PUBLICATIONS

(FIRST PAGE)

Biointerface Research in Applied Chemistry
Open-Access Journal (ISSN: 2069-5837)

Article
Volume 13, Issue 1, 2023, 97
https://doi.org/10.33263/BRIAC131.097

Effect of Double Mutation (L452R and E484Q) in RBD of Spike Protein on its Interaction with ACE2 Receptor Protein

Chainee Das [1], Pranab Jyoti Hazarika [1], Ankita Deb [1], Priya Joshi [1], Dorothy Das [1], Venkata Satish Kumar Mattaparthi [1,*]

[1] Molecular Modeling and Simulation Laboratory, Department of Molecular Biology and Biotechnology, Tezpur University, Tezpur, Assam, 784028, India; chaineedas97@gmail.com (C.D.); prnbhaz01@gmail.com (P.J.H.); ankita.deb12@gmail.com (A.D.); prjsh001@gmail.com (P.J.); dorthyds.1010@gmail.com (D.D.); mvenkatasatishkumar@gmail.com (V.S.K.M.), venkata@tezu.ernet.in (V.S.K.M.);
* Correspondence: mvenkatasatishkumar@gmail.com (V.S.K.M.); venkata@tezu.ernet.in (V.S.K.M.);
Scopus Author ID 54962670000
Received: 10.11.2021; Accepted: 10.12.2021; Published: 12.02.2022

Abstract: The severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) caused coronavirus disease 2019 (COVID-19) pandemic has become a global health issue. Recently, the SARS-CoV-2 strain (B.1.617 double mutant variant) has raised alarms in India and other nations. B.1.617 variant was found to contain two key mutations (L452R and E484Q) in the RBD region of the spike protein. In this work, we have focussed on the effect of the double mutations in spike protein on its binding to the host cell receptor protein, angiotensin-converting enzyme 2 (ACE2). From the molecular dynamics simulation, we observed that the L452R and E484Q double mutant (DM) in spike protein utilizes unique strategies to achieve stable binding to ACE2 compared to the spike protein's wild type (WT). Using MM-GBSA/MM-PBSA algorithms, we found that the binding affinity between spike protein-containing DM and ACE2 is high (GB_{TOT} = -47.09 kcal mol^{-1}, PB_{TOT}= -19.93 kcal mol^{-1}) in comparison with spike protein WT and ACE2 (GB_{TOT} =-31.79 kcal mol^{-1}, PB_{TOT}= -6.33 kcal mol^{-1}). Stable binding of spike protein to ACE2 is essential for virus entry. They should understand interactions between them while designing drugs and treatment modalities to target or disrupt this interface.

Keywords: SARS-CoV-2; Coronavirus; ACE2 receptor; Double mutant, B.1.617; molecular dynamics; spike protein; COVID-19.

1. Introduction

The ongoing spread of an infectious Coronavirus disease 2019 (COVID-19), caused by Severe Acute Respiratory Syndrome-Coronavirus-2 (SARS-CoV-2), an enveloped positive-stranded RNA virus into the community, poses exceptional challenges for the healthcare system due to high incidence and long incubation time [1]. SARS-CoV-2 is a novel coronavirus isolated on January 7, 2020 [2,3] by the Chinese Center for Disease Control and Prevention. The SARS-CoV-2 spike glycoprotein (spike protein) has gained significant attention since the outbreak of the COVID-19 pandemic due to its role in viral pathogenesis and immune response [4]. As of now, the vaccines that target spike protein, being used for COVID-19, provide host cells with a genetic transcript (mRNA or adenovirus) that ribosomes translate into a mutated spike protein. However, the nature and effect of mutations on the nascent spike protein remain

Biointerface Research in Applied Chemistry
Open-Access Journal (ISSN: 2069-5837)

Article
Volume 13, Issue 3, 2023, 235
https://doi.org/10.33263/BRIAC133.235

Computational Investigation on the Efficiency of Small Molecule Inhibitors Identified from Indian Spices against SARS-CoV-2 Mpro

Chainee Das [1], Dorothy Das [1], Venkata Satish Kumar Mattaparthi [1,*]

[1] Molecular Modeling and Simulation Laboratory, Department of Molecular Biology and Biotechnology, Tezpur University, Tezpur, Assam, 784028, India; chaineedas97@gmail.com (C.D.); dorthyds.1010@gmail.com (D.D.); mvenkatasatishkumar@gmail.com, venkata@tezu.ernet.in (V.S.K.M.);
* Correspondence:mvenkatasatishkumar@gmail.com, venkata@tezu.ernet.in(V.S.K.M.);

Scopus Author ID 54962670000
Received: 1.01.2022; Accepted: 5.02.2022; Published: 6.06.2022

Abstract: Recently, small compounds from Indian spices (Carnosol, Arjunglucoside-I, and Rosmanol) have been identified as SARS-CoV-2 main protease (Mpro) inhibitors. The structural dynamics and characteristic features of binding of these small molecules to the SARS-CoV-2 Mpro are not well understood. Here, we have constructed the potential of mean force (PMF) for dissociating Mpro-small molecule inhibitor complexes from the umbrella sampling simulations using the weighted histogram analysis method. Mpro-small molecule inhibitor complexes exhibited relatively higher dissociation energy values than the alpha-ketoamide-Mpro complex (positive control) from the PMF calculations. We found that binding affinity between protein and ligand is higher in Mpro-Arjunglucoside-I complex [ΔG_{bind} = -19.74 kcal mol^{-1} from MM-GBSA and ΔG_{bind} = -9.13 kcal mol^{-1} from MM-PBSA] than in other three SARS-CoV-2 small molecule complexes. The MM-GBSA/MM-PBSA calculations revealed that the small molecule inhibitors studied in this work have substantially higher binding affinity for Mpro. We found the residues present in SARS-CoV-2 Mpro's binding pocket contributed the most binding free energy to SARS-CoV-2 Mpro-small molecule interactions. Our findings emphasize the structural and binding features of the identified small molecule inhibitors with SARS-CoV-2 Mpro, which could be relevant in developing therapeutic candidates to combat SARS-CoV-2.

Keywords: MM-GBSA; MM-PBSA; **the** potential of mean force; molecular dynamics; per residue energy decomposition; COVID 19.

1. Introduction

A unique strain of SARS-CoV-2 coronavirus was first detected in Wuhan, a city in China's Hubei Province with a population of 11 million people, in December 2019, following a pneumonia outbreak with no clear reason. The virus has spread to more than 200 countries and territories around the world, and on March 11, 2020, the World Health Organization (WHO) declared it a pandemic[1, 2]. There was 288,767,991 laboratory-confirmed coronavirus disease 2019 (COVID-19) infection worldwide as of the 1st of January 2022, with 5,455,634 recorded fatalities. On 16 March 2020, outside of China, the number of cases and deaths surpassed those within the country [3]. SARS-CoV-2 belongs to the coronavirinae family of single-stranded RNA viruses, divided

Letters in Applied NanoBioScience
Open-Access Journal (ISSN: 2284-6808)

Article
Volume 12, Issue 4, 2023, 118
https://doi.org/10.33263/LIANBS124.118

Effect of Mutations in the SARS-CoV-2 Spike RBD Region of Delta and Delta-Plus Variants on its Interaction with ACE2 Receptor Protein

Chainee Das [1], Dorothy Das [1], Venkata Satish Kumar Mattaparthi [1,*]

[1] Molecular Modeling and Simulation Laboratory, Department of Molecular Biology and Biotechnology, Tezpur University, Tezpur, Assam, 784028, India; chaineedas97@gmail.com (C.D.); dorthyds.1010@gmail.com (D.D.); mvenkatasatishkumar@gmail.com (V.S.K.M.), venkata@tezu.ernet.in (V.S.K.M.)
* Correspondence: mvenkatasatishkumar@gmail.com (V.S.K.M.); venkata@tezu.ernet.in (V.S.K.M.);
Scopus Author ID 54962670000
Received: 26.03.2022; Accepted: 29.04.2022; Published: 18.09.2022

Abstract: The outbreak of severe acute respiratory syndrome coronavirus 2 (SARS CoV-2) has undergone multiple significant mutations since its detection in 2019 in Wuhan, China. The emergence of new SARS-CoV-2 variants that can spread rapidly and undermine vaccine-induced immunity threatens the end of the COVID-19 pandemic. The delta variant (B.1.617.2) that emerged in India challenges efforts to control the COVID-19 pandemic. In addition to Delta, so-called Delta Plus sub-variants (B.1.617.2.1 and B.1.617.2.2) have become a new cause of global concern. Here we compare the interaction profile of RBD of the spike protein of the Delta and Delta-Plus variant of SARS-CoV-2 with the ACE2 receptor. From the molecular dynamics simulation, we observed the spike protein of Delta and Delta-Plus variant of SARS-CoV-2 utilizes unique strategies to have stable binding with ACE2. Using MM-GBSA/MM-PBSA algorithms, we found the binding affinity of spike protein of the Delta- variant-ACE2 complex is indeed high (GB_{TOT} = -39.36 kcal mol^{-1}, PB_{TOT}= -17.52 kcal mol^{-1}) in comparison with spike protein of Delta-Plus variant-ACE2 Complex (GB_{TOT} = -36.83 kcal mol^{-1}, PB_{TOT} = -16.03 kcal mol^{-1}). Stable binding of spike protein to ACE2 is essential for virus entry, and the interactions between them should be understood well for the treatment modalities.

Keywords: SARS-CoV-2; coronavirus; ACE2 receptor; Delta-Plus, B.1.617; molecular dynamics; spike protein; COVID-19.

1. Introduction

Coronavirus disease 2019 (COVID-19), a disease caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has killed over 5.4 million people globally, making it the deadliest global health catastrophe since the 1918 influenza pandemic. The virus has continued to strike destruction since the World Health Organization (WHO) proclaimed it a global pandemic on March 11, 2020, with many countries seeing numerous waves of breakouts. Adaptive mutations can alter the pathogenic capacity of a virus in its genome. Even a single amino acid substitution can significantly impact a virus's ability to elude the immune system, making vaccine development difficult. SARS-CoV-2, like other RNA viruses, is prone to genetic evolution as it adapts to new human hosts, creating various variants with distinct characteristics from the ancestral strains. Periodic genomic sequencing of viral samples aids in the detection of new SARS-CoV-2 genetic variations circulating in populations, particularly in

Biointerface Research in Applied Chemistry
Open-Access Journal (ISSN: 2069-5837)

Article
Volume 13, Issue 4, 2023, 358
https://doi.org/10.33263/BRIAC134.358

Impact of Mutations in the SARS-CoV-2 Spike RBD Region of BA.1 and BA.2 Variants on its Interaction with ACE2 Receptor Protein

Chainee Das [1], Venkata Satish Kumar Mattaparthi [1,*]

[1] Molecular Modeling and Simulation Laboratory, Department of Molecular Biology and Biotechnology, Tezpur University, Tezpur, Assam, 784028, India; chaineedas97@gmail.com (C.D.); mvenkatasatishkumar@gmail.com (V.S.K.M.), venkata@tezu.ernet.in (V.S.K.M.);
* Correspondence: mvenkatasatishkumar@gmail.com (V.S.K.M.); venkata@tezu.ernet.in (V.S.K.M.);
Scopus Author ID 54962670000
Received: 10.05.2022; Accepted: 21.06.2022; Published: 17.09.2022

Abstract: The COVID-19 pandemic started at the onset of 2020 and still thriving due to its continuous mutation and evolution into new strains. Omicron strain has been recently categorized as a variant of concern(VoC) by WHO and based on mutations, it is divided into BA.1 and BA.2. In this study, we compared the interaction profile of RBD of the spike protein of the BA.1 and BA.2 variant of SARS-CoV-2 with ACE2 receptor. From the molecular dynamics simulation study, we observed the spike protein of BA.1, and BA.2 variant utilizes unique strategies to have a stable binding with ACE2. The binding affinity of the spike protein of the BA.2 variant-ACE2 complex is indeed high (GBTOT=-23.87 kcal/mol) in comparison with the spike protein of BA.1 variant-ACE2 complex (GBTOT=5.38 kcal/mol). Stable binding of spike protein to ACE2 is essential for virus entry, and the interactions between them should be understood well for the treatment modalities.

Keywords: BA.1; BA.2; ACE2 receptor; SARS-CoV-2; spike protein; molecular dynamics; COVID-19.

1. Introduction

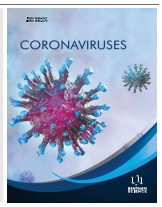
Strange pneumonia endemic with symptoms including fever, dry cough, lethargy, and gastrointestinal problems first appeared in late December 2019 at the Huainan Seafood Wholesale Market in Wuhan, Hubei, China [1]. However, the virus was hastily named 2019-nCoV, after which renamed SARS-CoV-2. Coronaviruses take their understanding from the precise spikes with rounded pointers that enhance their surface, which reminded virologists of the appeal of the sun's atmosphere as its corona [2]. The earliest recounted infected person fell sick on 1 December 2019. However, that person did not have a reference to the later wet marketplace cluster while within side the preceding case may moreover be handed off on 17 November. Two-thirds of the initial case cluster has been related to the marketplace [3]. Molecular clock evaluation indicates that the index case may have been infected between mid-October and mid-November 2019. As of 6 May 2022, more than 6,272,189 deaths have been attributed to COVID-19, with the primary loss of life in Wuhan on 9th January 2020. These numbers range with the aid of the community and, over time, stimulated via way of means of sorting out the volume, healthcare, treatment options, authorities' response, time for the cause

Send Orders for Reprints to reprints@benthamscience.net

Coronaviruses, 2023, *4*, e041023221709

RESEARCH ARTICLE

Efficiency of CAT and L-SIGN as Alternative or Co-receptors for SARS-CoV-2 Spike Protein



Chainee Das[1] and Venkata Satish Kumar Mattaparthi[1,*]

[1]*Department of Molecular Biology and Biotechnology, Molecular Modelling and Simulation Laboratory, Tezpur University, Tezpur, 784 028, Assam, India*

ARTICLE HISTORY

Received: May 30, 2023
Revised: July 30, 2023
Accepted: August 10, 2023

DOI:
10.2174/0126667975262159230927074645

Abstract: ***Background*:** The COVID-19 disease, which is caused by SARS-CoV-2, has been spreading rapidly over the world since December 2019 and has become a serious threat to human health. According to reports, SARS-CoV-2 infection has an impact on several human tissues, including the kidney, gastrointestinal system, and lungs. The Spike (S) protein from SARS-CoV-2 has been found to primarily bind ACE2. Since the lungs are the organ that COVID-19 is most likely to infect, the comparatively low expression of this recognized receptor suggests that there may be alternative co-receptors or alternative SARS-CoV-2 receptors that cooperate with ACE2. Recently, many candidate receptors of SARS-CoV-2 other than ACE2 were reported to be specifically and highly expressed in SARS-CoV-2 affected tissues. Among these receptors, the binding affinity of CAT and L-SIGN to the S protein has been reported to be higher in one of the recent studies. So, it will be significant to understand the binding interactions between these potential receptors and the RBD region of the S protein.

***Objective*:** To perform a computational analysis to check the efficiency of the alternative receptors (CAT and L-SIGN) of the SARS-CoV-2 on its binding to the Receptor Binding Domain (RBD) of Spike protein (S protein).

***Methods*:** In this study, we compared the interaction profile of the RBD of the S protein of SARS-CoV-2 with CAT and L-SIGN receptors.

***Results*:** From the molecular dynamics simulation study, the S protein employs special techniques to have stable interactions with the CAT and L-SIGN receptors (ΔG_{bind} = -39.49 kcal/mol and -37.20 kcal/mol, respectively).

***Conclusion*:** SARS-CoV-2 may result in greater virulence as a result of the S protein-CAT complex's stability and the greater affinity of spike protein for the CAT receptor.

Keywords: CAT, L-SIGN, ACE2 receptor, SARS-CoV-2, spike protein, molecular dynamics, COVID-19.

1. INTRODUCTION

The coronavirus disease that has been a threat to human health and society was caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) [1]. According to the phylogenetic analysis of the whole viral genome consisting of 29,903 nucleotides, the virus was found to be most closely related to a group of SARS-like coronaviruses that had previously been detected in bats in China with 89.1% nucleotide similarity [2]. More than 6,873,799 fatalities had been documented globally as of May 2023, and the figure continues to rise. Fever, cough and myalgia or fatigue were found to be the common symptoms of COVID-19 illness and sputum production, headache, hemoptysis, and diarrhea were found to be lesser common symptoms. Complications included acute respiratory distress syndrome, RNAaemia, acute cardiac injury and secondary infection [3]. Infectivity-based natural selection was discovered as the mechanism for SARS-CoV-2 evolution and transmission. Studies suggest that the RBD co-mutations will have high chances to grow into dominating variants which may be the main cause for the transition of CoV [4-7]. In order to develop possible antiviral drugs against this virus, it is imperative that the pathways of SARS-CoV-2 entry into the host be thoroughly studied [8]. The entry of the SARS-CoV-2 into the host cell is said to be dependent on the spike (S) protein and binding to the major functional receptor ACE2 [9]. A receptor-binding domain (RBD) is a key part of a virus located on the spike domain that allows it to dock to body receptors to gain entry into cells and lead to infection. RBD is a short immunogenic

*Address correspondence to this author at the Department of Molecular Biology and Biotechnology, Molecular Modelling and Simulation Laboratory, Tezpur University, Tezpur, 784 028, Assam, India; Tel: +91-3712-275443; +91-8811806866; Fax: +91-3712-267005/26700;
E-mails: mvenkatasatishkumar@gmail.com; venkata@tezu.ernet.in

2666-7975/23 $65.00+.00

Letters in Applied NanoBioScience
Open-Access Journal (ISSN: 2284-6808)

Article
Volume 13, Issue 2, 2024, 96
https://doi.org/10.33263/LIANBS132.096

Computational Investigation on the Impact of Mutations in the SARS-CoV-2 Spike RBD Region of BA.2.12.1 and BA.4 Variants on its Interaction with ACE2 Receptor Protein

Chainee Das [1], Ambika Mohta [1], Venkata Satish Kumar Mattaparthi [1,*]

[1] Molecular Modeling and Simulation Laboratory, Department of Molecular Biology and Biotechnology, Tezpur University, Tezpur, Assam, 784028, India; chaineedas97@gmail.com (C.D.); mohtaambika16@gmail.com (A.K.) mvenkatasatishkumar@gmail.com, venkata@tezu.ernet.in (V.S.K.M.);
* Correspondence: mvenkatasatishkumar@gmail.com, venkata@tezu.ernet.in (V.S.K.M.);
Scopus Author ID 54962670000
Received: 19.05.2023; Accepted: 11.08.2023; Published: 30.06.2024

Abstract: SARS-CoV-2 is an ongoing pandemic due to mutations in the Spike protein that give rise to multiple lineages and sub-lineagesin over time. The spike protein plays a major role in receptor recognition and cell entry with the help of the ACE2 receptor protein. Since the immune evasion mechanism has developed, mutations in the RBD region have increased infectivity and posed a serious threat. Along with the lineage of Omicron, the pathogenicity of several other omicron sub-lineages, including BA.4, BA.2, BA.2.12.1, BA.5, and others, has increased. BA.2.12.1 and BA.4 share almost 31 common mutations with BA.2. This study involves physiochemical, structural characterization, and binding properties of the spike protein of BA.4 and BA.2.12.1 variants using various online tools, Molecular dynamics, and other computational approaches. Based on the docking studies, BA.2.12.1 is more stable than BA.4 in binding with the ACE2 receptor. It has been found that BA.2.12.1 (ΔG_{bind} = -16.65 kcal/mol) has a higher binding affinity than BA.4 (ΔG_{bind} = -4.53 kcal/mol) with ACE2 according to calculations of binding free energy using the MM-GBSA approach. The overall stability of the BA.2.12.1 strain may make it more virulent than the BA.4 type strain.

Keywords: BA.2.12.1; BA.4; ACE2; RBD (receptor-binding domain); spike protein; COVID-19.

1. Introduction

Coronaviruses are lipid membrane-encapsulated viruses produced from the host cell and contain viral surface proteins inside. The genome of each corona strain is a single-stranded RNA with positive polarity and a base sequence oriented in the 5′–3′ direction [1]. Viral infections and contagious diseases pose a danger to population control, and that is due to their error-prone (RdRp) RNA-dependent RNA polymerase, which is responsible for duplicating genetic material and homologous recombination [2]. Since then, numerous mutations have taken place, resulting in multiple strains of SARS-CoV-2, including Alpha (B.1.1.7 lineages), Beta (B.1.351 lineages), Gamma (P.1 lineages), Delta (B.1.617.2 lineages), Lambda variant (C.37), Mu variant (B.1.621) Epsilon (B.1.427 and B.1.429), Eta (B.1.525), Iota (B.1.526), Kappa (B.1.617.1) 1.617.3, Mu (B.1.621, B.1.621.1), Zeta (P.2), Omicron (B.1.1.529, BA.4, BA.4.1, BA.2, BA.3, BA.4 and BA.5 lineages) [3-6].

Letters in Applied NanoBioScience
Open-Access Journal (ISSN: 2284-6808)

Article
Volume 13, Issue 4, 2024, 191
https://doi.org/10.33263/LIANBS134.191

Computational Investigation on the Physiochemical, Structural, and Binding Features of BA.2.75 and BA.2.75.2 Omicron Variants of SARS-CoV-2

Chainee Das [1], Venkata Satish Kumar Mattaparthi [1,*]

[1] Molecular Modeling and Simulation Laboratory, Department of Molecular Biology and Biotechnology, Tezpur University, Tezpur, Assam, 784028, India; chaineedas97@gmail.com (C.D.); mohtaambika16@gmail.com (A.K.) mvenkatasatishkumar@gmail.com (V.S.K.M.), venkata@tezu.ernet.in (V.S.K.M.);
* Correspondence: mvenkatasatishkumar@gmail.com ; venkata@tezu.ernet.in (V.S.K.M.);
Scopus Author ID 54962670000
Received: 21.06.2023; Accepted: 23.11.2023; Published: 28.08.2024

Abstract: Recently, several Omicron variants, including BA.2.75 and its sub-lineage BA.2.75.2, have demonstrated even better immune evasion and are responsible for waves of infections across the globe. BA.2.75 has been found in at least 15 nations and has become more prevalent in India. Additionally, BA.2.75.2 has expanded quickly, and it carries additional mutations R346T, F486S, and D1199N, suggesting a more extensive escape from neutralizing antibodies. This study analyzed physiochemical and structural characteristics of the spike protein (S protein) of BA.2.75 and BA.2.75.2 variants by employing various online tools, Molecular dynamics, and other computational approaches. The mutations G446S, R493Q, Q498R, N501Y, and N505H present in the RBD region of S protein of BA.2.75 and BA.2.75.2 were found to play a significant role in the binding of RBD of spike to ACE2. From the RMSD, RMSF, and inter-molecular hydrogen bond analyses, we found the S protein (BA.2.75)-ACE2 complex to have enhanced stability than the S protein (BA.2.75.2)-ACE2 complex. Also, we found the binding free energy value for the S (BA.2.75) -ACE2 complex (GBTOT= -20.03kcal/mol) to be relatively higher than the S (BA.2.75.2) -ACE2 complex (GBTOT= -15.19kcal/mol). The overall stability of the S protein (BA.2.75)-ACE2 complex may result in higher virulence of the strain.

Keywords: SARS-CoV-2; coronavirus; ACE2 receptor; BA.2.75; BA2.75.2; spike protein; COVID-19.

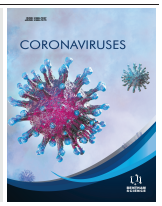
1. Introduction

The ongoing spread of an infectious Coronavirus disease 2019 (COVID-19), caused by Severe Acute Respiratory Syndrome-Coronavirus-2 (SARS-CoV-2), an enveloped positive-stranded RNA virus in the community, poses exceptional challenges for the healthcare system due to high incidence and long incubation time [1]. Since the start of 2022, most worldwide outbreaks have been caused by the coronavirus Omicron variants, constantly evolving. The Omicron variants raise worries that they could be associated with higher transmissibility, decreased vaccination effectiveness, and a higher risk of reinfection [2, 3]. ' 'The subvariants BA.4 and BA.5 of Omicron were found to be widespread in Europe and America, but in May 2022, a new sub-lineage, BA.2.75, was discovered in India and was found to have been responsible for a wave of viral infections that originated in India and spread throughout the

Coronaviruses, 2025, *6*, e130624230993

RESEARCH ARTICLE

Computational Design of Peptide Inhibitors Targeting the SARS-CoV-2 Main Protease



Chainee Das[1] and Venkata Satish Kumar Mattaparthi[1,*]

[1]*Molecular Modelling and Simulation Laboratory, Department of Molecular Biology and Biotechnology, Tezpur University, Tezpur, 784 028, Assam, India*

ARTICLE HISTORY

Received: April 07, 2024
Revised: May 30, 2024
Accepted: June 03, 2024

DOI:
10.2174/0126667975319992240612053235

Abstract: ***Background*:** The novel coronavirus disease also known as COVID-19 was first detected in December 2019 in Wuhan, China and was caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and its effect can still be seen in some parts of the world due to the lack of effective antiviral drugs and vaccines for treatment and controlling the pandemic. Chymotrypsin-like protease (3CLpro), also known as the main protease (Mpro) of SARS-CoV-2 plays a vital role during its replication process of the pathogen's lifecycle and is therefore considered a potential drug target for COVID-19. Hence, targeting the Mpro is an appealing approach for drug development because of its significant role in viral replication and transcription and therefore can act as an attractive drug target to combat COVID-19 as confirmed by researchers through numerous studies so far. Although small molecules dominate the field of drug market so far, peptide inhibitors still represent a class of promising candidates because of their similarity to endogenous ligands, high affinity, and low toxicity. It has been validated that therapeutic peptides can effectively and selectively inhibit the protein-protein interactions in viruses. Hence, it is necessary to design potential peptide inhibitors in order to inhibit the impact of the disease.

***Objective*:** To design peptide inhibitors against the SARS-CoV-2 Main Protease using computational methods.

***Methods*:** This study involves the development of potential target peptides that can act against the Mpro in a competitive mode against histone deacetylase (HDAC2) which had a high-confidence interaction with Mpro. Based on the interaction between Mpro and HDAC2, 13 peptides were designed out of which based on toxicity, binding affinity and binding site prediction, two peptides (peptide2 and peptide4) were screened and subjected to MD simulation.

***Results*:** Our study shows that the two peptides bind to the active site of the Mpro and it attains a higher stability upon binding to the peptides. We also found out that the Mpro has a strong binding affinity with both the peptides (GB_{TOT} = -72.85 kcal/mol for Mpro-peptide2 complex and GB_{TOT} = -46.36 kcal/mol for the Mpro-peptide4 complex).

***Conclusion*:** Even though declaring those peptides as future potent drug candidates would require more analysis and trials, our analysis will surely add value to the future findings and these findings could aid in the development of novel SARS-CoV-2 Mpro peptide inhibitors. These findings could aid in the development of novel SARS-CoV-2 Mpro peptide inhibitors.

Keywords: COVID-19, SARS-CoV-2, 3CLpro, HDAC2, MD simulation, peptide inhibitor.

1. INTRODUCTION

With rising levels of transmissibility and infectivity, the Coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has strained human health and public safety worldwide [1]. According to the World Health Organization (WHO), the COVID-19 pandemic has resulted in more than 703,874,696 confirmed cases and more than 6,965,332 confirmed deaths by March 2024 [2]. In the recent past, the world faced significant social, economic, and political chaos due to the COVID-19 disease. Due to the lack of globally approved antiviral drugs for treatment and vaccines against the pandemic, a number of cases and/or mortalities are still being observed in some parts of the globe. Supportive treatment and the use of repurposed drugs are the mainstays of current patient therapy [3]. The scientific community is now search-

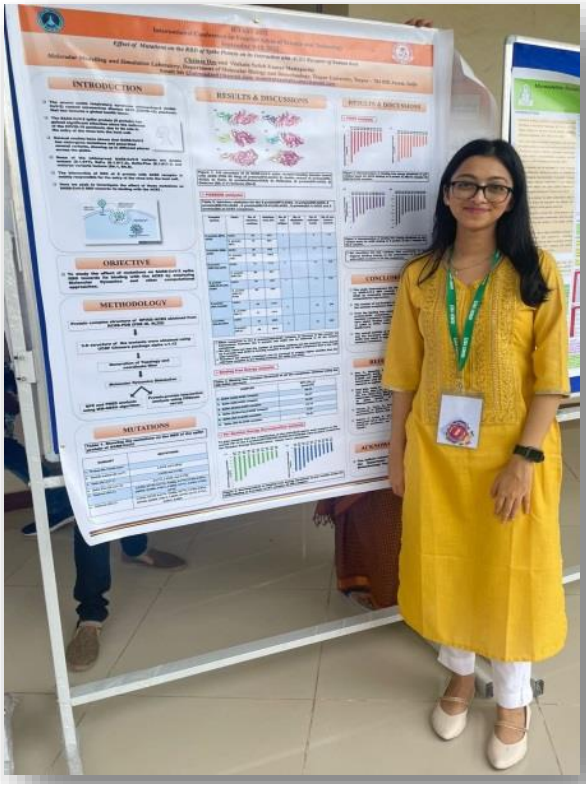
*Address correspondence to this author at the Molecular Modelling and Simulation Laboratory, Department of Molecular Biology and Biotechnology, Tezpur University, Tezpur, 784 028, Assam, India;
E-mails: mvenkatasatishkumar@gmail.com, venkata@tezu.ernet.in

2666-7975/25 $65.00+.00

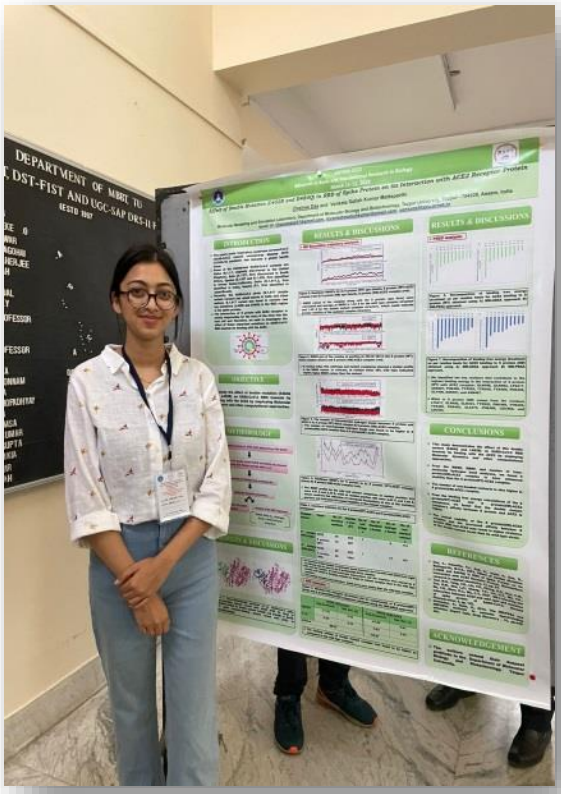
SEMINAR

CONFERENCES

WORKSHOPS

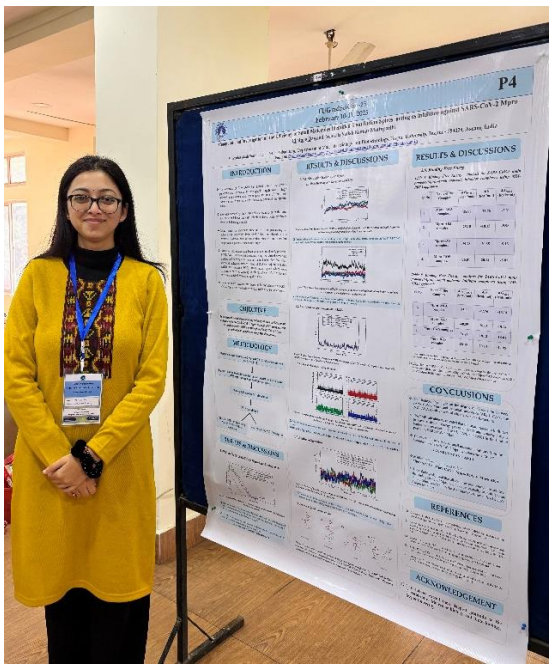


ICFAST-2022, University of Hyderabad



ABTRiB-2022, Department of Molecular Biology and Biotechnology, Tezpur University

Research at the Interface of Chemical, Biological and Material Sciences- 2023; Dept. of Chemical sciences, Tezpur University



TU Science Graduate Research Conclave 2025, Tezpur University