International Journal of Engineering Research & Technology (IJERT)
ISSN: 2278-0181
Vol. 9 Issue 11, November-2020

In Silico Analysis of Various Antiviral Compounds Against Spike Protein of COVID 19 using Docking Methods

C. Shanmathi. [1], P. Ponmurugan[2], N.Karthik [3]*, M.Anita[3], A.Ezhilarasu[3], A.Rohini[4]
[1]Department of Chemical Engineering, National Institute of Technology, Trichy -620015,Tamil Nadu, India
[2]Department of Botany, Bharathiar University, Coimbatore- 641 046, Tamil Nadu, India
[3]Department of Microbiology,Selvamm Arts and Science College, Namakkal-637 003, Tamil Nadu, India
[3]*Corresponding author: Assistant Professor, Department of Biotechnology,Selvamm Arts and Science College, Namakkal-637 003, Tamil Nadu, India
[4]Department of Biochemistry,Annai Violet Arts and science College,Chennai-600053,Tamil Nadu,India

***Abstract*:- The current examination assessed the adequacy of hostile to viral compounds against the objective protein, Spike protein of COVID19 utilizing in silico approach. Structure based docking studies was performed using PyRx 8.0 tool to retrieve potential candidates with high affinities binding against antiviral compound models with several targeted proteins repositories. The chosen target protein was 6LU7. Molecular docking was carried out using various anti-viral compounds with the target protein of microorganisms.Free vitality of restricting was recorded for the compound with its objective. Nine different compounds were docked with the target protein, within which was found to own higher binding affinity. Therefore, the current study plays a guiding role in developing new inhibitors with better binding affinities with the virulent protein of pathogens, followed by invention of novel drug to treat viral infections.**

Keywords: Spike protein, COVID 19, PyRx8.0

1. INTRODUCTION

Pneumonia of unknown cause was detected in Wuhan of Hubei province in China and reported first on 31st December 2019 [3]. On 30thJanuary, 2020 the outbreak was declared as Public Health Emergency of International Concern. On 11thFebruary ,2020 the new corona virus disease was named as COVID 19 by World Health Organization (WHO). The WHO declared it as world pandemic on March 11, 2020. In exception to Antarctic the virus contact the majority parts of the globe [9]

COVID 19 is a communicable disease caused by newly discovered corona virus. These are RNA group virus which will infect mammals and birds [6]. This cause the intense tract infection. there's no medication or vaccine yet discovered to forestall the human corona infectious. The National Institute of Health (NIH) stated that this virus is believed to own genetic similarity to bat corona virus [8]. The virus either directly via close contact and respiratory droplets of sneeze and cough or indirectly via contact through contaminated surfaces. this can be associated with SARS (Severe Acute Respiratory Syndrome) and MERS (Mideast Respiratory Syndrome). The Symptoms of corona virus include Fever, dry Cough and difficulty in breathing [9]. It takes a minimum of of 5-6 days to indicate symptoms when the person is affected from virus. The foremost promising test for the identification of virus is RT - PCR technique.

The COVID 19 belongs to the subfamily Orthocoronavirinae,within the family Coronaviridae, order Nidovirales, and realm Riboviria. COVID 19 is an enveloped, positive sense single stranded RNA genome encoding quite 20 proteins. This has higher binding affinity with human ACE2. this is often wrapped duringa icosahedral protein shell.The genome size of Covid ranges from around 26 to 32 kilobases, one among the greatest among RNA viruses. they need characteristic club-shaped spikes that project from their surface, which in electron micrographs create a picture paying homage to the solar corona, from which their name derives [12].

Novel approach of drug design and docking studies may be utilised for the invention of some therapeutic drug candidates against COVID 19. These in silico techniques can minimize the time and efforts within the pipeline of drug discovery. These techniques include study of the protein structure answerable for the disease or disorder, then identifying a ligand molecule which may have potent activities [1]. Molecular docking techniques are study of interaction of the ligand with the molecule at situation. The site is that three-dimensional site of molecule which directly effects the activity of the protein. Although the activity is often either positive or negative but still it helps medicinal chemist to proceed on rational path [7].

The interaction ligands are measured as binding affinity at receptor binding sites. The less the binding affinity to the receptor at the prescribed site is that the more practical. For measuring certain values, the CHARMM force fields are used. Although the values differ marginally from system to system, and from software to software. this is often due to the variations within the systemsgenetic algorithm [7].We performed the docking of some antiviral compounds with COVID 19 Spike protein main protease in complex with an inhibitor N3.

International Journal of Engineering Research & Technology (IJERT)
ISSN: 2278-0181
Vol. 9 Issue 11, November-2020

1.1 S Protein:

The S protein (spike protein) consists of an Ectodomain region (ED), Intracellular domain and TM region. it's a kind I-transmembrane (TM) protein which appears as clove shaped. The ED region consists of two receptor binding domains (RBD), S1 and trimeric stalk containing S2 subunit associated on C-terminal [4], [5]. When S protein associates, the virion appears as trimeric and appears sort of a crown structure. This structure is termed as Corona virus. The S protein is found to own potential role in viral entry inside the host. The activation of host immune re-pose against the virus by S protein has been reported. This protein is taken into account as a possible target for drug discovery because S1 domain and host ACE2 for SARS-CoV and di-peptidyl peptidase-4 (DPP4) for MERS-CoV related to host and viral membrane fusion mediated by S2 segment potentiate the CoV to release its RNA in host cell [10].

2. MATERIALS AND METHODS:

2.1 Preparation of Receptor:

The target protein, Spike protein of COVID 19 was obtained from PBD database (https://www.rcsb.org). The SDF file format of PBD ID: 6LU7 was downloaded for docking studies.

2.2 Preparation of Ligand:

PubChem Compound Database contains approved synthetic portrayal data gave to clarify substances in PubChem substance. Structures stored within PubChem Compounds are pre- clustered and cross-referenced by identity and similarity groups.Theaflavin (CID: 135403798), Theaflavin-3-gallate (TF2A) (CID: 7Q307578), Theaflavin-3-3'-digallate (CID: 135403795), Hydroxychloroquine (CID: 3652) , Zanamivir (CID: 60855), Peramivir (CID: 154234), BaloxavirMarboxil(CID: 124081896), Oseltamivir phosphate (CID: 78000), Galangin (CID: 5281616) structures were retrieved from the PubChem Compound Database.

2.3 ADME studies:

SWISS ADME studies are used for predicting the pharmacokinetics and physicochemical properties. Molecules that follow the Lipinski's rule with no violations are listed. the method involves the assessment of Absorption, Distribution, Metabolism and Excretion (ADME).

2.4 PyRx

PyRx could be a Virtual Screening programming for Computational Medication Revelation which will be utilized to screen libraries of mixes against potential medication targets. The macromolecules are docked with small molecules withthe assistance of virtual screening method. the pc aided docking method is extremely useful in identifying the lead drug compound and made the drug discovery procedure easier. PyRx may be a Python artificial language which willrun in any modern computer from PC to super computer [2].

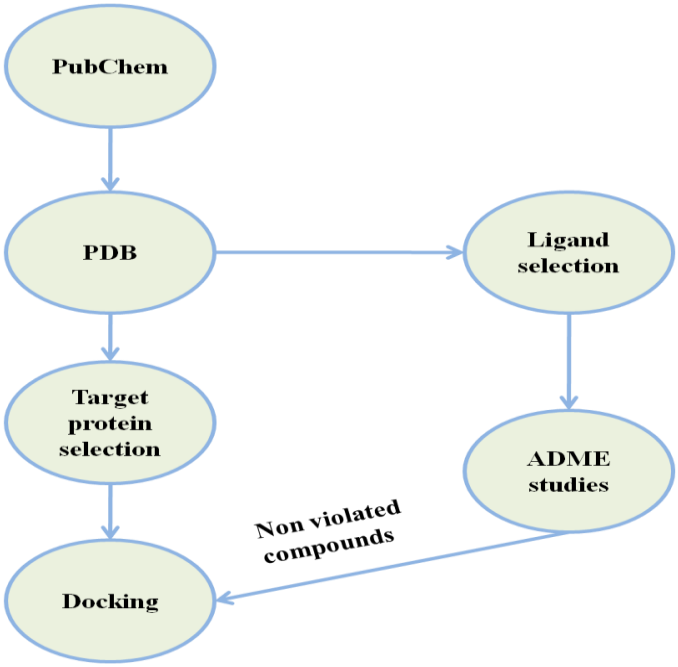


Fig 1: Steps involved in the docking study

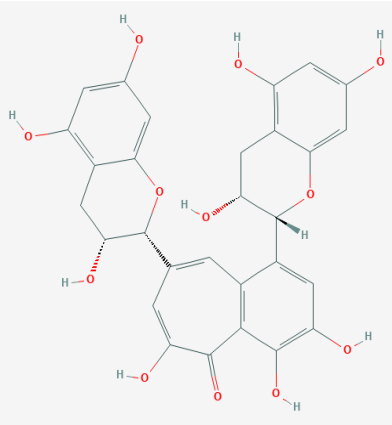
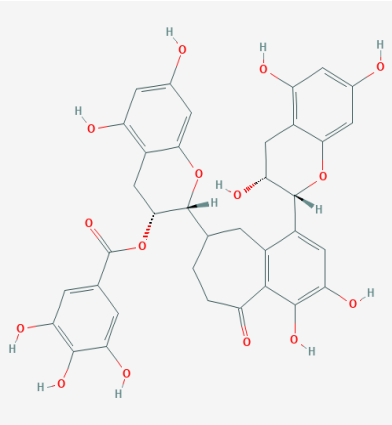
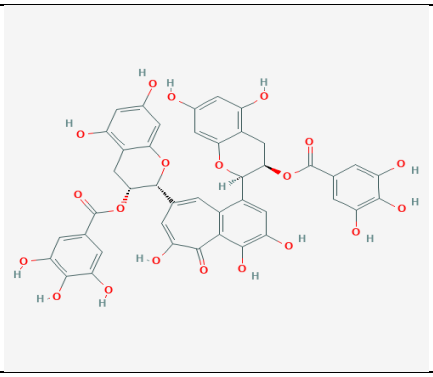
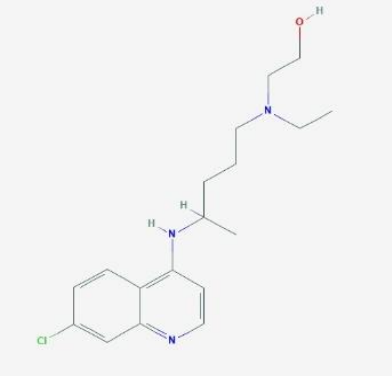
3. RESULT:

3.1 TARGET AND LIGAND PREPARATION:

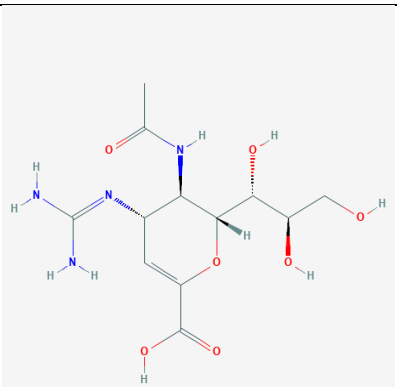
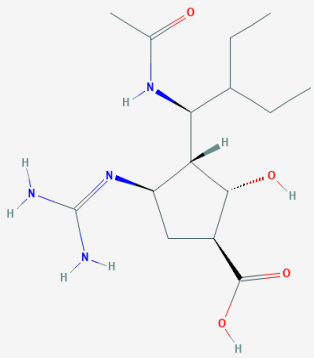
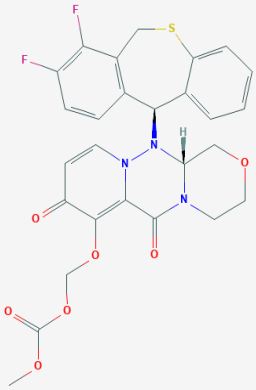
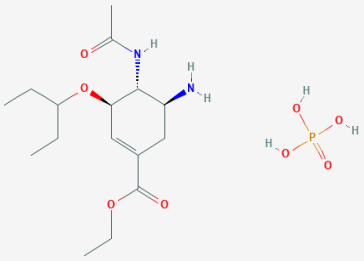
Table 3.1 gives the list of drug compounds used for docking studies

International Journal of Engineering Research & Technology (IJERT)
ISSN: 2278-0181
Vol. 9 Issue 11, November-2020

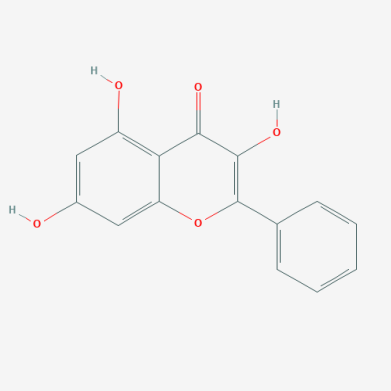
Table 3.1: List of ligand molecules

S.No	Drug	Structure	Target protein	PubChem ID
1.	Theaflavin		6LU7	135403798
2.	Theaflavin-3-gallate		6LU7	71307578
3.	Theaflavin-3-3'-digallate		6LU7	135403795
4.	Hydroxychloroquine		6LU7	3652

International Journal of Engineering Research & Technology (IJERT)
ISSN: 2278-0181
Vol. 9 Issue 11, November-2020

5.	Zanamivir		6LU7	60855
6.	Peramivir		6LU7	154234
7.	Baloxavir		6LU7	124081896
8.	Oseltomivir phosphate		6LU7	78000

International Journal of Engineering Research & Technology (IJERT)
ISSN: 2278-0181
Vol. 9 Issue 11, November-2020

9.	Galangin		6LU7	5281616

3.2 VIRTUAL SCREENING:

PyRx 8.0was accustomed perform the virtual screening of library of 9 molecules. The results from virtual screening are listed within the Table 3.2. The interaction with RMSD zero are considered to be the simplest.

Table 3.2: Virtual screening

Ligand	Binding Affinity (kcal/mol)
Theaflavin	-7.6
Theaflavin-3'-O-gallate	-8.5
Theaflavin 3,3'-digallate	-7.5
Hydroxychloroquine	-4.9
Zanamivir	-5.8
Peramivir	-5.5
Baloxavirmarboxil	-6.9
Oseltamivir phosphate	-4
Galangin	-6.8

3.3 ADME studies:

The SWISS ADME studies were performed for the library of ligand molecules. The ADME properties of H- donor, H- acceptor, LogP value and Molecular weight were determined. Some compounds violated these drug likeness properties. The non-violated compounds are then used for future studies.

COMPUND	MOLECULAR FORMULA	H-DONOR	H-ACCEPTOR	MOL.WT	LogP	VIOLATIONS
Theaflavin	C29H24O12	9	12	564.49 g/mol	1.84	3
Theaflavin-3'-O-gallate	C36H32O15	10	15	704.63 g/mol	1.74	3
Theaflavin 3,3'-digallate	C43H32O20	13	20	868.70 g/mol	0.73	3
Hydroxychloroquine	C18H26ClN3O	2	3	335.87 g/mol	3.58	0
Zanamivir	C12H20N4O7	7	8	332.31 g/mol	0.42	0
Peramivir	C15H28N4O4	5	5	328.41 g/mol	1.04	0
Baloxavirmarboxil	C27H23F2N3O7S	0	9	571.55 g/mol	3.68	1
Oseltamivir phosphate	C16H31N2O8P	5	9	410.40 g/mol	1.48	0
Galangin	C15H10O5	3	5	270.24 g/mol	2.08	0

4. DISCUSSION:

The virtual screening and ADME studies reveal that Galangin has higher binding of -6.8 kcal/mol as compared with other compounds. Although Theaflavin-3-gallate has higher binding affinity of -8.5 kcal/mol, it doesn't satisfy the Druglikeness properties. Other compounds like Hydroxychloroquine has binding affinity of -4.9 kcal/mol, Zanamivir has binding affinity of -5.5 kcal/mol, Peramivir has binding affinity of -5.5 kcal/mol and Oseltomivir phosphate has binding affinity of -4 kcal/mol.

5. CONCLUSION:

The In-silicoscreening of biologically active compounds were distributed towards the Spike protein of COVID 19. The molecular docking studies revealed that Galangin showed higher binding affinity by satisfying ADME properties. The interaction study helped us to grasp that Galangin may be employed in drug discovery process.
Further in vivo studies are often applied to search out the character of the ligand molecule in future.

6. REFERENCES:

[1] Pratyush K, Asnani A, Chaple D and Bais A. (2020). In silico screening and molecular docking of bioactive agents towards human coronavirus receptor. GSC Biological and Pharmaceutical Sciences, 11(1), 132-140.
[2] Dallakyan S, Olson AJ. Small-molecule library screening by docking with PyRx. *Methods Mol Biol*. 2015;1263:243-250. doi:10.1007/978-1-4939-2269-7_19

International Journal of Engineering Research & Technology (IJERT)
ISSN: 2278-0181
Vol. 9 Issue 11, November-2020

[3] Isaac I Bogoch, Alexander Watts, Andrea Thomas-Bachli, Carmen Huber, Moritz U G Kraemer, Kamran Khan, Pneumonia of unknown aetiology in Wuhan, China: potential for international spread via commercial air travel, *Journal of Travel Medicine*, Volume 27, Issue 2, March 2020, taaa008, https://doi.org/10.1093/jtm/taaa008
[4] Rani, Ruchi; Singh, Ankur; Pareek, Akshay; Tomar, Shailly (2020): In Silico Guided Drug Repurposing to Combat SARS-CoV-2 by Targeting Mpro, the Key Virus Specific Protease. ChemRxiv, https://doi.org/10.26434/chemrxiv.12030345.v1
[5] Saddala MS, Kiran JAP, Rani UA (2016) In Silico Drug Design and Molecular Docking Studies of Potent Inhibitors against Cathepsin-L (Ctsl) for Sars Disease. J Res Development 4: 145. doi:10.4172/ 2311-3278.1000145
[6] Donald C. Hall and Hai-Feng Ji, Travel Medicine and Infectious Disease,
[7] https://doi.org/10.1016/j.tmaid.2020.101646
[8] Narkhede RR, Cheke RS, Ambhore JP, Shinde SD. The Molecular Docking Study of Potential Drug Candidates Showing Anti-COVID-19 Activity by Exploring of Therapeutic Targets of SARS-CoV-2. EJMO 2020;4(3):185–195.
[9] Zhou, P., Yang, X., Wang, X. *et al.* A pneumonia outbreak associated with a new coronavirus of probable bat origin. *Nature* **579,** 270–273 (2020). https://doi.org/10.1038/s41586-020-2012-7
[10] World Health Organization (WHO) :https://www.who.int/emergencies/diseases/novel-coronavirus-2019
[11] Jin, Z., Du, X., Xu, Y. *et al.* Structure of M^{pro} from SARS-CoV-2 and discovery of its inhibitors. *Nature* (2020). https://doi.org/10.1038/s41586-020-2223-y.
[12] Corona Virus: https://en.wikipedia.org/wiki/Coronavirus