Repurposing of Medicinal plants used in Siddha formulations as Potential Protease Inhibitors of COVID-19: An in silico approach

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Background:

The Coronavirus disease (COVID-19) caused by the virus SARS-CoV-2 has become a global pandemic in a short time has infected about 1,203,959 patients and brought forth death rate about 64,788 among 206 countries as mentioned by WHO in the month of April 2020. Currently, there is no specific treatment or vaccine for fighting against this infectious disease and scientists agree that possible therapeutic may arise through drug repositioning. Herbal medicine are achieving attention because of the extensive therapeutics like potent antiviral, immunomodulatory, anti-inflammatory, and anti-oxidant properties.

Materials and methods

This study was planned to screen herbs from Siddha that have the potential to increase host immune system as well as blocking virus entry in host cells. Official Siddha formulation Kabasura Kudineer, Nilavembu Kudineer, and Novel Siddha formulation – JACOM are already being in use as antiviral, immunomodulatory, anti-inflammatory, and antioxidant. 54 molecules identified and surveyed via docking study. Docking study was performed using Maestro interface (Schrödinger Suite, LLC, NY).

Results:

Out of these 54 Phytoconstituents, 30 Phytoconstituents were found to interact with > 2 protein structures of COVID-19. The docking results indicate that amongst the reported molecules 4 out 5 protein structure (PDB ID: 5R7Y, 5R7Z, 5R80, 5R81 and 5R82) showed promising results of binding to COVID-19 enzyme. So this formulations may be useful as a therapeutic and/or prophylactic agent for restricting viral attachment to the host cells.

Discussion:

The drug repurposing study provide an insight in terms of binding of active ingredients present in different plants used in formulations and targets enzymes for treatment of the COVID19

Key words:

COVID-19, SARS-CoV-2, Siddha Medicine, Medicinal plants, AYUSH.

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Introduction:

COVID–19 disease caused by the novel coronavirus SARS-CoV–2 has been declared as a global pandemic by WHO first emerged in China [1]. SARS-CoV-2 has spread across all continents, as of latest situation report on June 30, 2020 by WHO, a total of 87, 08 008 cases with a mortality of 4, 61,715 have been reported [2]. In India there are 4, 10 461 cases and 13, 254 deaths as on June 30, 2020 these data correspond the imminent risk facing the country. Transmission of virus spreads via droplets, physical contact with infected individuals, contaminated surfaces [3]. COVID-19 commonly reported symptoms are fever, headache, vomiting, chills, dyspnea, nausea, sore throat, coughing up blood, shortness of

breath, myalgia, diarrhea, and malaise. The severe infection leads to pneumonia, acute respiratory distress syndrome (ARDS) and sometimes multi-organ failures such as kidney failure, and even death [4]. Coronaviruses (CoVs) are the family of Coronaviridae with four gene era (alpha, beta, gamma and delta), and only the alpha and beta- strains are identified to be pathogenic to human [5, 6]. Middle East respiratory syndrome (MERS) virus (MERS-CoV) and SARS-CoV are the other similar agents previously known Coronaviruses [7, 8]. In whole genome sequence analysis SARS-CoV-2 showed higher SARS-CoV genome sequence homology than that of MERS-CoV [9]. Siddha holistic approach will be helpful in combating COVID 19 using both therapeutic and non-therapeutic interventions with disease condition [10]. Presently, quarantine and symptomatic treatment protocol for disease management exists and there is no antiviral drugs or vaccines available. Therefore, it is necessary to develop a treatment for COVID-19. Based on the Siddha Medicine advisory given by Ministry of AYUSH for COVID-19 mentioned stage of medicines for treatment, prophylaxis, and convalescence. These medicines are indicated for symptom management and prophylaxis. However these medicines are in practice for viral diseases like Dengue and Chikungunya in vogue for the past two decades. Kabasura Kudineer and Nilavembu Kudineer, an official Siddha formulation described in Siddha manuscript Citta Vaittiyattirattu [11] is used for *Aiyacuram* (phlegmatic fevers) *Pitthacuram* (hemorrhagic fevers) and is a dependable Siddha prescription for fever [11]. Further, we choose another herbal formulation called "JACOM" a coded novel drug due to its Neuraminidase inhibition potential against inactivated influenza virus H1N1(Patent no.201741016901 A, Dated 18.05.2018) [12]. With the introduction of new and more efficient screening assays and prediction methods, the efficacy of herbal drugs can be effectively used during viral outbreaks [13]. In-silico studies happened in Kabasura Kudineer, and JACOM [14] Nilavembu Kudineer [15] against SARS-CoV-2 spike protein which supports and increase the scope of these medicines in drug repurposing areas.

Till precise treatment is available for COVID-19, the use of known antiviral, immunomodulatory, anti-inflammatory, and antioxidant property herbal drugs is a useful approach. In this study, docking studies were performed over binding pocket of COVID-19 to find the potential small molecule to combat COVID-19.

Materials and methods:

Platform for molecular modelling

The computational investigations were performed using the Schrodinger software (Maestro 11.4, Schrodinger 2017-4).

Ligand preparation

Total 54 Phytoconstituents were selected to perform the molecular docking studies to screen and identify the potent antiviral agents specifically for COVID-19 [16]. PubChem database was used to extract out the 3D chemical structures of the selected molecules. 3D and geometry optimizations with energy minimization of ligands were executed using algorithms monitored in Schrödinger Maestro v 11.4 [17]. LigPrep module (Schrodinger, LLC, NY, USA, 2009) was used from the Maestro builder panel to prepare ligand and generate 3D structure of the ligands by adding hydrogen atoms and removing salt and ionizing at pH (7 ± 2) [18]. Energy minimization was performed using OPLS_2005 force field by using the standard energy function of molecular mechanics and RMSD cut off 0.01 Å to generate the low-energy ligand isomer [19].

Preparation of protein structures and grid generation

To combat the current situation of COVID-19 protein structure of COVID-19 main protease with co-crystallized structure(PDB IDs:5R7Y, 5R7Z, 5R80, 5R81, 5R82, having resolution < 2 Å, R-Value Free < 0.30, R-Value Work < 0.25) were selected and obtained from Protein Data Bank (http://www.rscb.org) with good resolutions [20-24].Protein structure was prepared using protein preparation wizard in Maestro panel. During preparation of protein bond orders were assigned and hydrogen atoms were added as well. Water molecules were removed within 3 Å of het groups [25]. Finally, OPLS-2005force field was applied to minimize the structure of protein (Schrodinger, LLC, NY, USA, 2009) [26]. Further receptor grid boxes were generated using “Glide's Receptor Grid Generation” module at the active site (with the radius of 20 Å around the crystal structure) of co-crystallized ligand with the computing cubic box of 10Å × 10Å × 10Å [27].

Molecular docking

Molecular docking is a structure-based drug design approach to identify the essential amino acid interactions between the selected protein and generated ligands with low energy conformation [28]. Minimum interaction of the ligands characterized by the scoring function which used to foretell the binding affinity with the receptor. Glide Standard precision (SP), docking protocol was applied without smearing any constrain. Flexible docking with Glide Standard precision (SP) protocol was performed to predict the binding affinity and ligand efficiency as inhibitor of COVID-19 target [29]. Concluding energy assessment was done with the dock score. Visualization of docked ligands was done by Maestro interface (Schrödinger Suite, LLC, NY) [30].

$$\text{Dock score} = a \times vdW + b \times Coul + Hbond + Metal + Lipo + BuryP + RotB + Site$$

Where, a and b are co-efficient constant for vdW and Coul, respectively. vdW = van der Waals energy; Coul = Coulomb energy; Hbond = Hydrogen bonding with receptor; Metal = Binding with metal; Lipo=Constant term for lipophilic; Bury P=Buried polar group penalty; Rot B = Rotatable bond penalty; Site = active site polar interaction [31].

3. Results

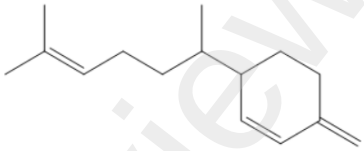
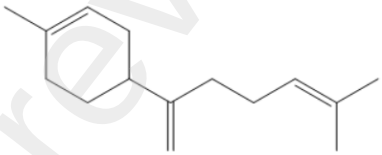
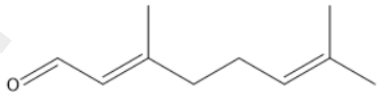
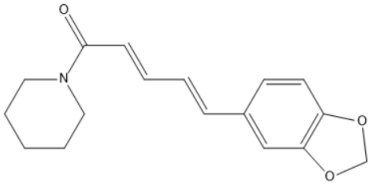
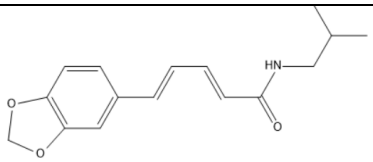
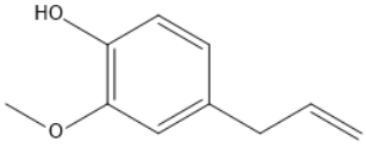
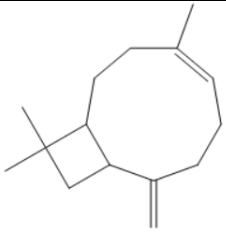
Docking studies were performed to find a potential Phytoconstituents for treating COVID-19, molecular docking studies were performed over three polyherbal Siddha formulation which includes 56 Phytoconstituents on the binding pocket of enzyme COVID-19 (PDB ID: 5R7Y, 5R7Z, 5R80, 5R81 and 5R82). Pharmacological action of each plant included in the formulation was given in Table 1. Also, the list of Phytoconstituents which included in docking study is depicted in Table 2, 3, 4.

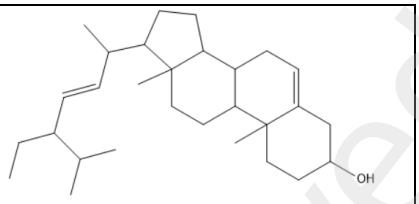
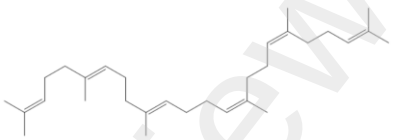
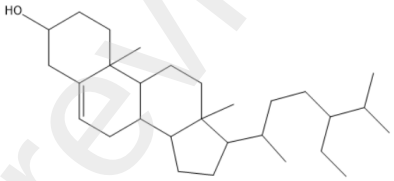
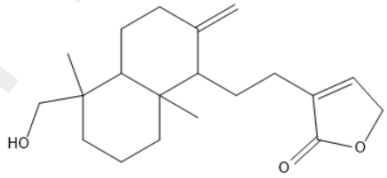
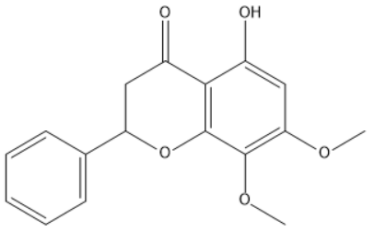
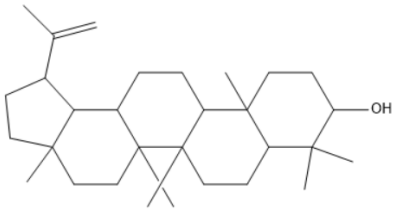
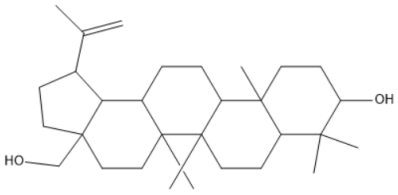
Table 1: List of Individual plants and their Pharmacological activity [32,33,34,35,36,37,38,39,40,41,42,43,44,45]

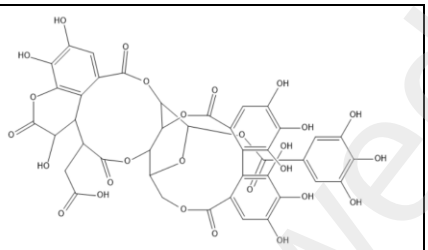
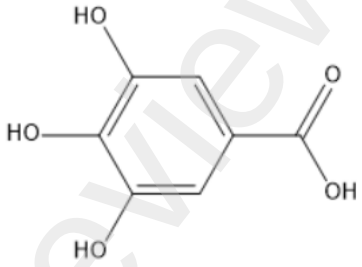
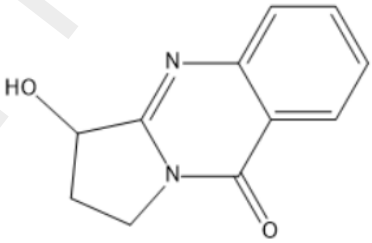
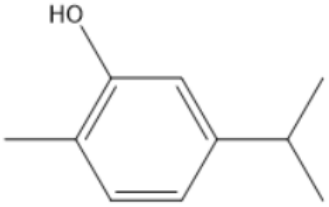
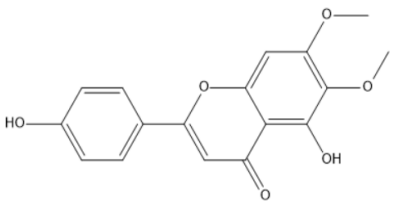
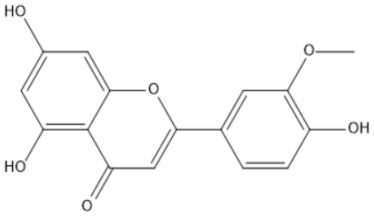
Botanical Name	Pharmacological activity
Zingiber officinale	Antioxidant, Anticancer, Anti-Inflammatory, Antiemetic, Antipyretic, Analgesic, Anti-Inflammatory, Antiviral, Antimicrobial, Immunomodulatory, Expectorant, Hepatoprotective
Piperlongum L	Antifungal, Ant Amoebic, Antimicrobial, Respiratory Stimulation, Antiasthmatic, Antioxidant, Immunomodulatory, Bioavailability Enhancement, Antiviral, Expectorant, Hepatoprotective

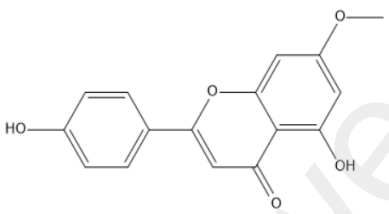
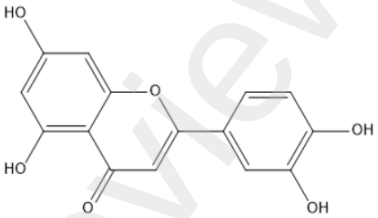
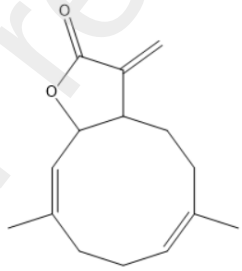
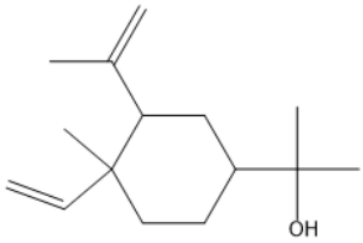
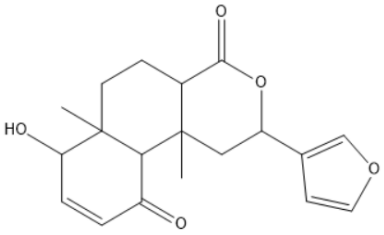
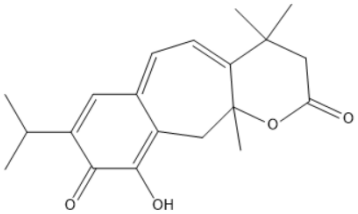
Syzygiumaromaticum	Antimicrobial, Analgesic, Antioxidant, Anticancer, Anthelmintic, Antiulcer, Anti-Inflammatory, Anti-Depressant, Bone Preserving, Antipyretic, Antithrombotic, Expectorant
*Tragiainvolucrata*L	Anti-Inflammatory, Analgesic, Diuretic And Anthelmintic, Antimicrobial
Anacycluspyrethrum	Anti-Inflammatory**,** Antioxidant, Antimicrobial, Immunomodulatory, Antipyretic
Andrographispaniculata	Anticancer, Anti-Inflammatory, Angiogenic, Antivenom, Antidiabetic, Antimalarial, Antimicrobial
Hygrophilaauriculata	Antimicrobial, Antipyretic, Anti-Inflammatory
Terminaliachebula	Antiviral, Antimicrobial, Immunomodulatory, Expectorant
*Justiciaadhatoda*L.	Antimicrobial, Antipyretic, Expectorant, Bronchodilator
Plectranthusamboinicus	Antimicrobial
Saussurealappa	Antiviral, Antimicrobial, Antipyretic
Tinosporacordifolia	Antiviral, Antimicrobial, Immunomodulatory, Antipyretic,
Clerodendrumserratum	Antimicrobial, Expectorant
*Sidaacuta*Burm.f.L	Antiviral, Antimicrobial, Antipyretic
*Cypreusrotundus*L.	Antiviral, Antimicrobial, Antipyretic
*Justiciaadathoda*L.	Antimicrobial, Expectorant
CaricaPapaya	Antibacterial, Antioxidant, Antipyretic, Insecticidal, Antimicrobial
Andrographispaniculata	Antiviral, Antipyretic
Ocimumtenuiflorum	Antibacterial, Antiviral, Antifungal, Antiprotozoal, Antimalarial, Anthelmintic, Antidiarrheal, Analgesic, Antipyretic, Anti-Inflammatory, Antiallergic, Antihypertensive, Cardio Protective, Central Nervous System (CNS) Depressant, Memory Enhancer, Anti-Hyper Cholesterolaemic, Hepatoprotective, Antidiabetic, Antiasthmatic, Antithyroid, Antioxidant, Anticancer, Chemopreventive, Radioprotective, Immunomodulatory,
Vetiveria zizanioides	Inflammatory, Antibacterial, Antifungal, And Anti-Malarial, Anti-Tubercular, Anti-Hyperglycaemic, Anti-Hepatoprotective And Antioxidant Activity.
Santalum album	Antipyretic, Antiscabietic, Diuretic, Expectorant, Stimulant, Anti-Inflammatory, Anti-Mitotic, Antiviral,
Piper nigrum	Antihypertensive, Antiplatelet, Antioxidant, Antitumor, Anti-Asthmatics, Analgesic, Anti-Inflammatory, Anti-Diarrheal, Antispasmodic, Antidepressants, Immunomodulatory,
Hedyotis corymbose	Antibacterial, Antioxidant, Analgesic, Hepatoprotective, Anticancer
Plectranthus vettiveroides	Antioxidant Activity, Anticancer
Trichosanthes cucumerina	Anti-Inflammatory

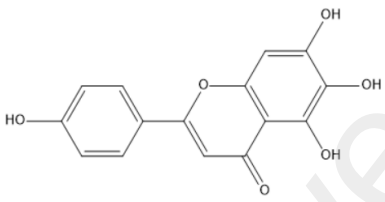
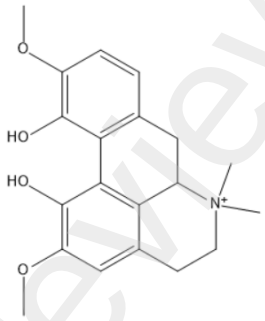
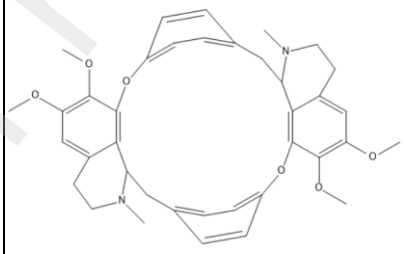
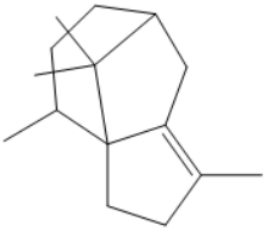
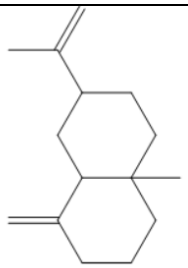
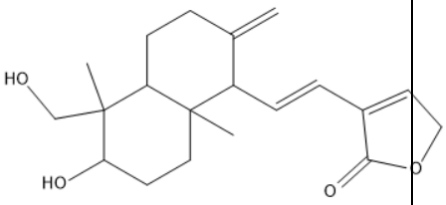
Table 2: List of Phytoconstituents of Medicinal plants used in Siddha formulations docked against COVID-19

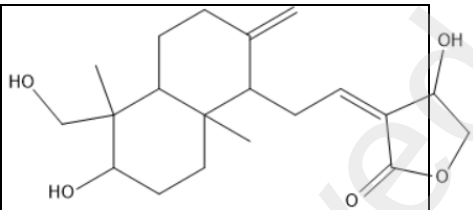
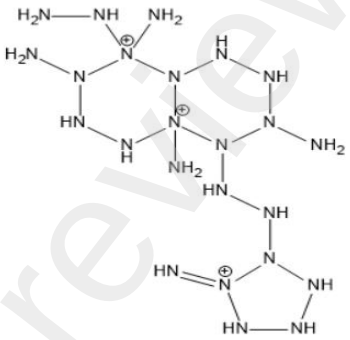
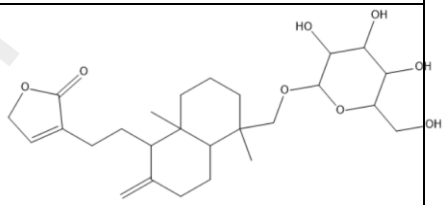
Plant name	Compound Name	Structure
Zingiber officinale Rosc	b-sesquiphellandrene	
	b-bisabolene	
	Geranial	
*Piperlongum*L	Piperine	
	Piperlonguminine	
Syzygiumaromaticum	Eugenol	
	b-Caryophyllene	

*Tragiainvolucrata*L	Stigmosterol	
Anacycluspyrethrum	Squalene	
	g-Sitosterol	
Andrographispaniculata	Andrograpanin	
	5-Hydroxy-7,8-dimethoxyflavanone	
Hygrophilaauriculata (Schum.)Heine	Lupeol	
	Betulin	

Terminaliachebula Retz.	Chebulagicacid	
	Gallicacid	
*Justiciaadhatoda*L.	Vasicinone	
Plectranthusamboinicus(Lour) Spreng	Carvacrol	
	Cirsimaritin	
	Chrysoeriol	

	6-Methoxygenkwanin	
Saussurealappa(Falc.)Lipsh	Luteolin	
	Costunolide	
	Elemol	
Tinosporacordifolia(Willd.)MiersexHook.f&Thoms	Tinosponone	
Clerodendrumserratum	Bharangin	

	Scutellarein	
*Sidaacuta*Burm.f.L	Magnoflorine	
	Cycleanine	
*Cypreusrotundus*L.	Cyperene	
	b-selinene	
Andrographis paniculate	14-deoxy-11,12-didehydroandrographide	

	Andrographolide	
	Deoxyandrographolide	
	neoandrographolide	
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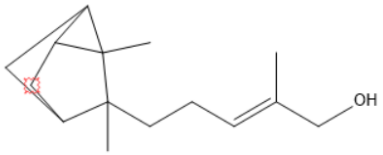
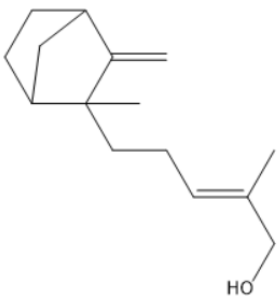
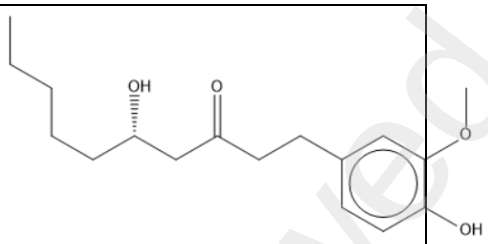
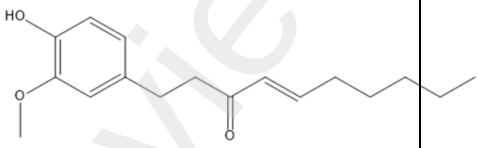
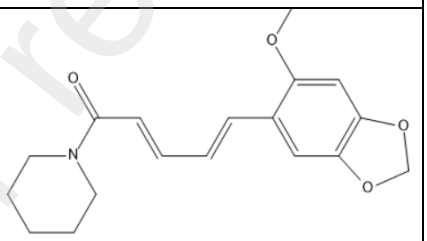
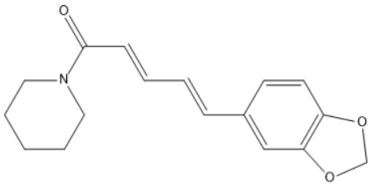
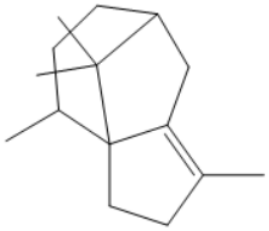
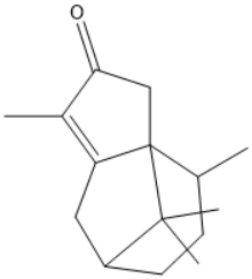
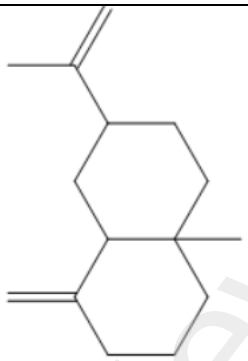
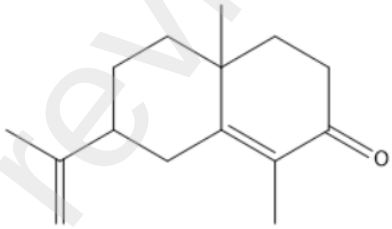
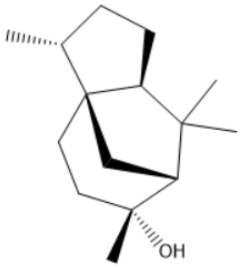
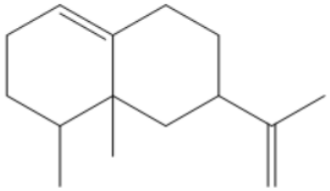
Santalum album	A Santalol	
	B Santalol	

Zingiber officinale	Gingerol	
	Shagaol	
Piper nigrum	Wisanine	
	Piperine	
Cyperus rotundus	Cyperene	
	Cyperotundone	

	ß-selinene	
	a-cyperone	
	Cedrol	
	Valencene	
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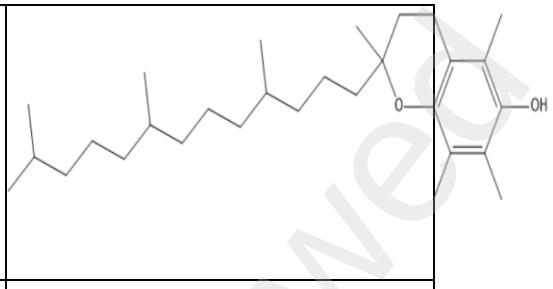
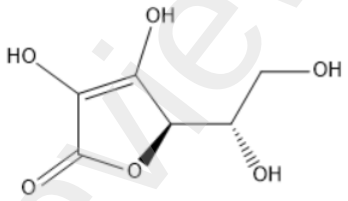
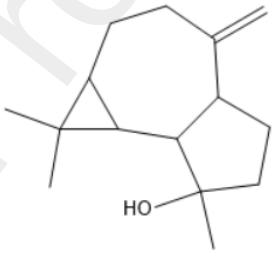
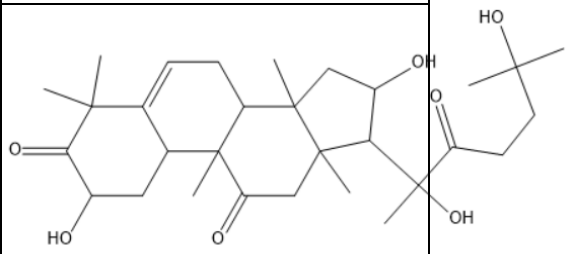
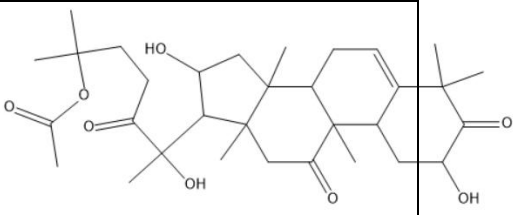
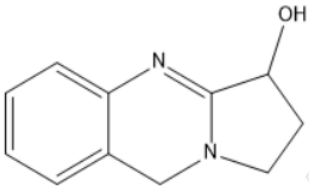
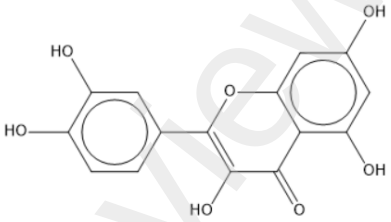
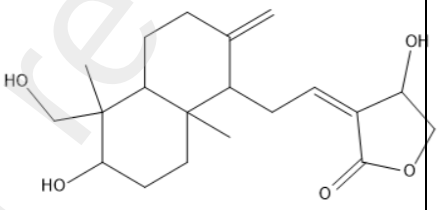
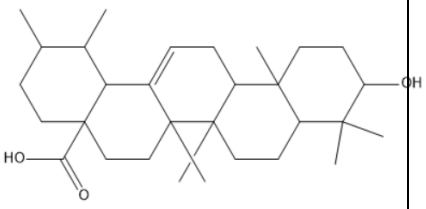
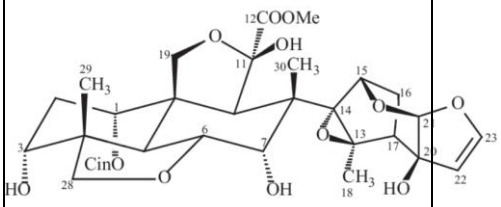
	Vitamin B	
	Vitamin C	
Plectranthus vettiveroides	Spathulenol	
	androstan-17-one 3-ethyl-3-hydroxy- (5a)	
Trichosanthes cucumerina	23, 24-dihydrocucurbitacin D	
	23,24-dihydrocucurbitacin B	

*Justiciaadathoda*L.	Vasicine	
CaricaPapaya	Quercetin	
Andrographispaniculata Burm.f.Nees	Andrographolide	
Ocimumtenuiflorum	Ursolicacid	
Meliaazedarach	Meliacine	

All these 54 Phytoconstituents were docked against the target enzyme COVID-19 and ranked based on their dock score. Phytoconstituents having dock score of -6 or less are considered better agent for inhibition of the COVID-19. A comparative analysis can be done by referring to Table 3. This table represents the list of active Phytoconstituents obtained after docking studies. These active Phytoconstituents have dock score value of

-6 or lower. Total 30 Phytoconstituents showed binding interactions with different COVID-19 structures of PDB ID 5R7Y, 5R7Z, 5R80, 5R81 and 5R82.

Table 3: Comparative docking study on COVID 19 enzymes of all Phytoconstituents

PDB ID	**5R7Y**	**5R7Z**	**5R80**	**5R81**	**5R82**
Phytoconstituents	**docking score**	**docking score**	**docking score**	**docking score**	**docking score**
Vasicinone	-6.492	-7.498	-6.778	-7.445	-6.098
Vasicine	-6.828	-7.522	-6.765	-7.31	-6.111
Chebulagic acid	-4.951	-7.641	-6.609	-6.646	-7.202
Piperine	-6.097	-7.166	-6.26	-7.098	-5.696
Cirsimaritin	-5.553	-7.398	-6.021	-6.834	-6.481
Luteolin	-7.129	-6.625	-6.764	-6.469	-6.925
5-Hydroxy-7,8-dimethoxyflavanone	-5.607	-6.611	-7.09	-6.572	-6.145
Scutellarein	-6.635	-6.932	-6.557	-6.585	-7.031
Chrysoeriol	-6.843	-6.81	-5.649	-6.579	-6.552
6- Methoxy genkwanin	-6.532	-6.611	-6.037	-6.434	-5.72
Bharangin	-6.379	-6.434	-5.152	-6.457	-4.943
Piperlonguminine	-6.28	-6.098	-5.325	-6.364	-5.192
Magnoflorine	-6.03	-5.419	-5.754	-6.409	-5.343
Carvacrol	-6.026	-6.568	-6.06	-6.594	-5.898
Tinosponone	-5.979	-6.5	-5.128	-5.608	-5.822
Gallic acid	-5.715	-5.677	-5.418	-6.12	-5.555
b-Caryophyllene	-5.679	-5.749	-6.002	-6.198	-5.421
Quercetin	-6.446	-6.811	-6.552	-6.525	-6.653
Ursolic acid	-5.329	-6.433	-3.694	-4.262	-4.7
androstan-17-one 3-ethyl-3-hydroxy- (5a)	-6.686	-6.677	-5.096	-5.635	-5.59
23,24-dihydrocucurbitacin B	-6.609	-6.594	-4.715	-6.532	-6.299
cucurbitacin B	-6.427	-6.335	-4.24	-6.11	-6.408
Cedrol	-6.384	-5.566	-6.061	-6.22	-5.744
Vitamin B	-6.328	-6.769	-5.024	-5.861	-4.182
Wisanine	-5.495	-7.247	-6.146	-6.645	-5.064
14-deoxy-11,12-didehydroandrographide	-4.853	-6.46	-5.118	-6.434	-6.331
deoxyandrographolide	-4.811	-5.99	-5.126	-5.677	-5.584
b-selinene	-5.014	-5.811	-5.194	-6.305	-4.726
Spathulenol	-5.726	-5.961	-6.501	-5.766	-5.212
Andrographolide	-5.014	-5.811	-5.194	-6.305	-4.726
Lupeol	-5.513	-5.138	-4.036	-3.576	-4.282

Betulin	-5.334	-5.03	-3.324	-4.626	-5.639
Cyperene	-5.286	-5.049	-5.048	-5.037	-4.924
Elemol	-5.146	-4.673	-5.263	-4.478	-5.099
Eugenol	-5.034	-4.704	-5.126	-5.307	-4.474
Stigmosterol	-4.723	-5.299	-5.443	-5.415	-4.979
Cycleanine	-4.634	----	-4.537	-4.037	-----
Squalene	-4.61	-5.84	-5.156	-5.558	-4.329
b-sesquiphellandrene	-4.575	-5.107	-4.998	-5.002	-4.288
b-bisabolene	-4.338	-5.156	-5.451	-5.342	-4.044
Costunolide	-4.317	-5.616	-5.667	-5.701	-4.839
g-Sitosterol	-4.137	-5.232	-5.261	-4.677	-4.14
Geranial	-3.486	-3.833	-4.005	-3.434	-3.66
Vitamin C	-5.643	-5.354	-4.505	-4.998	-4.767
a-cyperone	-5.271	-4.875	-5.5	-5.186	-5.276
B Santalol	-5.235	-5.062	-5.411	-5.151	-4.127
23, 24-dihydrocucurbitacin D	-5.038	-4.994	-4.417	-4.652	-5.357
Valencene	-4.994	-5.246	-5.477	-5.509	-4.736
Cyperotundone	-4.991	-5.011	-5.197	-5.234	-5.127
A Santalol	-4.899	-5.028	-5.824	-5.294	-4.414
Gingerol	-4.276	-4.82	-4.066	-3.47	-3.749
Shagaol	-3.861	-3.903	-3.734	-4.317	-2.778
9-octadecenamide	-1.91	-2.069	-1.676	-2.016	-0.541
Hexadecanoic acid	-1.05	-0.521	-0.018	-0.044	0.368

Out of these 30 Phytoconstituents, Vasicinone, Vasicine, Chebulagic acid, Piperine, Cirsimaritin, Luteolin, 5-Hydroxy-7,8- dimethoxyflavanone and many more were found to interact with more than 2 protein structures of COVID-19. Importantly amongst all Phytoconstituents Vasicine, Vasicinone, Luteolin, Scutellarein and Quercetin binds to all the protein structures of COVID -19 with dock score of less than -6. Moreover, Chebulagic acid, Piperine, Cirsimaritin, 5-Hydroxy-7,8- dimethoxyflavanone, Chrysoeriol, 6-Methoxy genkwanin, Carvacrol, 23,24-dihydrocucurbitacin B and cucurbitacin B also showed promising results in 4 out of 5 protein structures of COVID-19. Interestingly, half of the ingredients of the Kabasura Kudineer, Nilavembu Kudineer, and JACOM formulations showed excellent results in in silico docking studies.

Docking interactions of some of active Phytoconstituents based on docking studies are depicted in Figure 1 to 4. Vasicinone, Luteoline and Scutellarein interacted with all the

protein structures of COVID 19. Binding interaction of them with PDB ID 5R7Z, 5R7Y and 5R82 is showed in figure 1, 2 and 3 respectively.

Hydroxyl group of Vasicinone forms H-bond with amino acid Glu 166 and Pi-pi stacking interaction is also visible between amino acid Hie 41 and phenyl ring which is same as binding in case of Lopinavir and Remdesevir [44]. Four hydrogen bonds can form between OH group of Luteoline with Asn 142, Hie 41, Gln 192 and Thr 190. Also pi-pi stacking is observed between Phenyl ring and amino acid Hie 41.

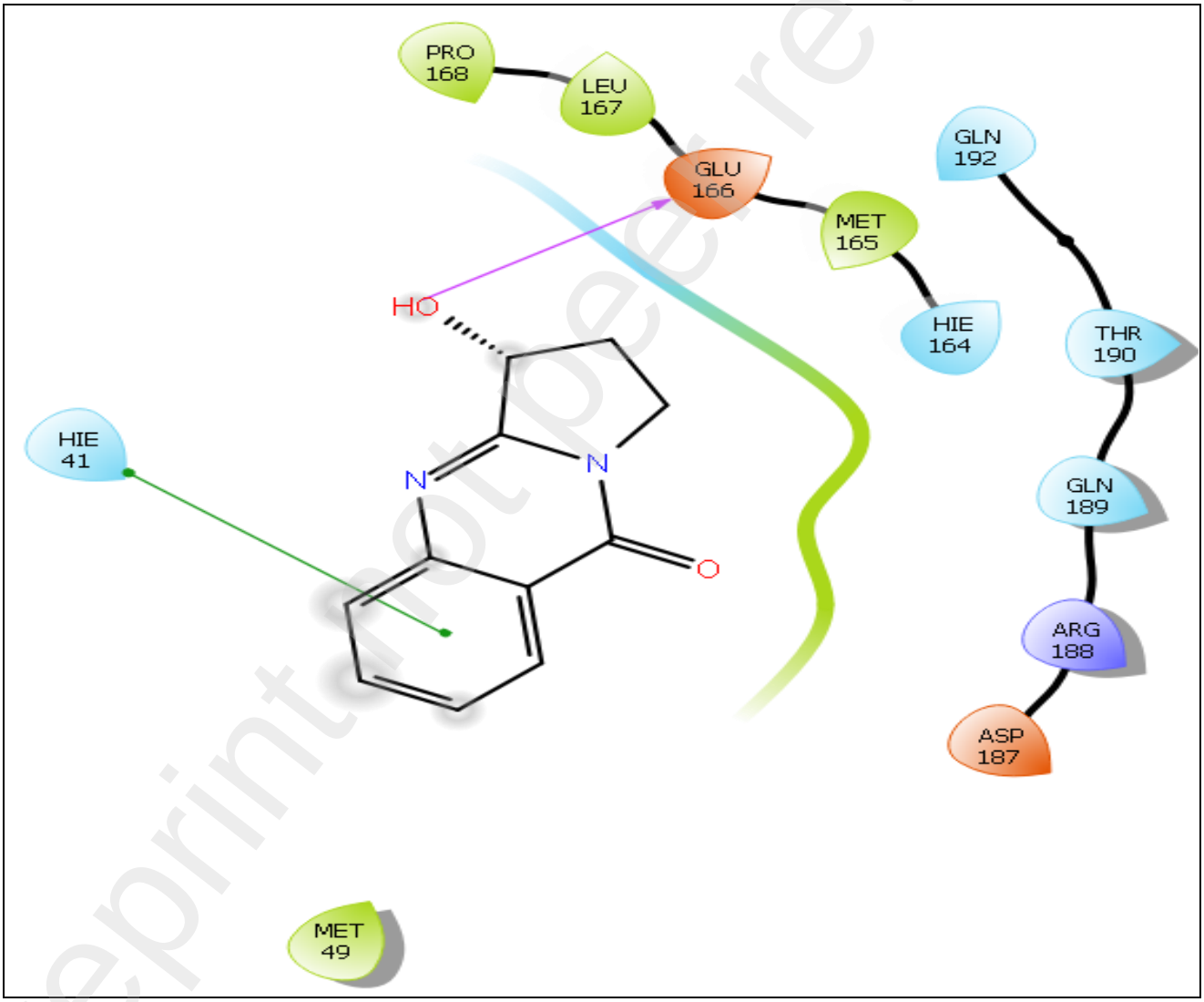


Figure 1: Docking interaction of Vasicinone with 5R7Z

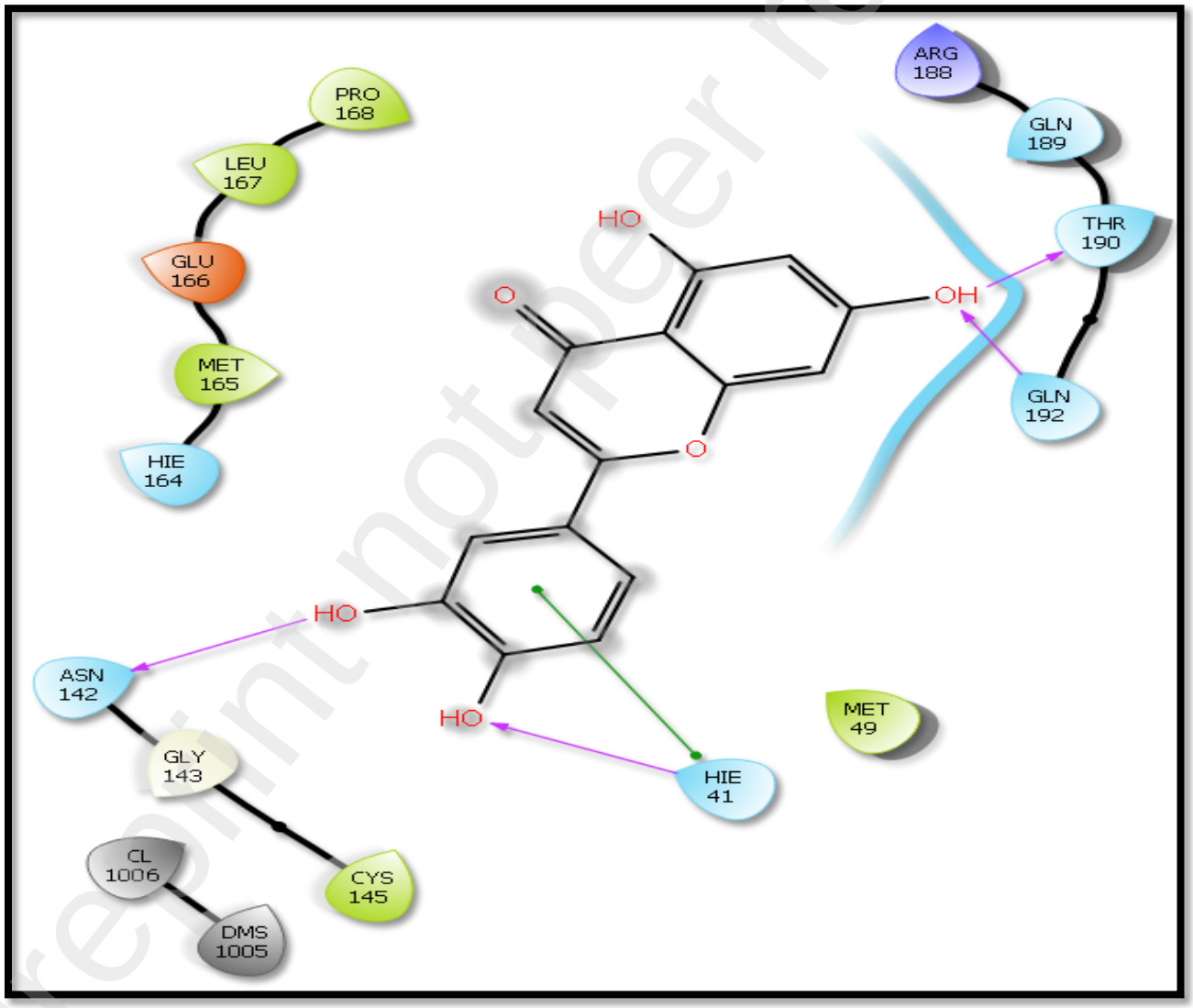


Figure 2: Docking interaction of Luteoline with 5R7Y

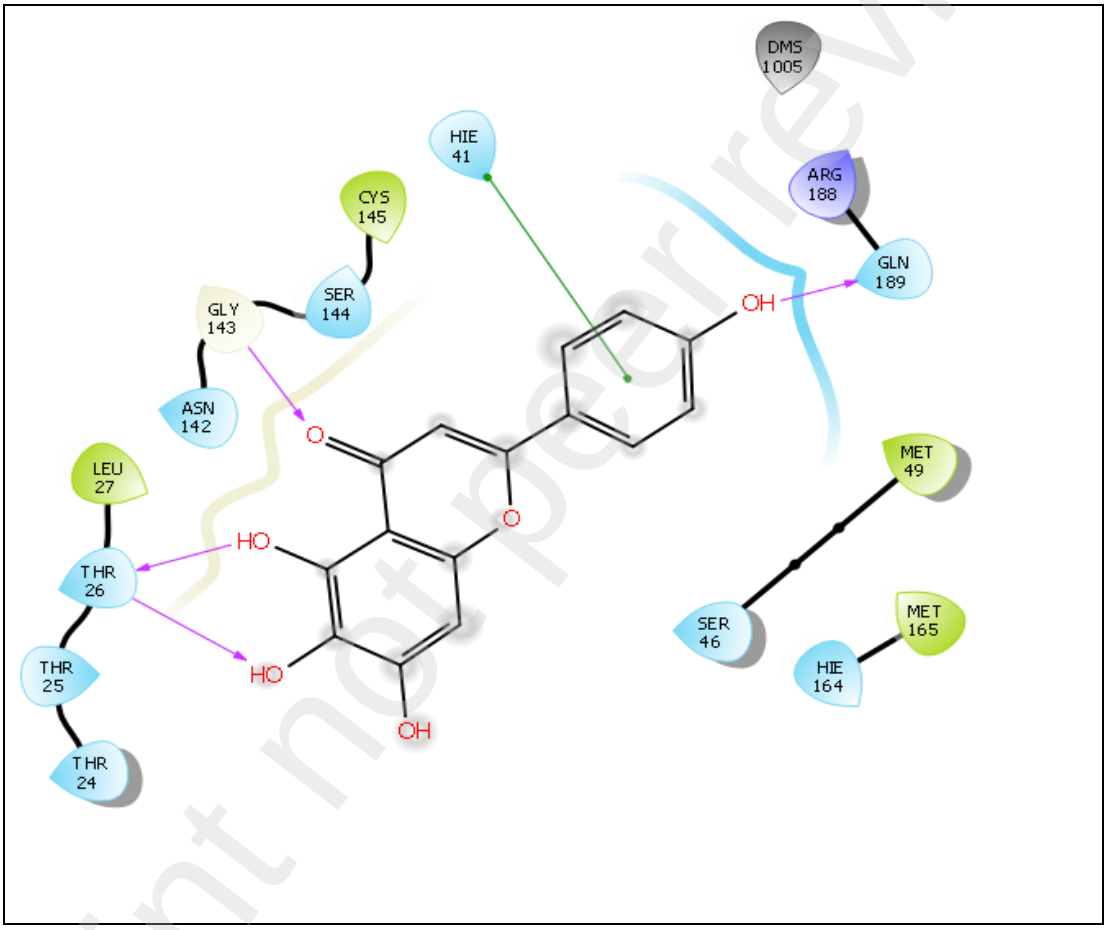


Figure 3: Docking interaction of Scutellarein with 5R82

As Scutellarein also exhibit good binding interaction with COVID 19 enzyme, a binding image of Scutellarein with 5R82 is given in Figure 3. Hydroxyl group of Scutellarein forms H- bond with amino acids Thr 26, Gln 189. Also 4-oxo chromene group of Scutellarein forms H-bonding interaction with Gly 143. More over phenyl ring of scutellarein is responsible for the pi-pi stacking interaction with Hie 41.

Docking interaction diagram of Protease inhibitor Chebulagic acid, is shown in Figure 4 with PDB ID 5R7Z. Chebulagic acid shows Many H- Bonding interaction with protein 5R7Z. In this case, Carbonyl group of acid form H- bond with Gln 189. Additionally, Ser 46 and Asn 142 froms H- bond with Carbonyl group of Ester. Further OH group on Phenyl ring can form H-bonding interaction with different Amino acids like Thr 26, Asn 142, Glu 166.

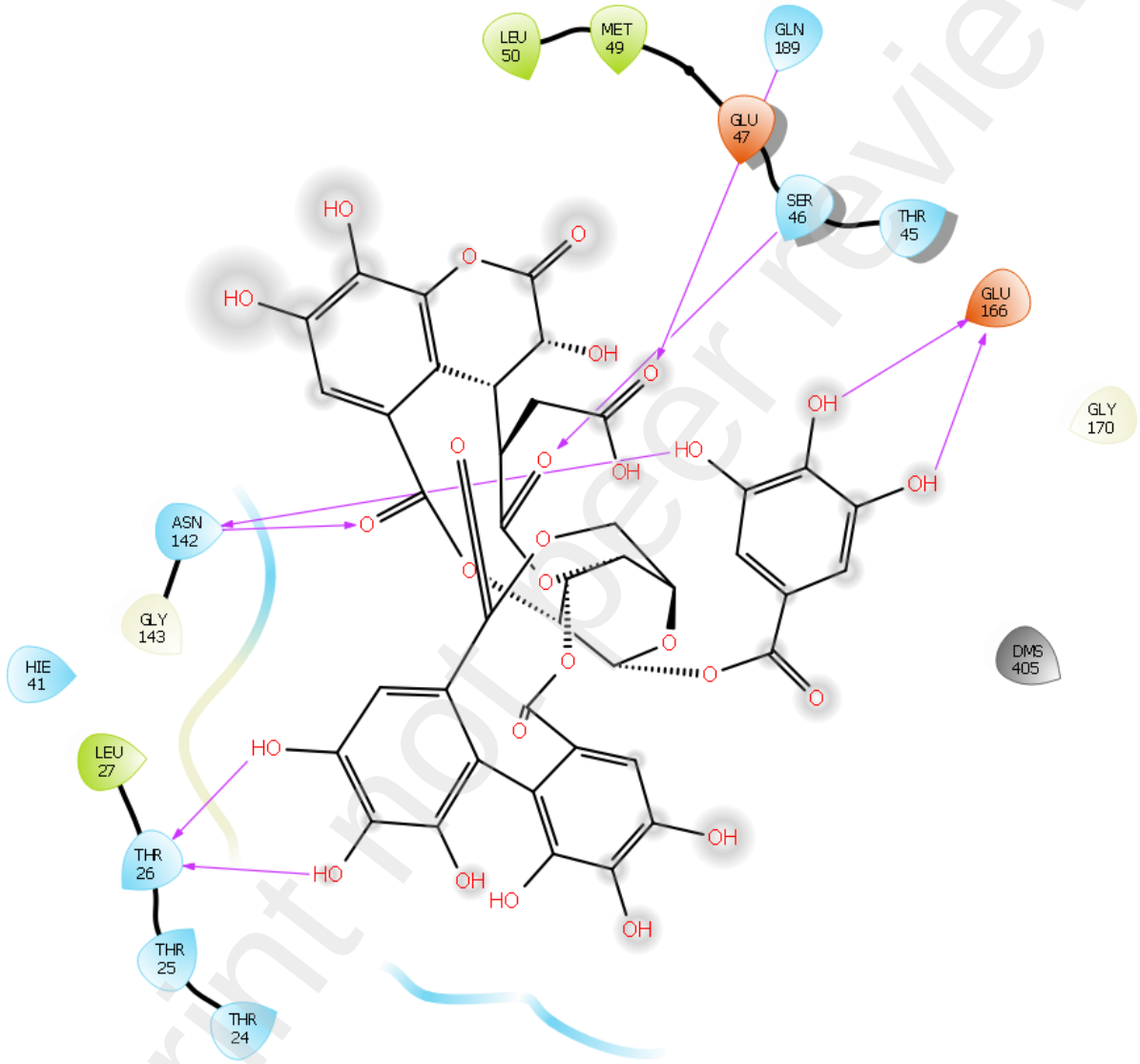


Figure 4: Docking interaction of Chebulagic acid with 5R7Z

Based on these docking score and interactions, it is estimated that Kabasura Kudineer, Nilavembu Kudineer and JACOM Siddha polyherbal formulations can be effective in treating the COVID 19 infections.

Conclusion:

To combat the life-threatening COVID-19 infection, Several Pre-clinical and Clinical studies are ongoing using antiviral and immunomodulatory drugs. Protease inhibitors plays a important role as potential candidate for COVID-19.

In this work, docking studies were performed on 54 Phytoconstituents known for its antiviral activities. In this study also many protease inhibitors showed remarkable binding interactions with COVID-19 enzymes. Vasicinone, Luteoline and Scutellarein found be more useful. Vasicinone inhibits protein synthesis and interacts with 5R7Z and 5R81 enzymes with dock score values of -7.498 and -7.445. The dock score values of Luteolin with 5R7Y are -7.129. The dock score values of Scutellarein with 5R82 are -7.031 respectively. As per docking score half of the ingredients of the formulations showed excellent results in in silico docking studies. These phytoconstituents showed promising results in Insilco, however pre-clinical and clinical studies should be impart in COVID-19 patients.

Disclosure statement

No potential conflict of interest was reported by the author(s).

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