Identification of novel inhibitors of Angiotensin-converting enzyme 2 (ACE-2) receptor from *Urtica dioica* to combat coronavirus disease 2019 (COVID-19)

Shobha Upreti

Kumaun University

Jyoti Sankar Prusty

National Institute of Technology, Raipur

Satish Chandra Pandey

Kumaun University

Awanish Kumar

National Institute of Technology, Raipur

Mukesh Samant (✉ mukeshsamant@gmail.com)

Kumaun University

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Abstract

The pandemic outbreak of coronavirus (SARS-CoV-2) is rapidly spreading across the globe, so the development of anti-SARS-CoV-2 agents is urgently needed. Angiotensin-converting enzyme 2 (ACE-2), a human receptor that facilitates entry of SARS-CoV-2, serves as a prominent target for drug discovery. In the present study, we have applied the bioinformatics approach for screening of a series of bioactive chemical compounds from Himalayan stinging nettle (*Urtica dioica*) as potent inhibitors of ACE-2 receptor (PDB ID: 1R4L). The molecular docking was applied to dock a set of representative compounds within the active site region of target receptor protein using 0.8 version of the PyRx virtual screen tool and analyzed by using discovery studio visualizer. Based on the highest binding affinity, 16 compounds were shortlisted as a lead molecule using molecular docking analysis. Among them, β -sitosterol was found with the highest binding affinity -12.2 Kcal/mol and stable interactions with the amino acid residues present on the active site of the ACE-2 receptor. Similarly, Luteoxanthin and Violaxanthin followed by rutin also displayed stronger binding efficiency. We propose these compounds as potential lead candidates for the development of target specific therapeutic drugs against COVID-19.

Introduction

SARS-CoV-2 belongs to the group of RNA viruses. Coronavirus is classified as alpha and beta (origin: bats and rodents), gamma and delta (origin: avian species) [1]. In around 2002 a beta-coronavirus crossed species barrier and moved from bats to a mammalian host and then to humans causing SARS outbreak [2]. Another beta coronavirus involved in causing the solemn malady like MERS (Middle East Respiratory Syndrome) began in 2012 [3]. The coronavirus we have been dealing lately, liable for the COVID-19 (Coronavirus Disease 2019) pandemic also belongs to the group of beta- coronavirus [4]. Full-length sequencing of the genome of this virus suggests its closeness to the strains found in bats, thus proposing its origin from the bats [2]. Its resemblance to the SARS CoV (SARS-Coronavirus) has given it the name, SARS-CoV 2 (SARS-coronavirus 2) [5]. The S protein (Spike protein) of SARS CoV binds to the cell surface receptors. SARS-CoV-2 a (+) single-stranded RNA virus fasten similar receptor as SARS-CoV i.e. ACE 2 (Angiotensin-Converting Enzyme 2) to infect the host [4], which was not the case of MERS-CoV S protein which targets DPP4 [6,7], not ACE2. ACE2, a molecule present mostly on the surface of blood vessels, and epithelium of the intestine and lungs is imperative in controlling immune reaction and flow of blood [8]. As per record of August 17, the total numbers of confirmed cases are 21,828,928 while the casualties caused are about 773,000 in 215 nations. Presently USA, Brazil, India, Russia, South Africa, Peru and Mexico are the most affected countries.

The counts of infection and casualty caused makes it clear that this is a dreadful virus which is in a great need to be contemplated and subsequently cured. It will take more than a year to develop an effective vaccine [9] hence, there is an urgent need to develop effective drugs against this disease. The progress of compelling medicines is not easy and will take longer than assumed, inturn impeding the management of this pandemic issue. Therefore to get over this, a rapid technique that can open paths for the development of some effective drugs i.e. molecular docking has been used in our study. Sofar several

natural compounds have been evaluated for their anti-SARS and anti-MERS activity moreover lately many investigators have been working on the repurposing of these natural products to combat SARS CoV-2 infection [10,11] but none of these compounds have been tested for phase III clinical trials. In this study we have focused on various compounds of *Urtica dioica* as these compounds have shown excellent anticancerous and antiviral activities [12], further *Urtica dioica* grow abundantly in Uttarakhand Himalaya as fodder and medicinal plant so to start with, virtual Scanning of various phytochemicals present in *Urtica* spp. was done which would control SARS-CoV-2 in the host cell. Our study involved the ACE2 receptor [13] as the target for these phytochemicals.

Materials And Methods

Building the Phytochemical Library

Various servers were searched (PubMed, Carrot2 and DLAD4U) to commence studies in different research papers, and about 41 compounds from the plant *Urtica dioica* were collected. *Urtica* was undertaken in this study due to its various therapeutic role against viral infections [14]

Protein selection and preparation

ACE-2 the Protein which has formed the major target for this virus in humans was retrieved from the database PDB (URL: <https://www.rcsb.org>) with PDB ID: 1R4L. Also, the selection of target protein for docking study is based on their X-Ray diffraction. The selected protein should not have protein break in entire 3D conformation and to meet requirements of docking analysis, protein should be in the form of PDB formats. X-ray crystallographic structure of 1R4L (Angiotensin Converting Enzyme-2 (ACE2)) was prepared for molecular docking in such a way that all hetero atoms (water, ions, etc.) were removed. By using the chimera tool, protein binding sites of the chain are selected and others are removed.

Ligand Preparation

Pubchem (URL: <https://pubchem.ncbi.nlm.nih.gov>) was used to retrieve 2D structures of the phytochemicals in SDF format and further using open babel (software) these compounds were converted to PDB format. The reference molecule used in the entire docking analysis is Remdesivir with Pubchem CID-121304016 were retrieved from Pubchem.

Phylogeny and homology modeling

MSA was done to check the similarities between the molecules present in the branch of the RAS system occurring in the lungs. Amino acid sequence of the target ACE2 (PDB ID:1R4L) along with the active site of ACE (AAH36375.1), the mature chain of DPP4 (sp|P27487.2), ADAM17 (sp|P78536.1) and MasR (sp|P35410.1), and also amino acid sequence of the protein AT1R(NP_114038.4), AT2R (NP_000677.2) and Collectrin (AAG09466) were retrieved from the database NCBI (URL: www.ncbi.nlm.nih.gov) in FASTA format and later these sequences were scanned for their similarities using Clustal W. Furthermore, a phylogenetic tree was developed using the aligned sequences.

Molecular docking

An *In silico* approach for ligand and receptor docking analysis was employed to examine structural complexes of the 1R4L (target protein) with *Urtica dioica* compounds (ligand molecule) in order to emphasize structural conformation of this protein target specificity. In the present investigation, we use PyRx virtual screening tool which uses both Vina and Auto Dock 4.2 with Lamarckian genetic algorithm as scoring function and contributes higher docking accuracy [15,16].

The target protein was defined as the total number of atoms of 5218; the number of residues is 655 with unique five chains. The chemical structure of macromolecule was determined by X-Ray Crystallography with a resolution of 3.00 Å. We continue to the preparation of target by eliminating the bound ligands and water molecules through UCSF Chimera tool. Also, we remove all chains except Chain A as it shows only ligand binding site chain. Then we introduced it into the PyRx tool by remarked as macromolecule in PyRx workflow. In this method, the protein and ligand molecules were converted to their proper readable file format (pdbqt) using auto dock tools. All docking studies were performed as blind docking which was set in the grid box and encompasses all possible ligand-receptor complex and dimensions were X= 39.021, Y= 4.078 and Z= 22.898 to dock all the ligands where 8 maximum exhaustiveness was calculated for each ligand. All other parameters of software were kept as default and all bonds contained in ligand were allowed to rotate freely, considering receptor as rigid. The final visualization of the docked structure was performed using Discovery Studio Visualizer 3.0. Before testing potentiality of the *Urtica dioica* compounds against 1R4L, a broad-spectrum anti-viral drug i.e. remdesivir was also used [17].

Results

Phylogenetic analysis

The phylogenetic relationship of ACE-2 (1R4L) and various enzymes involved in the Renin-Angiotensin System (ACE, ADAM17, Mas-R, AT1R and AT2R) along with a few other important homologs of ACE2 (collectrin and DPP4) was evaluated (Fig. 1). The phylogeny indicated that ACE-2 is only 12.825% similar to ACE, 9.553% to ADAM17, 10.648% to AT1R, 10.324% to AT2R, 8.898% to MASR, 4.655% to collectrin and 12.413% to DPP4. Such low level of similarity confirms that ACE-2 is distantly related to these enzymes, further strengthening our hypothesis to evaluate the ACE-2 receptor as a potential drug target.

3.2 Molecular docking

ACE-2 is the best target for inhibiting the 2019-nCoV, due to higher affinity of spike (S) glycoprotein of SARS-Cov-2. Spike (S) glycoprotein plays the most important role in viral attachment, fusion and entry into the host cell. CoV entry into the host immune system is mediated by transmembrane spike glycoprotein which forms homotrimers protruding from the viral surface and gives CoVs a crown-like appearance by forming spikes on their surface. S protein binds to a membrane receptor on the host cells, angiotensin-converting enzyme 2 (ACE2; EC 3.4.17.23) mediating the viral and cellular membrane fusion, which represents the critical initial stage of the infection [18,19]. Molecular docking studies were carried

out between receptor proteins (ACE-2) and its inhibitors (*Urtica dioica* compounds). Table 1, consists of all the compounds with their IUPAC names, structures of ligands, docking scores, and necessary H-bond formation with possible active residues by ligands with targets required for inhibition of receptor of COVID-19. After successfully docking of these compounds into target ACE-2, the result displays various modes of ligand-receptor interactions are generated with a particular docking score. The binding mode with the least binding energy is regarded as the best mode of binding as it is most stable for the ligand. Most of the compounds showing their inhibitory action by representing lower binding energy score (higher docking scores) compared with the binding energy of remdesivir (-8.7 kcal/mol), the standard anti-viral drug. Fig. 2, indicates the Co-ordination center and size of the active sites present in targeted protein (Chain A of 1R4I) generated from the PyRx virtual screening tool. Before conducting the virtual screening, molecular docking protocol was validated by docking the reference ligand Remdesivir into binding pocket obtained from the target protein ACE-2. The docked ligand was superimposed to compare with an experimental ligand. Generally, RMSD value is used to validate the docking studies. The RMSD value between the experimental ligand and docked ligand (Remdesivir) was 0.0 angstrom, which was perfectly acceptable. The result displays that docked reference molecule, remdesivir exhibited well-established hydrogen bonds with multiple amino acid residues in receptor active pocket showed in Fig. 3. The figure also indicates the formation of four conventional hydrogen bond with Tyr⁵¹⁰ (2.72 Å), Arg⁵¹⁴ (2.94 Å), Glu³⁹⁸ (2.16 Å) and Asp²⁰⁶ (2.67 Å) has been observed. The virtual screening of all *Urtica dioica* compounds (n=41) was performed by the docking approach in the active sites of target protein using the PyRx tool. From molecular docking analysis, a total of 16 compounds were screened which showed binding energy ranging from -12.2 to -8.8 kcal/mol against Covid-19 receptor ACE-2 and their ligand-receptor 3D interaction images are shown in Fig. 4. The binding energy of the reference molecule, Remdesivir was -8.7 kcal/mol. All these screened leads showed lower and significant binding energy and novel hydrogen bonding interactions with active residues of target receptor in comparison to the reference molecule. Thus, the docking studies suggest that screened compounds may have the same mechanism of action as the reference molecule. The 3d interaction image of 19 compounds with target ACE-2 in Fig. 5 reveals that, binding in the pocket of chain A with the affinity range from -8.6 to -5.8 kcal/mol. In comparison to the reference molecule, it shows lower docking scores (higher binding energy) but these ligands show stronger interaction with the target and may be considered as a good inhibitor of ACE-2. Furthermore, in Fig. 6, the docking of ACE-2 target with *Urtica dioica* compounds using docking procedure revealed that compound 6, 8, 16 and 30 were bounded by hydrophobic pockets containing amino acid residues whereas compound 10 and 18 were involved with hydrophobic and electrostatic pockets containing residues, though these compounds exhibited lower binding affinity to the target protein. These compounds do not exhibit any stronger interactions like H-bond with the target. Therefore, these were surprisingly low as compared to the reference molecule, indicating docking programs often failed to find out the correct binding mode.

Discussion

The intricacy of SARS CoV-2 has doomed the world right now owing to the lack of availability of any effective drug or vaccine, however, some synthetic antiviral drugs such as lopinavir/ritonavir [20,21], remdesivir [21] as well as other antimalarial drugs hydroxychloroquine and chloroquine [21] currently used to treat SARS CoV-2 patients have various side effects, therefore natural compounds are in a great need to be explored. Natural compounds can boost immunity [22,23] and cure a range of viral diseases. One of the most widely distributed plants with various medicinal properties is *Urtica dioica*. This particular plant has been noteworthy because of its antiviral, antioxidant, antiulcer, analgesic, anti-inflammatory, hepatoprotective, immune-modulatory, anti-colitis, anti-diabetic and anti-cancer effect [12]. In this study we have explored *Urtica*, which exhibits a range of bioactive compounds that can target ACE-2, an important enzyme of the RAS system and a decisive target for internalization of SARS CoV-2, thus docking of these compounds with ACE-2 will certainly serve to surmount the viral load. Most crucial molecules of the RAS system including ACE2 are present in the lungs therefore lungs are the most affected organ from this virus [24]. ACE, an enzyme present in the lung tissue converts angiotensin I to angiotensin II, which can either bind to AT1R or AT2R where it induces Vasconstriction or Vasodilation respectively [24]. ACE2 another enzyme present in the lung tissue acts on Angiotensin II and converts it into Ang1-7 which in turn binds to the Mas-R leading to vasodilation [24]. ACE-2 comes to the surface only when glycosylated, during SARS CoV-2 infection S (spike) protein of the virus binds to the ACE-2 receptors which result in the internalization of the virus further the viral genome is released into the cytosol where its replication and translation takes place to assemble newly formed virion which are later exocytosed (Fig. 7). As RAS system consists of various enzymes therefore to get a clear vision that ACE2 will make a good target for the natural compounds, we have executed its homology with the enzymes/proteins from the RAS system and some other homologs of ACE2 and found that it is distantly related to all the other 7 enzymes.

Results generated from molecular docking of various compounds of *Urtica* with the target ACE2 gave us some compounds with an overwhelming response. These compounds are thought to inhibit ACE2 by causing various structural changes or by affecting glycosylation (without glycosylation ACE2 will not come to the surface) thus impeding path for the virus to enter the host cell [25,26]. An *In silico* approaches have been established as an important part of various drug discovery programs, from leading finds to its optimization; methodologies such as ligand or targeted based computational screening procedures are broadly employed in many drug discovery studies [27-29]. Docking predicts the mode of interaction between target receptor protein and small ligand for established binding sites. Binding energy suggests the affinity of a specific ligand and strength by which a compound interacts with and binds to the pocket of a target protein. A compound with lower binding energy is preferred as a possible drug candidate. Currently, SARS-CoV-2 has become a prominent challenge for every researcher across the globe. The outbreak of this virus is spreading worldwide and causing several deaths. As we all know that no chemical vaccines are available for the treatment of the disease, we can use natural compounds that can help to stop the dissemination of coronavirus. SARS-CoV uses angiotensin-converting enzyme 2 (ACE 2) as a surface receptor that mediates the process of infection and transmission. In our study, we have applied a computational approach of drug repurposing in order to

identify a specific therapeutic agent against the COVID-19 receptor. Targeting ACE 2 protein can be efficient and leads to such changing of structural conformation which will not permit entering this virus inside the individual's immune systems. Therefore, About 41 compounds from *Urtica* were virtually scanned using PyRx virtual tool to build a phytochemical library. Later these compounds were docked with the enzyme ACE2. Out of 41 screened leads, only 16 compounds were selected based on their binding affinity and stronger interaction with the ACE 2 target. Out of 16 compounds, Beta-sitosterol (Compound 13) exhibited best-docked score (-12.2 Kcal Mol⁻¹) with ACE2 protein with comparison to reference remdesivir compound. The native ligand attached in ACE2 protein is showing its inhibitory action by forming one hydrogen bond with Val²¹² (2.10 Å) and leu⁹⁵, Val²⁰⁹, Pro⁵⁶⁵, Leu³⁹¹, Ala⁹⁹ residues appear in a mostly hydrophobic binding pocket. In this study, we have first time reported various compounds from *Urtica dioica* for their anti-SARS activity, specifically targeting the ACE2 receptor. We have observed that many compounds from *Urtica* have shown better results than the reference molecule remdesivir, thus compounds from this particular plant can surely be evaluated for invitro study and clinical trial.

Declarations

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Author contributors Shobha upreti and Jyoti Sankar Prusty: Collected information and performed experiments and wrote the manuscript. **Satish Chandra Pandey:** Assisted in writing and modification of the manuscript. **Mukesh Samant and Awanish Kumar:** Conceptualization, Visualization, Investigation, Supervision, Validation, Writing- Reviewing and final Editing of the manuscript. All authors approve the final version of the manuscript.

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Compliance with ethical standards

Conflict of Interest The authors have declared no conflict of interest.

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Table

Due to technical limitations, table 1 is only available as a download in the supplemental files section.

Figures

ACE2 (1R4L) MSSSSWLLSLVAVTAQSTIEEQAKTFLDKFNHEADLFYQSSLASWYNTNITEENVQNMNAGDKWSAFLKEQSTLAQMYPLQEIQNLTKVLQALQALQNGSSVLSDEKSKRLNTIL
 ACE
 Collectrin
 DPP4 MKTPWKVLLGLGAAALVTITVPPVLLNKGTDADSRKTYTLTDYLNKTYRLKLYSLRWISDHELYKQENILVFNAEYGNSSVFLNSTDFEGHSINDYSISPDGQFILLEYN
 AT1R
 AT2R
 MasR
 ADAM17 MRQSLFLFTSVVPVFLAPRPDPDPGFGPHQRLEKLDLSLDYDILSLSNIQHSVKKRDLQSTHVTETLLTSALKRHKFLYLTSSTERFSQNFKVVVDGKNESEYTVKWDQFTHGVV

ACE2 (1R4L) NTMSTIYSTGKVCNPDPNQCCLLLEPGLNEIMANSLOYNRLWAWESWRSEVGKQLRPLYEEYVVLKNEMARANHYEDYGDYWRGDYEVNGVDGYDYSRQQLIEDVHTFEIKPLYEHL
 ACE
 Collectrin
 DPP4 VKQWRHSYASDYIDLNKRQLTEERI PNNTQWVTS PVGKLAAYVNDIYVKIEPNLPSYRITWTGKEDIIYNGITDWWYEEVEFSAYSALWWSNGTFLAYAQFNDTEVPLIEYSF
 AT1R SPKAPQLRGGVDFVATNSQVIKMLNSTEDGKIRIQDDCPKAGRHHYIFVMIPTLYSII FVVGIFGNSLVVIVYFYMKLKTVAS
 AT2R ATTSKNITSGLHGLVNIISGNNESTLNCQKPSD
 MasR FAESQISLSCSLCLHSGDQEAQPNLVSQLCGVFLQNETNETHMQMSMAVGGQALPLNIAPKAVLVSLCGVLLNGTVFWLLCCGATN
 ADAM17 GEPDSVLARIHDDVDIIRINTDGAENIEPLWRFNVDTKDKRMLVYKSEDIKNVSRQSPKVCGLKVDNEELLPKGLVDRPEPEELVHRVKRRADPDMKNTCKLLVADHRFRYRGM

ACE2 (1R4L) HAYVRKLMNAPSYISPIGCLP-----AHLLGDMWGRFWTNLSLTVFPGQKPNIDVTAMVDQADAQRIFKEAEKFFVSVGLPNMTQGFWEN
 ACE
 Collectrin
 DPP4 YSDESILQPKTVRVPYKAGAVNPTVKFFVNTDSLSVYTNATSIQTAPASMLIDGHYLCDVTWATQERISLQWLRIQNSVMDICDYDESSGRWNCLVARQHIMESTTGWGRFRPS
 AT1R
 AT2R
 MasR
 ADAM17 RGEESTTTNYLIELIDRVDDIYRNTSDWNAAGFKG--YGTQIEQIRILKSPQEVKPGKHYNMAKSYNPEEKDAWDVKMLLEQFSFDIAEASKVCIAHLFTYQDFDMGTGLLAYVGSRA

ACE2 (1R4L) --SMLTDPGNVQKAVCHPTAWDLGKG--DFRILMCTKVTMDDFLTAHHEMGHIQYDNAYAA--QPFLLRNGANE-----
 ACE
 Collectrin
 DPP4 EPFHTLDGNSFYKIIISNEEGYRHICYFQIDKKDCTFIITKTGWEVIEALTSYLYISN--EYKGMPPGGRNLYKQLSDYTKVTCLSCELNPERCQYSVSFSEAKYYQLRCSGGLP
 AT1R VFLLTCLSIDRYLAIVHPMKSLRRLRMLVAKVTCIIWLLAGLASLPALIRHNVFFIENTNITVCAPHYES
 AT2R IFITTCMSVDYQSVLYPFLS--QRNRPNQASYIVPLVWCMACLSLPTTFYFRDVRTI EYLGVNACIMAFPEEK
 MasR LCLLVAISTERCVCVLPFIWYRCHRPKYSNVVCTLLWGLPFCINIVKSLFLTYWKHVKV
 ADAM17 NSHGGVCPCAYYSVPGKKNIYLSGLSTKYNKGLITLKEADLVTHLGHNFGEHDPGLAECAPNEDQGGKYVMYPIAVSGDHENKMFNSCSKQSIYKTESKAQECFQERSNKKVC

ACE2 (1R4L) -----GFHEAVGEIMSLAATPKHLKSIIGLLSPDFQEDNETEINFLKQA-----
 ACE
 Collectrin
 DPP4 LYTLHSSVNDKGLRVLEDNSALDK-----MLQNVQMPKGLDFIILNETKFWYQMLPPHFDKSKYPLLLDYAGPCSQKADTVFRLNWTATYLASTEN
 AT1R
 AT2R
 MasR
 ADAM17 GNSRVDGECECDPGIMYLNNDTCNSDCTLEKGVQCSDRNSPCCKNCQFETAQKKQCAEINATCKGVSYCTGNSSECPPPGNAEDDTYCLDLGKCKDGKCIFFCEREQQLESCACNETDN

ACE2 (1R4L) -----LTIVGTLPTFYMLEKWRWMVFKGEIPKQDQMKWEMKREIVGVPEVPVPHDETCDPASLHVNSDYSFIRYYTRTLYQFQEAALCQAAKHEGLHKCD
 ACE
 Collectrin
 DPP4 IIVASFDGRSGGYGDKIMHAIINRLGTFEVEDQIEAARQFSKMGFVONKRIATWGSYGGYVTSMLVSGSGGVFKCGIAVAPVSRWEYDYSVYTERYMGLPTEPDNLHYRNVSTVMSRA
 AT1R
 AT2R
 MasR
 ADAM17 SKVCVRDLSGRCVPPYDAEQNLFLKKGKPCVTFGCDNKGCEKRVQDVIERFWDIDQLSINTFGKFLADNIVGSVLYFSLIFWIPFSLILVHCVDKLDKQYESLSLFHPSNVEMLSS

ACE2 (1R4L) ISNSTEAGQKLFNMLRLGKSEPWTLALENVGAKNMNVRPLNLYFELFTWLKQDNKNSFVGWSTDWSPYAD-----
 ACE
 Collectrin
 DPP4 ENFKQVEYLLIHGTADDNVHFQQAQISKALVDVGDFQAMWYTD EHGIASSSTAHHQIYTHMSHFQKQCFSLP-----
 AT1R
 AT2R
 MasR
 ADAM17 MDSASVRIIKFPAPQTPGRGLQAPVTPSAPAPKLDHQRMIDQIEDPSTDSHMDDEGFEKDPFPNSSAKSFEDLTDHPVTRSEKASFKLQRQNRVDSKETEC

A

B

Figure 1

Multiple sequence alignment and phylogenetic relationship among ACE-2 (PDB ID:1R4L) and other important enzymes involved in RAS system (A) The protein sequences were aligned by the ClustalW 2.1 algorithm using the Network Protein Sequence Analysis (NPS@) online tool, and aligned sequences were graphically viewed by the Easy Sequencing in PostScript (ESPrpt) program. (B) Phylogenetic analysis was conducted on ClustalW 2.1-aligned sequences using the Poisson model method of MEGA v5.2 by the

NJ method and bootstrap analysis (1000 repeats). The sequence of 1R4L is distantly related to other enzymes involved in the RAS system.

Figure 2

Creation of text files for active sites in target protein in PyRx tool

Figure 3

Visuals of docking interactions of Remdesivir ligand molecule. A) 3D interaction poses of the ligand with 1R4L. B) 2D interactions of the ligand with 1R4L

Figure 4

Docking interactions showing novel binding interactions with the highest docking score (binding energy from -12.2 to -8.8 kcal/mol).

Figure 5

3D docking poses of Ligands with 1R4L target (Lower docking score comparison to remdesivir, binding energy from -8.6 to -5.8 kcal/mol)

(30) β -carotene

(10) Ethyl stearate

(6) n- Tetracosane

(8) n- Hexacosane

(16) Benzofuran,2,3,-dihydro

(18) 1-Dodecanamine, N,
N-dimethyl

Figure 6

Representation of docking of the compound with 1R4L shows lower binding energy but no H-bond formation.

Figure 7

ACE-2 Role in SARS CoV-2 Infection: Angiotensin I is converted to Angiotensin II by the action of ACE. Angiotensin II can either bind to AT1R or AT2R where it induces Vasoconstriction or Vasodilation respectively. ACE-2 acts on Angiotensin II and converts it into Ang1-7 which in turn binds to the Mas-R leading to vasodilation. ACE-2 comes to the surface only when glycosylated, during SARS CoV-2 infection S (spike) protein of the virus binds to the ACE-2 receptors which result in internalization of the virus further the viral genome is released into the cytosol where its replication and translation takes place to assemble newly formed virion which are later exocytosed. The phytochemical here are thought to act in two ways by inhibiting the glycosylation of ACE-2 (step 1 to 10 are blocked) or by making structural changes in ACE-2 (step 3 to 10 blocked)

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [Table1.docx](#)