds, an integrated tool called Argus lab 4.0.1 and Auto dock tools 1.5.6 construct a virtual screening environment.

The programme provides interactive interfaces for setting up both the target protein's binding site and the screening chemical library. Each substance in the library is docked into the binding site following screening, producing the protein-compound interaction profiles of electrostatic, hydrogen-bonding, and van der Waals interactions. The programme then verifies the pharmacological interactions, groups the screening compounds for post-screening analysis based on interaction data and compound structures, ranks and visualises the screening compounds using the

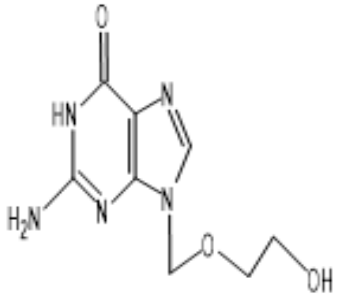
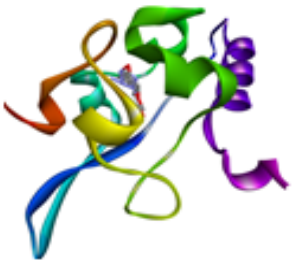
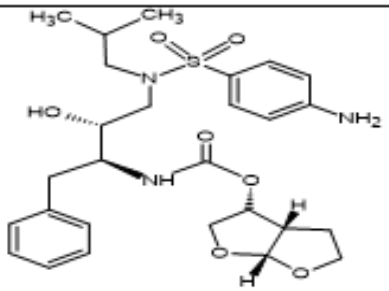
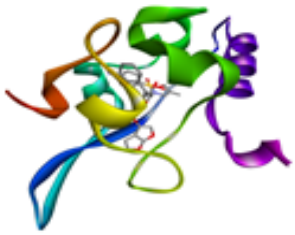
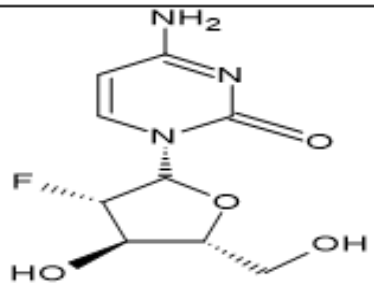
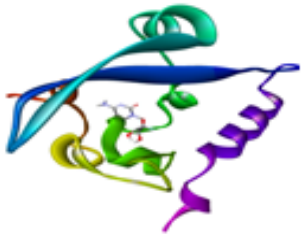
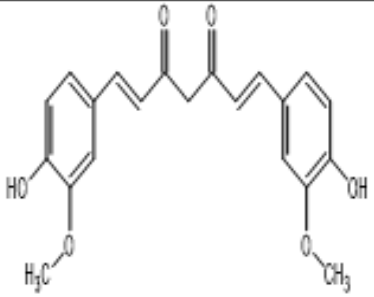
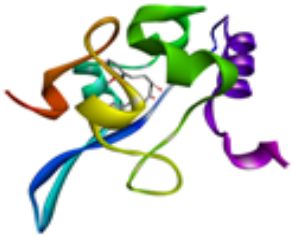
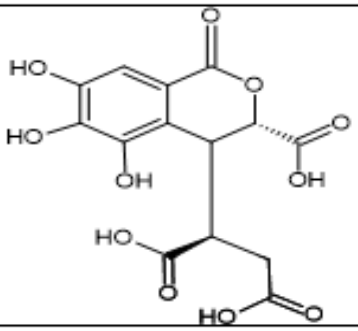
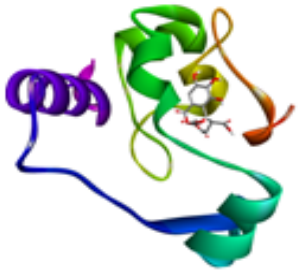
pharmacological interactions and energy-based scoring function.

IV. RESULTS AND DISCUSSION

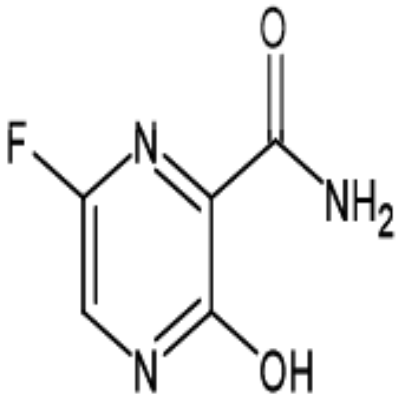
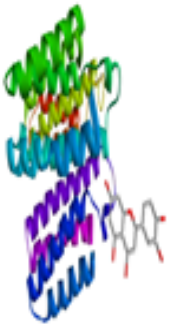
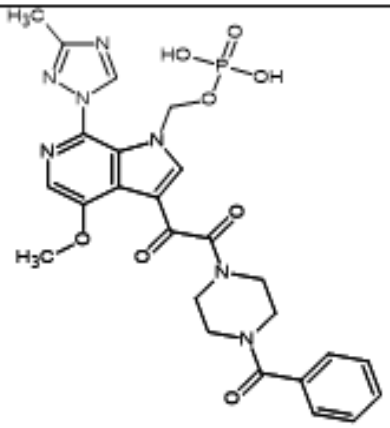
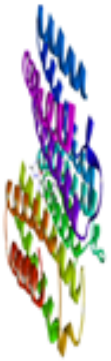
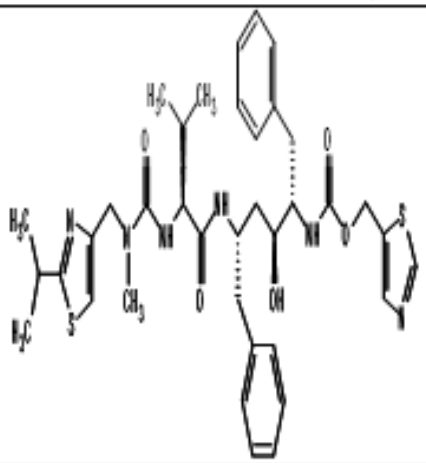
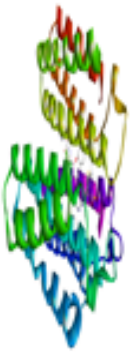
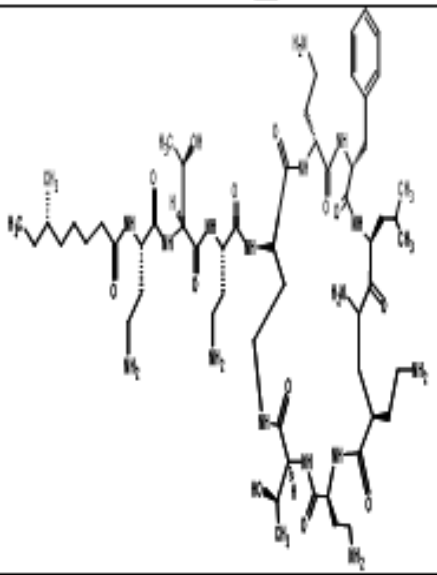
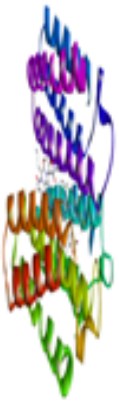
➢ *The Obtained Results are Tabulated below,*

This table shows the docked picture of drugs with proteins, 17 different antiviral drugs were docked with four different proteins.

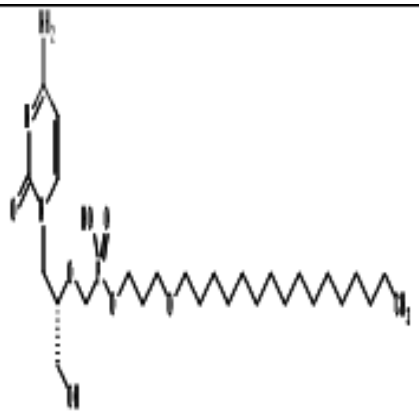
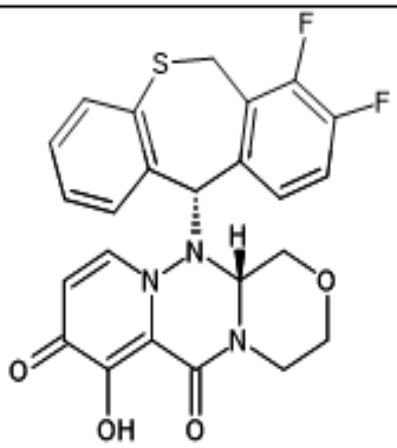
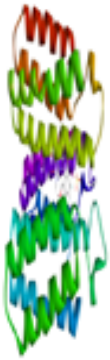
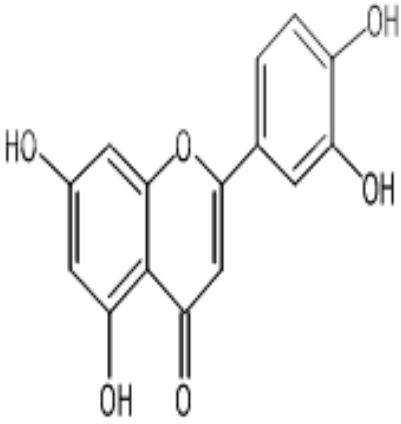
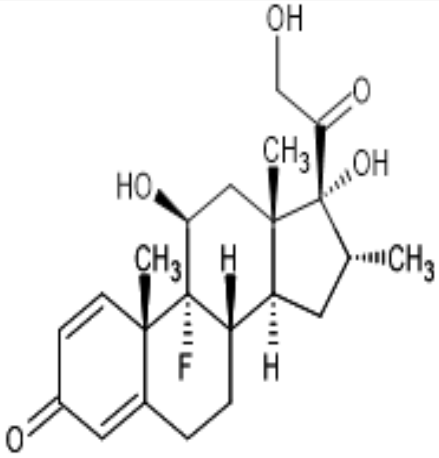
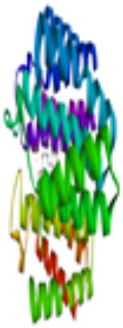
Table 1 The Docked Picture of Drugs with Proteins 1

S.NO	PROTEIN NAME	CHEMICAL NAME	STRUCTURE	CAPTURE	FINAL ENERGY
01.	6WZO	Acyclovir			Argus lab: -5.3 Auto dock: -6.9
02.	6WZO	Darunavir			Aurgus lab-nil Auto dock: -8.6
03.	6WZO	2 deoxy 2 fluro cytidine			Argus lab: -5.64 Auto dock: -5.1
04.	6WZO	Curcumin			Aurgus lab: -4.03 Auto dock: -7.4
05.	6WZO	Chebulic acid			Aurgus lab: -8.55 Auto dock: -5.6

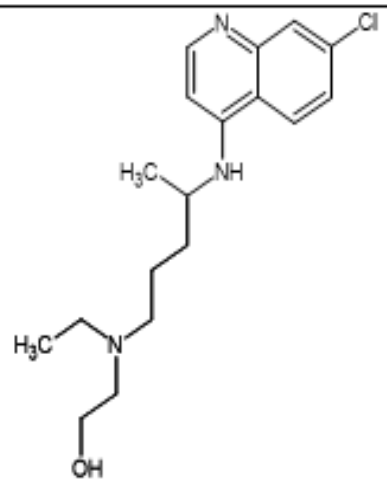
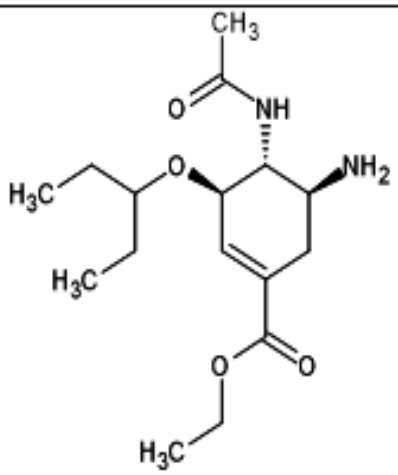
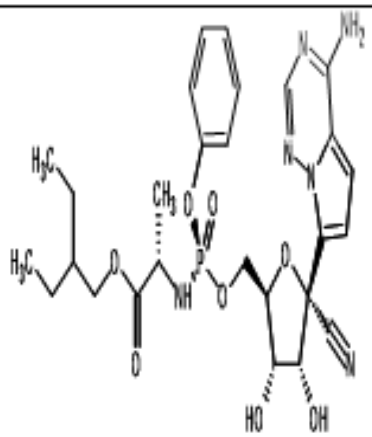
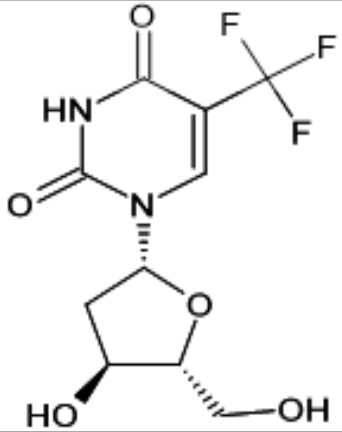
ISSN No:-2456-2165

06.	6WZO	Favipiravir			Argus lab: -4.74 Auto dock:-0.9
07.	6WZO	Fosetamivair			Argus lab: -624 Auto dock: 66.2
08.	6WZO	Ritonavir			Argus lab: -12.35 Auto dock: 85.5
09.	6WZO	Polymycin-B			Argus lab: NIL Auto dock: 154.7

ISSN No:-2456-2165

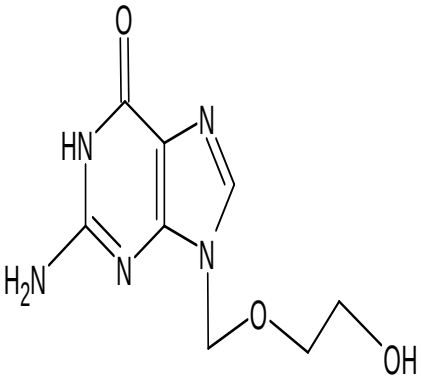
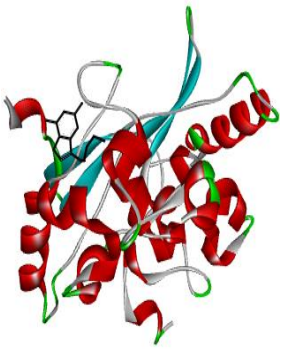
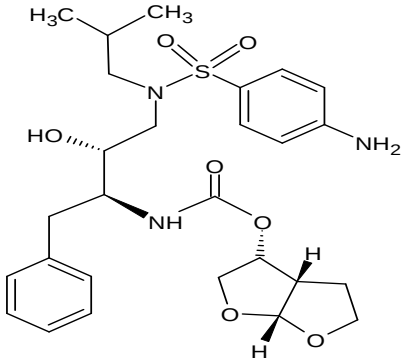
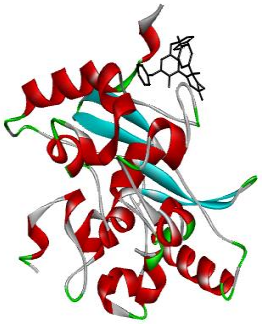
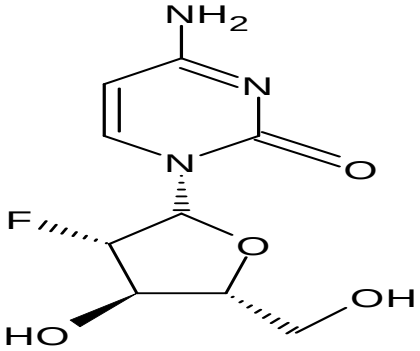
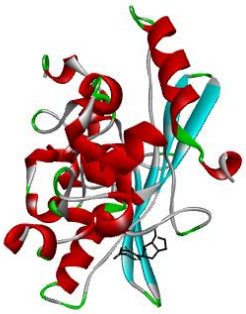
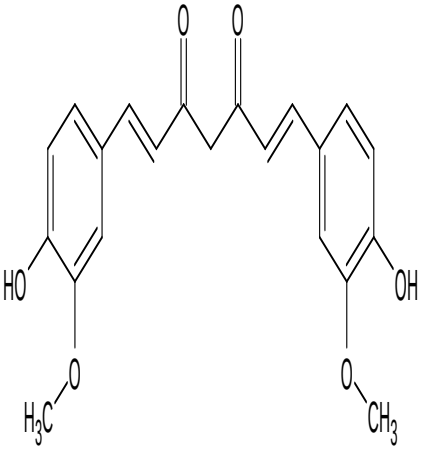
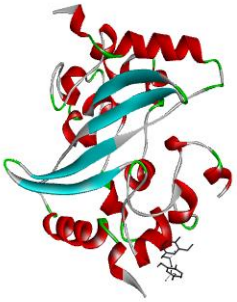
10.	6WZO	Brincidofovir			Argus lab: -9.04 Auto dock:17
11.	6WZO	Baloxavir			Argus lab:-9.36 Auto dock: 95.7
12.	6WZO	Luteolin			Argus lab: -7.48 Auto dock: 33.2
13.	6WZO	Dexamethasone			Argus lab:-8.86 Auto dock:46.5

ISSN No:-2456-2165

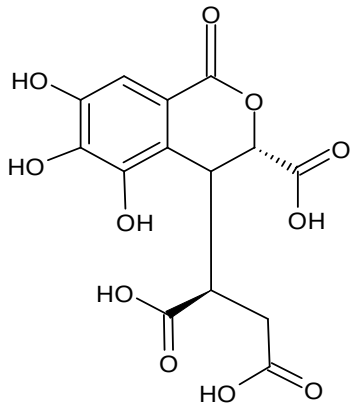
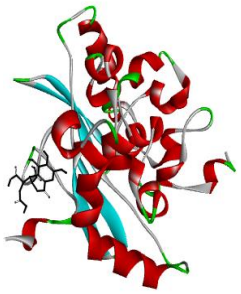
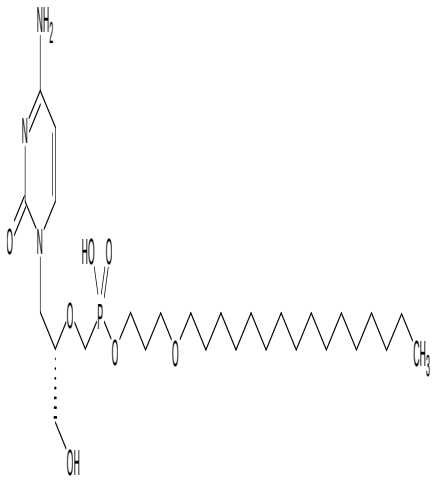
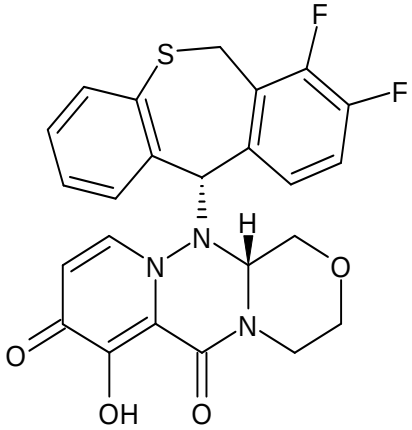
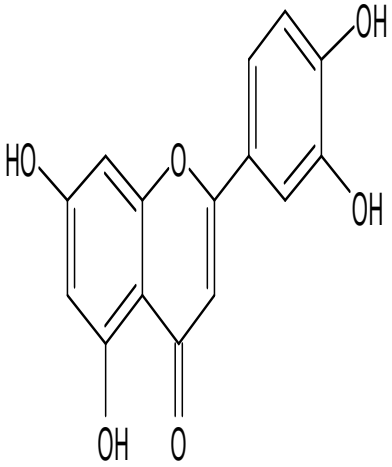
14.	6WZO	Hydrroxy chloroquine			Argus lab: -7.95 Auto dock:13.00
15.	6WZO	oseltamivir			Argus lab:-8.85 Auto dock: 15.7
16.	6WZO	Remdesivir			Argus lab: -8.37 Auto dock: 38.6
17.	6WZO	Trifuridine			Argus lab:-5.64 Auto dock: 11.7

ISSN No:-2456-2165

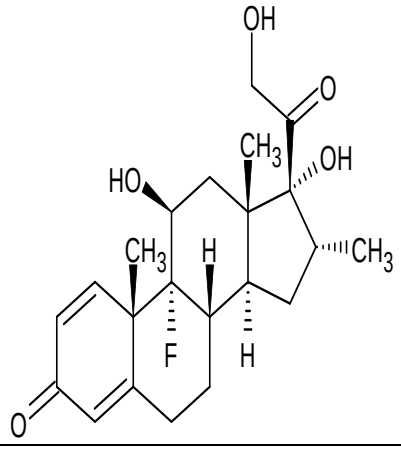
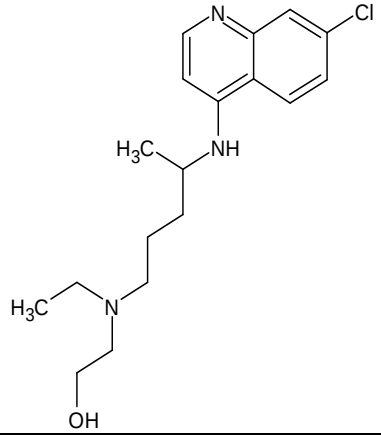
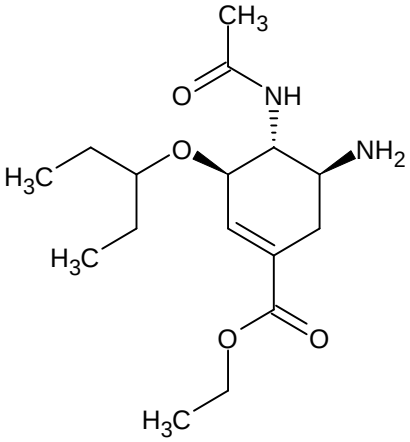
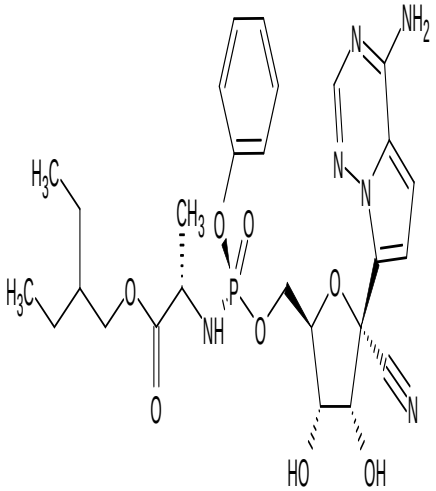
Table 2 The Docked Picture of Drugs with Proteins 2

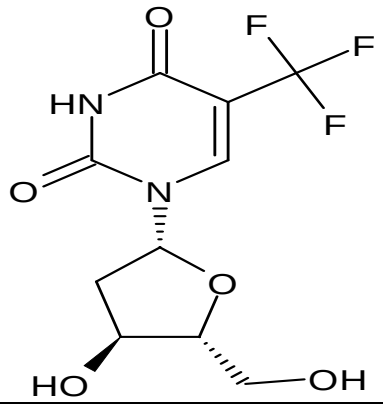
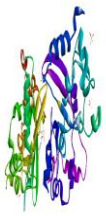
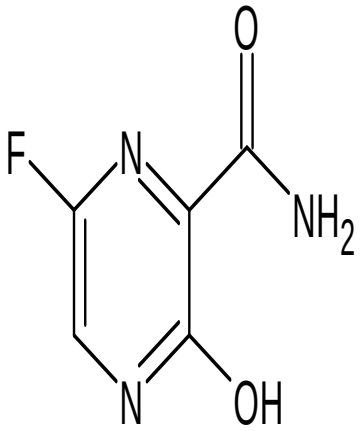
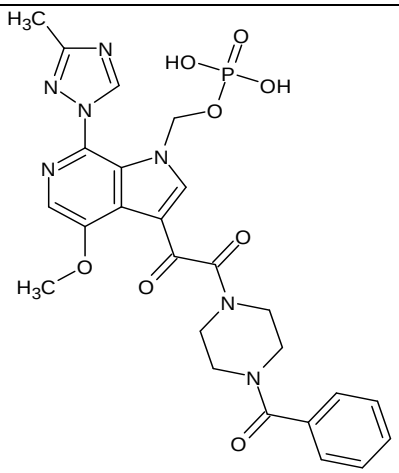
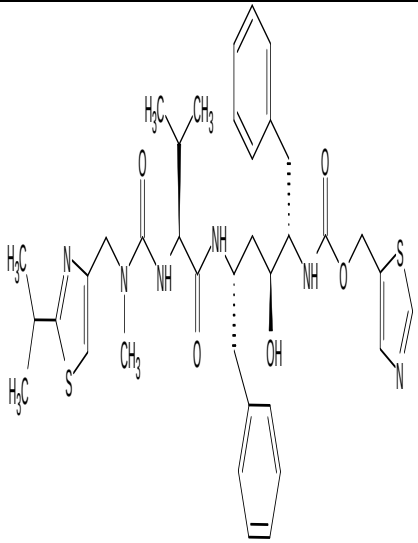
S.NO	PROTEIN NAME	CHEMICAL NAME	STRUCTURE	CAPTURE	FINAL ENERGY
01.	6WZQ	Acyclovir			Argus lab: -4.19 Auto dock: -4.4
02.	6WZQ	Darunavir			Aurgus lab:-12.81 Auto dock: -5.7
03.	6WZQ	2 deoxy 2fluro cytidine			Argus lab: -5.73 Auto dock: -5.0
04.	6WZQ	Curcumin			Aurgus lab: -4.416 Auto dock: -5.8

ISSN No:-2456-2165

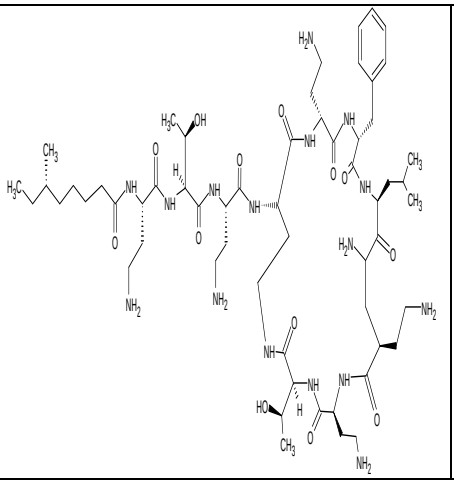
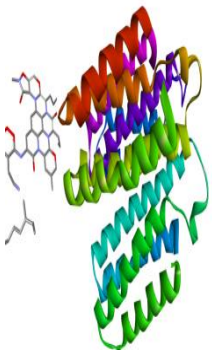
05.	6WZQ	Chebulic acid			Aurgus lab: -7.94 Auto dock: -5.1
06.	6WZQ	Brincidofovir			Argus lab: -9.21 Auto dock:-3
07.	6WZQ	Baloxavir			Argus lab:-10.7 Auto dock: -10.9
08.	6WZQ	Luteolin			Argus lab: -7.51 Auto dock: -8.9

ISSN No:-2456-2165

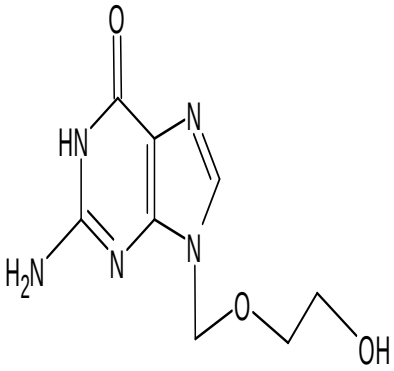
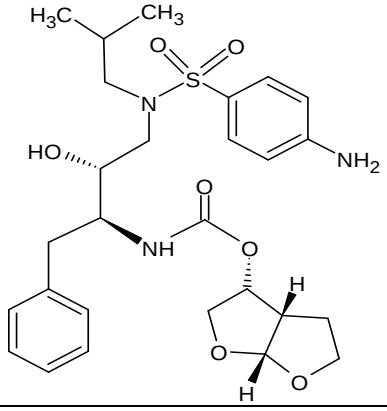
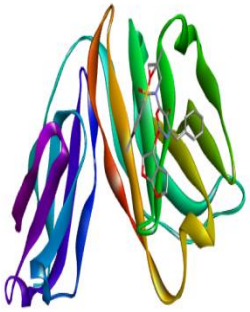
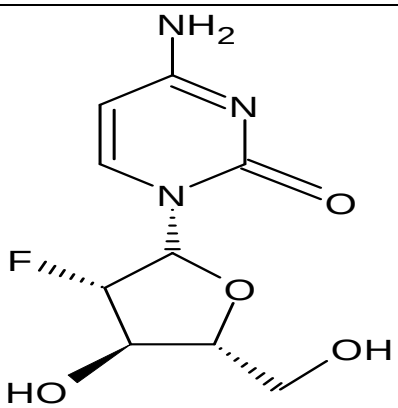
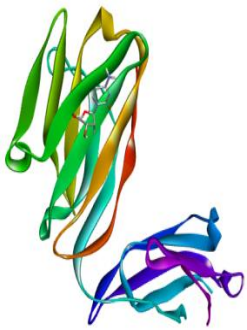
09.	6WZQ	Dexamethasone			Argus lab:- 10.40 Auto dock: -8.9
10.	6WZQ	Hydrroxy chloroquine			Argus lab: -8.37 Auto dock:- 5.6
11.	6WZQ	Oseltamivir			Argus lab: -8.72 Auto dock:- 5.0
12.	6WZQ	Remdesivir			Argus lab: -8.63 Auto dock: -7.7

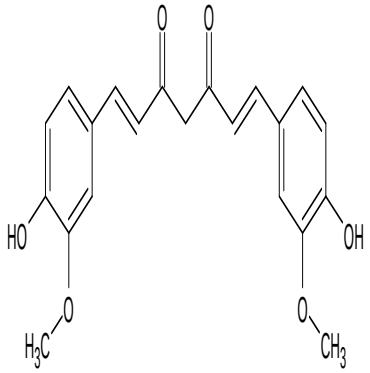
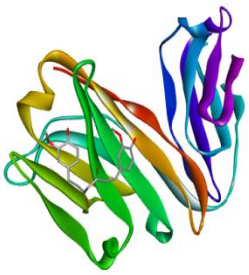
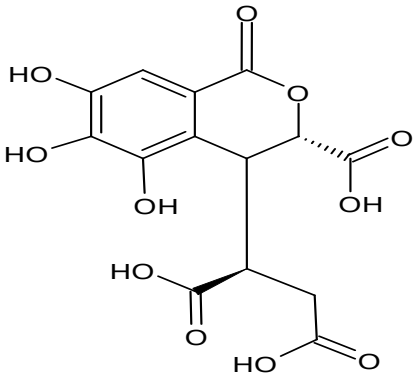
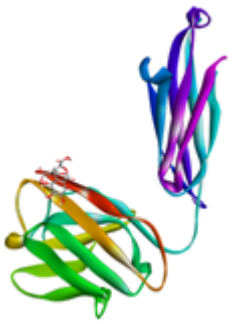
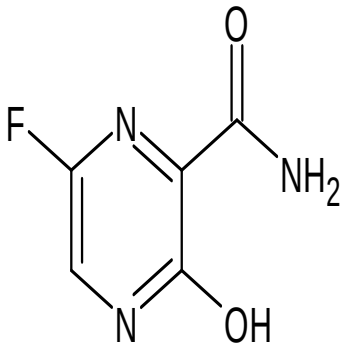
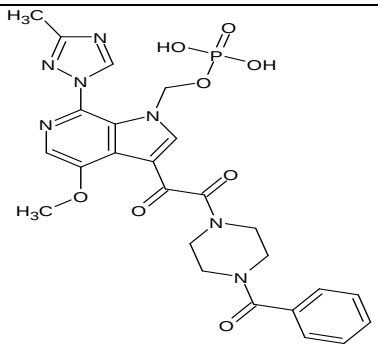
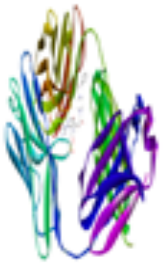
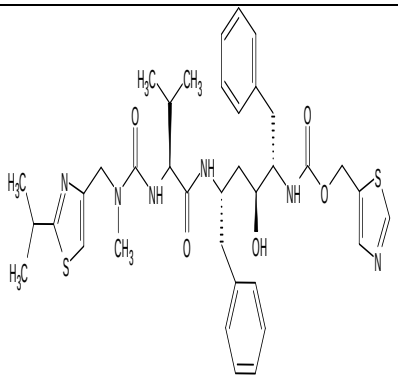
13.	6WZQ	Trifuridine			Argus lab: -5.40 Auto dock: -6.6
14.	6WZQ	Favipiravir			Argus lab: -4.82 Auto dock:- 5.0
15.	6WZQ	Fostemsavir			Argus lab: -5.76 Auto dock: - 8.4
16.	6WZQ	Ritonavir			Argus lab: -11.84 Auto dock: -10.0

ISSN No:-2456-2165

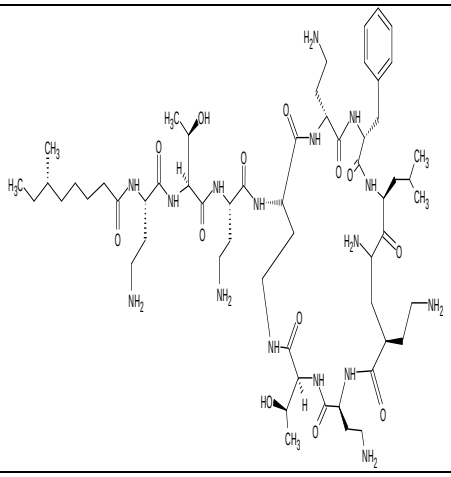
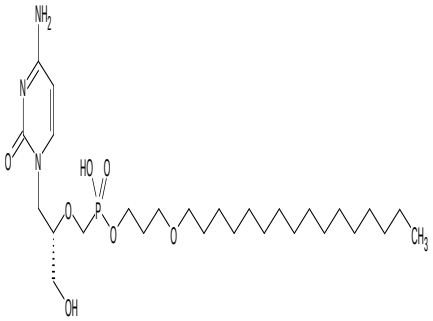
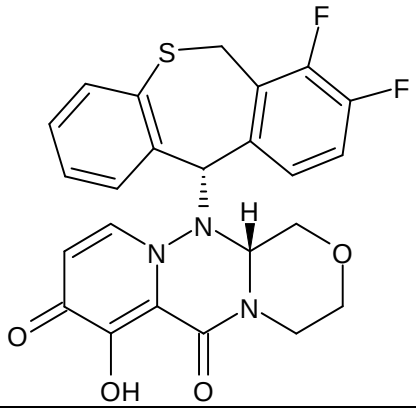
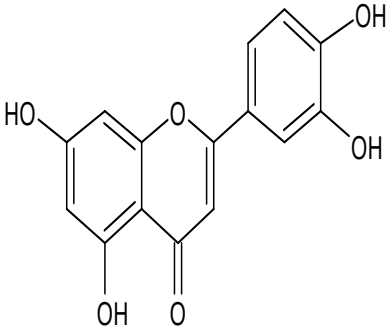
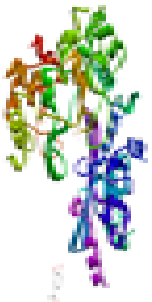
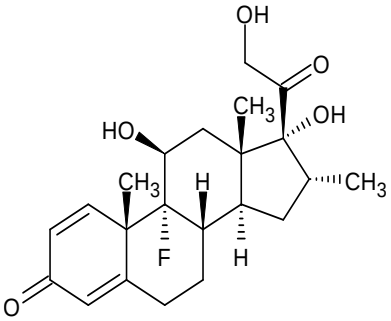
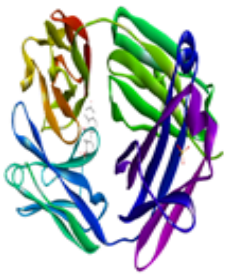
17.	6WZQ	Polymycin-B			Argus lab: NIL Auto dock: 16.3

Tablw 3 The Docked Picture of Drugs with Proteins 3

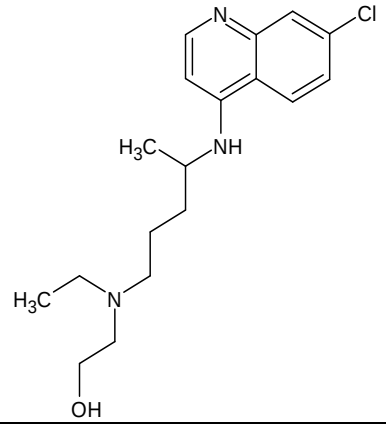
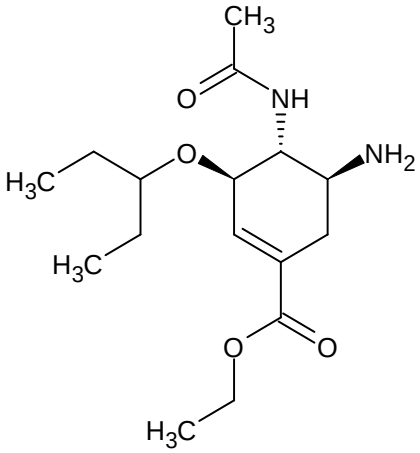
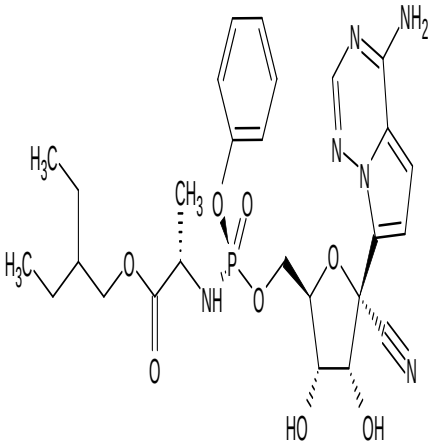
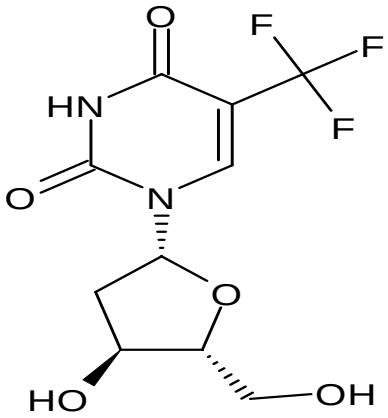
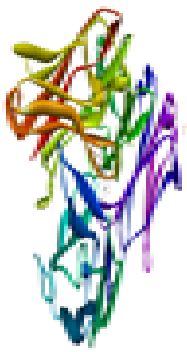
S.NO	PROTEIN NAME	CHEMICAL NAME	STRUCTURE	CAPTURE	FINAL ENERGY
01.	6XCA	Acyclovir			Argus lab: -4.22 Auto dock: -4.1
02.	6XCA	Darunavir			Aurgus lab: -10.30 Auto dock: -2.6
03.	6XCA	2 deoxy 2fluro cytidine			Argus lab: -5.54 Auto dock: -3.6

04.	6XCA	Curcumin			Aurgus lab: -2.5 Auto dock: -4.3
05.	6XCA	Chebulic acid			Aurgus lab: -7.41 Auto dock: -3.6
06.	6XCA	FAVIPIRAVIR			Argus lab: -4.81 Auto dock:- 4.5
07.	6XCA	FOSTEMSAVIR			Argus lab: -6.33 Auto dock: - 6.8
08.	6XCA	RITONAVIR			Argus lab: -12.32 Auto dock: -7.9

ISSN No:-2456-2165

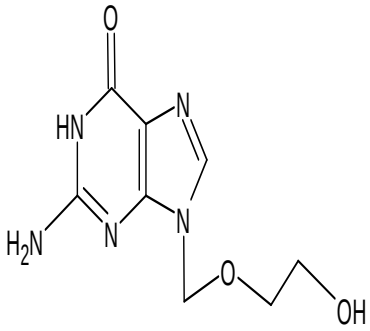
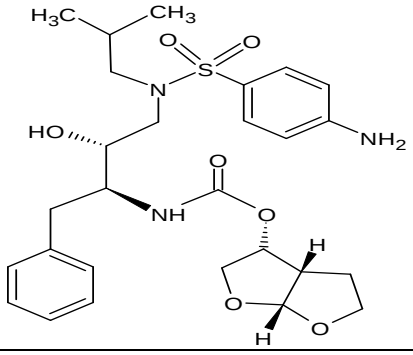
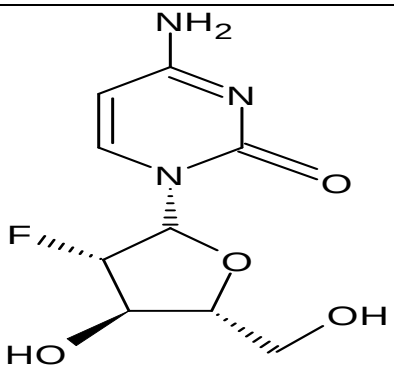
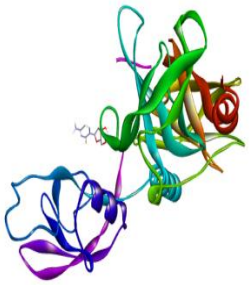
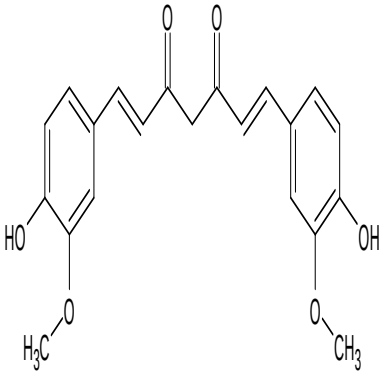
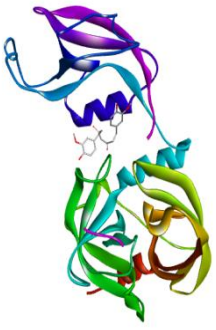
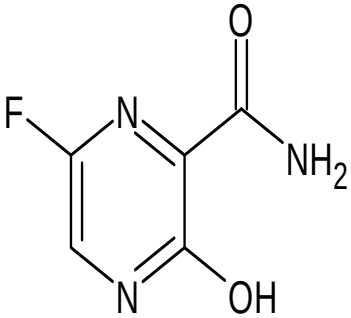
09.	6XCA	POLYMYXIN-B			Argus lab: NIL Auto dock: -6.2
10.	6XCA	Brincidofovir			Argus lab: -8.01 Auto dock:0.1
11.	6XCA	Baloxavir			Argus lab:-8.75 Auto dock: -8.3
12.	6XCA	Luteolin			Argus lab: -7.33 Auto dock: -6.4
13.	6XCA	Dexamethasone			Argus lab:-NIL Auto dock: -7.3

ISSN No:-2456-2165

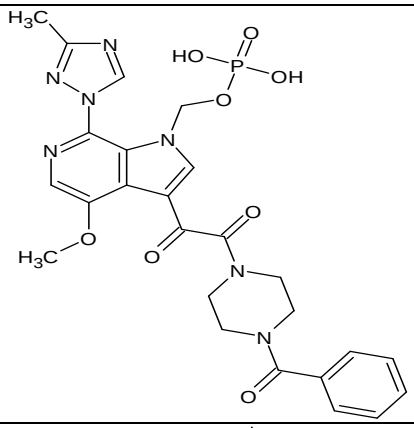
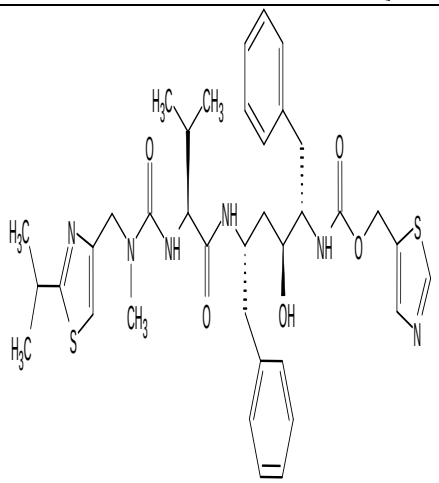
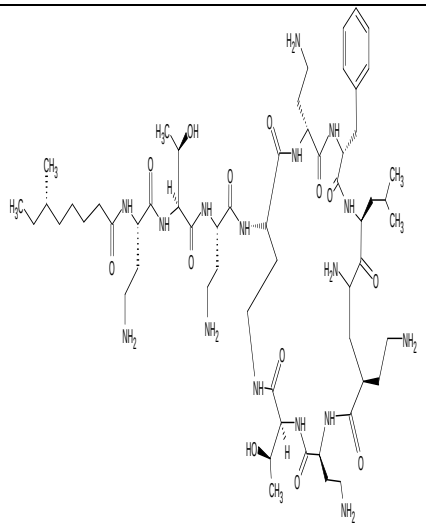
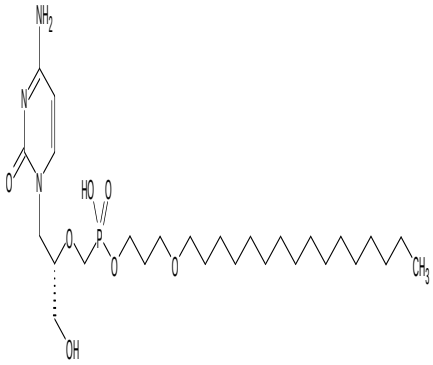
14.	6XCA	Hydrroxy chloroquine			Argus lab: -7.94 Auto dock:- 6.00
15.	6XCA	oseltamivir			Argus lab: -8.29 Auto dock: -5.8
16.	6XCA	Remdesivir			Argus lab: -9.84 Auto dock: -8.3
17.	6XCA	Trifuridine			Argus lab: -5.42 Auto dock: -7.3

ISSN No:-2456-2165

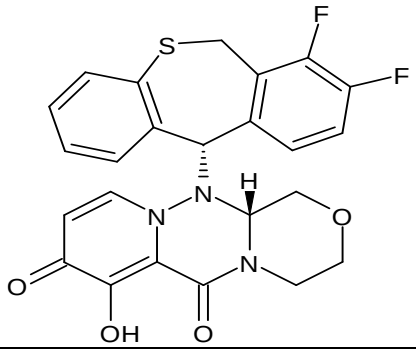
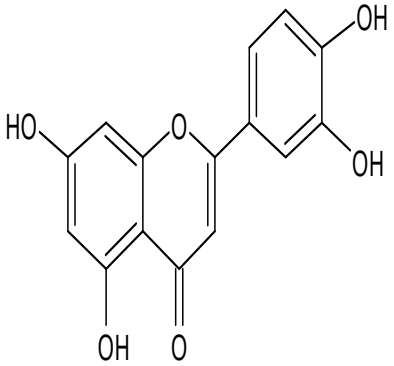
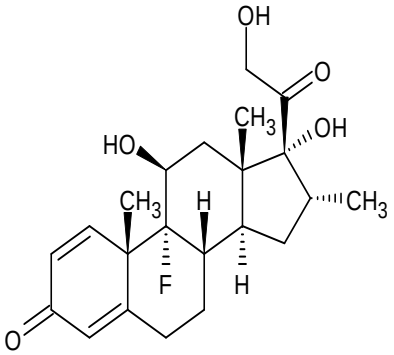
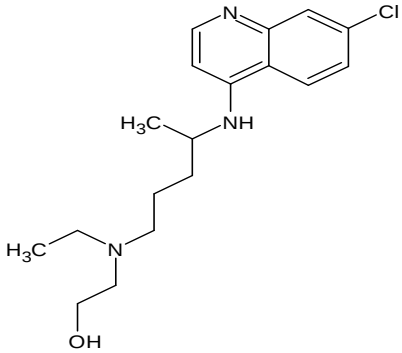
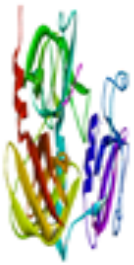
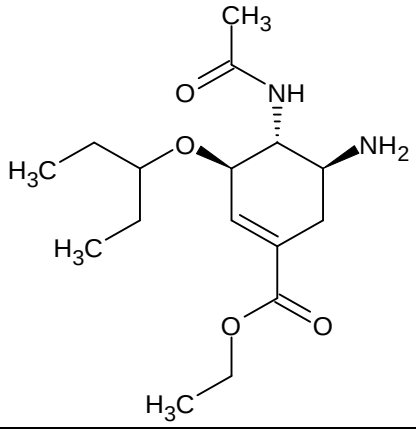
Table 4 The Docked Picture of Drugs with Proteins 4

S.NO	PROTEIN NAME	CHEMICAL NAME	STRUCTURE	CAPTURE	FINAL ENERGY
01.	7CO2	Acyclovir			Argus lab: -4.25 Auto dock: -4.6
02.	7CO2	Darunavir			Aurgus lab: -11.82 Auto dock: -6.5
03.	7CO2	2 deoxy 2fluro cytidine			Argus lab: -5.66 Auto dock: -5.3
04.	7CO2	Curcumin			Aurgus lab: -4.28 Auto dock: -5.4
05.	7CO2	Favipiravir			Argus lab: -4.82 Auto dock:- 4.8

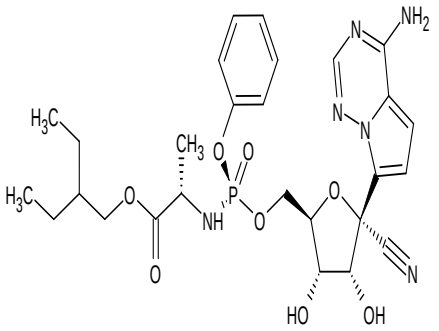
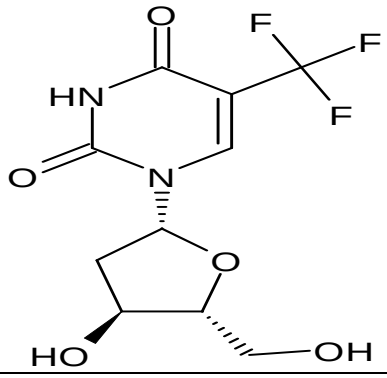
ISSN No:-2456-2165

06.	7CO2	Fostemsavir			Argus lab: -6.81 Auto dock: -6.9
07.	7CO2	Ritonavir			Argus lab: -15.03 Auto dock: -7.2
08.	7CO2	Polymycin-B			Argus lab: NIL Auto dock: 7.3
9.	7CO2	Brincidofovir			Argus lab: -7.36 Auto dock:-5

ISSN No:-2456-2165

10.	7CO2	Baloxavir			Argus lab:- 10.30 Auto dock: - 8.8
11.	7CO2	Luteolin			Argus lab: -9.45 Auto dock: - 7.4
12.	7CO2	Dexamethasone			Argus lab: NIL Auto dock: -5.6
13.	7CO2	Hydrroxy chloroquine			Argus lab: -9.85 Auto dock:- 6.1
14.	7CO2	oseltamivir			Argus lab: -8.16 Auto dock: -6.2

ISSN No:-2456-2165

15.	7CO2	Remdesivir			Argus lab: -9.02 Auto dock: -8.7
16.	7CO2	Trifuridine			Argus lab: -5.98 Auto dock: -7.2

V. FINDING OF INTERACTION

The ligand protein interaction can be simply viwed by click the 'ligand interactions' in the discovery studio file and note the amino acid which were involved in the **Hydrogen bonds, Electrostatic bond and Hydrophobic bonds.**

As the Anti-Viral agents are docked against SARS COVID main protease, the docking scores were obtained. From the results we can concluded that best binding energy of the compound.

However we can't say that only one drug out of these is the better one because the proteins are different (one is peptide binding protein and another one is imunne system protein and other two are viral proteins) and drugs are two types one is natural and others are synthetic. So, drugs possess different binding score with the different proteins

- *Note:-* For the binding of the proteins and drugs some of the bonds plays an important role suh as

- *Hydrogen bond*
- *Hydrophobic bonds*

The number of hydrogens bonds in the compound (weak electrostatic bonds between proton and electronegative of the compound) will estimate the better binding effects.

For eg: In this docking of acyclovir with 6WZO, the hydrogen bonds viz., ARG 256, ARG 271 makes pair with the nitrogen and oxygen with different position and PHE 274 make bond with other nitrogen and oxygen hence, this compounds has maximum binding affinity with this proteins (Fig.no.4). In case of Favipiravir it has only hydrogen bond so, it has leasst energy.

Hence, from this study one can know the insilico (a pre way before pre-clinical and clinical studies) way of docking of unknown drugs using different proteins.Once it was established then the further studies are developed such as invitro and invivo studies. It may help to procure economical balance, human resource and time management.

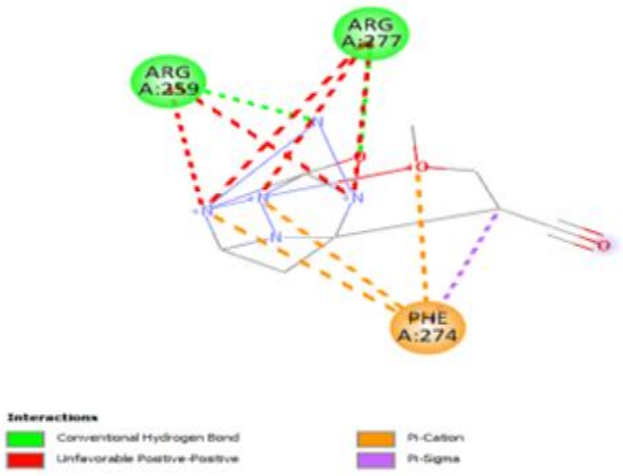


Fig 1 2D digram of Acyclovir with 6WZO

ISSN No:-2456-2165

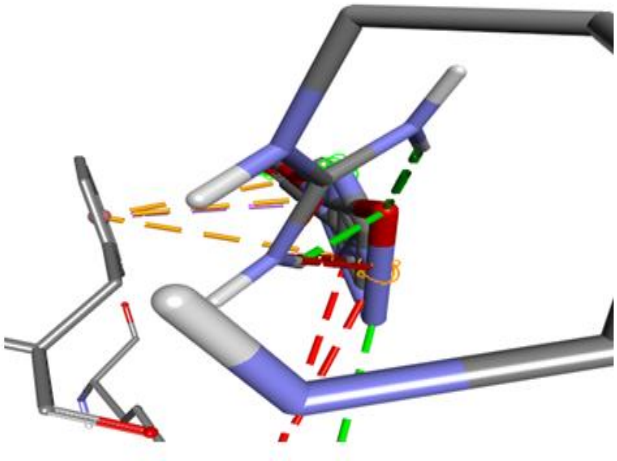


Fig 2 3D Digram of Acyclovir with 6WZO

VI. CONCLUSION

As the synthetic and natural drugs were docked against covid-19 main protease and the results were compared, this results shows that, when allopathic compounds are used for this infection its shows better activity and introducing the concept of drug repurposing. Drug repurposing eliminates the discovery of new compounds and wasting of time and money and as well as docking technology enhances the concept of repurposing of many antiviral agent against novel corona virus.

The medications using natural compounds were taken from approved bioactive compound databases using molecular docking techniques. These compounds from natural products were found to be capable of effectively inhibiting COVID-19 by acting on the primary protease (Mpro).

When compared to other drugs, the results of molecular docking revealed that the main compounds from the kabasura kudineer plants—chebulic acid and curcumin—may inhibit COVID-19.

- *Among the Synthetic Compounds ,*

- *2deoxy 2fluro cytidine (-5.71) - SARS COVID 19 Main protease*
- *Ritonavir (-15.3), Baloxavir (-10.9), curcumin (-4.3) – SARS COVID Neutralizing antibody .*

These findings urge additional in-vitro and in-vivo research on **Ritonavir, 2deoxy-2-fluoroctytidine, and Baloxavir.** They also support the traditional use of **Kabasura kudineer** as a preventative measure.

Although the drugs were developed, our own sanitation is very important in this pandemic period so follow the protocols of Govt. Wear mask, stay home and stay vaccinated.

ACKNOWLEDGMENT

The **Thirumathi Amma ACMEC Trust** and **Sakthi Arul Thiru Amma** are to be thanked for providing the necessary resources for the authors to complete their task successfully. We are grateful to **Dean Dr. T. Vetrichelvan** for his kind encouragement and help in getting our task done.

REFERENCES

[1]. Anonymous, https://en.wikipedia.org/wiki/Coronavirus
[2]. Anonymous, https://www .who.int
[3]. Rarey M, Kramer B, Lengauer T, Klebe G. A fast flexible docking method using an incremental construction algorithm. Journal of molecular biology. 1996 Aug 23;261(3):470-89.
[4]. Kitchen DB, Decornez H, Furr JR, Bajorath J. Docking and scoring in virtual screening for drug discovery: methods and applications. Nature reviews Drug discovery. 2004 Nov;3(11):935-49.
[5]. Morris GM, Lim-Wilby M. Molecular docking. InMolecular modeling of proteins 2008 (pp. 365-382). Humana Press.
[6]. Shoichet BK, McGovern SL, Wei B, Irwin JJ. Lead discovery using molecular docking. Current opinion in chemical biology. 2002 Aug 1;6(4):439-46.
[7]. Ferreira LG, Dos Santos RN, Oliva G, Andricopulo AD. Molecular docking and structure-based drug design strategies. Molecules. 2015 Jul 22;20(7):13384-421.
[8]. Tiwari SK, Agarwal S, Seth B, Yadav A, Nair S, Bhatnagar P, Karmakar M, Kumari M, Chauhan LK, Patel DK, Srivastava V. Curcumin-loaded nanoparticles potently induce adult neurogenesis and reverse cognitive deficits in Alzheimer's disease model via canonical Wnt/β-catenin pathway. ACS nano. 2014 Jan 28;8(1):76-103.
[9]. Suresh PS, Kumar A, Kumar R, Singh VP. An Insilco approach to bioremediation: Laccase as a case study. Journal of Molecular Graphics and Modelling. 2008 Jan 1;26(5):845-9.
[10]. Abdo Elfiky A. Ribavirin, Remdesivir, Sofosbuvir, Galidesivir, and Tenofovir against SARS-CoV-2 RNA dependent RNA polymerase (RdRp): A molecular docking study. Life sciences. 2020 Jul 15;253:117592.
[11]. Ahmet Aktaş A, Tüzün B, Aslan R, Sayin K, Ataseven H. New anti-viral drugs for the treatment of COVID-19 instead of favipiravir. Journal of Biomolecular Structure and Dynamics. 2021 Dec 12;39(18):7263-73.
[12]. Assia Belhassan A, Chtita S, Zaki H, Lakhlifi T, Bouachrine M. Molecular docking analysis of N-substituted oseltamivir derivatives with the SARS-Cov-2 main protease. Bioinformation. 2020;16(5):404.

[13]. Ismail Celik I, Onay-Besikci A, Ayhan-Kilcigil G. Approach to the mechanism of action of hydroxychloroquine on SARS-CoV-2: a molecular docking study. Journal of Biomolecular Structure and Dynamics. 2021 Sep 2;39(15):5792-8.
[14]. Md. Riad Chowdhury P. In silico investigation of phytoconstituents from Indian medicinal herb 'Tinospora cordifolia (giloy)'against SARS-CoV-2 (COVID-19) by molecular dynamics approach. Journal of Biomolecular Structure and Dynamics. 2021 Nov 22;39(17):6792-809.
[15]. Mohamed Hagar , Ahmed HA, Aljohani G, Alhaddad OA. Investigation of some antiviral N-heterocycles as COVID 19 drug: molecular docking and DFT calculations. International Journal of Molecular Sciences. 2020 Jan;21(11):3922.
[16]. Mohammad Mahfuz Ali Khan Shawan , Halder SK, Hasan MA. Luteolin and abyssinone II as potential inhibitors of SARS-CoV-2: An in silico molecular modeling approach in battling the COVID-19 outbreak. Bulletin of the National Research Centre. 2021 Dec;45(1):1-21.
[17]. Mostafa A. Hussien, Abdelaziz AE. Molecular docking suggests repurposing of brincidofovir as a potential drug targeting SARS-CoV-2 ACE2 receptor and main protease. Network Modeling Analysis in Health Informatics and Bioinformatics. 2020 Dec;9(1):1-8.
[18]. Ray M, Sarkar S, Rath SN. Druggability for COVID-19: in silico discovery of potential drug compounds against nucleocapsid (N) protein of SARS-CoV-2. Genomics & Informatics. 2020 Dec;18(4).
[19]. Sandra De Meyer , Bojkova D, Cinatl J, Van Damme E, Buyck C, Van Loock M, Woodfall B, Ciesek S. Lack of antiviral activity of darunavir against SARS-CoV-2. International Journal of Infectious Diseases. 2020 Aug 1;97:7-10.
[20]. Xuqiao Hu X, Zhou Z, Li F, Xiao Y, Wang Z, Xu J, Dong F, Zheng H, Yu R. The study of antiviral drugs targeting SARS-CoV-2 nucleocapsid and spike proteins through large-scale compound repurposing. Heliyon. 2021 Mar 1;7(3):e06387.
[21]. Anonymous: https://www.rcsb.org/.