Omicron favors neuropilin1 binding over ACE2: Increased infectivity and available drugs

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Omicron favors neuropilin1 binding over ACE2: Increased infectivity and available drugs

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Abstract

COVID-19 pandemic is continue with thousands of new cases every day around the world, even then different vaccines have been developed and proven efficacious against SARS-CoV-2. Several know antivirals drugs have been repurposed or tested against SARS-CoV-2 but we still don't have an effective therapeutic strategy to control this viral infection. Moreover, in the race of finding out an efficient antiviral, excess uses of antiviral drugs developed a selective pressure on the virus that results in the high frequency of mutations and the possible emergence of antiviral drug resistance against SARS-CoV-2. Omicron is a recently emerged, highly mutated variant of SARS-CoV-2, reported for high infectivity. In the present study we performed molecular docking analysis between available potential antiviral drugs (remdesivir, nirmatrelvir, molnupiravir, EIDD-1931, GS-441524, and favipiravir) and omicron S protein including S protein/ACE2 complex. Our results suggest high infectivity of omicron, however, the known antiviral drugs were found efficacious against omicron variant. Further, to investigate the high infectivity of omicron, we performed a docking experiment between omicron S protein and neuropilin1 (NRP1). Surprisingly, results suggests high affinities with NRP1 than ACE2. Overall, results suggest that omicron favors NRP1 binding over ACE2, the possible reason behind improved infectivity of omicron variant.

Keywords: Omicron, ACE2, Neuropilin1, SARS-CoV-2, antivirals, COVID-19,

Introduction

It's now almost two years when in December 2019, the first case of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was identified in Wuhan, China (1). Within no time, SARS-CoV-2 roll out throughout the world and WHO declared it as a global COVID-19 pandemic (2). Since then SARS-CoV-2 is continuously evolving and several variants have been reported which are categorized as variant being monitored (VBM), a variant of interest (VOI), variant of concern (VOC), and variant of high consequence (VOHC) (3). The first official variant of SARS-CoV-2 was characterized with a single mutation D614G in the spike (S) glycoprotein, which was associated with a high transmission rate and thus quickly become the prevailing global viral strain (4). Till now five variants of concern have been identified including Alpha, Beta, Gamma, Delta, and Omicron which all are associated with the increased transmission, infectivity, immune escape, and resistance to antibody neutralization (5, 6). Interestingly, SARS-CoV-2 spike glycoprotein is the hot spot where all the major mutations are reported in different variants (www.ecdc.europa.eu/en/covid-19/variants-concern).

Receptor binding domain (RBD) and amino (N)-terminal domain (NTD) of the S glycoprotein are especially reported to have mutations in different variants (7). Importantly, RBD of SARS-CoV-2 S glycoprotein is the first site of contact with its receptor on the host cell and thus played an essential role in viral transmissibility and infectivity as in the recently emerged omicron variant (8). It is well known that ACE2 is the human cell receptor for the SARS-CoV-2 entry into the cell that happens upon S glycoprotein encounter with ACE2 (9). Rapid mutations in the S glycoprotein of emerging SARS-CoV-2 variants not only determine its infectivity to host cell but also affects the efficacy of antiviral drugs by blocking its availability to antiviral drugs. There is no doubt that omicron has highly transmissible as within one month it is circulating worldwide (10).

Moreover, SARS-CoV-2 spike protein is the principal target for neutralizing antibodies/vaccines and in the case of highly mutated spike protein, chances of immune escape or resistance against neutralizing antibody increase. It has been already reported that omicron is successfully able to breach the immunity acquired from past infection or vaccination (11). Recent, studies observed that omicron is resistant to most of the antiviral mAbs and already questioned the clinical efficacy of these mAbs (12).

The efficacy of other direct-acting antiviral drugs and their efficacy against omicron is also questionable. The emergence of a highly mutated variant of SARS-CoV-2, such as omicron created an urgent pressure for effective antivirals.

By considering the above-mentioned facts about the omicron variant, we performed molecular docking analysis using available drugs and S glycoprotein of Wuhan and omicron variant. We compared the free binding energy of different drugs with S glycoprotein of Wuhan and omicron variant, and further check the effectiveness of drugs by docking analysis using S protein/ACE2 (for both S glycoprotein of Wuhan and

omicron variant) complex. As omicron reported highly transmissible, we performed the omicron S glycoprotein docking with neuropilin1 (a known human receptor for SARS-CoV-2) (13) and compared the binding affinities with ACE2.

Material and methods

Protein retrieval and preparation

SARS-CoV-2 Spike protein (Wuhan, PDB ID: 6VSB), and omicron S protein (PDB ID: 7T9J) are used as a target for different antiviral drugs used in the present study. The human receptor of SARS-CoV-2, Neuropilin1 (PDB ID: 2QQI), ACE2 (PDB ID: 1R42), and its complex with Wuhan S protein (PDB ID: 6M0J) and omicron S protein (PDB ID: 7T9K) are used to determine the infectivity of SARS-CoV-2 variants and subsequent antiviral drug efficacy. All the target proteins and complexes for the docking studies were retrieved in PDB format from the RCSB PDB database (<http://www.rcsb.org>). Further, target protein and complex structure modification were carried out by removing preoccupied ligand, ions, and water (H₂O) molecules by using Chimera 1.15 (<https://www.cgl.ucsf.edu/chimera/>). Active site residues of target proteins were predicted by using an online tool, Fpocket (<https://bioserv.rpbs.univ-paris-diderot.fr/services/fpocket/>) (14). Next, after active site residue prediction, target proteins were modified again by using Chimera 1.15 to remove chains that are not involved in the active site.

Ligand preparation

3D structures of all the drugs used in the present study (Remdesivir, CID: 121304016; Nirmatrelvir, CID: 155903259; Molnupiravir, CID: 145996610; EIDD-1931, CID: 197020; GS-441524, CID: 44468216; Favipiravir, CID: 492405) are downloaded from the PubChem (<https://pubchem.ncbi.nlm.nih.gov/>) in SDF format. All the SDF format structures were prepared in PDB format for docking, by using Chimera 1.15 (<https://www.cgl.ucsf.edu/chimera/>).

Molecular docking

Molecular docking experiments were performed by using HDock online server <http://hdock.phys.hust.edu.cn/> (15). The best protein-drug or protein-protein complex was selected from among the top ten conformers based on docking score scoring (free binding energy, kcal/mol). Next, protein-drug or protein-protein docked complexes were selected for further, analysis of non-bonded interactions. The interaction analysis was conducted using PyMOL (16) and Discovery Studio visualization (17) software packages.

Results

Highly mutated omicron spike protein and its transmissibility

The omicron variant of SARS-CoV-2 is first detected in South Africa in November 2021 and subsequently, the sequence was deposited to the GISAID (Global Initiative on Sharing All Influenza Data) database. Due to the high transmissibility, the omicron variant was rolled out throughout the world within a short period of one month. Within this period several genomic sequences were submitted for the omicron and their genomic analysis revealed significant differences in comparison to the known SARS-CoV-2 variants. Observed genomic differences of the omicron variant are following its high transmissibility and independent evolution from other known variants of SARS-CoV-2 (18). Omicron spike was observed to have 37 mutations when compared to Wuhan variant spike protein. The highest number of mutations, 15 were found in receptor-binding domain (RBD) of spike protein (Fig1). The Omicron variant has only 6 unique mutations out of its all 61 mutations while the rest already exists in the known variants of SARS-CoV-2. However, results showed that omicron could potentially escape the two doses of vaccines with a 33 to 44 fold reduction in antibody neutralization capabilities (19). Interestingly, omicron has three sets of unique mutations that contribute to its increased transmissibility that following its worldwide spread within a short window of time. The spike protein mutations Q498R and N501Y (Fig1) contribute to its increased binding with ACE2 (20). Further, H655Y, N679K, and P681H triple mutations were observed to have an essential role in enhanced cleavage at the S1/S2 junction while N protein mutations R203K and G204R participate in efficient and fast replication that boosts the viral load and spread (21).

Omicron spike mutations don't make it resistant to available drugs

Omicron spread worldwide within a short period while we still have only a few approved antivirals to use in the clinical setting. The race for new potential antivirals is still going on as new variants of SARS-CoV-2 are appearing frequently. For a better understanding of the implications caused by omicron variant mutations on the existing antiviral and their use to treat omicron infections, we performed molecular docking analysis with omicron S protein and existing drugs including, remdesivir, nirmatrelvir, molnupiravir, EIDD-1931, GS-441524, and favipiravir (Fig2 to Fig7) (Table1). Upon comparing the docking results from both Wuhan variant S protein and Omicron S protein, we found remdesivir (-167.30 kcal/mol) highly effective against omicron, followed by molnupiravir (-157.50 kcal/mol). Moreover, remdesivir formed H-bonds with Phe970, Arg995, and Thr998, while molnupiravir formed H-bonds with Leu1034, Ser1037, and His1048 (Fig2 and Fig4). Favipiravir showed the lowest binding affinities with omicron (-105.81 kcal/mol), however, it was higher than the Wuhan variant (-92.76 kcal/mol). Interestingly, docking results suggested that remdesivir (-167.30 kcal/mol) is more efficient against omicron than the Wuhan variant (-157.85 kcal/mol). Overall docking results suggest remdesivir, molnupiravir, and EIDD-

1931 as effective antivirals against omicron, while the results are in agreement with the recent in vitro study (22), however, we observed reduced efficacy of nirmatrelvir, and GS-441524 against omicron in comparison to the Wuhan variant (Table1).

Omicron spike mutations allow strong binding with ACE2 and increase infectivity

To evaluate the binding of omicron S protein with ACE2, we performed a molecular docking experiment between ACE2 and S protein of Wuhan and omicron variant. We found increased binding affinities between omicron s protein and ACE2 (-264.22 kcal/mol) when compared to s protein of Wuhan variant (-259.88 kcal/mol). This suggests high infectivity of omicron than the Wuhan variant. To further, confirm the high infectivity and efficiency of available drugs, we performed molecular docking analysis between available drugs and s protein/ACE2 complex of both Wuhan and omicron variant (Fig8 to Fig13) (Table2). Docking results showed the highest free binding energy (-181.46 kcal/mol) for remdesivir that suggesting the effectiveness of remdesivir against highly infective omicron variant in comparison to the other drugs used in this study. Moreover, remdesivir formed H-bonds with Glu375 and Tyr515 at the receptor-binding surface (Fig8). Overall, all the studied drugs showed reduced free binding energy with omicron S protein/ACE2 complex, when compared to the binding free energies with the Wuhan S protein/ACE2 complex (Table2). This suggests a strong affinity of omicron S protein with ACE2 that result in high infectivity and reduced efficacy of drugs in comparison to the Wuhan variant, however, favipiravir is the exception of this observation that showed increased free binding energies when docked with omicron S protein/ACE2 complex (-104.97 kcal/mol), though that is the lowest among all studied drugs in the present study.

Omicron uses Neurophilin1 receptor to increase the infectivity

Neuropilin1 (NRP1) is recently reported as another potential receptor for SARS-CoV-2 spike protein that can play important role in viral infectivity (23). It has been shown that SARS-CoV-2 can directly bind to NRP1 upon the cleavage of the furin cleavage site and significantly enhance the viral entry thus infectivity (24). NRP1 could be a potential therapeutic target to combat the SARS-CoV-2 infection, however, much less attention was given to this receptor while few reports are available showing its potential role in SARS-CoV-2 entry and infection (25–27). Given facts about NRP1 in SARS-CoV-2 infectivity and increased transmissibility along with infectivity of omicron variant, we performed a molecular docking experiment between NRP1 and s protein of omicron and Wuhan variant. To our surprise, we found strong free binding energies for omicron S protein to NRP1 (-332.71 kcal/mol), which was significantly higher than free binding affinities between ACE2 and S protein of omicron (-264.22 kcal/mol) (Table3). Moreover, Tyr322, Lys373, Lys377, Asn386, Tyr1047, and Arg1107 amino acids at RBD of omicron S protein are involved

in conventional H-bonds formation with NRP1 binding site (TableS1) (Fig14A and B). Also, free binding energies between NRP1 and omicron S protein (-332.71 kcal/mol) were significantly higher than free binding energies between NRP1 and S protein of Wuhan variant (-312.61 kcal/mol). Interestingly, the S protein of the Wuhan variant itself (-312.61 kcal/mol) has higher free binding energies with NRP1 in comparison to the free finding energies between ACE2 (-259.88 kcal/mol) (Table3). In conclusion, NRP1 may serve as a better receptor for SARS-CoV-2 and probably play an essential role in its increased infectivity. Also as the docking results suggest omicron variant might prefer NRP1 over ACE2 or both simultaneously for the cellular entry that results in its high infectivity.

Limitations of the study

Despite being provided the docking-based evidence for strong binding of omicron S protein with NRP1 and other available drugs, the current study has some limitations. First of all, this study is based on in silico analysis using molecular docking and structural aspects of different SARS-CoV-2 receptors, S proteins of SARS-CoV-2 variants, and available drugs. Further, detailed in vitro and in vivo studies are required to fully confirm the insights provided by the present study. Second, this study is limited to the receptors or viral proteins and antiviral drugs whose 3d structures are known. Despite these limitations present study provided some important insights for increased infectivity of omicron variant and the efficacy of available antiviral drugs. These insights could be used or considered for the development of better treatment strategies and therapeutic drug development to mitigate the COVID-19 pandemic.

Conclusions

COVID-19 pandemic is going on with the frequent emergence of new variants, however, the unprecedented availability of technical and scientific advances made us a better understanding and thus management and development of efficient therapeutic strategies. Similarly, this in silico study provides a better understanding of the increased infectivity of the omicron variant. Results suggest that omicron acquired mutations result in high infectivity, however, available drugs are still effective and mitigate omicron infections. Our study also gives attention to the other SARS-CoV-2 human receptors such as NRP1. Molecular docking analysis suggests strong binding affinities of omicron S protein for NRP1, than ACE2. Possibly, omicron uses other NRP1 and other human receptors for SARS-CoV-2 and so showed high infectivity. Further, docking analysis with different potentially available antiviral drugs confirms their efficacy against the SARS-CoV-2 omicron variant. None of the mutations of omicron or other variants of SARS-CoV-2 reported contributing to drug resistance to date, however, we cannot rule out the possibilities for the emergence of drug resistance in the future. Overall, using the insights from the present study, further

detailed studies are required for better management and development of therapeutic strategies to combat the COVID-19 pandemic.

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Conflict of interest

Authors declare no conflict of interest.

Author contribution

PB and DR experimented. PB wrote the manuscript and conceptualize the manuscript. SMM and PB did proofread and supervise the whole work.

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Data availability

All the original contributions/data of the present study are included in the manuscript and supplementary material. Corresponding author can be contacted for further enquiries.

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Tables and legends to the figures

Table1. Determination of binding free energy (kcal/mol) from the docking analysis of Omicron and Wuhan variant's S protein with clinically potential available drugs.

Drug	Binding free energy (kcal/mol)	
	Wuhan S protein	Omicron S protein
Remdesivir	-157.85	-167.30
Nirmatrelvir	-151.28	-138.66
Molnupiravir	-160.96	-157.50
EIDD-1931	-130.27	-135.08
GS-441524	-145.37	-123.09
Favipiravir	-92.76	-105.81

Table2. Determination of binding free energy (kcal/mol) from the docking analysis of Omicron and Wuhan variant's S protein/ACE2 complex with clinically potential available drugs.

Drug	Binding free energy (kcal/mol)	
	Wuhan S protein /ACE2 complex	Omicron S protein/ACE2 complex
Remdesivir	-180.51	-181.46
Nirmatrelvir	-170.60	-153.96
Molnupiravir	-167.45	-153.61
EIDD-1931	-141.91	-130.79
GS-441524	-149.93	-141.26
Favipiravir	-96.54	-104.97

Table3. Determination of binding free energy (kcal/mol) from the docking analysis of Omicron and Wuhan variant's S protein with Neuropilin1 and ACE2.

Receptor	Binding free energy (kcal/mol)	
	Wuhan S protein	Omicron S protein
Neuropilin1	-312.61	-332.71
ACE2	-259.88	-264.22

Figure1. SARS-CoV-2, omicron variant mutations. Spike trimer figure derived from a cryo-electron microscopy structure (PDB ID: 7T9J) using Pymol software package.

Figure2. Molecular docking of remdesivir with omicron S protein (upper panel) and Wuhan S protein (Lower panel). Remdesivir showed in yellow color (stick model 3D model). On the right side, respective 2D interaction figures are shown where conventional hydrogen bonds are shown as green dotted lines and discs while van der Waals interactions are shown as light green dotted lines and discs. Remdesivir presented as a yellow color ball and stick model (2D model).

Figure3. Molecular docking of nirmatrelvir with omicron S protein (upper panel) and Wuhan S protein (Lower panel). Nirmatrelvir showed in yellow color (stick model 3D model). On the right side, respective 2D interaction figures are shown where conventional hydrogen bonds are shown as green dotted lines and discs while van der Waals interactions are shown as light green dotted lines and discs. Nirmatrelvir presented as a yellow color ball and stick model (2D model).

Figure4. Molecular docking of molnupiravir with omicron S protein (upper panel) and Wuhan S protein (Lower panel). Molnupiravir showed in yellow color (stick model 3D model). On the right side, respective 2D interaction figures are shown where conventional hydrogen bonds are shown as green dotted lines and discs while van der Waals interactions are shown as light green dotted lines and discs. Molnupiravir presented as a yellow color ball and stick model (2D model).

Figure5. Molecular docking of EIDD-1931 with omicron S protein (upper panel) and Wuhan S protein (Lower panel). EIDD-1931 showed in yellow color (stick model 3D model). On the right side, respective 2D interaction figures are shown where conventional hydrogen bonds are shown as green dotted lines and discs while van der Waals interactions are shown as light green dotted lines and discs. EIDD-1931 presented as a yellow color ball and stick model (2D model).

Figure6. Molecular docking of GS-441524 with omicron S protein (upper panel) and Wuhan S protein (Lower panel). GS-441524 showed in yellow color (stick model 3D model). On the right side, respective 2D interaction figures are shown where conventional hydrogen bonds are shown as green dotted lines and discs while van der Waals interactions are shown as light green dotted lines and discs. GS-441524 presented as a yellow color ball and stick model (2D model).

Figure7. Molecular docking of favipiravir with omicron S protein (upper panel) and Wuhan S protein (Lower panel). Favipiravir showed in yellow color (stick model 3D model). On the right side, respective 2D interaction figures are shown where conventional hydrogen bonds are shown as green dotted lines and discs while van der Waals interactions are shown as light green dotted lines and discs. Favipiravir presented as a yellow color ball and stick model (2D model).

Figure8. Molecular docking of remdesivir with omicron S protein/ACE2 complex (upper panel) and Wuhan S protein/ACE2 complex (Lower panel). Remdesivir showed in yellow color (stick model 3D model). On the right side, respective 2D interaction figures are shown where conventional hydrogen bonds are shown as green dotted lines and discs while van der Waals interactions are shown as light green dotted lines and discs. Remdesivir presented as a yellow color ball and stick model (2D model).

Figure9. Molecular docking of nirmatrelvir with omicron S protein/ACE2 complex (upper panel) and Wuhan S protein/ACE2 complex (Lower panel). Nirmatrelvir showed in yellow color (stick model 3D model). On the right side, respective 2D interaction figures are shown where conventional hydrogen bonds are shown as green dotted lines and discs while van der Waals interactions are shown as light green dotted lines and discs. Nirmatrelvir presented as a yellow color ball and stick model (2D model).

Figure10. Molecular docking of molnupiravir with omicron S protein/ACE2 complex (upper panel) and Wuhan S protein/ACE2 complex (Lower panel). Molnupiravir showed in yellow color (stick model 3D model). On the right side, respective 2D interaction figures are shown where conventional hydrogen bonds are shown as green dotted lines and discs while van der Waals interactions are shown as light green dotted lines and discs. Molnupiravir presented as a yellow color ball and stick model (2D model).

Figure11. Molecular docking of EIDD-1931 with omicron S protein/ACE2 complex (upper panel) and Wuhan S protein/ACE2 complex (Lower panel). EIDD-1931 showed in yellow color (stick model 3D model). On the right side, respective 2D interaction figures are shown where conventional hydrogen bonds are shown as green dotted lines and discs while van der Waals interactions are shown as light green dotted lines and discs. EIDD-1931 presented as a yellow color ball and stick model (2D model).

Figure12. Molecular docking of GS-441524 with omicron S protein/ACE2 complex (upper panel) and Wuhan S protein/ACE2 complex (Lower panel). GS-441524 showed in yellow color (stick model 3D model). On the right side, respective 2D interaction figures are shown where conventional hydrogen bonds are shown as green dotted lines and discs while van der Waals interactions are shown as light green dotted lines and discs. GS-441524 presented as a yellow color ball and stick model (2D model).

Figure13. Molecular docking of favipiravir with omicron S protein/ACE2 complex (upper panel) and Wuhan S protein/ACE2 complex (Lower panel). Favipiravir showed in yellow color (stick model 3D model). On the right side, respective 2D interaction figures are shown where conventional hydrogen bonds are shown as green dotted lines and discs while van der Waals interactions are shown as light green dotted lines and discs. Favipiravir presented as a yellow color ball and stick model (2D model).

Figure14. Molecular docking analysis of neuropilin1 with omicron S protein (A) and Wuhan S protein (B). Neuropilin1 showed as a yellow-colored ball and stick model while S protein (both omicron and Wuhan) showed as green and purple ribbon. Zoomed interaction image showed on the right side, where hydrogen bonds are represented by the dotted red lines.

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Figures

Figure 1

SARS-CoV-2, omicron variant mutations. Spike trimer figure derived from a cryo-electron microscopy structure (PDB ID: 7T9J) using Pymol software package.

Figure 2

Figure2. Molecular docking of remdesivir with omicron S protein (upper panel) and Wuhan S protein (Lower panel). Remdesivir showed in yellow color (stick model 3D model). On the right side, respective 2D interaction figures are shown where conventional hydrogen bonds are shown as green dotted lines and discs while van der Waals interactions are shown as light green dotted lines and discs. Remdesivir presented as a yellow color ball and stick model (2D model).

Figure 3

Molecular docking of nirmatrelvir with omicron S protein (upper panel) and Wuhan S protein (Lower panel). Nirmatrelvir showed in yellow color (stick model 3D model). On the right side, respective 2D interaction figures are shown where conventional hydrogen bonds are shown as green dotted lines and discs while van der Waals interactions are shown as light green dotted lines and discs. Nirmatrelvir presented as a yellow color ball and stick model (2D model).

Figure 4

Molecular docking of molnupiravir with omicron S protein (upper panel) and Wuhan S protein (Lower panel). Molnupiravir showed in yellow color (stick model 3D model). On the right side, respective 2D interaction figures are shown where conventional hydrogen bonds are shown as green dotted lines and discs while van der Waals interactions are shown as light green dotted lines and discs. Molnupiravir presented as a yellow color ball and stick model (2D model).

Figure 5

Molecular docking of EIDD-1931 with omicron S protein (upper panel) and Wuhan S protein (Lower panel). EIDD-1931 showed in yellow color (stick model 3D model). On the right side, respective 2D interaction figures are shown where conventional hydrogen bonds are shown as green dotted lines and discs while van der Waals interactions are shown as light green dotted lines and discs. EIDD-1931 presented as a yellow color ball and stick model (2D model).

Figure 6

Molecular docking of GS-441524 with omicron S protein (upper panel) and Wuhan S protein (Lower panel). GS-441524 showed in yellow color (stick model 3D model). On the right side, respective 2D interaction figures are shown where conventional hydrogen bonds are shown as green dotted lines and discs while van der Waals interactions are shown as light green dotted lines and discs. GS-441524 presented as a yellow color ball and stick model (2D model).

Figure 7

Molecular docking of favipiravir with omicron S protein (upper panel) and Wuhan S protein (Lower panel). Favipiravir showed in yellow color (stick model 3D model). On the right side, respective 2D interaction figures are shown where conventional hydrogen bonds are shown as green dotted lines and discs while van der Waals interactions are shown as light green dotted lines and discs. Favipiravir presented as a yellow color ball and stick model (2D model).

Remdesivir

Omicron

Wuhan

S protein/ACE2 complex

Figure 8

Molecular docking of remdesivir with omicron S protein/ACE2 complex (upper panel) and Wuhan S protein/ACE2 complex (Lower panel). Remdesivir showed in yellow color (stick model 3D model). On the right side, respective 2D interaction figures are shown where conventional hydrogen bonds are shown as green dotted lines and discs while van der Waals interactions are shown as light green dotted lines and discs. Remdesivir presented as a yellow color ball and stick model (2D model).

Nirmatrelvir

Omicron

Wuhan

S protein/ACE2 complex

Figure 9

Molecular docking of nirmatrelvir with omicron S protein/ACE2 complex (upper panel) and Wuhan S protein/ACE2 complex (Lower panel). Nirmatrelvir showed in yellow color (stick model 3D model). On the right side, respective 2D interaction figures are shown where conventional hydrogen bonds are shown as green dotted lines and discs while van der Waals interactions are shown as light green dotted lines and discs. Nirmatrelvir presented as a yellow color ball and stick model (2D model).

Molnupiravir

Omicron

Wuhan

S protein/ACE2 complex

Figure 10

Molecular docking of molnupiravir with omicron S protein/ACE2 complex (upper panel) and Wuhan S protein/ACE2 complex (Lower panel). Molnupiravir showed in yellow color (stick model 3D model). On the right side, respective 2D interaction figures are shown where conventional hydrogen bonds are shown as green dotted lines and discs while van der Waals interactions are shown as light green dotted lines and discs. Molnupiravir presented as a yellow color ball and stick model (2D model).

Figure 11

Molecular docking of EIDD-1931 with omicron S protein/ACE2 complex (upper panel) and Wuhan S protein/ACE2 complex (Lower panel). EIDD-1931 showed in yellow color (stick model 3D model). On the right side, respective 2D interaction figures are shown where conventional hydrogen bonds are shown as green dotted lines and discs while van der Waals interactions are shown as light green dotted lines and discs. EIDD-1931 presented as a yellow color ball and stick model (2D model).

Figure 12

Molecular docking of GS-441524 with omicron S protein/ACE2 complex (upper panel) and Wuhan S protein/ACE2 complex (Lower panel). GS-441524 showed in yellow color (stick model 3D model). On the right side, respective 2D interaction figures are shown where conventional hydrogen bonds are shown as green dotted lines and discs while van der Waals interactions are shown as light green dotted lines and discs. GS-441524 presented as a yellow color ball and stick model (2D model).

Favipiravir

Omicron

Wuhan

S protein/ACE2 complex

Figure 13

Molecular docking of favipiravir with omicron S protein/ACE2 complex (upper panel) and Wuhan S protein/ACE2 complex (Lower panel). Favipiravir showed in yellow color (stick model 3D model). On the right side, respective 2D interaction figures are shown where conventional hydrogen bonds are shown as green dotted lines and discs while van der Waals interactions are shown as light green dotted lines and discs. Favipiravir presented as a yellow color ball and stick model (2D model).

Figure 14

Molecular docking analysis of neuropilin1 with omicron S protein (A) and Wuhan S protein (B).

Neuropilin1 showed as a yellow-colored ball and stick model while S protein (both omicron and Wuhan) showed as green and purple ribbon. Zoomed interaction image showed on the right side, where hydrogen bonds are represented by the dotted red lines.