Evaluation of Yashtimadhu (Glycyrrhiza glabra) active Phytochemicals Against Novel Coronavirus (SARS-CoV-2)

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Research Article

Keywords: COVID-19; SARS-CoV-2; Phytochemicals; Ayurvedic herbs; Molecular docking; Pharmacokinetics

Posted Date: May 5th, 2020

DOI: https://doi.org/10.21203/rs.3.rs-26480/v1

Abstract

Corona Virus Disease 2019 (COVID-19) caused by a novel coronavirus emerged from Wuhan, China in December 2019. It has spread to more than 205 countries and become pandemic now. Currently, there are no FDA approved drugs or vaccines available and hence several studies are going on in search of suitable drug that can target viral proteins or host receptor for the prevention and management of COVID-19. The search for plant-based anti-viral agents against the SARS-CoV-2 is promising because several of plants have been shown to possess anti-viral activities against different viruses. Here, we used molecular docking approach to explore the use of Indian Ayurvedic herbs, Yashtimadhu in prevention and management of COVID-19. In the present study we have evaluated the effectiveness of phytochemicals found in Yashtimadhu against Main Protease (Mpro), Spike (S) protein and RNA-dependent RNA polymerase (RdRp) of SARS-CoV-2 as well as human angiotensin converting enzyme 2 (ACE2) receptor and furin protease. Apart from this, we have also performed in-silico drug-likeness and predicted pharmacokinetics of the selected phytochemicals found in the Yashtimadhu. Our study shows that several phytochemicals found in this plant have potential to bind with important proteins of SARS-CoV-2 which are essential for viral infection and replication. Overall our study provides scientific basis in terms of binding of active ingredients present in Yashtimadhu with SARS-CoV-2 target proteins. Our docking studies reveal that Yashtimadhu may inhibit the viral severity by interfering with viral entry as well as its multiplication in the infected persons. Thus Yashtimadhu may be helpful in the prevention and management of the COVID-19.

Introduction

SARS-CoV-2 is the seventh coronavirus (CoV) known to infect humans; SARS-CoV, MERS-CoV and SARS-CoV-2 has caused three recent major global epidemics, whereas HKU1, NL63, OC43 and 229E are associated with mild symptoms [1; 2]. Presently, there are no specific drugs or vaccines approved for SARS-CoV-2. As compared to SARS-CoV and MERS-CoV, SARS-CoV-2 virus exhibits faster human-to-human transmission and high infectivity rate. Hence, World Health Organization (WHO) has declared it as a global emergency. Researchers from all-over the world are trying to find possible cure for this infectious disease, COVID-19. Phylogenetic analysis show that SARS-CoV-2 has very high nucleotide sequence identity with SARS-CoV (79.7%) [3]. The envelope and nucleocapsid proteins of SARS-CoV-2 are two evolutionarily conserved regions, with sequence identities of 96% and 89.6%, respectively. Like other CoVs, SARS-CoV-2 has a positive-sense single-stranded RNA as genome and four structural proteins, namely the S (spike), E (envelope), M (membrane), and N (nucleocapsid) proteins in which, N protein holds the RNA genome, and the S, E, and M proteins together create the viral envelope. CoVs infect host cells using their spike proteins on the surface by making interaction with cognate receptors present on the host cell surface. The spike proteins of SARS-CoV-2 has high affinity to the cellular receptor angiotensin-converting enzyme 2 (ACE2) for their entry inside the cells [4]. The higher binding affinity of SARS-CoV-2 spike protein to the human receptor ACE2 is due to presence of functional polybasic furin cleavage site at the S1–S2 boundary in the spike glycoprotein [5]. Zoonosis is common among CoVs and they can be transmitted

from one animal species to another, animals to humans, and humans to humans [6; 7]. Currently, in search of an effective therapeutics against SARS-CoV-2, researchers are screening existing broad-spectrum anti-virals, small molecule libraries, FDA approved drug libraries and rational drug design approach [3; 8]. Apart from these, exploring traditional Ayurvedic plants for the management of COVID-19 both as prophylaxis and therapeutic purpose will be an alternate approach.

Ayurvedic medicines are used in Indian subcontinent since the Vedic period and they have long history for treatment of viral diseases [9; 10; 11]. Yashtimadhu *(Glycyrrhiza glabra),* is one of the most potent rasayana drugs in Ayurveda (also known as Licorice and Mulethi) used alone or in combination with other herbs in preparation of several Ayurvedic medicines and food supplements worldwide for centuries. Commercially, Yashtimadhu is added to chewing gum, chocolate candy, cigarettes, smoking mixtures, chewing tobacco and snuff as sweetening agents [12]. It possesses several beneficial effects including treatment of various respiratory disorders such as cough, cold and flu [12]. Yashtimadhu and its active ingredients have significant anti-inflammatory property [13; 14; 15; 16]. Clinically, Yashtimadhu has been used for prevention and treatment of oral mucositis after radio- and chemo- therapy in cancer patients [17]. The most important bioactive compounds of Yashtimadhu, Glycyrrhizin was shown to inhibit SARS-CoV replication as well as inhibits adsorption and penetration of the virus at early stage of the replicative cycle [18; 19].

In the present study, the phytochemicals of Yashtimadhu were docked with different viral proteins (such as spike, main protease, RNA dependent RNA polymerase) and also with host cell receptors & protease (such as human ACE2 and furin). Our study predicted that many of the phytochemicals found in Yashtimadhu possess significant affinity towards functional region of viral proteins including spike, proteases, and polymerase as well as host surface receptor and protease. Our study provides a scientific justification for consumption of Yashtimadhu in consultation with Ayurvedic practitioner for the prevention of viral infection, pathogenicity and reducing disease-severity in COVID-19 patients. This can also be combined with the conventional treatment for management of COVID-19.

Materials And Methods

List of the phytochemicals found in Yashtimadhu: Yashtimadhu have an array of the phytochemicals. Some of well-known phytochemicals include, Abscisic, Apioside, Glabridin, Glabrin A, Glabrin B, Glycyrrhetic acid (also known asglycyrrhetinic Acid), Glycyrrhizin (also known as Glycyrrhizic Acid/ Glycyrrhizinic Acid), Hispaglabridin, Isoliquiritigenin, Isoliquiritin, Licochalcone A, Liquiritigenin, Liquiritin, Liquiritin Apioside, Prenyllicoflavone A, Salicyclic Acid, Shinflavanone, Shinpterocarpin, Sitosterol, Stigmasterol, Syringic acid, Trans-Ferulic acid. 3D structures of these different phytochemicals were downloaded from PubChem (https://pubchem.ncbi.nlm.nih.gov) in structure-data file (SDF).

Ayurvedic usage of Yashtimadhu: In Ayurveda, Yashtimadhu is being used either alone or in combination with different other herbs. This can be consumed as powder or tablets or as a component of Ayurvedic kadha (decoction). Traditionally Yashtimadhu powder is consumed by mixing with honey or ghee.

Protein structures: In order to study the mode of interaction of different phytochemicals with various SARS-CoV-2 proteins and receptors found on virus and host cells, molecular docking was performed. We have used following PDB ID's 6lu7 (SARS-CoV-2 main protease), 6m0j (SARS-CoV-2 spike), 6m71 (SARS-CoV-2 RdRp), 6m0j (ACE2) and 5mim (proprotein convertase, furin). All the protein structures were retrieved from protein data bank (www.rcsb.org) and cleaned using USCF Chimera software [20].

Molecular docking: PyRx virtual screening tool was used for preparation of the input files and performing molecular docking using Vina wizard [21]. For preparation of protein input files, all water molecules, ligands and ions were removed from *.pdb files. The polar hydrogens were added to protein structure and prepared files were saved in *.pdbqt format. The molecule's energy was minimized using energy minimization tools of PyRx virtual screening software and ligands were saved in *.pdbqt format after adding polar hydrogens for further docking process. 2D interaction of the ligand and protein was visualized using Discovery Studio Visualizer. Region-specific docking was performed against SARS-CoV-2 main protease and spike protein as well as for human ACE2 & Furin protease. Following AutoDock Vina docking parameters such as (center_x = -16.69, center_y = 27.23, center_z = 68.46, size_x = 36.65, size_y = 42.12, size_z = 50.40), (center_x = -32.483, center_y = 26.077, center_z = 7.923, size_x = 52.974, size_y = 46.699, size_z = 30.699), (center_x = -25.0997, center_y = 19.903, center_z = 3.047, size_x = 78.872, size_y = 67.603, size_z = 35.866) and (center_x = 32.41, center_y = -37.97, center_z = -11.64, size_x = 71.93, size_y = 55.05, size_z = 47.46) were used for SARS-CoV-2 main protease (PDB ID: 6LU7), SARS-CoV-2 spike (PDB ID: 6m0j), human ACE2 (PDB ID: 6m0j) and furin (PDB ID: 5MIM) respectively. For docking RdRp (PDB ID: 6m71) NSP7 and NSP8 was removed from the NSP12 and grid box for docking parameter was set at the NSP12-NSP7 and NSP12-NSP8 interface. Docking parameters used for NSP12 were center_x = 112.289, center_y = 131.245, center_z = 141.597, size_x = 83.597, size_y = 69.959, size_z = 45.240.

In-silico drug-likeness and pharmacokinetic property prediction: After performing molecular docking, in-silico drug-likeness and important pharmacokinetic properties of the selected phytochemicals which bind will SARS-CoV-2 spike, Mpro, RdRp and human ACE2 & Furin proteins were predicted using pkCSM online prediction platforms [22]. This online server calculates pharmaceutically applicable properties such as molecular weight, octanol-water partition coefficient (LogP), number of H-bond donor, number of H-bond acceptor and number of rotatable bonds. In addition it also calculates ligands Absorption, Distribution, Metabolism, Excretion and Toxicity (ADMET) parameters like water solubility, human intestinal absorption, total clearance, AMES test, human maximum tolerated dose, hepatotoxicity and many more parameters.

Results

Our molecular docking study revealed that different phytochemicals found in Yashtimadhu have significant binding affinity with various SARS-CoV-2 proteins i.e main protease, spike & RdRp and host macromolecular targets such as human ACE2 and furin proteins (Table 1). SARS-CoV-2 spike protein interacts with the host ACE2 receptor present on the surface of the host cells for their entry. Furin (a kind of proprotein convertase) is another protease found in the host cells which acts on the viral spike protein and facilitates the interaction of spike with the human ACE2. Figure 1, shows the predicted binding of

important phytochemicals found in Yashtimadhu against SARS-CoV-2 spike protein and their different protein residues which are involved in the interaction. Some of the important phytochemicals present in this plant are Glycyrrhetic acid, Shinflavanone, Glycyrrhizin and Glabridin. Their predicted binding energies are -8.3, -7.8 and -7.2kcal/mol respectively. Figure 2, shows the predicted binding of some key phytochemicals of Yashtimadhu against human ACE2 receptor and their different protein residues which are involved in the interaction. These phytochemicals are Shinpterocarpin, Apioside, Glabridin, Glycyrrhetic acid, Liquiritin apioside and Shinflavanone. Their predicted binding energies are -8.2, -7.8, -7.7, -7.6, -7.5 and -7.4kcal/mol respectively. Figure 3, shows the predicted binding of some important phytochemicals of Yashtimadhu against human furin protease and different protein residues which are involved in the interaction. These phytochemicals are Shinpterocarpin, Apioside, Glycyrrhizin, Shinflavanone, Glabrin B, Glycyrrhetic acid, Liquiritin, Glabridin, Glabrin A and Prenyllicoflavone A. Their predicted binding energies are -8.6, -8.5, -8.5, -8.5, -8.4, -8.3, -8.3, -8.2, -8.2 and -8.1kcal/mol respectively.

The SARS-CoV-2 main protease (Mpro), plays a pivotal role in viral gene expression and replication. Crucial maturation cleavage events within the viral precursor polyprotein are mediated by the Mpro. Figure 4, shows the predicted binding of important phytochemicals of Yashtimadhu against Mpro and different protein residues which are involved in the interaction. These phytochemicals are Glabrin B, Shinflavanone, Glycyrrhetic acid, Shinpterocarpin, Glabridin, Hispaglabridin A, Liquiritin apioside, Licochalcone A, Apioside, Prenyllicoflavone A, Liquiritigenin, Isoliquiritin and Isoliquiritigenin. Their predicted binding energies are -8.9, -8.4, -8.2, -8.1, -8.1, -8.0, -7.9, -7.9, -7.9, -7.7, -7.7, -7.5 and -7.5 kcal/mol respectively.

The RNA-dependent RNA polymerase (RdRp, also named NSP12) is the central component of SARS-CoV-2 replication/transcription machinery. Figure 5, shows the predicted binding of important phytochemicals of Yashtimadhu against RdRp and their different protein residues which are involved in the interaction. These phytochemicals are Liquiritin apioside, Shinflavanone, Glycyrrhizin, Glycyrrhetic acid, Hispaglabridin A and Prenyllicoflavone A. Their predicted binding energies are -8.8, -8.5, -8.4, -8.4, -8.3 and -8.3kcal/mol respectively.

The phytochemicals which bind to all the selected studied molecules such as SARS-CoV-2 spike, Mpro, RdRp and human ACE2 & Furin were analysed for their in-silico drug-likeness and pharmacokinetics using pkCSM server [22] (Table 2). Some of the phytochemicals do not follow the Lipinski's rule of five for all the parameters. ADMET properties calculated with the aid of pkCSM server shows that predicted intestinal absorption of the phytochemicals such as Glabridin, Glycyrrhetic acid, Hispaglabridin A, Prenyllicoflavone A, Shinflavanone, Shinpterocarpin and Isoliquiritigenin are high i.e 94.164, 100, 92.325, 92.154, 93.109, 96.183 and 91.096 % respectively. Except Glabrin B none of the studied phytochemicals predicted to have hepatotoxicity (Table 2).

Discussion

Traditional herbal medicines are gaining attention as potential alternative sources of therapy for diverse diseases across many countries. Medicinal plants and natural products are being accepted widely due to the perception that they may have fewer side effects as compared to synthetic molecules. Use of herbs

and phytochemicals has a long history in the management of various respiratory diseases [23; 24; 25]. In European countries, several species of herbs have been used against flu and common cold[26]. In India, use of spices and herbs for treatment of various diseases including cough, cold and flu is a common practice with recorded history of several thousands of years [27; 28]. Recently, Maurya and Sharma (2020), have predicted that phytochemicals found in traditional Indian Ayurvedic Kadha have significant potential to bind with important SARS-CoV-2 proteins and human receptor and may be beneficial in boosting host immunity and managing symptoms of COVID-19 [29].

The Yashtimadhu root has been significantly used for ages in Indian system of Ayurvedic medicine, in ancient Egyptian medicine and in traditional Chinese medicine [30; 31]. It had already been known for its antiviral properties [32; 33; 34]. Yashtimadhu root contains a variety of phytochemicals such as flavonoids like Glycyrrhizin, Liquiritigenin, and Glabridin that had antiviral activity against the SARS coronavirus [19; 35]. Phytochemicals, triterpenoids found in Yashtimadhu root especially glycyrrhizic acid and glycyrrhetinic acid that were found to be extremely potent against the SARS-CoV [19; 35].

The therapeutics which prevent the CoV severity may work on several specific targets such as virus structural proteins which block virus binding with host cell receptors, or inhibiting the virus's self-assembly process (such as spike and nucleocapsid proteins); some may be acting on critical functional proteins and enzymes which prevent the virus RNA synthesis and replication (such as main protease, RdRp and helicase); some act on CoV virulence factors (such as Nsp1, Nsp3c and ORF7a) and some act on host's specific receptors or enzymes, preventing virus from entering into host's cells (such as ACE2, furin). It is well-known that SARS-CoV viral genome encodes more than 20 proteins, among which two proteases i.e 3-chymotrypsin-like protease (main protease, Mpro) and papain-like protease (PLpro) are vital for virus replication [36]. They cleave the two translated polyproteins (PP1A and PP1AB) into individual functional components, resulting in release of 16 non-structural proteins (NSPs)[37].

CoVs spike protein is a main glycosylated protein that interacts with the host by binding to host cell receptors to mediate virus invasion and determine viral tissue or host tropism [38]. Spike protein is the main structural protein of CoVs and assembles into a special corolla structure on the surface of the virus as a trimer. The host ACE2 has been proved by many studies to be the specific receptor for the spike receptor binding domain (RBD) of SARS-CoV. Spike of CoV is cleaved into S1 and S2 by the host cell protease furin during infection. The modified spike glycoprotein can interact with the cell surface receptor ACE2. The S1 subunit, which contains the RBD, binds with host cell surface receptors, and the S2 subunit mediates virus-cell and cell-cell membrane fusion. Initial interactions between the S1 domain and its host receptor (ACE2), and subsequent S2 segment mediated fusion of the host and viral membrane allows the viral RNA genome to enter inside the host cells. Thus, these proteins represent as important targets for designing drug [38]. Spike structural integrity and cleavage activation play a key role in virus invasion and virulence.

Very recently, Wang et al (2020) presented the crystal structure of the C-terminal domain of SARS-CoV-2 spike protein in complex with human ACE2 and reported that amino acid residues S19, Q24, T27, F28, D30, K31, H34, E35, E37, D38, Y41, Q42, L45, L79, M82, Y83, N330, K353, G354, D355 and R357 of the

human ACE2 interact with amino acid residues K417, G446, Y449, Y453, L455, F456, Y473, A475, G476, E484, F486, N487, Y489, F490, Q493, G496, Q498, T500, N501, G502 and Y505 of C-terminal domain of SARS-CoV-2 spike protein [39]. Our study shows that different phytochemicals found in the Yashtimadhu have significant binding affinity with viral spike, host ACE2 & furin proteins (Figure 1, 2, 3). Phytochemical found in Yashtimadhu, interact with few of these amino acid residues or the residues which are lying near to them. This indicates that phytochemicals found in the Yashtimadhu can interfere with the interaction of the virus with the host cells and can slow down the viral entry. The spike protein is also known to activate the immune response of the host cell towards CoVs [38]. The S1 domain of spike acts as a major antigen on the surface of the virus [40]. Binding of the phytochemicals with the spike may also minimize the immune response mediated by it.

Thus SARS-CoV-2 Mpro is considered as a promising druggable target because it plays vital role in viral gene expression and replication and are crucial for maturation cleavage events of viral precursor polyprotein. Our study shows that an array of phytochemicals have significant binding affinity with the SARS-CoV-2 Mpro (Fig 4).

The RNA-dependent RNA polymerase is the central module of CoVs replication/transcription machinery and an excellent target for new therapeutics development. RdRp, catalyses the synthesis of viral RNA and thus plays a central role in the replication and transcription cycle of SARS-CoV-2 in association with nsp7 and nsp8 as co-factors. Co-factor snsp7 and nsp8 are essential for proper functioning of the RdRp. Our docking study shows that many of the phytochemicals found in the Yashtimadhu bind on the interface region of the nsp12 where nsp7 or nsp8 co-factor binds (Fig 5). This indicates that the binding of the phytochemical can slow down the RdRp activity resulting in decrease in the virulence.

Our in-silico drug-likeness and pharmacokinetic prediction study shows that many of the active phytochemicals found in the Yashtimadhu such as Glabridin, Glycyrrhetic acid, Hispaglabridin A, Prenyllicoflavone A, Shinflavanone, Shinpterocarpin and Isoliquiritigenin do not have any predicted hepatotoxicity and show very high (>90%) intestinal absorption (Table 2). This indicates that after consumption of Yashtimadhu the active phytochemicals will be absorbed and can interact with the viral spike, Mpro and other proteins along with the human receptor and proteins needed by CoV during infection.

During the SARS-CoV infection, human lung epithelial cells are among the first targets for viral entry. In response to viral multiplication and host cell damage, lung epithelial cells secrete inflammatory mediators to initiate and exacerbate host innate inflammatory responses, causing detrimental immune-mediated pathology within the lungs in certain cases. In a very recent study, Huang et al (2020) have shown that the patients infected with SARS-CoV-2 had high amounts of IL1b, IFNγ, IP10, and MCP1, which can mediate cytokine storm associated multi-organ damage. At the same time, SARS-CoV-2 infection also initiates increased secretion of T-helper-2 (Th2) cytokines (eg, IL4 and IL10) which suppress inflammation [41]. The increased secretion of inflammatory mediators was also associated with moderation of helper T cell responses in COVID-19 patients. There are several reports showing that Yashtimadhu and its phytochemicals have significant anti-inflammatory property [13; 14; 15; 16]. Our study predicts that many

of the phytochemicals such as Apioside, Beta-sitosterol, Glabridin, Glabrin B, Glycyrrhetic acid, Glycyrrhizin, Hispaglabridin A, Isoliquiritin, Licochalcone A, Liquiritigenin, Liquiritin apioside, Liquiritin, Prenyllicoflavone A, Shinflavanone, Shinpterocarpin and Stigmasterol found in Yashtimadhu, have significant binding affinity with more than two inflammatory mediators (Supplementary Table 1). This indicates Yashtimadhu may reduce the inflammatory response and will boost the immunity of the host.However, this molecular docking study needs further validation by in vitro and in vivo experiments.

In conclusion, based on the molecular docking study, usage of Yashtimadhu may be beneficial in prevention of SARS-CoV-2 infection and can reduce the severity in the infected person. Thus in consultation with Ayurvedic practitioner, Yashtimadhu can be taken as immunity booster and also as prophylaxis in prevention and management of COVID-19.

Declarations

Acknowledgement: The author would like to thank Dr S. Santosh Kumar, Radiation Biology & Health Sciences Division, Bhabha Atomic Research Centre, Mumbai for his valuable constructive suggestions and critical review of the article.

Declaration of Conflicting Interests: The author declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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Tables

Table 1: Docking score against SARS-CoV-2 spike, main protease & RdRp and human ACE2 & Furin

Table 1					
Compounds	**Target molecules; binding energy (kcal/mol)** (Only those phytochemicals are included in the table which have binding energy ≤ - 7.0)				
	SARS-CoV-2 spike protein (PDB ID: 6m0j)	**SARS-CoV-2 main protease (PDB ID: 6lu7)**	**SARS-CoV-2 RdRp (PDB ID: 6m71)**	**Human ACE2 (PDB ID: 6m0j)**	**Human Furin (PDB ID: 5mim)**
Native ligand (N3)		-7.6			
Phytochemicals					
Apioside	-7	-7.9	-7.8	-7.8	**-8.5**
Glabridin	-7.2	**-8.1**	-7.8	-7.7	**-8.2**
Glabrin B	-7.3	**-8.9**	**-8**	-7.3	**-8.4**
Glycyrrhetic acid	**-8.3**	**-8.2**	**-8.4**	-7	-7.8
Glycyrrhizin	-7.3	-7.3	**-8.4**	-7.3	**-8.5**
Hispaglabridin A	-7.3	**-8**	**-8.3**	-7	-7.7
Liquiritin	-7.1	-7.4	-7.9	-7.2	**-8.3**
Prenyllicoflavone A	-7	-7.7	**-8**	**-8.2**	**-8.1**
Shinflavanone	**-7.8**	**-8.4**	**-8.5**	-7.4	**-8.5**
Shinpterocarpin	-7.2	**-8.1**	-7.8	**-8.2**	**-8.6**
Liquiritin apioside		-7.9	**-8.8**	-7.5	-7.9
Isoliquiritigenin		-7.5	-7.7	-7	-7
Glabrin A		-7.3	-7.9		**-8.2**
Liquiritigenin		-7.7	-7.2	-7.3	
Isoliquiritin		-7.5			-7.9
Licochalcone A		-7.9			-7.4
Stigmasterol			-7.9		-7.9
Beta-sitosterol					-7.2

Table 2- In-silico ADMET prediction of the selected phytochemicals found in Yashtimadhu

Table 2

Phytochemicals	MW	LogP	No. of rotatable bonds	No. of HBA	No. of HBD	Water solubility (log mol/L)	Intestinal absorption (human) (% Absorbed)	Total Clearance (log ml/min/kg)	AMES toxicity	Max. tolerated dose (human) (log mg/kg/day)	Hepatotoxicity
Apioside	564.5	-1.485	7	14	8	-2.851	17.411	-0.054	No	0.446	No
Glabridin	324.4	4.001	1	4	2	-3.646	94.164	0.121	No	-0.395	No
Glabrin B	835	-2.554	8	11	9	-2.93	10.645	10.645	No	0.491	Yes
Glycyrrhetic acid	470.7	6.413	1	3	2	-3.329	100	-0.114	No	0.196	No
Glycyrrhizin	822.9	2.246	7	13	8	-2.892	0	-0.304	No	0.389	No
Hispaglabridin A	392.5	5.509	3	4	2	-4.649	92.326	0.41	No	0.019	No
Liquiritin	418.4	0.277	4	9	5	-3.354	46.076	0.342	Yes	0.186	No
Prenyllicoflavone A	390.5	5.889	5	4	2	-4.57	92.154	0.399	Yes	-0.017	No
Shinflavanone	390.5	5.792	3	4	1	-6.226	93.109	0.58	No	0.489	No
Shinpterocarpin	322.4	4.186	0	4	1	-3.694	96.183	0.106	No	-0.33	No
Liquiritin apioside	550.5	-1.258	1	13	7	-3.103	18.25	0.436	No	0.055	No
Isoliquiritigenin	256.3	2.7	3	4	3	-3.06	91.096	0.087	No	0.118	No

Figures

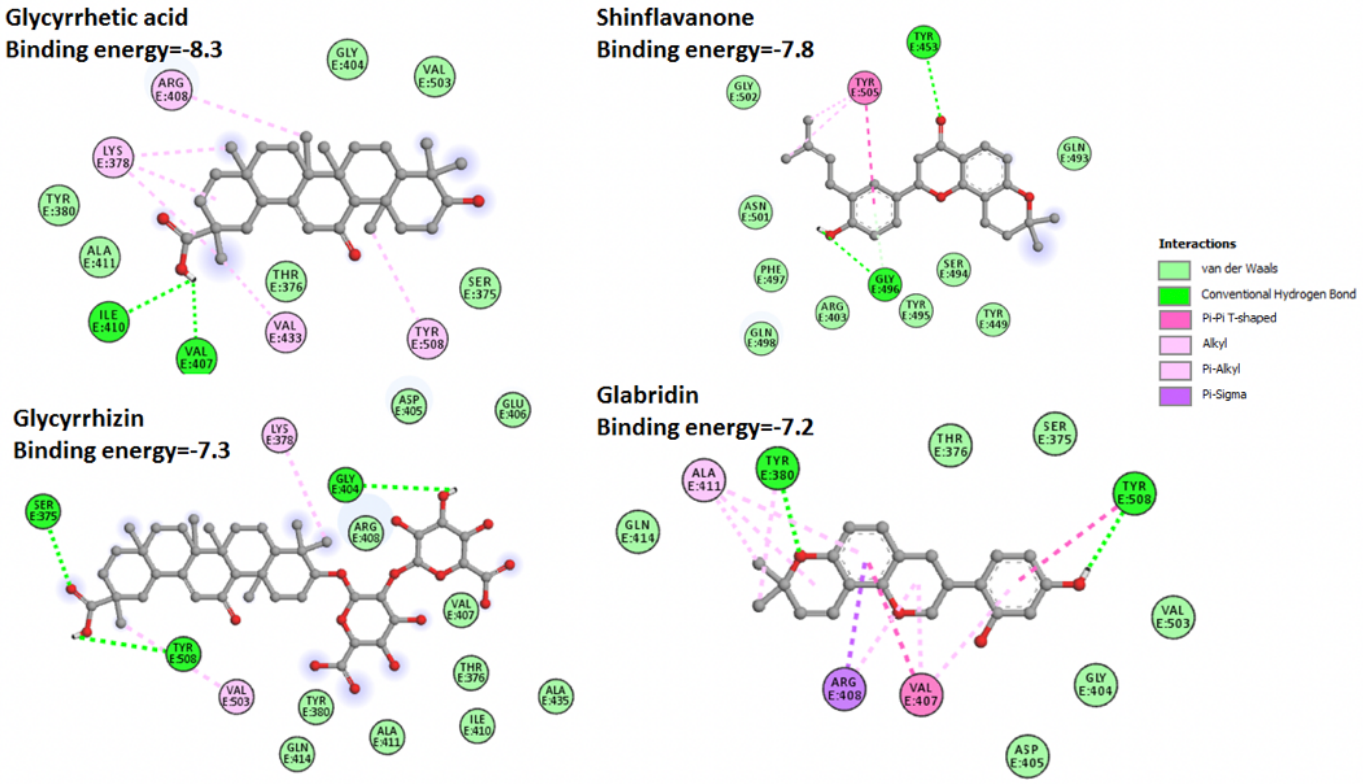

Figure 1

The predicted binding and 2D interaction of selected phytochemicals from Yashtimadhu against SARS-CoV-2 Spike CTD (PDB ID: 6M0J) and their different protein residues which are involved in the interaction.

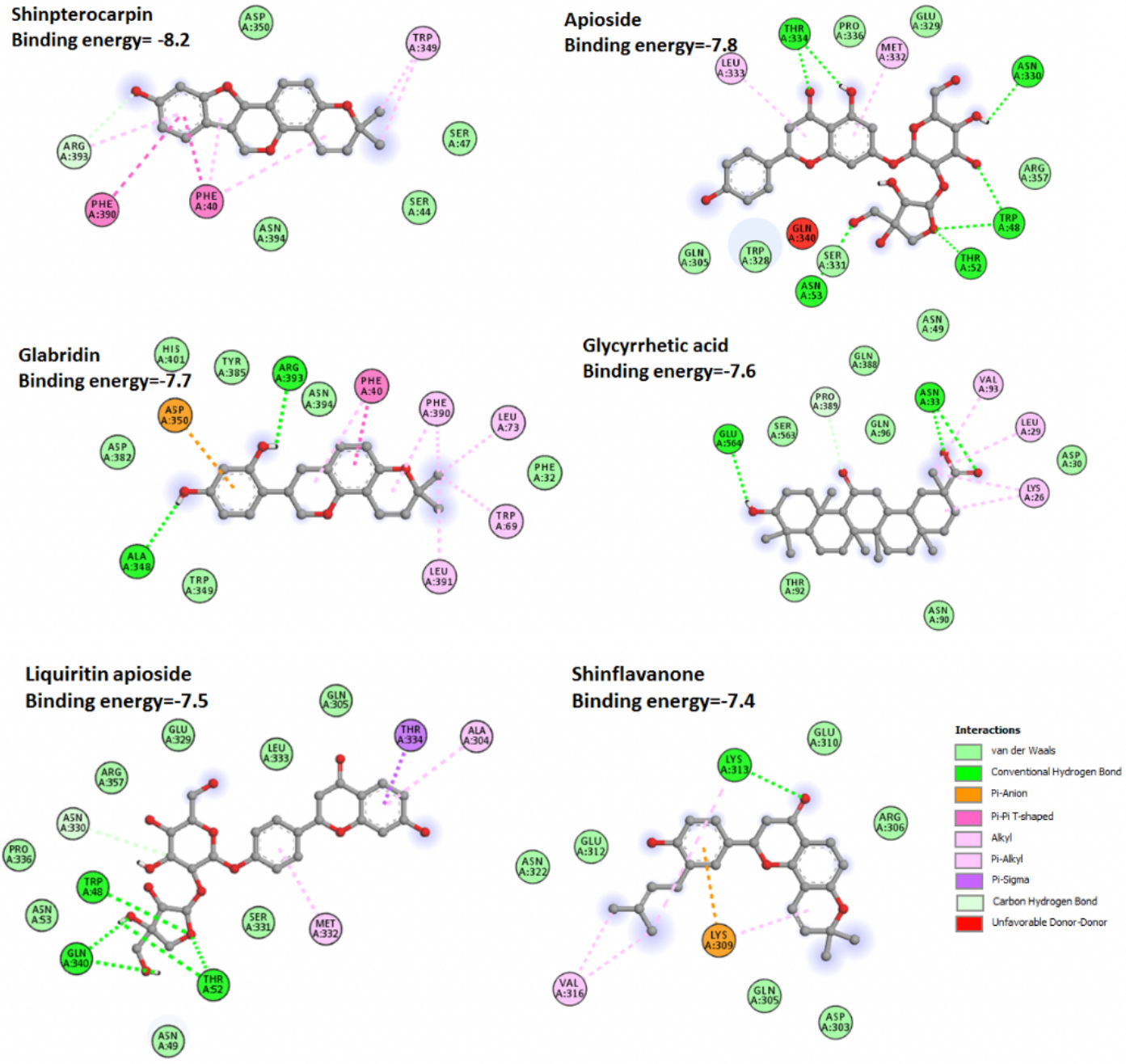

Figure 2

The predicted binding and 2D interaction of selected phytochemicals from Yashtimadhu against human ACE 2 receptor (PDB ID: 6M0J) and their different protein residues which are involved in the interaction.

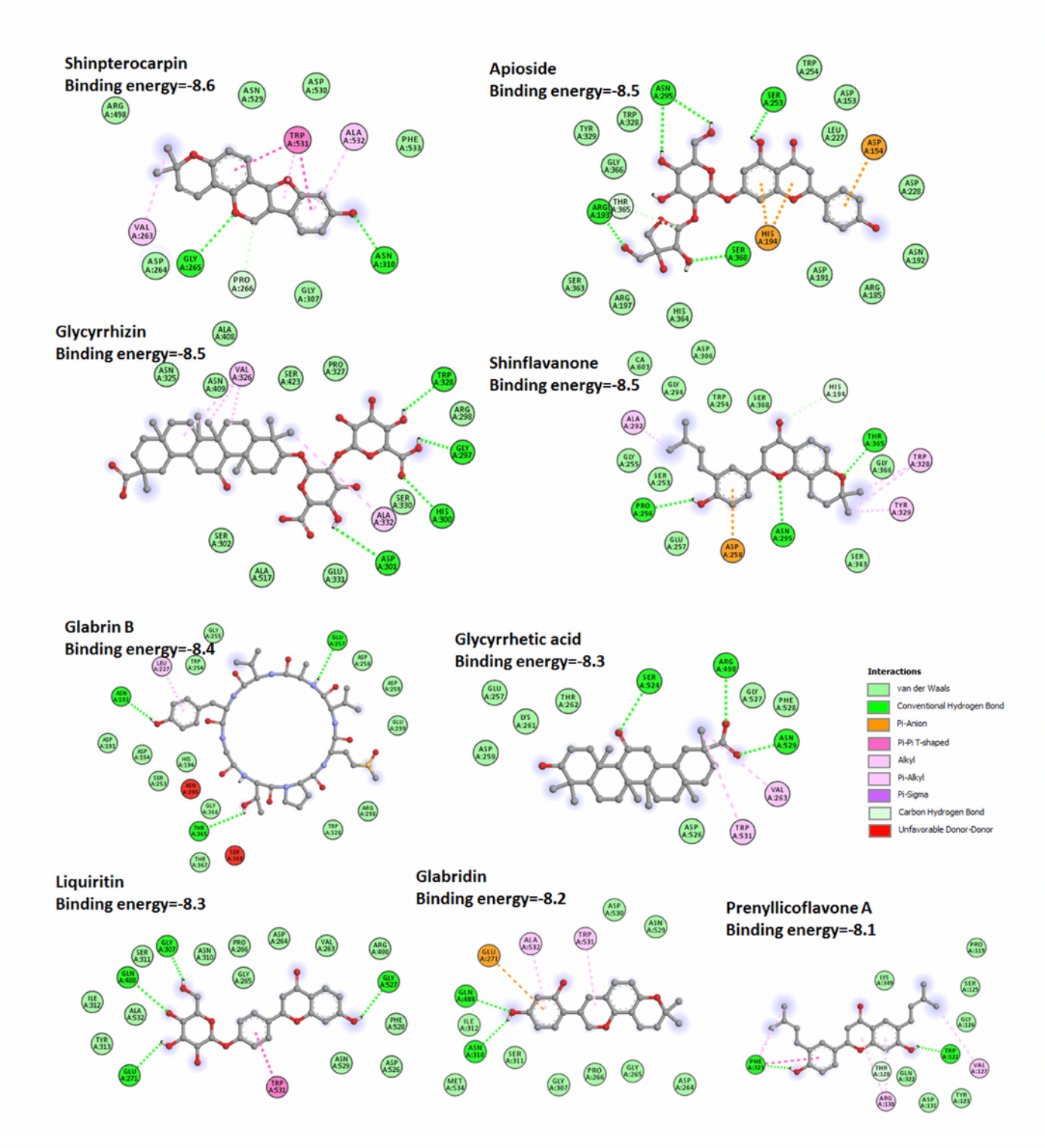

Figure 3

The predicted binding and 2D interaction of selected phytochemicals from Yashtimadhu against human furin protease (PDB ID: 5MIM) and their different protein residues which are involved in the interaction.

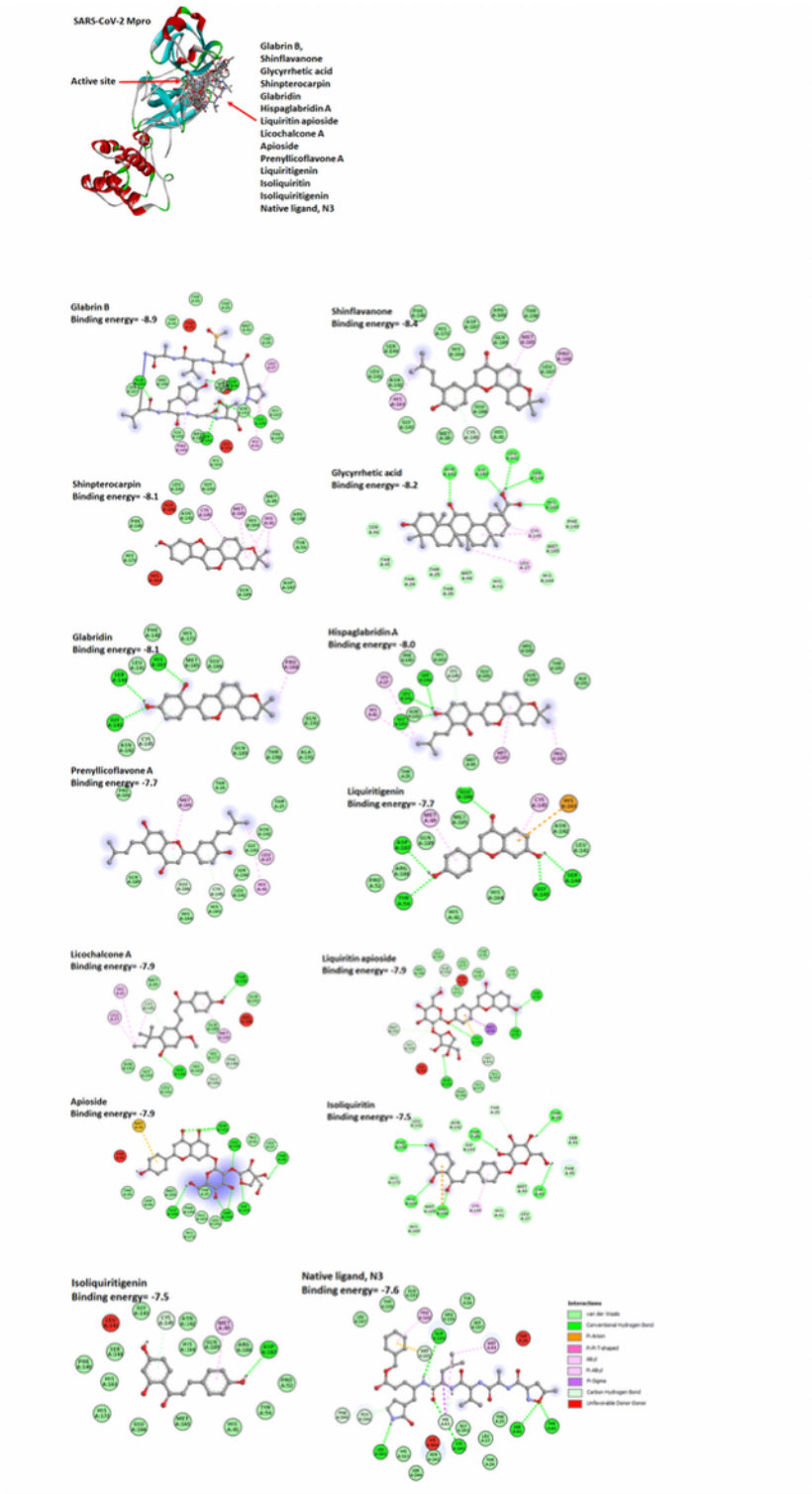

Figure 4

The predicted binding and 2D interaction of selected phytochemicals from Yashtimadhu against SARS-CoV-2 Mpro (PDB ID: 6LU7) and their different protein residues which are involved in the interaction.

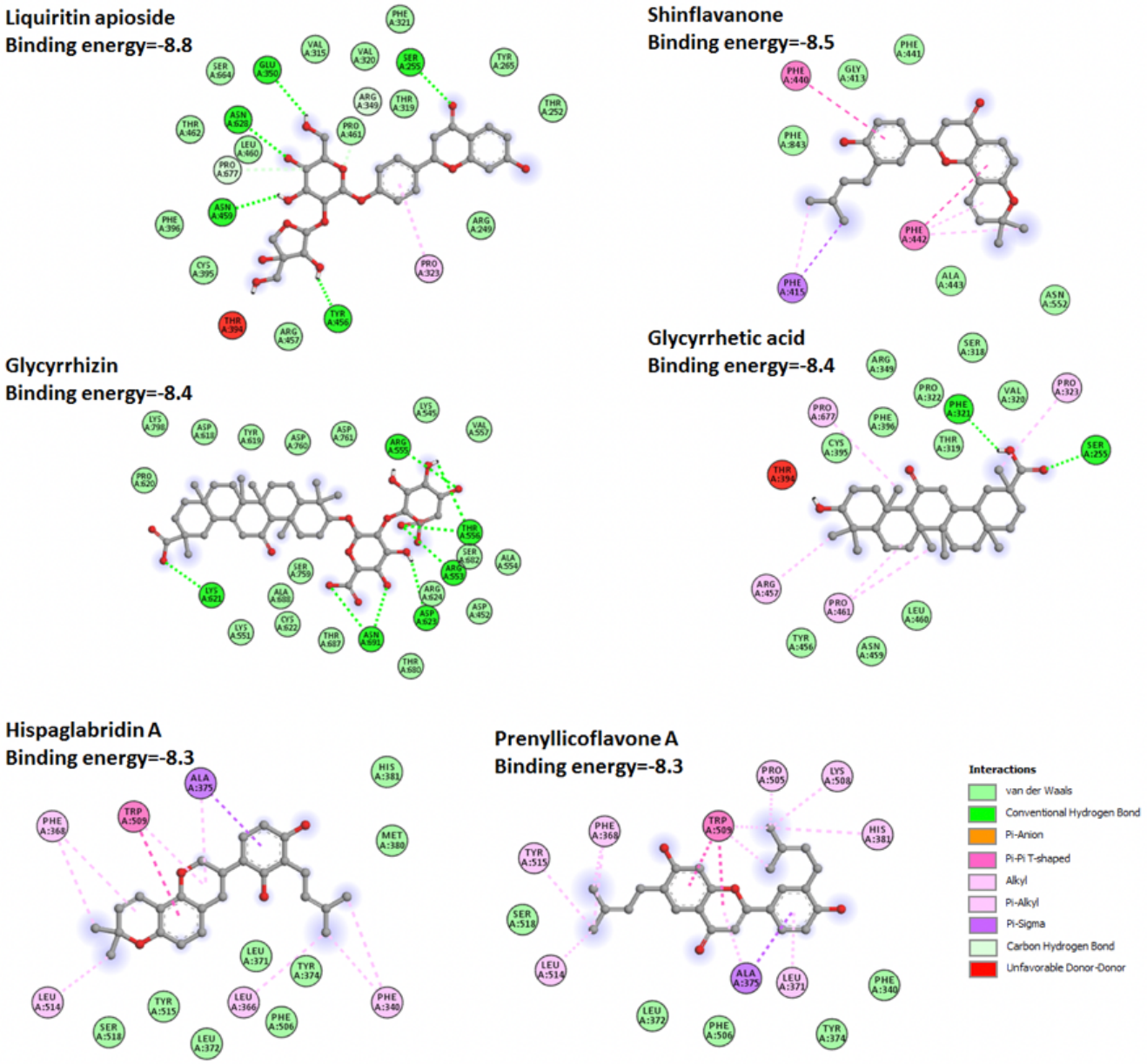

Figure 5

The predicted binding and 2D interaction of selected phytochemicals from Yashtimadhu against SARS-CoV-2 RNA dependent RNA polymerase (PDB ID: 6M71) and their different protein residues which are involved in the interaction.

Supplementary Files

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