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SCREENING OF POTENTIAL LIGANDS FOR THE MAIN PROTEASE OF THE SARS-COV-2 CORONAVIRUS BY USING MOLECULAR DOCKING

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Abstract. An RNA virus from the Coronaviridae family, a subgroup of Coronavirinae, was first identified in late 2019 as the cause of severe acute respiratory infection in China.[1] Despite the fact that clinical guidelines have been developed for the treatment of a new coronavirus infection, there are currently no specific medicine of preventing and treating a new coronavirus infection.[2]

Various viral proteins are considered among drug targets, including: RNA-dependent RNA polymerase, papain-like protease, main protease and viral surface proteins (S-protein and TMPRSS2).[2] The main protease is a promising drug target because it is required for protein processing and viral replication.[2] In this study, molecular docking of 56 ligands with clinically proven inhibitory action against heterogeneous group of enzymes was carried out in order to study the possibility of inhibiting the main protease SARS-CoV-2 (PBD ID: 6LU7, resolution 2.16 Å). SARS coronavirus 3CL protease (PBD ID: 2GX4, resolution 1.93 Å) was selected as a control macromolecule. Molecular docking and assessment of binding sites were performed using AutoDock Tools 1.5.6 software. The results are shown in Table 1.

Table 1. Molecular docking results with SARS-CoV-2 major protease

Strong binding energy, small cluster sizes		Weak binding energy, large cluster sizes	
Ligand's INN	Binding E, kkal/mol; number of conformations in the largest cluster	Ligand's INN	E связывания, ккал/моль; number of conformations in the largest cluster
Caspofungin	-15,31; 2	Isophlurophate	-4,09; 23
Saquinavir	-14,14; 4	Riamilovir	-6,02; 70
Nelfinavir	-13,33; 5	Captopril	-6,31; 15
Indinavir	-12,76; 2	Mefloquine	-6,90; 37
Remikiren	-13,67; 2	Ribavirin	-8,01; 12

Thus, the best potential medical drugs – coronavirus's protease inhibitors among compounds explored may be heterogenic group molecules (antiviral agents, indirect anticoagulants, as well as mammal enzymes blockers). In prospect, it is planned to elicit common characteristics of viral enzyme's best inhibitors.

References

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2. Pharmacological therapeutics targeting RNA-dependent RNA polymerase, proteinase and spike protein: from mechanistic studies to clinical trials for COVID-19 / Huang J., Song W., Huang H. [et al.] // Journal of clinical medicine. – 2020. Vol. 9.