
Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Materials Today: Proceedings 46 (2021) 11169–11176

Contents lists available at ScienceDirect

Materials Today: Proceedings

journal homepage: www.elsevier.com/locate/matpr

# Modeling novel Anti-Viral peptides (AVPs) with in-silico docking simulations against corona virus

Aditi Sharma [a], Kumud Pant [b,*], Akshara Pande [c], Somya Sinha [b], Bhasker Pant [c]

[a] Deparment of Life Sciences, Graphic Era Deemed to be University, Dehradun, Uttarakhand, India
[b] Department of Biotechnology, Graphic Era Deemed to be University, Dehradun, Uttarakhand, India
[c] Department of Computer Sciences, Graphic Era Hill University, Dehradun, Uttarakhand, India

ARTICLE INFO

*Article history:*
Received 31 December 2020
Received in revised form 9 February 2021
Accepted 11 February 2021
Available online 27 February 2021

*Keywords:*
Corona virus
Anti-Viral peptides
Modeling
Simulation
Docking

ABSTRACT

The havoc created by Corona virus has been dealt with using various integrative approaches adopted by laboratories through-out the world. Use of anti-viral peptides (AVPs) although new but has shown tremendous potential against many pathogens. Previously AVPs have been designed against spike protein of corona virus which is the major entry mediating molecule. Using various in-silico strategies, in this research work AVPs have been modeled against lesser studied viral proteins namely ORF7a protein, Envelope protein (E), Nucleoprotein (N), and Non-Structural protein (Nsp1 and Nsp2). The predicted AVPs have been docked against various host as well as viral proteins. The interaction of small AVPs seems capable of interfering with binding between viral protein and its host counterpart. Therefore, these AVPs can act as a deterrent against novel corona virus, which requires further validation through laboratory techniques.

Selection and peer-review under responsibility of the scientific committee of the International Conference on Technological Advancements in Materials Science and Manufacturing.

## 1. Introduction

Corona virus (CoVs) has been known to be linked with significant disease outbreak in East Asia and the Middle East since past two decades. The pandemic of severe acute respiratory syndrome (SARS) and the Middle East respiratory syndrome (MERS) has occurred during 2002 and 2012 respectively. Recently, in late 2019, emergence of a novel corona virus namely severe acute respiratory syndrome corona virus 2 (SARS-CoV-2) has become the leading cause of corona virus disease 2019 (COVID-19) which has given rise to major health threat and an ongoing pandemic throughout the world [1]. Corona viruses are the member of Coronaviridae family (subfamily Coronavirinae), which causes infection in a wide range of hosts leading to symptoms and diseases like common cold and eventually fatal consequences such as SARS and MERS. Presently COVID-19, SARS-CoV-2 is believed to fall under one of the seven members of the corona virus family infecting humans; although, this novel virus is genetically different. There were only six CoVs until 2020 which were known to infect humans involving human CoV 229E (HCoV- 229E), HCoV-NL63, HCoV-OC43, HCoV-HKU1, SARS-CoV, and MERS-CoV. Out of these, SARS-CoV and MERS-CoV have led to the major outbreaks with high mortality rates while others have been found to be linked with mild upper-respiratory-tract illness [2,3]. As the evolution of this novel CoV-2 has caused a high public health threats worldwide, hence there is a great need to control this outbreak by utilizing various novel technologies like use of anti-virals, cell and gene therapies, immunomodulators, neutralizing antibodies and much more [4,5]. Out of these, many recent evidences have been observed highlighting the functional properties of antiviral proteinaceous compounds as a defensive barrier and it has also been identified that some antimicrobial peptides can show their activity against a wide range of viruses, hence termed as antiviral peptides (AVPs) [6,7,8]. These molecules when acquired by using bioinformatics tools are termed as designed or artificial AVPs which can be obtained through bait studies involving testing of an artificial peptide interacting against a specific target like a surface glycoprotein or a vital viral enzyme, it can also be derived using in-silico approach by utilizing specific software that are designed to predict peptides [9,10,11]. There are various advantages associated with the utilization of antiviral peptides including inhibition of protein–protein interactions, an alternative against diseases which are difficult to target, availability of advance technologies that will

* Corresponding author.
*E-mail addresses:* pant.kumud@gmail.com, kumud.pant@geu.ac.in (K. Pant).

https://doi.org/10.1016/j.matpr.2021.02.377
2214-7853/
Selection and peer-review under responsibility of the scientific committee of the International Conference on Technological Advancements in Materials Science and Manufacturing.

enhance peptide half-life and shorter market time [12]. Along with various advantages, there are certain side effects related with peptide drugs and minute drug tolerance in comparison to chemical drugs. Meanwhile, the peptide based treatment is highly specific, besides this there is a need of special storage circumstances for peptide drugs in order to avoid inactivation of protein functions leading to low oral bioavailability and the tendency of rapid metabolism [13].

Therefore the need for novel therapeutics in the form of AVPs against essential viral proteins, as a boost in the research against the same, cannot be denied. Previously anti-viral peptides have been designed against fusion protein and spike protein of corona virus [14,15]. Moreover the use of anti-viral peptides against SARS-CoV2, SARS-CoV, MERS-CoV, SARS-related CoVs, and other respiratory viruses has been documented [16].

Realizing the therapeutic potential of these peptides, in this research work the lesser explored proteins of CoV-2 as novel drug targets have been used for designing AVPs. The proteins include ORF7a, Envelope protein (E), Nucleoprotein (N), Nsp1 and Nsp2. The ORF7a protein of Severe acute respiratory syndrome corona virus 2 (2019-nCov) has been found located in the host endoplasmic reticulum membrane, host endoplasmic reticulum-Golgi intermediate compartment membrane and host Golgi apparatus membrane. Its length is 121 with molecular weight 13.744 Da and interacts with the spike glycoprotein, M protein, E protein, ORF3a protein, human SGT, host ITGAL and host BST2. It takes part in biological process like modulating viral host G0/G1 transition checkpoint, suppressing viral host Tetherin activity and suppressing viral host type I interferon-mediated signaling pathway. It functions as an antagonist of host Tetherin (BST2), by binding to BST2 thereby interfering with its glycosylation and in-turn disrupting its antiviral effect along with this, it may also suppress siRNA and may bind to host ITGAL, thereby playing a role in attaching and modulating leukocytes. Envelope protein (E) of SARS-CoV-2 has a major role in viral morphogenesis and assembly but the short length of the protein lessens the probability of finding AVPs [17]. The next protein is Nucleoprotein (N) responsible for packaging the positive strand viral genome RNA into a helical ribonucleocapsid (RNP) and also plays a fundamental role during virion assembly through its interactions with the viral genome and membrane protein M [18]. The other viral protein is replicase polyprotein 1a which is cleaved into 11 chains of host translation inhibitor nsp1, 3C-like proteinase (3CL-PRO; 3CLp) and various non– structural proteins [19].

In this research paper an attempt has been made to piece-together novel AVPs against the mentioned target viral as well as host proteins using various in-silico resources. The confirmation of anti-viral activity through further laboratory experimentation could be a major boost in fighting against ever invading microorganisms with the proof that 'solution to the problem lies within the problem itself'.

## 2. Materials and methods

ViralZone has been used for retrieving information on corona virus intearactome [20]. From the interactome, proteins other than spike have been considered for predicting AVPs. The significant server cum databases for prediction, analysis and storage of AVPs are AVPpred [21], APD3 [22], CAMPR3 [23] and HIPdb [24]. AVPpred is the first database and server developed using peptides with experimentally proven antiviral activity with implementation done using machine learning models, therefore has been chosen for analysis and prediction.

Profile ALIgNEment (PRALINE), a flexible multiple sequence alignment tool, is another software to be used in this research work. It has numerous advantages besides having user friendly interface and easily interpretable output [25,26]. The software has been applied for multiple sequence alignment of target viral protein so as to select most conserved stretch of residues to be tested further as anti-viral peptide.

The predicted anti-viral peptide(s) are docked or checked for the interaction ability with host and viral protein using publicly available servers. For peptide-protein docking or interaction prediction and ab-initio docking algorithm based tool MDockPeP has been used. This server docks all-atom, flexible peptide to receptor and later docked poses are ranked based on statistical potential-based scoring function, ITScorePeP [27,28].

Another downloadable software iGemDock, a virtual screening tool with facility for post screening analysis, has been used for predicting interaction analysis of viral non-spike proteins with predicted AVPs [29].

LIGPLOT + downloadable servers have been used for analysis of interacting residues between receptor and ligands [30,31]. This server allows observation of all kind of bonds as well as interacting residues between modeled peptide and host protein.

The CASTp (Computed Atlas of Surface Topography of proteins) server at http://sts.bioe.uic.edu/castp/ is used for predicting pockets and also cavities on protein on which ligands can bind [32].

The various servers and software as mentioned above have been used for prediction of novel AVPs through analysis performed at various levels against major virulent proteins of Corona virus.

## 3. Results and discussion

The strategy of finding anti-viral peptide as a deterrent has been previously explored for spike protein of the virus by Torres Jesús

**Table 1**
Viral proteins for AVP designing.

| S. No | Name of the viral interactome protein | Interacting host (human) protein | Uniprot ID of viral protein |
|---|---|---|---|
| | ORF7a | Tetherin (BST2), ITGAL, SGTA | P0DTC7 |
| | Envelope protein (E) | MPP5 | P0DTC4 |
| | Nucleoprotein (N) | SMAd3 | P0DTC4 |
| | Nsp1 | 40S ribosome | P0DTC1 |
| | Nsp2 | PHB | P0DTC1 |
| | ORF6 | KPNA2 | P0DTC6 |

| Amino Acid Polarity | Hydrophobic | Hydrophilic |
|---|---|---|
| | 3(37 %) | 5 (63 %) |

| Amino Acid Charge | +vely charged | -vely charged | Neutral Amino acid |
|---|---|---|---|
| | 2(25 %) | 2(25 %) | 4 (50 %) |

| Amino Acid Surface exposure | Surface exposed | Burried |
|---|---|---|
| | 5(62 %) | 3 (38 %) |

| Disorder | Disorder-promoting | Order-promoting | Disorder-order neutral |
|---|---|---|---|
| | 5(62 %) | 3(37 %) | 0 (1 %) |

| Flexibility | Highly flexibility | Low flexibility |
|---|---|---|
| | 5(62 %) | 3 (38 %) |

**Fig. 1.** Physiochemical properties for predicted AVP through AVPpred.

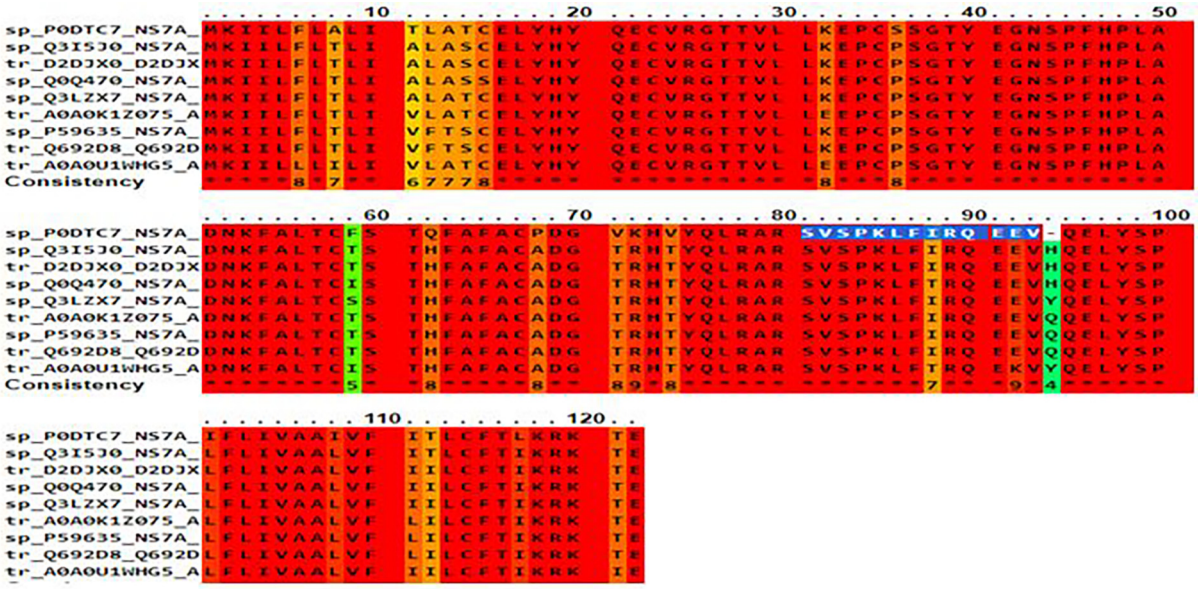


**Fig. 2.** Multiple sequence alignment of various ORF7a proteins.

et al. [33]. Therefore, the lesser explored viral proteins have been considered for designing anti-viral peptides and are tabulated in table 1.

In the preliminary step PODTC7 homologs were aligned through PRALINE on-line server. The homologues with more than 80% similarity were included as a part of analysis. For analysis of peptides with antiviral potential, multiple sequence alignment was performed to find the most conserved residues. These residues were predicted to have very important role on interaction with host protein. The residues were investigated for their anti-viral property using AVPred server accessible at http://crdd.osdd.net/servers/avppred/ [21]. Only one conserved sequence was found to have AVP with good probability (KLFIRQEE). Its various physiochemical properties are shown in Fig. 1. The amphiphilic character of peptides and overall hydrophobicity is responsible for anti-viral characteristics. As can be seen in Fig. 1 although the hydrophobicity value of predicted AVP is lesser but other characteristics like surface exposed residues, disorder promotion and flexibility may be good enough for peptide to have anti-viral properties.

The presence of conserved amino acids as predicted through PRALINE server for PODTC7 is shown in Fig. 2 [25,26]. Majority of the aligned portion is found to have good conservancy score. Therefore to reveal the most suitable amino acid residue fragment the entire sequence was checked for anti-viral properties in sliding window of 1 through AVPred server. The physiochemical properties of the predicted AVP are exhibited in Fig. 3. In Fig. 3 the variation in hydrophobicity throughout the peptide is shown in green line along Y axis. The frequency of alpha helix seems to be on an increasing trend which is again a prerequisite for effective anti-viral activity of a peptide. The similar variation in properties for other predicted peptide is indicative of effect of varying amino acid composition on anti-viral property.

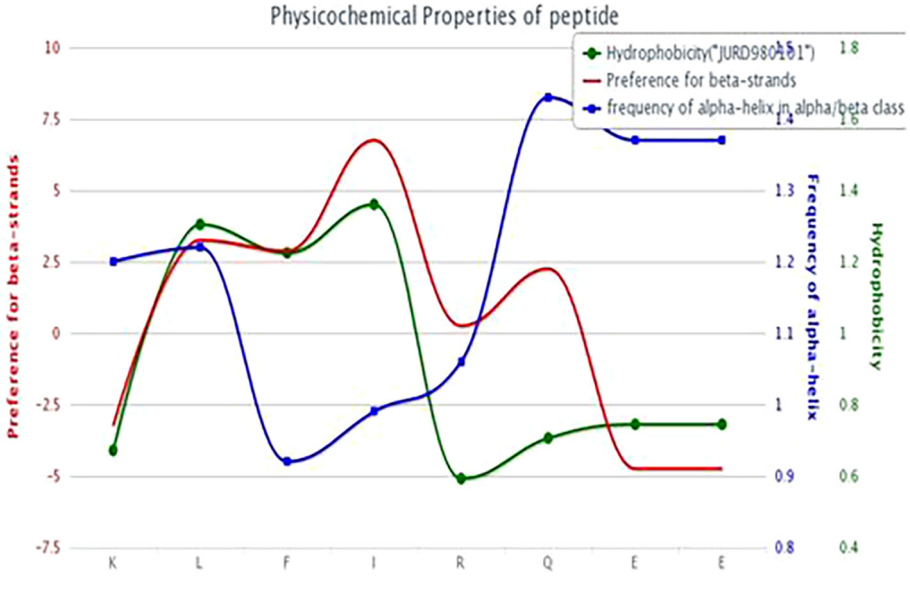


**Fig. 3.** Various physiological properties predicted through AVPpred server.

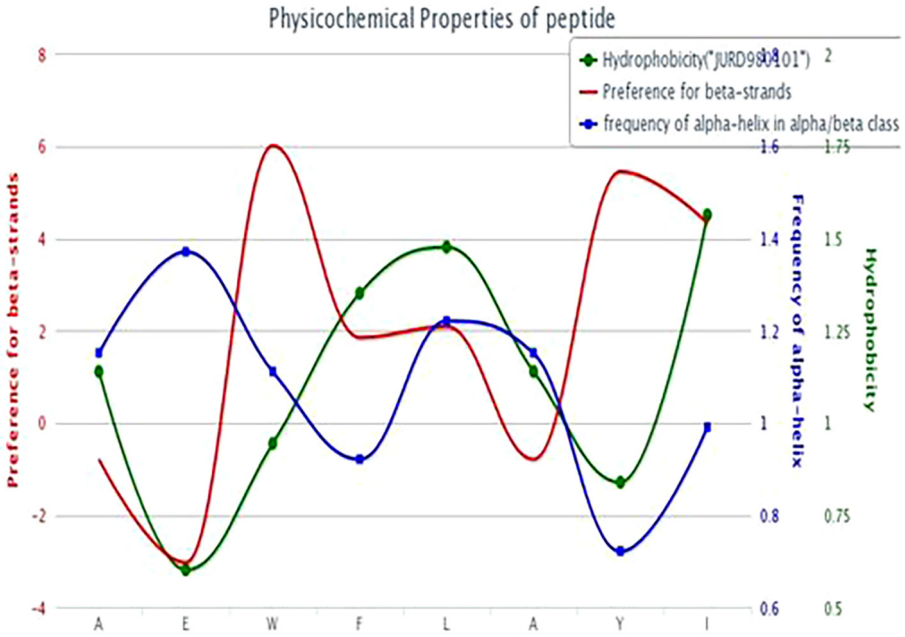


**Fig. 4.** Physiochemical properties of predicted peptide ISSFKWDL.

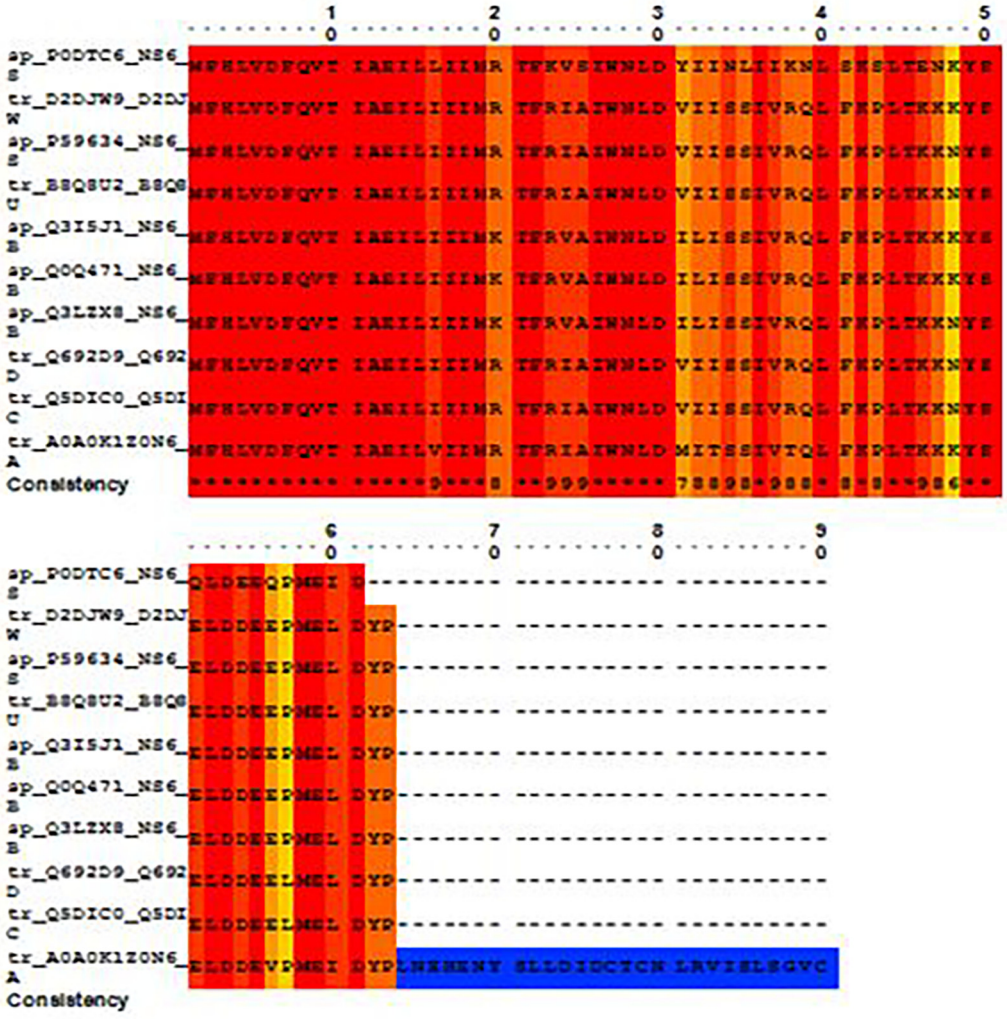


**Fig. 5.** P0DTC6 multiple sequence analysis with homologues.

**Table 2**
Predicted AVP.

| AVP sequence |
|---|
| KLFIRQEE from P0DTC7<br>ISSFKWDL and AEWFLAYI from P0DTC1 |

**Table 3**
Viral proteins used for interaction analysis with all predicted AVPs.

| Viral Target Protein (PDB ID) |
|---|
| 6 W37 ORF7a protein<br>7JIR (1564–1878) Papain-Like Protease<br>7K3G envelop small membrane protein<br>6M3M (41–174) Nucleoprotein<br>6WZO (247–364) Nucleoprotein6Y2E (3264–3569) Replicase polyprotein 1a<br>7CZ4 (1025–1195) Replicase polyprotein 1a |

**Table 4**
Interaction energy through MDockPep server for predicted AVP and host target protein.

| AVP | Target Protein | Docking Score |
|---|---|---|
| KLFIRQEE-Q10589 | Tetherin (BST2) | −129.0 |
| KLFIRQEE-O43765 | SGTA | −132.4 |
| ISSFKWDL-O43765 | SGTA | −129.8 |
| AEWFLAYI-O43765 | SGTA | −139.5 |

The next interactome protein chosen for our analysis was P0DTC4 which is an envelope protein of the virus. Since no AVPs were detected through AVPpred server therefore this protein was not considered for further analysis. For P0DTC6 (ORF6) also no AVP was detected. The next in the sequence was P0DTC1 which is an interacting protein of SAR-CoV-2. The analysis through AVPpred server revealed two AVPs in the protein. The sequence of predicted AVP is ISSFKWDL and AEWFLAYI. The physiochemical properties of one of the peptide predicted peptide ISSFKWDL is shown in Fig. 4. Although the dip in hydrophobicity for E (Glutamic acid) and Y (Tyrosine) is prominent but increase in hydrophobicity is observed at regular intervals for rest of the amino acid residues. The conserved residues for this protein found through multiple sequence alignment of all known Nsp1 have been shown in Fig. 5. Finally the AVPs predicted are tabulated in table 2.

The predicted anti-viral peptides have been tested for binding ability with both host as well as viral proteins. The various viral proteins are mentioned in table 3. The 3D structure of viral proteins has been obtained from Protein Data Bank (PDB) databank. For nucleoprotein two structures with ID 6M3M and 6WZO were considered for analysis since they represent different region of the big nucleoprotein. Similar is the case with replicase polyprotein 1a where two PDB IDs are analyzed for predicting binding interactions. The choice of viral proteins has been expanded so as to uncover the region binding best with the predicted AVPs and with the best resolution.

The interaction or docking of predicted AVPs (from table 2) with host target protein (shown in table 1), has been done with MDockPeP server. The interacting energies are shown in table 4. The energies are result of cumulative effect of weak interactions between peptide and host proteins. Only the top scoring models or the models with best docking score are tabulated. The best interactions are thermodynamically most favored one. The more is the energy dissipated or released stronger or better is the interaction.

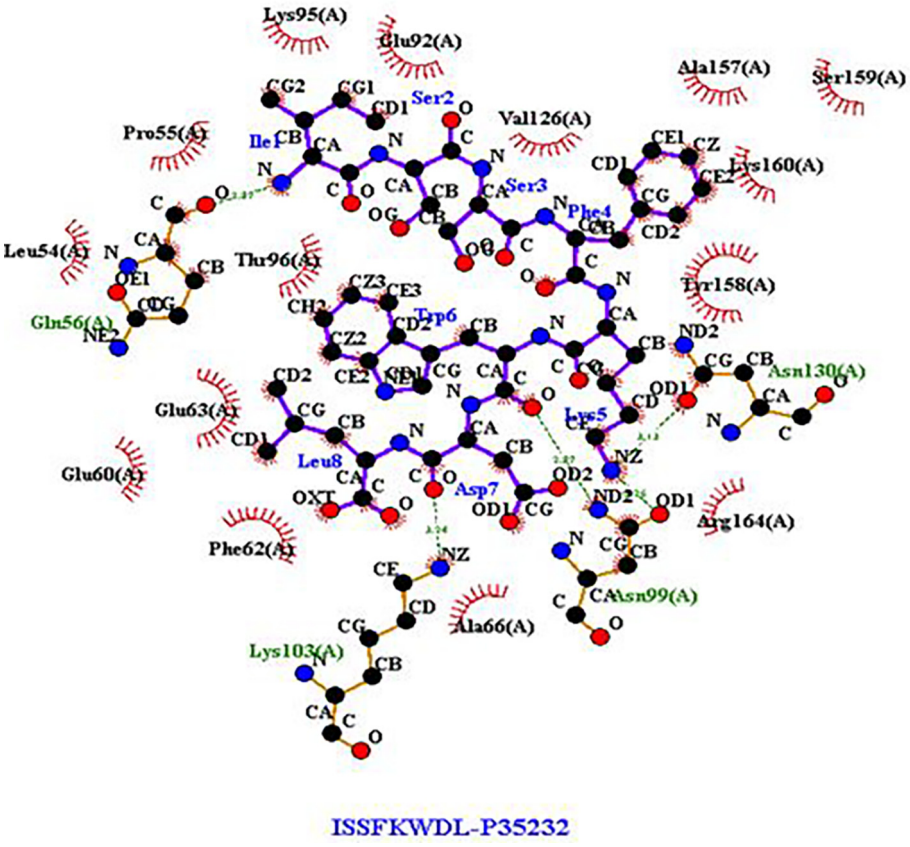


**Fig. 6.** Interaction of predicted 1st AVP with P35232.

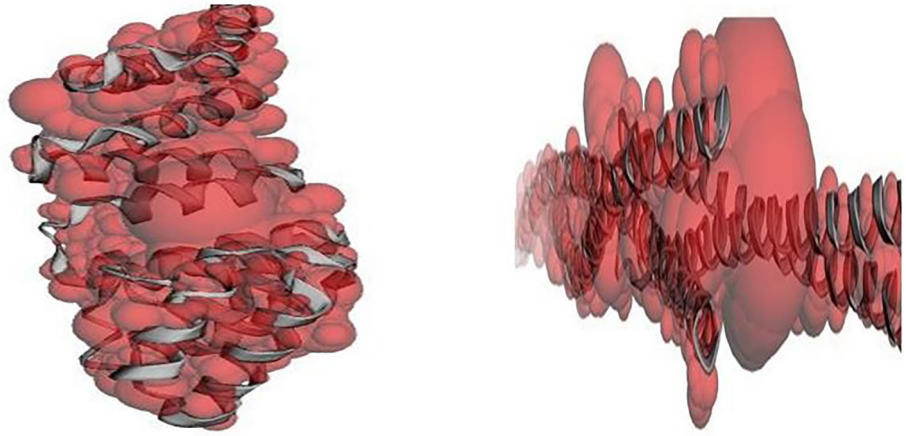


**Fig. 7.** The entire proteins involved in forming ligand binding pocket.

**Table 5**
Docking energy through iGemDock stand alone software for predicted AVP and viral target protein.

| Compound | Docking Energy | Interacting residues | | | | |
|---|---|---|---|---|---|---|
| 6w37-avp1KLFIRQEE | -93.5 | H-S-HIS-4 | H-M-LYS-17 | H-M-PRO-19 | H-S-ASP-54 | |
| | | -8.8639 | -3.0038 | -3.5 | -6.81366 | |
| | | H-S-HIS-58 | H-S-TYR-60 | V-S-LYS-17 | V-S-PRO-19 | |
| | | -7.30817 | -8.24613 | -4.09607 | -6.04051 | |
| | | V-M-ASP-54 | V-S-ASP-54 | V-S-HIS-58 | | |
| | | -4.60494 | -10.6028 | -9.42057 | | |
| 6y2e-avp1KLFIRQEE | -116.2 | H-M-PHE-3 | H-S-ARG-4 | H-S-TRP-207 | V-M-PHE-3 | V-S-GLU-290 |
| | | -3.03877 | -8.80672 | -3.01678 | -4.08197 | -6.11148 |
| | | V-M-ARG-4 | V-S-LYS-5 | V-S-TYR-126 | V-S-LYS-137 | V-S-PHE-291 |
| | | -4.95356 | -13.1438 | -4.37825 | -6.56988 | -5.88561 |
| | | V-M-LEU-282 | V-M-GLY-283 | V-M-SER-284 | V-S-GLU-288 | |
| | | -6.46131 | -9.85755 | -6.44016 | -10.2025 | |
| 7jir-avp1KLFIRQEE | -89.5 | H-S-LYS-157 | H-S-GLU-161 | H-S-GLU-167 | H-S-TYR-268 | |
| | | -5.45772 | -3.42134 | -14.3324 | -4.2391 | |
| | | H-S-GLN-269 | V-M-LEU-162 | V-S-LEU-162 | V-S-ASP-164 | |
| | | -3.20301 | -7.61083 | -4.06287 | -8.8238 | |
| | | V-S-TYR-264 | V-S-TYR-268 | V-S-GLN-269 | | |
| | | -5.02632 | -9.56913 | -15.9983 | | |
| 7k3g-avp1KLFIRQEE | -134.7 | H-S-ASN-15 | H-S-ASN-15 | H-S-ASN-15 | H-S-GLU-8 | V-S-THR-11 |
| | | -12.8433 | -4.75794 | -8.27143 | -16.7365 | -9.84079 |
| | | H-S-ASN-15 | V-M-THR-11 | V-S-THR-11 | V-S-ASN-15 | V-S-ASN-15 |
| | | -6.55402 | -4.26457 | -5.5744 | -8.23096 | -5.95392 |
| | | V-S-THR-9 | V-S-THR-11 | V-S-GLU-8 | V-S-THR-11 | |
| | | -5.54411 | -21.0968 | -10.2307 | -12.7403 | |
| 7cz4-avp1KLFIRQEE | -107.1 | H-M-GLY-130 | V-M-GLY-48 | V-M-VAL-49 | V-M-ALA-129 | |
| | | -3.5 | -5.83789 | -4.28172 | -11.0469 | |
| | | V-M-GLY-130 | V-M-ILE-131 | V-S-ILE-131 | V-S-PHE-132 | |
| | | -11.0526 | -11.2298 | -8.92634 | -4.42544 | |
| | | V-S-PRO-136 | V-S-ASP-157 | V-S-LEU-160 | | |
| | | -5.2915 | -7.60569 | -6.37918 | | |
| 6m3m-avp1KLFIRQEE | -114.5 | H-S-ASP-64 | H-S-ARG-90 | H-S-ASP-104 | V-S-GLN-59 | V-S-PRO-107 |
| | | -4.10618 | -3.5 | -9.02287 | -9.69948 | -9.36151 |
| | | V-M-HIS-60 | V-M-GLY-61 | V-S-LYS-62 | V-S-ARG-9 | V-M-ASP-104 |
| | | -7.88932 | -5.28644 | -4.0696 | -5.60899 | -5.33711 |
| | | V-S-ASP-104 | V-M-LEU-105 | V-M-SER-106 | | |
| | | -12.6266 | -5.67852 | -7.09034 | | |

*H-S (Hydrogen bond side chain), H-M (Hydrogen bond main chain), V-S (Vanderwalls bond side chain), V-M (Vanderwalls bond main chain)

The docking between various viral target proteins (mentioned in table 3) with AVP sequences (from table 2) is done through iGemDock software and depicted through LigPLOT, one has been shown in Fig. 6 [29–31]. The same has been generated for rest of the proteins also. The interacting energies are summarized in table 5. From table 5 it is found that envelope small membrane protein interacts best with predicted anti-viral peptide out of all viral proteins.

In Fig. 7 the pocket forming residues or active site residues of various host proteins are depicted. The prediction is made through CASTp server which signifies the amino acid residues that are a part of active site (32). For both Q10589, BST2_HUMAN Bone mar-

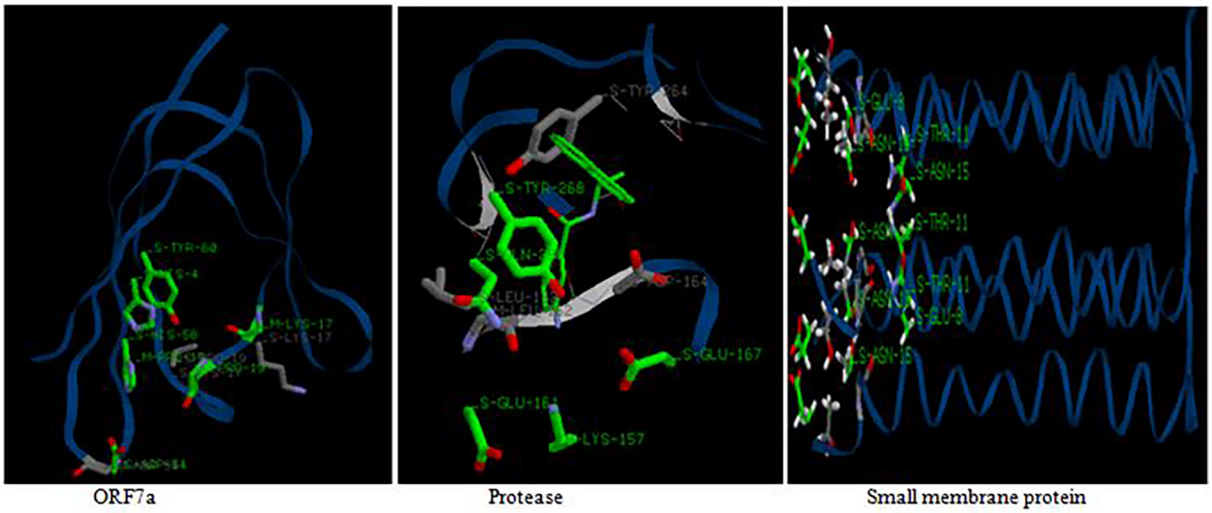


**Fig. 8.** Interacting residues of predicted AVP with ORF7a protein (6 W37), Papain like Protease (7JIR) and (7K3G) envelop small membrane protein.

**Table 6**
Amino acid residues of pocket, predicted through CASTp server.

| Receptor | Chain | SeqID | AA | Chain | SeqID | AA | Chain | SeqID | AA | Chain | SeqID | AA |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| P35232, PHB_HUMAN Prohibitin | A | 63 | LYS | A | 96 | PHE | A | 169 | SER | B | 62 | GLN |
| | A | 64 | PRO | A | 98 | PRO | A | 170 | LEU | B | 63 | LYS |
| | A | 65 | ILE | A | 106 | ILE | A | 171 | THR | B | 64 | PRO |
| | A | 66 | ILE | A | 112 | GLU | A | 172 | HIS | B | 65 | ILE |
| | A | 68 | ASP | A | 113 | ASP | A | 173 | LEU | B | 66 | ILE |
| | A | 69 | CYS | A | 115 | ASP | A | 175 | PHE | B | 68 | ASP |
| | A | 70 | ARG | A | 116 | GLU | A | 176 | GLY | B | 69 | CYS |
| | A | 71 | SER | A | 143 | ARG | A | 177 | LYS | B | 70 | ARG |
| | A | 72 | ARG | A | 144 | GLU | A | 178 | GLU | B | 71 | SER |
| | A | 73 | PRO | A | 147 | SER | A | 180 | THR | B | 72 | ARG |
| | A | 93 | ARG | A | 167 | ASP | A | 181 | GLU | B | 73 | PRO |
| | A | 95 | LEU | A | 168 | VAL | | | | B | 93 | ARG |
| | B | 95 | LEU | B | 167 | ASP | C | 64 | PRO | C | 95 | LEU |
| | B | 98 | PRO | B | 168 | VAL | C | 64 | PRO | C | 98 | PRO |
| | B | 106 | ILE | B | 169 | SER | C | 65 | ILE | C | 106 | ILE |
| | B | 107 | PHE | B | 170 | LEU | C | 66 | ILE | C | 107 | PHE |
| | B | 110 | ILE | B | 171 | THR | C | 68 | ASP | C | 110 | ILE |
| | B | 111 | GLY | B | 172 | HIS | C | 69 | CYS | C | 113 | ASP |
| | B | 113 | ASP | B | 173 | LEU | C | 70 | ARG | C | 114 | TYR |
| | B | 114 | TYR | B | 177 | LYS | C | 71 | SER | C | 114 | TYR |
| | B | 115 | ASP | B | 178 | GLU | C | 72 | ARG | C | 115 | ASP |
| | B | 116 | GLU | B | 181 | GLU | C | 73 | PRO | C | 116 | GLU |
| | B | 143 | ARG | C | 62 | GLN | C | 74 | ARG | C | 143 | ARG |
| | B | 147 | SER | C | 63 | LYS | C | 93 | ARG | C | 144 | GLU |
| | C | 147 | SER | C | 167 | ASP | C | 170 | LEU | C | 173 | LEU |
| | C | 148 | ARG | C | 168 | VAL | C | 171 | THR | | | |
| | C | 151 | SER | C | 169 | SER | C | 172 | HIS | | | |

row stromal antigen tetherin and O43765, SGTA_HUMAN the entire protein has been found to be involved in forming active site or ligand binding site as shown in Fig. 7. Similar to Fig. 6 the interacting residues of modeled peptides with viral proteins are also depicted in Fig. 8, predicted through iGemDock.

The AVPs designed through in-silico approach have been found to bind with important residues of protein, mentioned in table 1 and table 3 and also predicted through CASTp shown in table 6. The effect of predicted AVPs in blocking the active site residues has been studied in conjunction with the amino acid residues involved in pocket or cavity prediction for various receptor proteins that are mentioned in table 1 and 3.

The designed AVPs show optimum binding with both host as well as viral proteins. This binding can prevent the viral protein from binding to natural target of host protein. The bound peptide fragments to viral non-spike proteins can block the viral proteins from functioning properly therefore acting as anti-viral agents.

## 4. Conclusion

In this research work anti-viral peptides or AVPs have been designed using computational approach against proteins other than spike of Corona virus. The designed AVPs are tested for their ability to prevent binding of pathogen proteins with host proteins. In principle deterrent proteins can be designed both against host and pathogen. The same principle has been tested here with binding induced between host and viral proteins and predicted AVPs. The AVPs in-fact can block the active sites of host as well as pathogen thereby preventing further activities.

The disruption caused at various levels by the effect of global COVID-19 outbreak has prioritized the immediate and urgent treatment therapies. In this concern, we believe that the production of AVPs could represent the most promising treatment strategy. In our study, the AVPs designed through in-silico approach have been found to bind with important residues of protein mentioned in table 1 and 3. This binding can prevent the viral protein from binding to natural target of host protein, therefore acting as anti-viral agents. AVPs being simple with its primary structure and versatile functional properties may prove to be potential candidate in facing COVID-19 and several other emerging outbreaks in unpredictable future. We have explored the in-silico facet of AVPs prediction providing basis for its in-vitro analysis. Still there are certain aspects involving their potential utilization in clinical treatment and promising antiviral activity along with studying prophylactic reactions concerned against COVID-19 which are needed to be investigated in near future.

## CRediT authorship contribution statement

**Aditi Sharma:** Conceptualization, Writing - original draft. **Kumud Pant:** Conceptualization, Methodology. **:** . **Akshara Pande:** Writing - original draft. **Somya Sinha:** Data curation. **Bhasker Pant:** Supervision, Software.

## Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

## Acknowledgement

The authors are highly thankful to Graphic Era Deemed to be University, Dehradun, Uttarakhand, Department of Biotechnology for providing facility to carry out this work.

## References

[1] A.J. Rodriguez-Morales, D.K. Bonilla-Aldana, G.J. Balbin-Ramon, A.A. Rabaan, R. A. Sah, A. Paniz-Mondolfi, P. Pagliano, S. Esposito, History is repeating itself probable zoonotic spillover as the cause of the 2019 novel corona virus epidemic, Infez Med 28 (2020) 3–5.
[2] Zhu N, Zhang D, Wang W, Li X, Yang B, Song J, Zhao X, Huang B, Shi W, Lu R, Niu P, Zhan F, Ma X, Wang D, Xu W, Wu G, Gao GF, Tan W. China, Novel Corona virus Investigating and Research Team. A novel corona virus from patients with pneumonia in China, 2019. N Engl J Med 2020;382:727–733.
[3] X. Wei, X. Li, J. Cui, Evolutionary perspectives on novel corona viruses identified in pneumonia cases in China, Natl Sci Rev 7 (2020) 239–242.
[4] V.J. Munster, M. Koopmans, N. Van Doremalen, D. Van Riel, E. de Wit, A novel corona virus emerging in China-key questions for impact assessment, N Engl J Med 382 (2020) 692–694.
[5] , FDA (2020), at https://www.who.int/emergencies/diseases/novel-corona virus-2019/advice-for-public/myth-busters.
[6] A. Falco, V. Mas, C. Tafalla, L. Perez, J.M. Coll, A. Estepa, Dual antiviral activity of human alpha- defensin-1 against viral haemorrhagic septicaemia rhabdovirus (VHSV) Inactivation of virus particles and in-duction of a type I interferon-related response, Antiviral Res 76 (2007) 111–123.
[7] L.R. Crack, L. Jones, G.N. Malavige, V. Patel, G.S. Ogg, Human antimicrobial peptides LL-37 and human β-defensin-2 reduce viral replication in keratinocytes infected with varicella zoster virus, Clin Exp Dermatol 37 (2012) 534–543.
[8] S.E. Altmann, C.R. Brandt, P.B. Jahrling, J.E. Blaney, Antiviral activity of the EB peptide against zoonotic poxviruses, Virol J 6 (2012) 1–6.
[9] K. Okazaki, H. Kida, A synthetic peptide from a heptad repeat region of herpesvirus glycoprotein B inhibits virus replication, J Gen Virol 85 (2004) 2131–2137.
[10] V. Tiwari, J. Liu, T. Valyi-Nagy, D. Shukla, Anti-heparan sulfate peptides that block herpes simplex virus infection in vivo, J Biol Chem 286 (2011) 25406–25415.
[11] C. Mooney, N.J. Haslam, G. Pollastri, D.C. Shields, Towards the improved discovery and design of functional peptides: common features of diverse classes permit generalized prediction of bioactivity, PLoS One 7 (2012) 1–12.
[12] A.A. Kaspar, J.M. Reichert, Future directions for peptide therapeutics development, Drug Discov Today 18 (17–18) (2013) 807–817.
[13] B.J. Bruno, G.D. Miller, C.S. Lim, Basics and recent advances in peptide and protein drug delivery, Ther Deliv 4 (11) (2013) 1443–1467.
[14] Rongsong Ling, Yarong Dai, Boxuan Huang, Wenjie Huang, Jianfeng Yu, Xifeng Lu, Yizhou Jianga. In silico design of antiviral peptides targeting the spike protein of SARS-CoV-2. Peptides 2020;130(170328).
[15] S. Manna, T. Chowdhury, P. Baindara, S.M. Mandal, Fusion Protein Targeted Antiviral Peptides: Fragment-Based Drug Design (FBDD) Guided Rational Design of Dipeptides Against SARS-CoV2, Current Protein & Peptide Science 21 (10) (2020).
[16] Arun Suria Karnan Mahendran, Yin Sze Lim, Chee-Mun Fang, Hwei-San Loh, and Cheng Foh Le. The Potential of Antiviral Peptides as COVID-19 Therapeutics. Front Pharmacol. 2020;11(575444).
[17] https://covid-19.uniprot.org/uniprotkb/P0DTC7
[18] https://covid-19.uniprot.org/uniprotkb/P0DTC9
[19] https://covid-19.uniprot.org/uniprotkb/P0DTC1
[20] C. Hulo, E. de Castro, P. Masson, L. Bougueleret, A. Bairoch, I. Xenarios, P. Le Mercier, ViralZone: a knowledge resource to understand virus diversity, Nucleic Acids Res 39 (2011) 576–582.
[21] N. Thakur, A. Qureshi, M. Kumar, AVPpred: collection and prediction of highly effective antiviral peptides, Nucleic Acids Res 40 (2012) W199–W204.
[22] G. Wang, X. Li, Z. Wang, APD3: The antimicrobial peptide database as a tool for research and educa- tion, Nucleic Acids Res 44 (2015) D1087–D1093.
[23] F.H. Waghu, R.S. Barai, P. Gurung, S. Idicula-Thomas, CAMPR3: a database on sequences, structures and signatures of antimicrobial peptides, Nucleic Acids Res 44 (2015) D1094–D1097.
[24] A. Qureshi, N. Thakur, M. Kumar, HIPdb: a database of experimentally validated HIV inhibiting pep- tides, PLoS One 8 (2013) e54908.
[25] J. Heringa, Two strategies for sequence comparison: profile-preprocessed and secondary structure- induced multiple alignment, Computers & Chemistry 23 (3–4) (1999) 341–3648.
[26] J. Heringa, Local weighting schemes for protein multiple sequence alignment, Comput Chem 26 (2002) 459–477.
[27] X. Xu, C. Yan, X. Zou, MDockPeP: An ab-initio protein-peptide docking server, J Comput Chem 39 (2018) 2409–2413.
[28] C. Yan, X. Xu, X. Zou, Fully Blind Docking at the Atomic Level for Protein-Peptide Complex Structure Prediction, Structure 24 (2016) 1842–1853.
[29] K.C. Hsu, Y.F. Chen, S.R. Lin, et al., iGEMDOCK: a graphical environment of enhancing GEMDOCK using pharmacological interactions and post-screening analysis, BMC Bioinformatics 12 (2011) S33, https://doi.org/10.1186/1471-2105-12-S1-S3.
[30] Berman HM, Battistuz T, Bhat TN, Bluhm WF, Bourne PE, Burkhardt K, Feng Z, Gilliland GL, Iype L, Jain S, Fagan P, Marvin J, Padilla D, Ravichandran V, Schneider B, Thanki N, Weissig H, Westbrook JD, Zardecki C. The Protein Data Bank Acta Crystallogr D Biol Crystallogr 2002;58(Pt 6 No 1):899–907.
[31] R.A. Laskowski, M.B. Swindella, LigPlot+: Multiple Ligand-Protein Interaction Diagrams for Drug Discovery, J. Chem. Inf. Model 51 (10) (2011) 2778–2786.
[32] W. Tian, C. Chen, X. Lei, J. Zhao, J. Liang, CASTp 3.0: computed atlas of surface topography of pro- teins, Nucleic Acids Res (2018;2;46(W1):W363–W367.).
[33] T. Jesús, L. Rogelio, C. Abraham, et al., Prediction of antiviral peptides derived from viral fusion proteins potentially active against herpes simplex and influenza A viruses, Bioinformation 8 (18) (2012) 870–874.