THEORETICAL AND EXPERIMENTAL EVALUATION OF THE ANTIVIRAL ACTIVITY OF ORGANIC ACIDS SPECTRUM AGAINST INFECTIOUS BRONCHITIS VIRUS

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The new betacoronavirus SARS-CoV-2 caused COVID-19 and the fifth pandemic of respiratory disease after the 1918 flu pandemic. There is an urgent need to find new antiviral drugs against respiratory coronaviruses but also to study the antiviral effect of well-known substances to identify new therapeutic approaches for people with COVID-19. An expanded search for new, effective antiviral drugs against coronaviruses is needed using both *in silico* and subsequent *in vitro* studies. The aim of this study was theoretical *in silico* and *in vitro* evaluation of the antiviral activity of several well-known organic acids against infectious bronchitis virus (IBV), the prototype strain of the *Coronaviridae* family.

The cytotoxic effect of organic acids was evaluated on a monolayer of cell culture BHK-21. Cultivation, accumulation, and determination of the infectious titer of IBV by cytopathic action were performed using cell cultures of chicken embryo fibroblasts and BHK-21. The antiviral effect of a substance was assessed by measuring its chemotherapeutic index. Possible mechanism of antiviral activity of a number of aminocarboxylic acids was studied with the use of molecular docking of the "protein-ligand" interaction with the "key-lock" modeling type. The spike protein and main protease of IBV were chosen as targets for modeling in .pdb format (Protein Data Bank). The structures of the ligands: 4-aminobutyl, 5-aminovaleric, 6-aminocaproic, 7-aminoheptanoic, 8-aminooctanoic acids, as well as methyl-6-aminohexonate were taken in .sdf format from Pubchem, and subsequently converted into 3d structures in .pdb using Avogadro® and Discovery Studio 3.5®. Results were visualized using AutoDock 4.2.6, PyMol® and Protein-Ligand Interaction Profiler®.

This study’s results, performed *in vitro*, showed that effective inhibition of virus reproduction in preventive and treatment regimens indicated that 4-aminobutyric acid and 6-aminocaproic acid affect the early stages of coronavirus reproduction. The results of molecular docking showed that the best binding of the amino acid to the spike protein was shown for 4-aminobutylic acid; however, 6-aminocaproic acid showed good binding energy with the main protease. In general, the binding energy of amino acids with the main protease was higher than with the spike protein, which can be explained by the complex structure of the spike protein and, probably, by another mechanism of its inhibition and should be explored in the future work.