Consensus docking and molecular dynamic for discovery of potential inhibitors of SARS-CoV-2 main protease

Roman S. Tumskiy\textsuperscript{1,*}, Anastasiia V. Tumskaia\textsuperscript{2}

\textsuperscript{1}Institute of Biochemistry and Physiology of Plants and Microorganisms (IBPPM RAS), Russian Academy of Sciences, 13 Prospekt Entuziastov, Saratov 410049, Russia
\textsuperscript{2}Chemistry Institute, Saratov State University, 83 Astrakhanskaya, Saratov 410012, Russia
E-mail: tumskiy_r@ibppm.ru

The X-Ray crystal structures of 3C-chymotrypsin-like protease for SARS-CoV (PDB ID: 3V3M) and SARS-CoV-2 (PDB ID: 7L0D) have been taken from the Protein Data Bank at 1.96 and 2.39 Å resolutions, respectively.

Conclusion

For the first time, multistep computer-aided molecular design with consensus docking were performed for discovery of novel possible SARS-CoV and SARS-CoV-2 3CLpro inhibitors among azachalcones derivatives (150 compound) by using multistep computer-aided molecular design with consensus docking.

Based on multistep rational design, several ligand libraries were created by using classical and non-classical bioisosteric replacements. After consensus docking of these libraries, the 18 new possible 3CLpro inhibitors were identified. By the molecular dynamic simulations data, complexes of 3CLpro with the most prospective novel inhibitors (compounds 84, 113 and 146) are well stable and have the acceptable ligand-inducing changes in the protein structure.