POLYPHENOLS AS POTENTIAL INHIBITORS OF SARS-COV-2 CORONAVIRUS: AN *IN SILICO* STUDY

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Relevance. Currently, the search for antiviral substances is carried out in two ways: 1. Repurposing existing and screening newly synthesized compounds. 2. Targeted search for natural biologically active substances, in most cases, using computer modeling. The main disadvantage of all currently used drugs is their fairly high toxicity and, as a consequence, the presence of side effects. In the development of new drugs for the treatment of COVID-19, polyphenolic compounds are of particular interest. Studies conducted by scientists from different countries have shown that plant polyphenols are promising polyfunctional compounds with great potential as active ingredients for the creation of new pharmaceutical substances with antiviral activity.

Considering the importance of early screening of bioactive compounds for potential drug discovery or prevention of viral infections, **the aim of this study** was to conduct a virtual screening of polyphenols for the potential to inhibit vital proteins of SARS CoV-2 coronavirus using a molecular docking method.

Materials and methods: In silico molecular screening of several SARS-CoV-2 non-structural proteins and natural polyphenolic compounds was performed using the molecular docking method. The structures of SARS-CoV-2 proteins: ADP-binding domain NSP3, main protease NSP5, RNA-dependent RNA polymerase NSP12, endoribonuclease NSP15 were obtained from the Protein Data Bank (PDB). The structures of 15 polyphenols of different groups isolated from Euphorbia ferganensis B.Fedtsch. and plants were identified by LC-MS, with interpretation of mass spectra, compared with those reported in the literature. The following public databases were used in the identification process: Chemical Entities of Biological Interest (ChEBI, https://www.ebi.ac.uk/chebi/), Chemical Compounds Deep Data Source (https://www.molinstincts.com/), ChemSpider (www.chemspider.com) and Phenol_Explorer (www.phenol-explorer.eu).

Results: The interactions of 15 gallic acid derivatives and 7 tannins with DNA-dependent RNA polymerase, NSP5, NSP12, and NSP6 enzymes were studied. As part of the analysis, the localization in the enzyme active site, the nature of interactions (hydrogen bonds, hydrophobic contacts, π-π stacking, etc.), and the amino acid residues involved in the binding were determined for each compound. In addition, the binding affinity values were calculated, which made it possible to quantitatively evaluate the strength and stability of the ligand-target complexes. According to the analysis results, hepta-galloyl-glucose, gallic acid, and protocatechuic acid showed high affinity for the NSP12 and NSP16 proteins of the SARS-CoV-2 virus. This allows us to recommend these compounds as potential inhibitors against the virus for further in vitro and in vivo studies. Based on the data obtained, the most promising compounds with a pronounced ability to inhibit the activity of DNA-dependent RNA polymerase are selected.

Conclusions: Hepta-galloyl-glucose, gallic acid and protocatechuic acid are considered as potential candidates for subsequent verification of antiviral activity in vitro and in vivo experiments. This approach represents an important step in the development of new natural antiviral drugs.