

***In-silico* Molecular Docking of Di-Rhamnolipids Targeting the SARS-CoV-2 Spike Receptor-Binding Domain: Potential Interference with ACE2-Mediated Viral Attachment**

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ABSTRACT

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) remains an important target for developing alternative antiviral strategies. In the present study, an *in-silico* approach was employed to investigate the potential of two di-rhamnolipid biosurfactants, L-rhamnosyl-L-rhamnosyl-C₁₂ and L-rhamnosyl-L-rhamnosyl-C₁₂-C₁₀ against the SARS-CoV-2 spike glycoprotein. Functional-domain and motif analyses identified the BCOV_S1_CTD and bCOV_S1_RBD regions as relevant interaction sites. Molecular docking revealed favorable binding of both rhamnolipids, with L-rhamnosyl-L-rhamnosyl-C₁₂ showing the strongest docking score (−6.8 kcal/mol), followed by L-rhamnosyl-L-rhamnosyl-C₁₂-C₁₀ (−6.2 kcal/mol), compared with L-rhamnose (−4.9 kcal/mol). The ligands interacted predominantly through hydrogen bonding and hydrophobic contacts involving residues such as ASP382, ARG393, PHE390, TRP349, and HIS401 within the receptor-binding region. These interactions suggest that the rhamnolipids may interfere with spike-mediated recognition and attachment to the human ACE2 receptor. In-silico toxicity assessment predicted L-rhamnosyl-L-rhamnosyl-C₁₂ to be non-carcinogenic, non-mutagenic, non-cytotoxic, and non-hepatotoxic, while both compounds complied with the Lipinski rule of five. However, the C₁₀ derivative showed predicted immunotoxicity and poor environmental biodegradability, emphasizing the need for further safety evaluation. Overall, L-rhamnosyl-L-rhamnosyl-C₁₂ emerges as a promising candidate for further experimental investigation as an antiviral biosurfactant targeting SARS-CoV-2 spike-mediated host-cell attachment. Experimental validation and molecular dynamics simulations are required to substantiate these computational predictions and determine the therapeutic potential of these compounds.

Keywords: L-rhamnosyl-L-rhamnosyl-C₁₂; L-rhamnosyl-L-rhamnosyl-C₁₂-C₁₀; Molecular docking; severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2); Spike glycoprotein.

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INTRODUCTION

The ongoing outbreak of the Coronavirus disease 2019 (COVID19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) which was first identified in December 2019 in Wuhan, Hubei, China and was spread over 188 countries. As of 17th August, 2020 more than 21.5 million cases were reported throughout the world and among them over 772000 peoples were deceased. In India, one of the infection hot spots faces more than 2.53 million infections and over 49,036 deaths [1]. This is worrisome statistics that India have shared almost 10% case of infections throughout the world. The common symptoms of these infections were included fever, cough, fatigue, shortness of breath, loss of smell and

taste and when the infection reaches to the severe stage then the people experience acute respiratory distress syndrome (ARDS) caused by the cytokine storm [2], multi-organ failure, septic shock, and blood clots [3, 4] leading to the fatality of the patient [5]. Biologically coronavirus possesses RNA as genetic material and covered with glycoprotein capsid and glycoprotein spike which interact with the angiotensin-converting enzyme 2 (hACE2) receptor of human attached to the cell membranes of cells in the lungs, arteries, heart, kidney, and intestines [6]. A wide array of antiviral and antiprotozoal drugs such as Chloroquine, Hydroxychloroquine, Lamivudin, Emtricitabine, remdesivir, favipiravir were applied to control this severe pandemic which is generally targeting the protease and nucleic acids of the SARS-CoV-2 virus [7]. But all were consequently shown less potent in clinical practices. In this context, new approaches need to be taken to combat this fatal pandemic.

Biosurfactants are potent alternatives due to their amphiphilic and lower cell toxic nature. Biosurfactants commonly destabilize the capsid glycoproteins and other hydrophobic compounds and wipe out the capsid layer to make the virus particle naked which leads to destroying the virus [5]. Biosurfactants are commonly utilized in several medical and pharmaceutical industries and these can be an effective alternative for a versatile application in coronavirus related treatments [8]. Among the biosurfactants, Rhamnolipid is one of the widest and medically important glycolipid biosurfactants that efficiently affect the cell membrane of several Gram-positive and negative bacteria and dismantle the cellular structure [9]. Application of this rhamnolipid as hand sanitizers and in cleaning agents to control this SARS-CoV-2 virus in every stage and incubation time with a potent antimicrobial surface destabilizing agent. Additionally, rhamnolipid can be used as a potential drug delivery system and can be applied in the face mask to control this virus [5]. The present study aimed to study the in-silico destabilization and blockage of the spike protein of the SARS-CoV-2

virus with the application of two derivatives of rhamnolipid elucidate the probable mode of action of the rhamnolipid with their toxicity profiles through the in-silico approaches.

Materials and methods:

Retrieval of sequence, phylogenetic, functional domain, and motif analysis: The protein sequence of the spike glycoprotein of SERS-CoV-2 (PDB ID: 6M0J) were retrieved from the RCSB PDB database (<https://www.rcsb.org/search>) and the homolog and orthologs of the sequence were searched using NCBI Blast server (Blast-p). The BLAST annotation was further checked by UniProt databases. Multiple sequence alignment of the sequences was aligned using the ClustalW method and the neighbor-joining (NJ) phylogenetic tree was constructed through MEGA7 [10] in Poisson method with 1000 bootstrap values replications. The functional domain of spike glycoprotein was predicted through ExPASy-PROSITE scan (<https://prosite.expasy.org/scanprosite/>) [11, 12] and the functional motifs in the protein sequence were also identified by motif search tool (<http://www.genome.jp/tools/motif/>) [13].

Physicochemical Characterization and Secondary structure Prediction: Physicochemical properties such as compositions of amino acids, instability, aliphatic indices, extinction coefficients, and grand average of hydropathicity (GRAVY) were calculated from Expasy ProtParam tool [14]. For calculation of theoretical isoelectric points (pI) and molecular weights, Sequence Manipulation Suite (SMS) Version 2 (<http://www.bioinformatics.org/sms2/proteiniep.html>) and (<http://www.bioinformatics.org/sms2/proteinmw.html>) were used, respectively. Prediction of secondary structure and assessment of the secondary elements such as helices, sheets, and turns were performed by PSIPRED v3.3 (<http://bioinf.cs.ucl.ac.uk/psipred/>) and CFSSP: Chou and Fasman Secondary Structure Prediction server (<http://cho-fas.sourceforge.net/>) [15, 16] software.

Homology modeling and evaluation of model:

The tertiary 3D structure of the SARS-CoV-2 virus was predicted through online Expasy SWISS-MODEL (ProMod Version 3.70) workspace [17] and offline Modeller9.13 [18] software. The QMEAN4 score of the predicted model was generated by SWISS sever and cross-checked in the SAVES server (<http://services.mbi.ucla.edu/SAVES/>). The overall quality of the model based on the highest overall quality factor generated by ERRAT (<http://services.mbi.ucla.edu/ERRAT/>).

Ramachandran plot was constructed to observe the dihedral angles ψ against ϕ in the energetically allowed regions of the amino acid of the SARS-CoV-2 spike glycoprotein by the SAVES server (<http://services.mbi.ucla.edu/SAVES/Ramachandra>

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n/) and RAMPAGE [19] server.

Protein–rhamnolipid Interaction: Spike protein of COVID-19 (PDB ID: 6M0J) was docked with two rhamnolipid derivatives such as L-rhamnosyl-L-rhamnosyl-C₁₂ and L-rhamnosyl-L-rhamnosyl-C₁₂-C₁₀ along with L-rhamnose as basic carbohydrate moiety, retrieved from pubchem server (<https://pubchem.ncbi.nlm.nih.gov/>). The spike protein was processed by removing all water molecules followed by the addition of polar hydrogen and Kollman charges and then the docking was performed using AutoDock Vina package according to standard protocol [7]. The docked structure was visualized using Biovia discovery studio visualizer client v20.0.1.

In-silico toxicity assessment

The *in-silico* toxicity assessment of the L-rhamnosyl-L-rhamnosyl-C₁₂, and L-rhamnosyl-L-rhamnosyl-C₁₂-C₁₀ was estimated by online tools and software including Pro-Tox II (http://tox.charite.de/prottox_II/index.php?site=com_pound_input) in KNIME platform [20]. The assessment of the environmental toxicity hazards was evaluated through admetSAR software (<http://lmmd.ecust.edu.cn/admetSar1/predict/>) [20]. The drug-likeness of the rhamnolipid was evaluated through the Lipinski Rule of Five using the online server <https://scfbio-iiitd.res.in/software/drugdesign/lipinski.jsp>.

Results and discussions:

Phylogenetic analysis, and Functional domain analysis: The SERS-CoV-2 spike glycoprotein (PDB ID: 6M0J) was isolated from the SERS-CoV-2 infected patient from Wuhan province, China [21]. The spike glycoprotein of SERS-CoV-2 (PDB ID: 6M0J; NCBI accession no.: P0DTC2.1) had a close similarity (100%) to the SERS-CoV-2 spike glycoprotein chain A (NCBI accession no.: 6XR8A) and several SERS-CoV-2 surface glycoproteins (99%) (Figure 1). The target SERS-CoV-2 spike glycoprotein (PDB ID: 6M0J) possessed four active sites i.e.

Betacoronavirus spike (S) glycoprotein S1 subunit N-terminal (NTD) domain profile (BCOV_S1_NTD; amino acids from 9 to 303), Betacoronavirus spike (S) glycoprotein S1 subunit C-terminal (CTD) domain profile (BCOV_S1_CTD; amino acids from 334 to 527), Coronavirus spike (S) glycoprotein S2 subunit heptad repeat 1 (HR1) region profile (COV_S2_HR1; amino acids from 896 to 1001), and Coronavirus spike (S) glycoprotein S2 subunit heptad repeat 2 (HR2) region profile (COV_S2_HR2; amino acids from 1143 to 1225) (Figure 2a). There were twelve functional motifs were identified from the SERS-CoV-2 spike glycoprotein (PDB ID: 6M0J) amino acid sequences (Figure 2b).

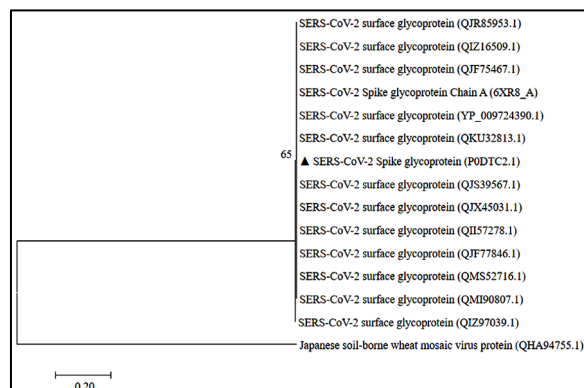
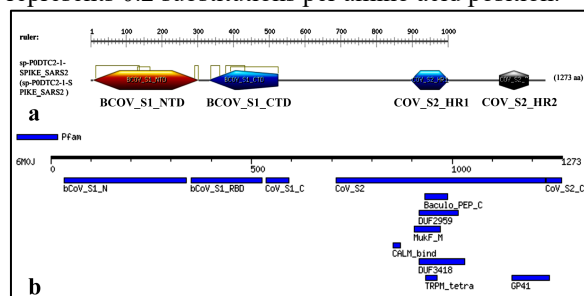


Figure 1: Unrooted neighbor-joining (NJ) phylogenetic tree of the spike glycoprotein (PDB ID: 6M0J) of SERS-CoV-2. Here the target protein was marked as a filled triangle. The bootstrap values (<50) were marked at the node of the clade. The bar represents 0.2 substitutions per amino acid position.



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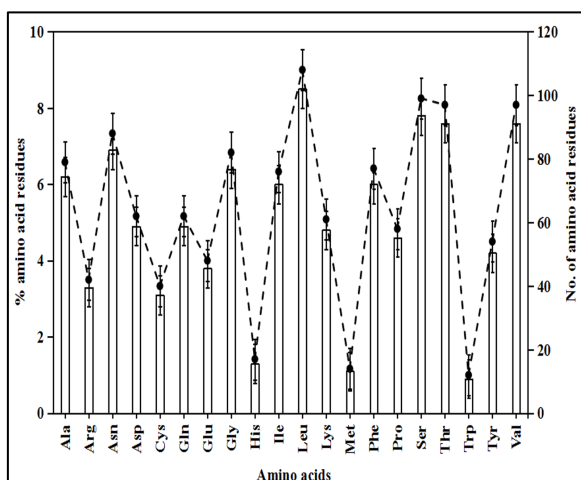


Figure 3: Amino acid composition (number and percentage) of the SERS-CoV-2 spike glycoprotein. Here dotted lines represent the number of amino acids and the hollow bar represents the percentage of the amino acid compositions.

Secondary structure prediction and homology modeling: The secondary structure of SERS-CoV-2 spike glycoprotein (PDB ID: 6M0J) possessed alpha helix 28.59%, extended strand 23.25%, beta-turn 3.38% and random coil 44.78% as secondary structure (Fig. 4a and b). Among the secondary structure components, the most stable components are alpha helices and extended strand as they form during the protein folding [12]. The 44.78% random coil were remained unfolded properly and devoid of secondary structure and have interacted with water. From the predicted result it can be proposed that the spike glycoprotein thermodynamically stable in nature.

Homology modeling refers to the three-dimensional nature of the target SERS-CoV-2 spike glycoprotein (PDB ID: 6M0J). The predicted built model had -1.26 QMEAN score which indicates the model was close to 0 and eventually a good model (Figure 4c). The QMEAN score refers to the global quality of the entire model of a three-dimensional target protein and to analyze the local per residue of different regions within a proposed model [22]. The good quality of the predicted model should be ranged between 0 to 1 [21] and our predicted model had normalized QMEAN score in comparison with non-redundant PDB structure was <1. In the SAVES server, the ERRAT generated overall quality factors of the target spike glycoprotein was 96.9636. The 3D model (Figure 4d) of the target SERS-CoV-2 spike glycoprotein (PDB ID: 6M0J) was estimated by the SWISS-MODEL workspace and the amino acids of the target protein were aligned to the template sequence (6xr8.1.A) which showed 100% identity with the target sequences. The Ramachandran plot (Figure 4e) depicted that the percentage of residues in the favored region was 92.3%, and in the additional allowed region was 7.7% whereas 0% was found in the outlier region. This observation was very much close to the

expected standard stable Ramachandran plot result [19]. Generally, a good Ramachandran plot should be stated where more than 90% of the amino acid residues lied in the most favored region [12].

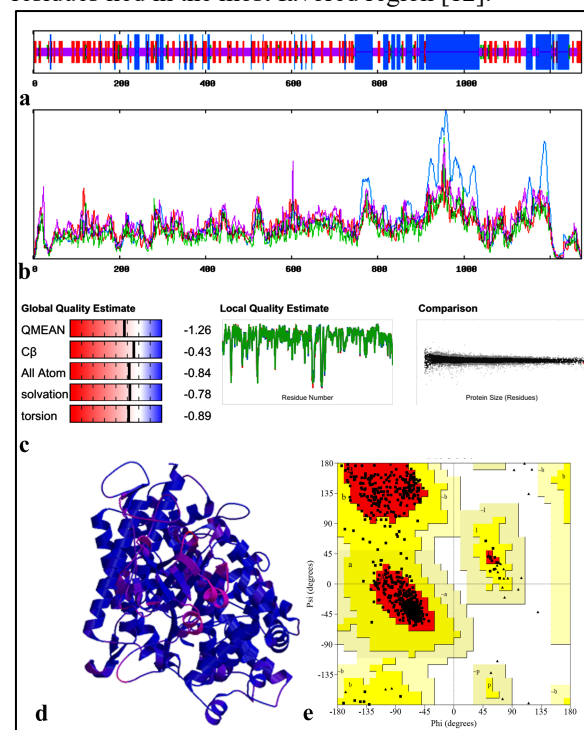


Figure 4: Secondary structure and homology modeling Prediction of spike glycoprotein of SERS-CoV-2. Here (a) and (b) represents the secondary structure of the targeted protein. Here, the blue color represents alpha-helix and extended strands and the red color represents the beta-turn. (c) QMEAN score and the global quality of the predicted model; (d) 3D structure of the spike glycoprotein obtained from homology modeling; (e) Ramachandran plot of the predicted model of the spike glycoprotein of SERS-CoV-2.

Protein-rhamnolipid Interaction: The target SERS-CoV-2 spike glycoprotein (PDB ID: 6M0J) was docked with two derivatives of rhamnolipids such as L-rhamnosyl-L-rhamnosyl-C₁₂ and L-rhamnosyl-L-rhamnosyl-C₁₂-C₁₀ along with their basic carbohydrate moiety L-rhamnose. The net energy of the molecular docking interactions was expressed as Xtra precision Glide score (XPG Score) which can be calculated as $XPG\ Score (kcal/mol) = a \cdot vdW + b \cdot Coul + Lipo + H-bond + Metal + BuryP + RotB + Site$, where, vdW, Coul, Lipo, H bond, metal, BuryP, Rot B, and Site denote van der Waals energy, Coulomb energy, lipophilic contacts, hydrogen-bonding, metal-binding, the penalty for buried polar groups, the penalty for freezing the rotatable bonds, and polar interactions with the residues in the active site, respectively. $a = 0.065$ and $b = 0.130$ are coefficient constants of van der Waals energy and Coulomb energy, respectively [23].

The ligand-protein interactions showed that the ligand L-rhamnosyl-L-rhamnosyl-C₁₂ docked with

ASP382A (2.1936 Å) by conventional hydrogen bond, ALA348A (2.75086 Å) by carbon-hydrogen bond, ARG393A (4.10496 Å) by hydrophobic alkyl bond, PHE40A (5.1876 Å, 4.5234 Å), TRP349A (4.2821 Å, 3.6173 Å), HIS378A (4.3263 Å), PHE390A (5.1782 Å, 4.2121 Å) by the hydrophobic pi-alkyl bond (Figure 5a, d, g, and j). The second rhamnolipid ligand *L*-rhamnosyl-*L*-rhamnosyl-*C*₁₂-*C*₁₀ was docked with HIS401A (2.8975 Å), ASP350A (2.8117 Å), TYR385A (2.5324 Å), PHE390A (2.1249 Å) by conventional hydrogen bond, ARG393A (3.5087 Å) by carbon-hydrogen bond, PHE40A (5.0878 Å), TRP349A (5.3574 Å, 5.0936 Å, 4.1683 Å), HIS378A (4.6994 Å), PHE390A (5.1528 Å), HIS401A (4.7576 Å) by the hydrophobic pi-alkyl bond (Figure 5b, e, h, and k). The control carbohydrate moiety *L*-rhamnose was docked with ALA348A (1.9806 Å, 2.8131 Å), ASP382A (2.9350 Å), TYR385A (2.3570 Å) by conventional hydrogen bond, ASP382A (2.6413 Å, 2.7563 Å) by carbon-hydrogen bond, and HIS401A (2.5258 Å) by pi-donor hydrogen bond (Figure 5c, f, i, and l). The XPG scores of the spike glycoprotein with *L*-rhamnosyl-*L*-rhamnosyl-*C*₁₂, *L*-rhamnosyl-*L*-rhamnosyl-*C*₁₂-*C*₁₀, and *L*-rhamnose were -6.8 kcal mol⁻¹, -6.2 kcal mol⁻¹, and -4.9 kcal mol⁻¹, respectively. From these XPG scores that both the rhamnolipids effectively bind to the SERS-CoV-2 spike glycoprotein (PDB ID: 6M0J) than the control *L*-rhamnose ligand. But between these two rhamnolipid ligands *L*-rhamnosyl-*L*-rhamnosyl-*C*₁₂ was best suited docked molecule than *L*-rhamnosyl-*L*-rhamnosyl-*C*₁₂-*C*₁₀.

Based on the cross-study of the protein structure and the ligand interactions, it was observed that the ligand was docked mainly in between the amino acid residues 334 to 527 which is the active site (BCOV_S1_CTD) of the spike glycoprotein as well as the functional motif (bCOV_S1_RBD) (Figure 2). These observations indicate that the rhamnolipid ligands effectively blocked the BCOV_S1_CTD active site as well as the bCOV_S1_RBD motif. Additionally, through the hydrophobic pi-alkyl bond both the rhamnolipids were bound with PHE40A residue of the protein which was the part of another active site BCOV_S1_NTD and functional motif bCOV_S1_N (Figure 2). This observation also

***In silico* toxicity assessment**

The probable toxicity of biosurfactant *L*-rhamnosyl-*L*-rhamnosyl-*C*₁₂ was predicted by *in-silico* analysis to check for its safe uses and disposals in the environment. The rhamnolipid has been predicted to be non-carcinogen, non-mutagenic, non-cytotoxic and non-hepatotoxic in nature by the Pro-tox II prediction tools. The Pro-tox II and AdmetSAR further predicted that the biosurfactant had LD₅₀ values of 190 mg kg⁻¹ body weight for its oral toxicity and 1.232 mg kg⁻¹ body weight for acute toxicity in rat. The ADME-Tox properties of the rhamnolipid predicted that the compound cannot

suggests that the rhamnolipid biosurfactant also dismantle the equilibrium of the active site (BCOV_S1_NTD) as well as the functional motif (bCOV_S1_N). From these studies, we can hypothesize that the rhamnolipid *L*-rhamnosyl-*L*-rhamnosyl-*C*₁₂ can be an effective blocker of the spike protein of SERS-CoV-2 which generally access the ACE2 receptor protein of the human system. Smith et al. proposed the similar hypothesis that biosurfactant effect on the outer capsid and spike protein and wipe off the glycolipid and hydrophobic coat by the formation of micelli surrounding the capsid and spike protein fractions. Consequently, the viral particle gets naked and in the open environment, the nucleic acid became destroyed similar to our hypothesis [5]. However, further experimental validation is essential to confirm the rhamnolipid and spike glycoprotein interactions.

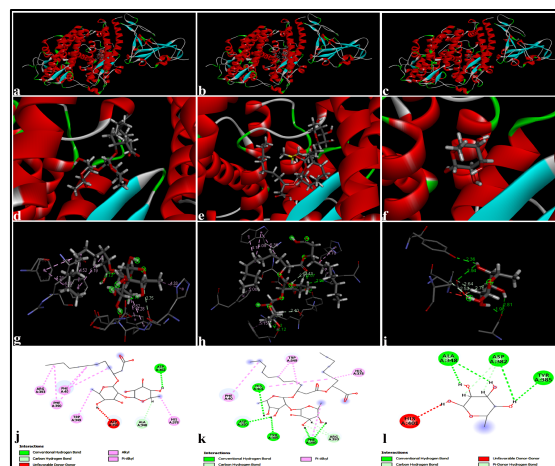


Figure 5: Molecular docking analysis of protein-ligand (*L*-rhamnosyl-*L*-rhamnosyl-*C*₁₂, *L*-rhamnosyl-*L*-rhamnosyl-*C*₁₂-*C*₁₀, and *L*-rhamnose) interactions against the SERS-CoV-2 spike glycoprotein. 'a', 'd', 'g', and 'j' represent the interaction of *L*-rhamnosyl-*L*-rhamnosyl-*C*₁₂ with the target protein (PDB ID 6M0J); and 'b', 'e', 'h', and 'k' represent the interaction of *L*-rhamnosyl-*L*-rhamnosyl-*C*₁₂-*C*₁₀ with the target protein (PDB ID 6M0J); and 'c', 'f', 'i', and 'l' represent the interaction of *L*-rhamnose with the target protein (PDB ID 6M0J).

cross the blood-brain barrier (0.5372), and unable to absorb in human intestine (0.6213) or Caco-2 cell line (0.7012), and non-inhibitor of P-glycoprotein (0.6607) and renal organic cation transporter (0.9051) and localized sub-cellularly at mitochondria (0.7275) with weak hERG (the human Ether-a-go-go-Related Gene) inhibitor (0.9521) (Table S2). However, the rhamnolipid *L*-rhamnosyl-*L*-rhamnosyl-*C*₁₂ has resistance to biological degradation in the environment (0.9451). The ligand *L*-rhamnosyl-*L*-rhamnosyl-*C*₁₂ was found to follow the Lipinski rule of five for drug likeliness with molecular mass 312 Da (<500 Da), hydrogen bond

donor 5, hydrogen bond acceptors 6 with log P score values -0.053101, and the molar refractivity of 77.145782. The *in-silico* toxicity has also been predicted that the rhamnolipid biosurfactant can be safely utilized in the human and rat model and safely disposed of in the environment. The low toxicity and inability to cross the blood-brain barrier or intestine or Caco-2 cell lines indicates the low penetration efficiency inside the human cells. The Lipinski rule of five also indicates the rhamnolipid may be used as a potent drug [20]. From all these observations it can be suggested that the rhamnolipid L-rhamnosyl-L-rhamnosyl-C₁₂ may be used as a drug to combat topical pathogens soon.

The probable toxicity of biosurfactants L-rhamnosyl-L-rhamnosyl-C₁₂-C₁₀ was also predicted through *in-silico* approaches for its safe uses and disposals in the environment. The rhamnolipid was predicted to be non-carcinogen, non-mutagenic, non-cytotoxic and non-hepatotoxic in nature although it was predicted as immunotoxic in nature. The Pro-tox II prediction tool also predicted that the rhamnolipid derivative was non-toxic to several nuclear receptor signaling such as Aryl hydrocarbon Receptor (AhR), Androgen Receptor (AR), Androgen Receptor Ligand Binding Domain (AR-LBD), Aromatase, Estrogen Receptor Alpha (ER), Estrogen Receptor Ligand Binding Domain (ER-LBD), Peroxisome Proliferator Activated Receptor Gamma (PPAR-Gamma) and stress response pathways such as Nuclear factor (erythroid-derived 2)-like 2/antioxidant responsive element (nrf2/ARE), Heat shock factor response element (HSE), Mitochondrial Membrane Potential (MMP), Phosphoprotein (Tumor Suppressor) p53, and ATPase family AAA domain-containing protein 5 (ATAD5). The probability of the nontoxic nature of the rhamnolipid derivative was more than 80% but it was predicted that the derivative can be targeted for toxicity development to the enzyme's amine Oxidase A and prostaglandin G/H Synthase 1. The Pro-tox II and AdmetSAR further predicted that the biosurfactants belong to the class 2 toxicity level with LD₅₀ values of oral toxicity was 10 mg/kg and 2.5223 mol/kg body weight for acute toxicity in rat. The ADME-Tox predicted that the rhamnolipid cannot cross the blood brain barrier (0.5286), and unable to absorb in human intestine (0.7589) or Caco-2 cell line (0.7643), and non-inhibitor of P-glycoprotein (0.6237) and renal organic cation transporter (0.9115) and localized sub-cellularly at mitochondria (0.7755) with weak hERG (the human Ether-a-go-go-Related Gene) inhibitor (0.9437), nontoxic in AMES test and not readily biodegradable in the environment (0.9429). The ligand was followed the Lipinski rule of five for drug likeness with molecular mass 312 Da (<500 Da), hydrogen bond donor 5, hydrogen bond acceptors 6 with logP score values -0.053101, and the molar refractivity 77.145782.

The *in-silico* toxicity profiles indicate that L-rhamnosyl-L-rhamnosyl-C₁₂ and its C₁₀ derivative possess generally favorable safety characteristics, including predicted absence of carcinogenicity, mutagenicity, cytotoxicity and hepatotoxicity. Their limited predicted intestinal, Caco-2 and blood-brain barrier permeability further suggests low systemic and neurological exposure. These findings are consistent with previous reports describing rhamnolipids as relatively low-toxicity biosurfactants with considerable biomedical and environmental potential [24, 25]. However, the predicted immunotoxicity of the C₁₀ derivative and poor biodegradability warrant experimental validation and ecological risk assessment. Importantly, Lipinski-compliant physicochemical properties support further investigation as topical antimicrobial candidates, but do not establish clinical drug-likeness alone [26].

Conclusion:

This study demonstrates the potential of di-rhamnolipid biosurfactants can be used as candidate antiviral molecules against SARS-CoV-2. Molecular docking revealed that L-rhamnosyl-L-rhamnosyl-C₁₂ showed the strongest interaction with the spike glycoprotein (-6.8 kcal/mol), followed by L-rhamnosyl-L-rhamnosyl-C₁₂-C₁₀ (-6.2 kcal/mol), with interactions concentrated within the BCOV_S1_CTD and receptor-binding regions. *In-silico* toxicity assessment further predicted favorable safety characteristics, including non-carcinogenic, non-mutagenic, non-cytotoxic and non-hepatotoxic properties, while both derivatives complied with the Lipinski rule of five. However, the predicted immunotoxicity and poor biodegradability of the C₁₀ derivative warrant further investigation. Overall, L-rhamnosyl-L-rhamnosyl-C₁₂ represents the more promising candidate for further antiviral development. Molecular dynamics, *in-vitro* antiviral assays, and *in-vivo* studies are required to validate these computational predictions and establish its therapeutic potential.

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