In Silico Testing of Some Protected Galactopyranose as SARS-CoV-2 Main Protease Inhibitors

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Abstract

An outbreak of novel Coronavirus disease (COVID-19 or 2019-nCoV) due to the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) has already demonstrated a fatal death toll all over the world. To cure this viral infection, a number of compounds of different categories have been investigated in silico. Some of the compounds showed better binding energy with COVID-19-related proteins. However, until now there is no appropriate drug except a vaccine. It was found that many antifungal drugs are used for COVID-19 patients in hospitals. Many monosaccharide esters have been reported to have antifungal potential. Thus, in the present study, some protected galactopyranose esters are chosen for molecular docking with SARS-CoV-2 main proteases (PDB id: 7BQY and 6LU7). A docking study revealed that galactopyranose esters ***5-8*** *have very good docking scores (-8.4 to -6.5 kcal/mol) compared to the standard drugs azithromycin, remdesivir, and hydroxychloroquine. To explain such good scores interaction between amino acid residues of proteins and compounds in their docked complexes are calculated and duly discussed in this study.*

Keywords: *COVID-19, Protected galactose, Molecular docking, Remdesivir, Sugar esters.*

1. Introduction

It is now established that severe respiratory problems, pneumonia, and fever symptoms containing death threatening disease caused by the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) is known as novel Coronavirus disease (COVID-19 or 2019-nCoV) [1-4]. After its outbreak in Wuhan, Hubei province, China in 2019, the world has been suffering huge death tolls, and was heading step by step crisis due to its severe symptoms with lethal complications, which needed hospitalization [5-7]. Many studies showed that patients with type 2 diabetes, obesity, heart disease, and high blood pressure enhanced health/death risk for COVID-19 patients in hospitals [8]. COVID-19 composed of a diverse group of viruses and has the ability to infect many different animals including triggering cytokine storm syndrome [9,10]. It is different from the previously reported

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coronaviruses and this new virus has earnest evidence compared to Middle East respiratory syndrome [11,12]. Many literatures described genomic characteristics, receptor use, and the basic virology of COVID-19, which helped to identify the mortality risk factors. Lack of proper medication enhanced death tolls and posed fatal health problems to every nation of the world. Consequently, every sector of social, economic, educational, developmental, and tourism growth have been hampered [13].

Although vaccines are now available and have demonstrated high efficacy in decreasing the severity of COVID-19 infections to reduce hospitalization severity and deaths, they are not able to prevent this virus transmission [14]. The identification, discovery, and implementation of active antiviral drugs against this virus are thus important to fight this pathogen [15]. In this respect, many researchers showed potentiality of a different kinds of drugs *in silico* against COVID-19. For example, phytochemicals present in herbal green tea (polyphenols like epicatechingallate, epigallocatechin gallate, and gallocatechin-3-gallate, etc.) have the ability to interact with the important residues of major protease (M^{pro}) of SARS-CoV-2 [16]. These polyphenolic compounds showed binding affinity with M^{pro} (−7.1 to −9.0 kcal/mol). Again, several antibiotic such as nucleoside related Molnupiravir (1a, Figure 1) when applied to COVID-19 patients (among 202 treated participants) are found to reduce the risk of death for moderate symptom containing patients [17]. Compounds having monosaccharide moiety (thio glucopyranoside) such as Auranofin (2; Figure 1) inhibits SARS-COV-2 replication in human cells at very low concentration (against Huh-7 cell line) [18] although different result was reported for other cell line (Human epithelial lung cancer Calu-3) [19].

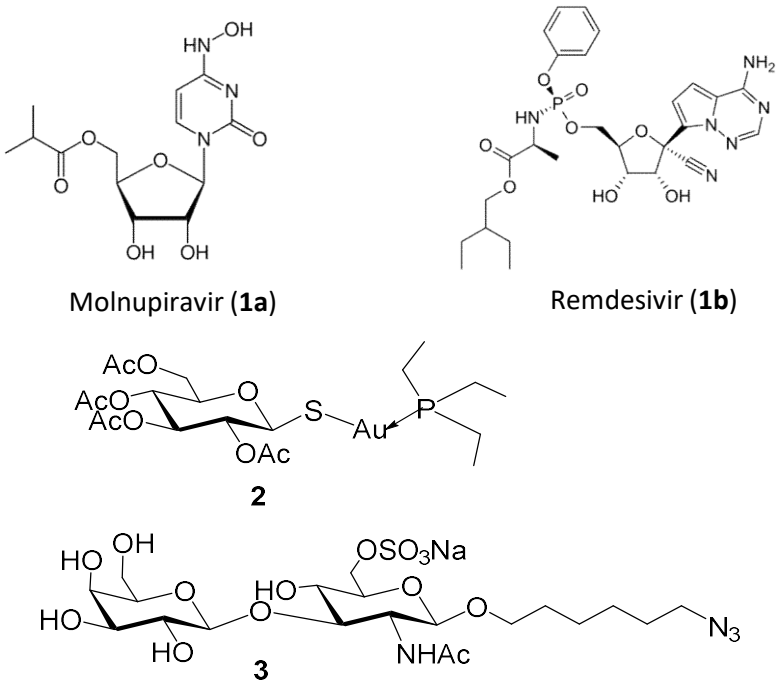

Figure 1. Anti-COVID-19 drug containing sugar unit(s).

Recently (2022), Lee et al. [20] reported that 6-sulfo *N*-acetyllactosamine (3) can inhibit the binding of the spike protein S1 subunit with blood group A RBCs. Thus, it reduces the interactions between the spike protein S1 subunit and ACE2. Many nucleosides are well-reported for their effectiveness against dengue virus, HIV, HBV, yellow fever virus, and Zika virus, etc. [21,22]. In an another positive approach, 16 nucleoside analogs are found to be highly potential against SARS-CoV-2 virus [23]. The carbohydrate-nucleosides include well-known antiviral drugs molnupiravir (1a) and remdesivir (1b). Moreover, some nucleosides have potentiality against resistant strains of pathogenic microorganisms [24]. Many monosaccharides with ester groups (known as sugar ester, SEs) possess

biological potentialities [25-30]. These SEs have many positive physicochemical, ADMET, and drug-likeness properties [31-36]. SEs can be synthesized using various methods under different conditions providing different positional selectivity [37-42]. With ester moieties, many of them showed *in silico* binding and hence inhibition against COVID-19 virus [43-48].

Although a plethora of different classes of compounds were tested and some can positively prevent COVID-19, no effective drugs are established for the treatment stage. Due to fatal risks of this viral infections, researchers are forced to search for new antiviral formulations. Based on biological potentiality of monosaccharides and related works [49-51], especially galactose esters [52], we aim to extend their investigation dealing with antiviral studies in the present pandemic situation.

2. Materials and methods

2.1. Galactopyranoside acyl esters

For anti-COVID-19 potentiality study, four acyl esters 5-8 of galactopyranose 4 were selected and their structures are presented in Figure 2. These compounds were already synthesized from D-galactose *via* 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (4) and characterized by our research group [53]. In all these esters 5-8, C-6 OH is substituted by an acyl group like pivaloyl, benzoyl, 2-chlorobenzoyl, and 4-chlorobenzoyl. Also, iospropylidene protection is present 2,3- and 4,5-positions of the pyranose ring.

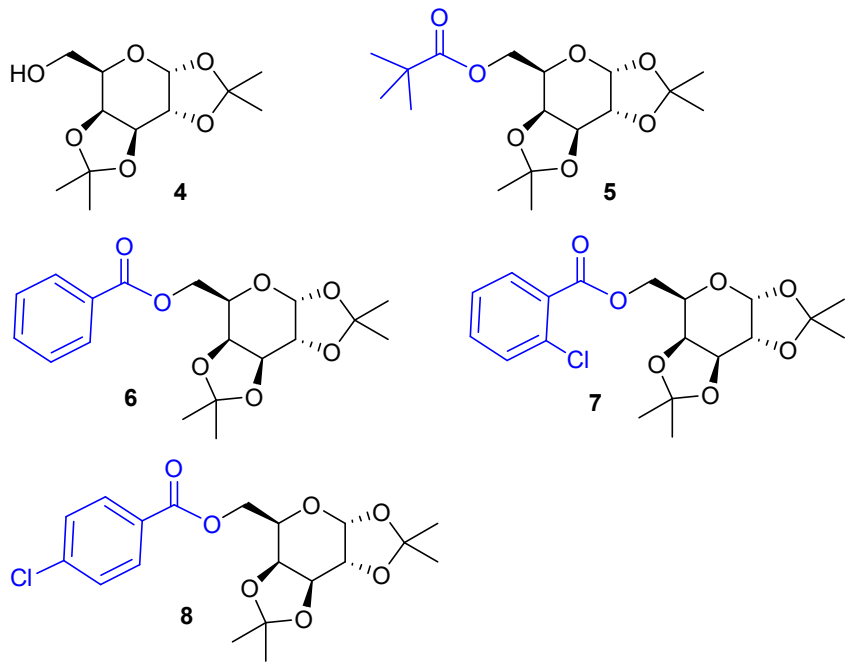

Figure 2. Protected galactopyranose 4-based sugar esters 5-8.

2.2. DFT based optimization

The original 2D and 3D geometry of galactopyranose was collected from PubChem (PubChem CID 6036). It was then opened in GaussView software and structures 4-8 were drawn keeping geometry intact [54]. After saving all the compounds separately, these were subjected for structural optimization. In this respect, the B3LYP hybrid density functional method in DFT (density functional theory) was used [55]. The basis set was 6-31G+ where optimization took several days in a core i3

laptop. These optimized structures of the compounds were saved and duly used during molecular docking. It should be noted that the optimized structures will show more accurate binding scores than the non-optimized molecules.

2.3. Method for molecular docking

In the last forty years, several molecular docking programs have been established. Many of the popular programs are in use to predict the binding conformations and interactions between compounds/ligands and protein binding sites [56]. Optimized structures of 4-8 (mentioned in section 2.1) in the sdf format were used for docking. In addition, three standard antibiotics sdf files were collected from PubChem. Two main proteases such as 7BQY and 6LU7 were also downloaded from the RCSB protein data bank (PDB). Unnecessary heteroatoms and water from 7BQY and 6LU7 were removed and saved as pdb file format. Swisspdb software was used for energy minimization of all the ligands. After energy minimization ligands were saved in pdbqt format.

Having all the ligands and proteins in useable formats, we used PyRx autodock vina for their molecular docking. After loading ligands and proteins, box size was fixed in the maximum dimension level (a command available in the software) and proceeded for auto docking. Docked complexes were opened in the DiscoveryStudio 4.5 (client), where necessary non-bond interactions were calculated.

3. Results and discussion

3.1. Optimized structures of the galactose esters

Conformational structures are important for carbohydrates [57] as molecular size and shape influences their binding with proteins. Thus, we checked the conformations of galactopyranose molecules from their optimized structures and these are presented in Figure 3. Due to the fusion of two five-membered acetonide rings to six-membered galactopyranose ring (**4**-**8**), the pyranose ring deviated from the regular chair conformation (Figure 3).

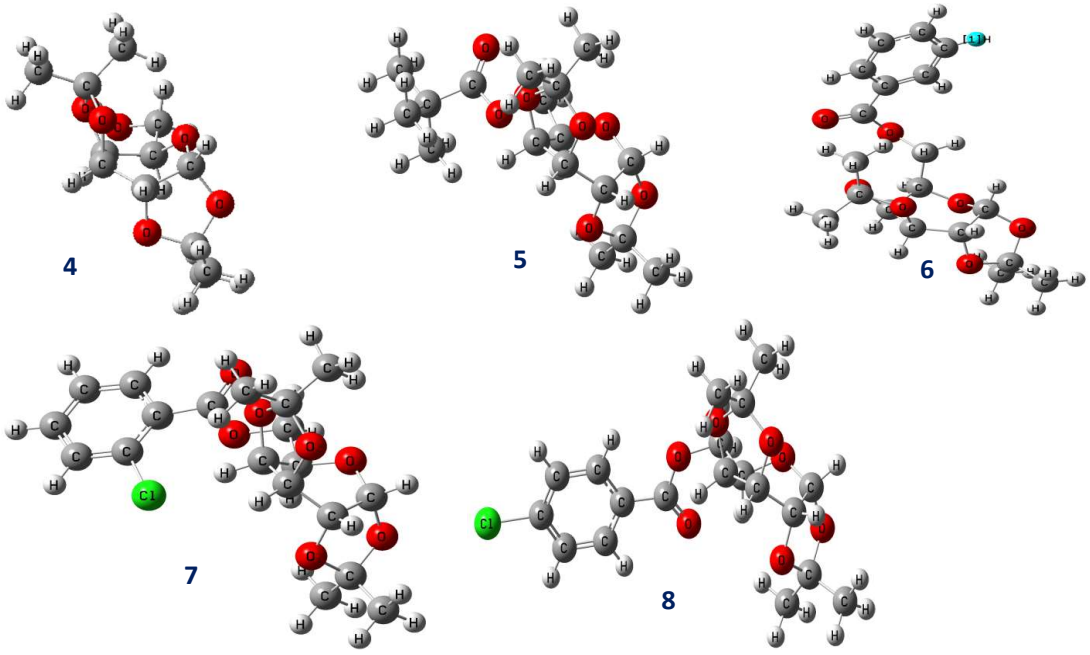

Figure 3. DFT optimized structures of galactopyranose (only backbones are presented).

3.2. Molecular docking: Binding affinity with SARS-CoV-2 main proteases

Several protective measures have been reported for the control of COVID-19 situation along with the administration of antiviral drugs [58]. It was observed that several SEs showed antifungal properties [59,60] and antifungal agents were reported to have antiviral efficacy, especially they were checked for anti SARS-CoV-19 tests *in vitro* [61]. Encouraged by these results, four galactopyranose esters 5-8 were selected for molecular docking with main proteases (7BQY and 6LU7). These compounds are protected at C-1,C-2 and C-3,C-4 positions as isopropylidene rings, which imposed some ring distortion in the original pyranose ring (section 3.1). Thus, esters 5-8 might have some special interaction with main proteases used. The molecular binding energy with the selected proteases are presented in Table 1 and Table 3.

Table 1. Molecular docking score (binding energy) with 7BQY.

Ligand/Drug	Binding energy (kcal/mol)	No. of H bond	No. of Hydrophobic bond	No. of van der Waal/ES bond	Total bonds
4	-6.2	5	3	0	8
5	-7.1	5	6	0	11
6	-7.4	7	3	0	10
7	-8.4	2	0	0	2
8	-7.3	2	8	0	10
Azithromycin	-6.7	6	1	0	7
Hydroxychloroquine	-6.4	6	3	1	10
Remdesivir	-7.5	7	1	0	8

ES = electrostatic; -6.0 kcal/mol is considered standard docking score.

Initial docking of the compounds with M^{pro} 7BQY showed that protected galactopyranose **4** has binding energy -6.2 kcal/mol, which increased upon esterification at the C-6 position of **4**. Pivaloyl ester **5**, benzoyl ester **6**, 2-chlorobenzoyl ester **7**, and 4-chlorobenzoyl ester **8** showed binding energy -7.1, -7.4, -8.4, and -7.3 kcal/mol, respectively. These results are found to be comparable with standard drugs used for the COVID-19 hospitalized patients such as azithromycin (-6.7 kcal/mol), hydroxychloroquine (-6.4 kcal/mol) and remdesivir (-7.5 kcal/mol). The highest binding energy was observed for the 2-chlorobenzoate **7**, which was better than all the standard drugs tested here (Table 1). It was observed that the binding energy is related to different interaction of the compounds (here termed as ligands) with the amino acid residues of the 7BQY (Figure 4 and Table 2). Interestingly, the best-docked compound **7** formed two H-bonds with THR111, and ILE152, which are similar to standard drug remdesivir (Table 2).

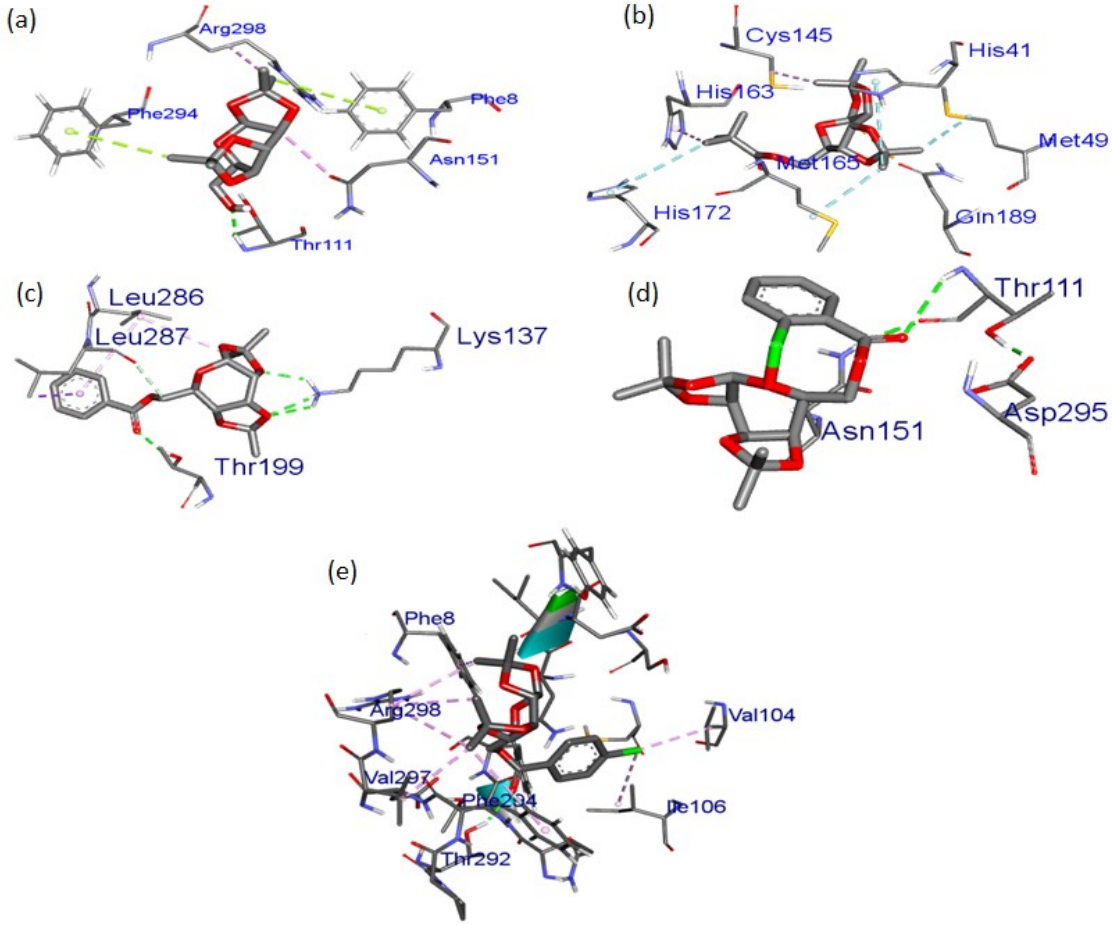

Figure 4. Non-bond interactions of 7BQY with ligands - (*a*) **4**; (*b*) **5**; (*c*) **6**; (*d*) **7**; and (*e*) **8**.

Table 2. Interaction of compounds with amino acid (AA) residues in compounds-7BQY complex.

Drug	Hydrogen bond		Hydrophobic bond		Van der Waals bond
	Interacting residue of amino acid	Distance (Å)	Interacting residue of amino acid	Distance (Å)	
4	THR111 ASN151 ASN151 GLN110 ASP295	2.08191 2.42152 2.87417 2.73666 2.8025	ARG298 PHE8 PHE294	4.54082 4.97707 4.14713	Absent
5	MET165 GLN189 HIS164 HIS164 GLN189	2.62542 2.54258 2.92302 2.70614 2.63827	MET165 MET49 CYS145 HIS41 HIS163 HIS172	4.1241 3.94271 4.37724 4.9025 4.65468 5.27312	Absent
6	LYS137 LYS137 LYS137 THR199	2.5559 2.36167 2.30771 2.19358	LEU286 LEU286 LEU287	4.8677 5.44459 4.21717	Absent

	ASP289 THR199 LEU287	2.66395 2.59192 2.06939			
7	THR111 ILE152	2.81125 2.68148			Absent
8	THR292 ASP153	2.12343 2.48906	VAL297 ARG298 ARG298 ARG298 VAL104 ILE106 PHE8 PHE294	4.17857 4.7455 4.26966 4.51154 4.02694 5.25525 5.04265 5.41539	Absent
Azithromycin	MET276 LEU287 ALA285 GLY275 ASP289 THR199	2.31792 2.3419 1.87656 2.65918 2.62422 2.64481	LEU286	5.28191	Absent
HCQ	ASP187 MET49 HIS164 MET49 LEU141 HIS163	2.16221 2.7717 2.60035 2.99932 2.84044 2.38572	MET49 MET165 HIS41	5.41684 4.11199 4.70795	Absent
Remdesivir	TYR154 ILE152 THR111 ASP153 THR111 ASP153 ASP295	2.24905 2.76088 2.86186 2.23244 2.51048 2.54508 2.87869	PHE294	4.5044	Absent

Note: TRP = Tryptophan, ASP = Aspartic acid, GLU = Glutamic acid, LEU = Leucine, THR = Threonine, ASN = Asparagine, GLN = Glutamine, PHE = Phenylalanine, ILE = Isoleucine, ARG = Arginine, VAL = Valine, SER = Serine, PRO = Proline, GLY = Glycine, HIS = Histidine, LYS = Lysine, TRP = TRPosine, CYS = Cysteine, MET = Methionine.

In the next stage, galactopyranose esters were docked with another M^{pro} 6LU7 and resulted binding energies are presented in Table 3. Here, ester compounds 6-8 have better binding energy (-6.9 to -7.5 kcal/mol) than the non-ester 4 (-6.3 kcal/mol) and standard antibiotics (-5.4 to -6.7 kcal/mol). The binding affinity of different esters 5-8 with 6LU7 are due to different non-bond interactions, which are shown in Figure 5 and Table 4. However, the binding energies for 6LU7 are slightly lower than the other M^{pro} 7BQY. In this case, also, the best-docked 7 formed three H-bonds with THR199, LEU287, and LEU287 which are in conformity with the standard drug remdesivir. Thus, these compounds should be valuable for future COVID-19 therapy [62,63].

Table 3. Molecular docking score (binding energy) with 6LU7.

Ligand/Drug	Binding energy (kcal/mol)	No. of H bond	No. of Hydrophobic bond	No. of van der Waal bond	Total bonds
4	-6.3	3	6	0	9
5	-6.5	6	2	0	8
6	-7.1	2	1	0	3
7	-7.5	3	1	0	4
8	-6.9	3	3	0	6
Azithromycin	-6.7	1	0	0	1
HCQ	-5.4	3	4	1	8
Remdesivir	-6.5	6	4	0	10

*For rigorous validation three standard drugs/antibiotics are also docked with 6LU7; HCQ = hydroxychloroquine.

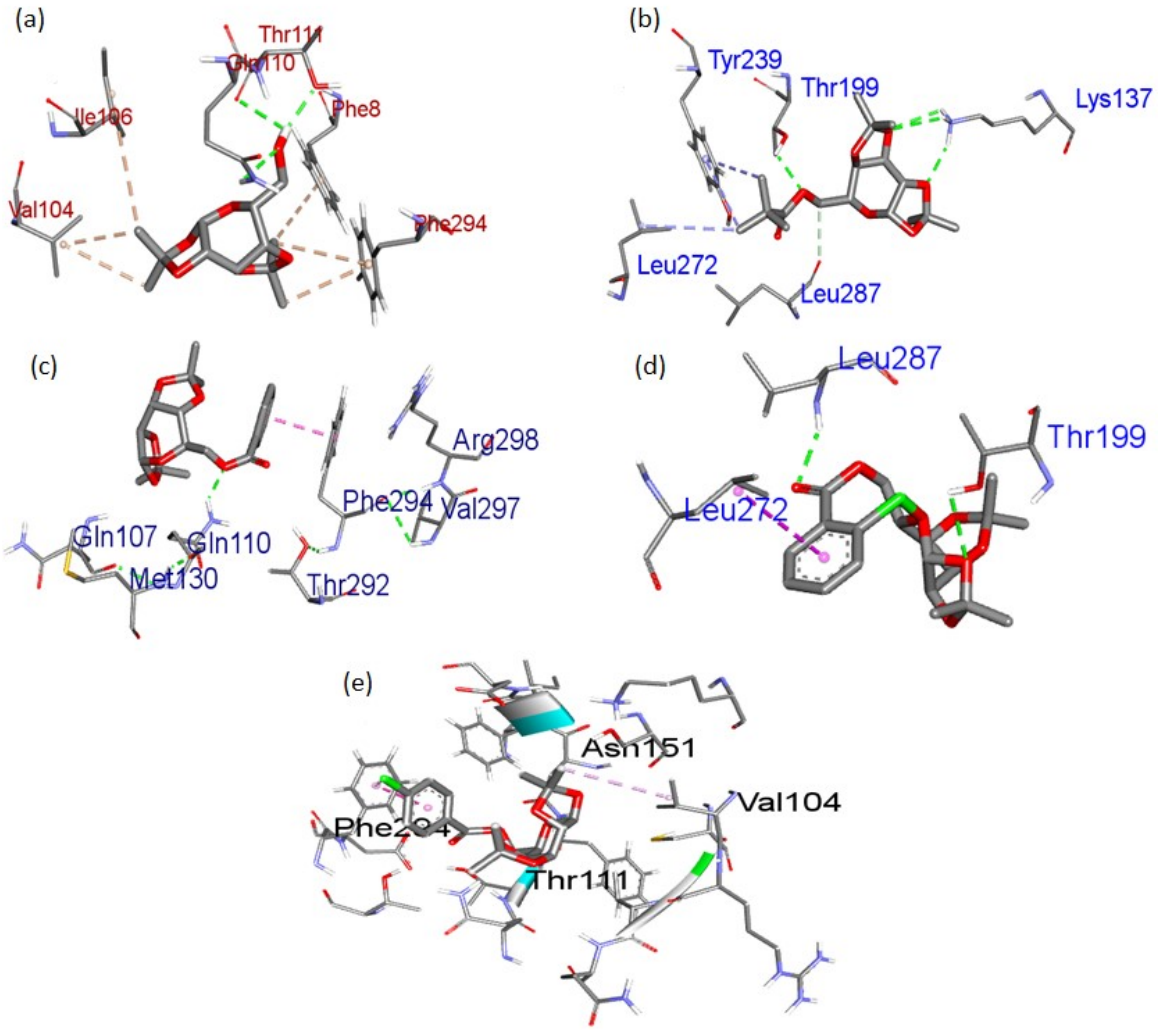

Figure 5. Non-bond interactions of 6LU7 with ligands - (*a*) **4**; (*b*) **5**; (*c*) **6**; (*d*) **7**; and (*e*) **8**.

Table 4. Interaction of compounds with amino acid (AA) residues in compounds-6LU7 complex.

Drug	Hydrogen bond		Hydrophobic bond		Van der Waals bond
	Interacting residue of amino acid	Distance (Å)	Interacting residue of amino acid	Distance (Å)	
4	GLN110 THR111 THR111	2.77255 2.60789 2.06335	VAL104 ILE106 VAL104 PHE8 PHE294 PHE294	3.8145 5.48623 4.04544 5.30905 4.34993 4.00344	Absent
5	LYS137 LYS137 LYS137 THR199 THR199 LEU287	2.8773 2.81353 2.15306 2.25645 2.89776 2.55337	LEU272 TYR239	 5.12811 5.11663	Absent
6	GLN110 THR111	2.01111 2.62796	PHE294 LEU272	3.74456 5.36564	Absent
7	THR199 LEU287 LEU287	2.88975 2.28916 2.84925	LEU272	5.36564	Absent
8	ASN151 SER158 THR111	2.77404 2.91259 2.13413	PHE294 VAL104 PHE294	3.73107 4.51593 5.00409	Absent
Azithromycin	ASP197	2.58858			Absent
HCQ	LYS137 TYR237 LEU287	2.03862 2.73424 3.58823	LEU287 TYR239 LEU272 LEU287	5.14494 5.2597 5.08956 5.4991	Absent
Remdesivir	THR199 LEU287 TYR237 ASP197 LEU287 TYR237	2.55616 2.29238 2.68334 2.15456 2.43253 2.83745	MET276 LEU286 LEU287 LEU272	4.3123 5.37822 4.4486 4.9742	Absent

Note: TRP = Tryptophan, ASP = Aspartic acid, GLU = Glutamic acid, LEU = Leucine, THR = Threonine, ASN = Asparagine, GLN = Glutamine, PHE = Phenylalanine, ILE = Isoleucine, ARG = Arginine, VAL = Valine, SER = Serine, PRO = Proline, GLY = Glycine, HIS = Histidine, LYS = Lysine, TRP = TRPosine, CYS = Cysteine, MET = Methionine.

4. Conclusion

Researchers found that administration of an antiviral drugs along with other protective measures (quarantine, isolation, etc.) allowed to control or decrease COVID-19 epidemic. While a limited number drugs are found effective to control the situation. More research and novel antiviral drugs are essential to control the COVID-19 situation. The present study clearly indicated that protected galactopyranose esters 5-8 have better binding effects with SARS-CoV-2 main proteases (7BQY and 6LU7). 2-Chlorobenzoate ester 7 possess better binding with both 7BQY and 6LU7 than the other esters (5-6, 8), non-ester galactopyranose 4, and standard drugs tested. For the efficient management of COVID-19 situation, more therapeutics that is effective is essential in addition to vaccine. The results present herein might help to establish carbohydrate-based antiviral drugs. However, more *in vitro* and *in vivo* analyses are necessary to establish these compounds as antiviral agents.

Conflicts of Interest

The authors declare that there are no conflicts of interest regarding the publication of this paper.

References

[1] Peng, Z., Xing-Lou, Y., Xian-Guang, W., Ben, H., Lei, Z., & Wei, Z. (2020). A pneumonia outbreak associated with a new coronavirus of probable bat origin. *Nature*, *579*(7798), 270–273. https://doi.org/10.1038/s41586-020-2012-7.

[2] Dhumad, A.M., Majeed, H.J., Harismah, K., & Zandi, H. (2021). In silico Approach on ribavirin inhibitors for COVID-19 main protease. *Bioint. Res. Appl. Chem*., *11(*6), 13924–13933. https://doi.org/10.33263/BRIAC116.1392413933

[3] Rout, J., Swain, B.C., & Tripathy, U. (2022) In silico investigation of spice molecules as potent inhibitor of SARS-CoV-2, Journal of Biomolecular Structure and Dynamics, *40*(2), 860–874, https://doi.org/10.1080/07391102.2020.1819879

[4] Rashdan, H.R.M, Abdelmonsef, A.H., Abou-Krisha, M.M., & Yousef, T.A. (2022). Synthesis and identification of novel potential thiadiazole based molecules containing 1,2,3-triazole moiety against COVID-19 main protease through structure-guided virtual screening approach. *Bioint. Res. Appl. Chem*., *12*(6), 8258–8270. https://doi.org/10.33263/BRIAC126.82588270

[5] Zhu, N., Zhang, D., Wang, W., Li, X., Yang, B., Song, J., et al. (2020). A novel Coronavirus from patients with pneumonia in China, 2019. *New Engl. J. Med.*, *382*, 727–733. https://doi.org/10.1056/NEJMoa2001017

[6] Prescott, H.C. (2021). Outcomes for patients following hospitalization for COVID-19. JAMA. *325(15)*, 1511–1512. https://doi.org/10.1001/jama.2021.3430

[7] Kordzadeh, A., & Saadatabadi, A.R. (2022). Effects of the temperature and the pH on the main protease of SARS-CoV-2: A molecular dynamics simulation study. *Bioint. Res. Appl. Chem*., *12*(6), 7239–7248. https://doi.org/10.33263/BRIAC126.72397248

[8] Zhang, L., Hou, J., Ma, F.Z. et al. (2021). The common risk factors for progression and mortality in COVID-19 patients: a meta-analysis. *Arch. Virol*., *166*, 2071–2087. https://doi.org/10.1007/s00705-021-05012-2

[9] Huang, C., Wang, Y., Li, X., Ren, L., Zhao, J., Hu, Y., et al. (2020). Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet*, *395*, 497–506. https://doi.org/10.1016/S0140-6736(20)30183-5

[10] Mehta, P., McAuley, D.F., Brown, M., Sanchez, E., Tattersall, R.S., Manson, J.J., et al. (2020).COVID-19: consider cytokine storm syndromes and immunosuppression. *Lancet*, *395*, 1033–1034. https://doi.org/10.1016/S0140-6736(20)30628-0

[11] Chen, C., Zhang, Y., Huang, J., Yin, P., Cheng, Z., Wu, J., Chen, S., Zhang, Y., Chen, B., Lu, M., Luo, Y., Ju, L., Zhang, J., & Wang, X. (2020). Favipiravir versus Arbidol for COVID-19: A randomized clinical

trial. *MedRxiv*. https://doi.org/10.1101/2020.03.17.20037432

[12] Md Nayeem, S., Sohail, E. M., Srihari, N. V., Indira, P., & Srinivasa Reddy, M. (2021). Target SARS-CoV-2: theoretical exploration on clinical suitability of certain drugs. *Journal of Biomolecular Structure and Dynamics*, 1-8. https://doi.org/10.1080/07391102.2021.1924262

[13] Hu, B., Guo, H., Zhou, P., & Shi, Z.-L. (2021). Characteristics of SARS-CoV-2 and COVID-19. *Nat. Rev. Microbiol.*, *19*, 141–154. https://doi.org/10.1038/s41579-020-00459-7

[14] Shah, A.S., Gribben, C., Bishop, J., Hanlon, P., Caldwell, D., Wood, R., Reid, M., McMenamin, J., Goldberg, D., Stockton, D., et al. (2021). Effect of vaccination on transmission of SARS-CoV-2. *New Engl. J. Med.*, *385*, 1718–1720. https://doi.org/10.1056/NEJMc2106757

[15] Tarighi, P., Eftekhari, S., Chizari, M., Sabernavaei, M., Jafari, D., & Mirzabeigi, P. (2021). A review of potential suggested drugs for coronavirus disease (COVID-19) treatment. *Eur. J. Pharmacol.*, *895*, 173890. https://doi.org/10.1016/j.ejphar.2021.173890

[16] Ghosh, R., Chakraborty, A., Biswas, A., & Chowdhuri, S. (2021). Evaluation of green tea polyphenols as novel corona virus (SARS CoV-2) main protease (Mpro) inhibitors – An in silico docking and molecular dynamics simulation study. Journal of Biomolecular Structure & Dynamics, *39*, 4362–4374. https://doi.org/10.1080/07391102.2020.1779818

[17] Fischer, W., Eron, J.J., Holman, W., Cohen, M.S., Fang, L., Szewczyk, L.J., Sheahan, T.P., Baric, R., Mollan, K.R., Wolfe, C.R., et al. (2021). Molnupiravir, an Oral Antiviral Treatment for COVID-19. *medRxiv*, https://doi.org/10.1101/2021.06.17.21258639

[18] Rothan, H.A., Stone, S., Natekar, J., Kumari, P., Arora, K., & Kumar, M. (2020). The FDA-approved gold drug auranofin inhibits novel coronavirus (SARS-COV-2) replication and attenuates inflammation in human cells. *Virology*, *547*, 7–11. https://doi.org/10.1016/j.virol.2020.05.002

[19] Cirri, D., Marzo, T., Tolbatov, I., Marrone, A., Saladini, F., Vicenti, I., Dragoni, F., Boccuto, A., & Messori, L. (2021). In vitro anti-SARS-CoV-2 activity of selected metal compounds and potential molecular basis for their actions based on computational study. *Biomolecules*, *11*, 1858. https://doi.org/10.3390/biom11121858

[20] Lee, Y.-K., Chang, W.-C., Prakash, E., Peng, Y.-J., Tu, Z.-J., Lin, C.-H., Hsu, P.-H., & Chang, C.-F. (2022). Carbohydrate Ligands for COVID-19 spike proteins. *Viruses*, *14*, 330. https://doi.org/10.3390/v14020330

[21] Kasthuri, M., Li, C., Verma, K., Russell, O.O., Dickson, L., McCormick, L., Bassit, L., Amblard, F., & Schinazi, R.F. (2020). Synthesis of 4'-substituted-2'-deoxy-2'-alpha-fluoro nucleoside analogs as potential antiviral agents. Molecules, *25*, 1258. https://doi.org/10.3390/molecules25061258

[22] Sari, O., Bassit, L., Gavegnano, C., McBrayer, T.R., McCormick, L., Cox, B., Coats, S.J., Amblard, F., & Schinazi, R.F. (2017). Synthesis and antiviral evaluation of 2',2',3',3'-tetrafluoro nucleoside analogs. Tetrahedron Lett., *58*, 642–644. https://doi.org/10.1016/j.tetlet.2017.01.006

[23] Schultz, D.C., Johnson, R.M., Ayyanathan, K. et al. (2022). Pyrimidine inhibitors synergize with nucleoside analogues to block SARS-CoV-2. Nature, *604*, 134–140. https://doi.org/10.1038/s41586-022-04482-x

[24] Zenchenko, A.A., Drenichev, M.S., Il'icheva, I.A., & Mikhailov, S.N. (2021). Antiviral and Antimicrobial Nucleoside Derivatives: Structural Features and Mechanisms of Action. Molecular Biology, *55*, 786–812. https://doi.org/10.1134/S0026893321040105

[25] Kabir, A.K.M.S., Matin, M.M., Mridha, M.A.U., & Shahed, S.M. (1998). Antifungal activities of some methyl 6-O-trityl-α-D-mannopyranosides, The Chittagong University Journal of Science, *22*(1), 41–46. ISSN: 1561-1167

[26] Matin, M.M., & Ibrahim, M. (2010). Synthesis of some methyl 4-O-octanoyl-α-L-rhamnopyranoside derivatives. Journal of Applied Sciences Research, *6*(10), 1527–1532. ISSN: 1816-157X

[27] Matin, M.M., & Chakraborty, P. (2020). Synthesis, spectral and DFT characterization, PASS predication, antimicrobial, and ADMET studies of some novel mannopyranoside esters. Journal of Applied Science & Process Engineering, *7*(2), 572–586. e-ISSN: 2289-7771

[28] Matin, M.M., Bhuiyan, M.M.H., Hossain, M.M., & Roshid M.H.O. (2015). Synthesis and comparative antibacterial studies of some benzylidene monosaccharide benzoates. Journal of the Turkish Chemical Society Section A: Chemistry, *2*(4), 12–21. e-ISSN: 2149-0120

[29] Rahman, M.A., Chakma, U., Kumer, A., Rahman, M.R., & Matin, M.M. (2023). Uridine-derived 4-aminophenyl 1-thioglucosides: DFT optimized FMO, ADME, and antiviral activities study. Biointerface Research in Applied Chemistry, *13*(1), 52.https://doi.org/10.33263/BRIAC131.052

[30] Kabir, A.K.M.S., Matin, M.M., & Kawsar, S.M.A. (1998). Synthesis and antibacterial activities of some uridine derivatives. The Chittagong University Journal of Science, *22*(1), 13–18. ISSN: 1561-1167

[31] Kabir, A.K.M.S., Matin, M.M., Sanaullah, A.F.M., Sattar, M.A., & Rahman, M.S. (2001). Antimicrobial activities of some lyxoside derivatives. Bangladesh Journal of Microbiology, *18*(1), 89–95. ISSN: 1011-9981

[32] Kabir, A.K.M.S., Matin, M.M., Bhuiyan, M.M.R., Rahim, M.A., & Rahman, M.S. (2005). Biological evaluation of some monosaccharide derivatives. International Journal of Agriculture & Biology, *7*(2), 218-221. ISSN: 1814-9596

[33] Hanee, U., Rahman, M.R., & Matin, M.M. (2021). Synthesis, PASS, in silico ADMET, and thermodynamic studies of some galactopyranoside esters. Physical Chemistry Research, *9*(4), 591-603. https://doi.org/10.22036/pcr.2021.282956.1911

[34] Siddikey, F., Roni, M.A.H., Kumer, A., Chakma, U., & Matin, M.M. (2022). Computational investigation of Betalain derivatives as natural inhibitor against food borne bacteria. Current Chemistry Letters, *11*(3), 309–320. http://dx.doi.org/10.5267/j.ccl.2022.3.003

[35] Rahman, M.A., Matin, M.M., Kumer, A., Chakma, U., & Rahman, M.R. (2022). Modified D-Glucofuranoses as New Black Fungus Protease Inhibitors: Computational Screening, Docking, Dynamics, and QSAR Study. Physical Chemistry Research, *10*(2), 195–209. https://doi.org/10.22036/pcr.2021.294078.1934

[36] Kumer, A., Chakma, U., & Matin, M.M. (2022). Bilastine based drugs as SARS-CoV-2 protease inhibitors: Molecular docking, dynamics, and ADMET related studies. Orbital: The Electronic Journal of Chemistry, *14*(1), 15–23. http://dx.doi.org/10.17807/orbital.v14i1.1642

[37] Zago, E., Joly, N., Chaveriat, L., Vincent Lequart, V., & Martin, P., (2021). Enzymatic synthesis of amphiphilic carbohydrate esters: Influence of physicochemical and biochemical parameters, *Biotechnology Reports*, *30*, e00631, https://doi.org/10.1016/j.btre.2021.e00631

[38] Kim, H. J., Kang, S. H., Choi, S. S., & Kim, E. S. (2017). Redesign of antifungal polyene glycosylation: engineered biosynthesis of disaccharide-modified NPP. *Applied Microbiology & Biotechnology*, *101*, 5131–5137. https://doi.org/10.1007/s00253-017-8303-8

[39] Kabir, A.K.M.S., & Matin, M.M. (1994). Regioselective acylation of a derivative of L-rhamnose using the dibutyltin oxide method. Journal of the Bangladesh Chemical Society, 7(1), 73–79. ISSN: 1022-016X

[40] Matin, M.M. (2008). Synthesis of D-glucose derived oxetane: 1,2-O-isopropylidene-4-(S)-3-O,4-C-methylene-5-O-methanesulfonyl-β-L-threo-pento-1,4-furanose. Journal of Applied Sciences Research, *4*(11), 1478–1482. ISSN: 1816-157X

[41] Kabir, A.K.M.S., Matin, M.M., Hossain, A., & Sattar, M.A. (2003). Synthesis and antimicrobial activities of some rhamno-pyranoside derivatives. Journal of the Bangladesh Chemical Society, *16*(2), 85–93. ISSN: 1022-016X

[42] Matin, M.M. (2006). Synthesis of some silyl protected 1,4-galactonolactone derivatives. Journal of Applied Sciences Research, 2(10), 753–756. ISSN: 1816-157X

[43] Kumbhar, P.S., Pandya, A.K., Manjappa, A.S., Disouza, J.I., & Patravale, V.B. (2021). Carbohydrates-based diagnosis, prophylaxis and treatment of infectious diseases: Special emphasis on COVID-19. Carbohydrate Polymer Technologies and Applications, *2*, 100052. https://doi.org/10.1016/j.carpta.2021.100052

[44] Islam, N, Islam, M.D., Rahman, M.R., & Matin, M.M. (2021). Octyl 6-O-hexanoyl-β-D-glucopyranosides: Synthesis, PASS, antibacterial, in silico ADMET, and DFT studies. Current Chemistry Letters, *10*(4), 413–

426. http://dx.doi.org/10.5267/j.ccl.2021.5.003

[45] Matin, M.M., Uzzaman, M., Chowdhury, S.A., & Bhuiyan, M.M.H. (2022). In vitro antimicrobial, physicochemical, pharmacokinetics, and molecular docking studies of benzoyl uridine esters against SARS-CoV-2 main protease. Journal of Biomolecular Structure and Dynamics, *40*(8), 3668-3680. https://doi.org/10.1080/07391102.2020.1850358

[46] Matin, P., Matin, M.M., Rahman, M.R., & Kumer, A. (2023). Synthesis, antifungal, and molecular docking studies of some new di-O-isopentanoyl glucopyranosides. Physical Chemistry Research, *11*(1), 149–157. https://doi.org/10.22036/PCR.2022.334577.2057

[47] Kumer, A., Chakma, U., Matin, M.M., Akash, S., Chando, A., & Howlader, D. (2021). The computational screening of inhibitor for black fungus and white fungus by D-glucofuranose derivatives using in silico and SAR study. Organic Communications, *14*(4), 305–322. https://doi.org/10.25135/agc.oc.116.2108.2188

[48] Matin, M. M., Bhuiyan, M. M. H., Debnath, D. C., & Manchur, M. A. (2013). Synthesis and comparative antimicrobial studies of some acylated D-glucofuranose and D-glucopyranose derivatives. International Journal of Biosciences, *3(*8), 279–287. http://dx.doi.org/10.12692/ijb/3.8.279-287

[49] Matin, P., Rahman, M.R., Huda, D., Bakri, M.K.B., Uddin, J., Yurkin, Y., Burko, A., Kuok, K.K., & Matin, M.M. (2022). Application of synthetic acyl glucopyranosides for white-rot and brown-rot fungal decay resistance in aspen and pine wood. *BioResources*, *17(*2), 3025–3041. https://doi.org/10.15376/biores.17.2.3025-3041

[50] James, A.A., Rahman, M.R., Huda, D., Aqlan, M.F.M., Matin, M.M., Bakri, M.K.B., Kuok, K.K., Rahman, M.M. (2022). Synthesis and characterization of novel nano-carbon mixture from Dabai (Canarium odontophyllum) nutshell. *BioResources*, *17*(3), 4452–4469. https://doi.org/10.15376/biores.17.3.4452-4469

[51] Khui, P.L.N., Rahman, M.R., Matin, M.M., & Bakri, M.K.B. (2022). Recycled Rubber Waste Plastic and its Composites. In: Recycled Plastic Biocomposites, Rahman, M.R. & Bakri, M.K.B. (Eds), 1st Ed, Woodhead Publishing/Elsevierpp 147–163. https://doi.org/10.1016/B978-0-323-88653-6.00014-6

[52] Matin, P., Hanee, U., Alam, M.S., Jeong, J.E., Matin, M.M., Rahman, M.R., Mahmud, S., Alshahrani, M.M., & Kim, B. (2022). Novel galactopyranoside esters: Synthesis, mechanism, in vitro antimicrobial evaluation and molecular docking studies. Molecules, *27*(13), 4125. https://doi.org/10.3390/molecules27134125

[53] Matin, M.M., & Azad, A.K.M.S. (2006). Synthesis of some protected 6-O-acyl-galactopyranose derivatives. Journal of Applied Sciences Research, *2*(12), 1199–1202. ISSN: 1816-157X

[54] Frisch, M. J., Trucks, G. W., Schlegel, H. B., Scuseria, G. E., Robb, M. A., et al. (2013). Gaussian 09W, Revision D.01. Gaussian, Inc., Wallingford CT.

[55] Lu, L., Hu, H., Hou, H., & Wang, B. (2013). An improved B3LYP method in the calculation of organic thermochemistry and reactivity. Computational and Theoretical Chemistry, *1015*, 64-71. https://doi.org/10.1016/j.comptc.2013.04.009.

[56] Veronika Temml, Zsofia Kutil, Z. (2021). Structure-based molecular modeling in SAR analysis and lead optimization. Computational and Structural Biotechnology Journal, *19*, 1431-1444. https://doi.org/10.1016/j.csbj.2021.02.018.

[57] Matin, M. M., Ibrahim, M., Anisa, T. R., & Rahman, M. R. (2022). Synthesis, characterization, in silico optimization, and conformational studies of methyl 4-O-palmitoyl-α-L-rhamnopyranosides. Malaysian Journal of Science, *41*(1), 91-105. https://doi.org/10.22452/mjs.vol41no1.6

[58] Torneri, A., Libin, P., Vanderlocht, J., Vandamme, A.-M., Neyts, J., & Hens, N. (2020). A prospect on the use of antiviral drugs to control local outbreaks of COVID-19. *BMC Medicine*, *18*(191). https://doi.org/10.1186/s12916-020-01636-4

[59] Matin, M. M., Bhuiyan, M. M. H., Kibria, S. M., & Hasan, M. S. (2022). Synthesis, PASS predication of antimicrobial activity and pharmacokinetic properties of hexanoyl galactopyranosides and experimental evaluation of their action against four human pathogenic bacteria and four fungal strains. *Pharmaceutical Chemistry Journal*, *56*(5), 627-637. https://doi.org/10.1007/s11094-022-02687-y

[60] Ristovski, J.T., Matin, M.M., Kong, R., Kusturica, M.P., Zhang, H. (2022). In vitro testing and

computational analysis of specific phytochemicals with antiviral activities considering their possible applications against COVID-19. *South African Journal of Botany*, 1–11. https://doi.org/10.1016/j.sajb.2022.02.009

[61] Narayanan, A., Narwal, M., Majowicz, S.A. et al. (2022). Identification of SARS-CoV-2 inhibitors targeting Mpro and PLpro using in-cell-protease assay. *Communications Biology*, *5*, 169. https://doi.org/10.1038/s42003-022-03090-9

[62] Niknam, Z., Jafari, A., Golchin, A., Pouya, F.D., Nemati, M., Rezaei-Tavirani, M., & Rasmi, Y. 2022). Potential therapeutic options for COVID-19: an update on current evidence. *Eur. J. Med. Res*., Vol.27, No.6. https://doi.org/10.1186/s40001-021-00626-3

[63] Mirtaleb, M.S., Mirtaleb, A.H., Nosrati, H., Heshmatnia, J., Falak, R., & Emameh, R.M. (2021). Potential therapeutic agents to COVID-19: An update review on antiviral therapy, immunotherapy, and cell therapy, *Biomedicine & Pharmacotherapy*, *138*, 111518. https://doi.org/10.1016/j.biopha.2021.111518