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Triazavirin – as a potential coronovirus M protease inhibitor 2019-nCoV

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In 2019, a novel Coronavirus 2019-nCoV was found to cause Severe Acute Respiratory symptoms and rapid pandemic in China, France, United States of America, Germany, Italy, Japan, Russia. In order to find candidate drugs for 2019-nCoV. We have carried out a computational study to screen for effective available drug Triazavirin which may work as inhibitor for the Mpro of 2019-nCoV.

The quantum chemical calculations have performed for the most stable conformation and optimized the using the Density Functional Theory

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(DFT/B3LYP) method with MidiX basis sets by the Gaussian 09W program package on a Pentium IV/4.28 GHz personal computer.

Triazavirin is an antiviral drug synthesized in Russia through a joint effort of Ural Federal University, Russian Academy of Sciences, Ural Center for Biopharma Technologies and Medsintez Pharmaceutical.

Triazavirin (TZV) is a synthetic analogue of the bases of purine nucleosides (guanine). It belongs to azoloazines – heterocyclic compounds structurally resembling the nitrogenous bases. Research on azoloazines began at the UPI in 1993.

Triazavirin has a wide spectrum of antiviral action and effectively inhibits not only many epidemic strains of influenza viruses type A such as H1N1 (swine flu), H3N2, H5N1 (avian influenza), H5N2, H7N3, H9N2, including the pandemic strain H1N1 pdm 2009, but also influenza viruses Type B. TZV has also been found to have antiviral activity against a number of other viruses including Tick-borne encephalitis virus, Forest-Spring Encephalitis virus and is also being investigated for potential application against the Coronavirus 2019-nCoV. The efficiency index of Triazavirin in animal experiments for influenza viruses Types A and B is 65–85%. The effectiveness of the drug against fever of Rift Valley, West Nile, tick-borne encephalitis and other dangerous infections has been established.

Clinical trials have confirmed the high therapeutic effect of Triazavirin; it was registered by the Ministry of Health of the Russian Federation as a medicament for the treatment of the influenza virus (registration certificate LP-002604).

The study of the crystal structure of the drug gives an idea about a set of spatial and electronic features that can be used in the search for responsible biological targets and molecular modeling of new useful compounds. The molecular docking approach used to model the interaction between a small molecule and a protein at the atomic level, which allow us to characterize the behavior of small molecules in the binding site of target proteins as well as to elucidate fundamental biochemical processes.

We have used Time Dependent Density Functional Theory (TD-DFT) for calculation of the electronic transitions of the lowest energy conformation of the title compound. The electronic properties such as EHOMO, ELUMO, HOMO-LUMO energy gap, dipole moment (μD), point group, Mulliken atomic charges, and natural charge of the title structure were calculated. The optimized molecular structures, molecular electrostatic potential (MEP) surface, HOMO and LUMO surfaces were visualized using GaussView 05 program. Interaction between structures of Coronavirus 2019-nCoV and Triazavirin has been investigated by HyperChem Profes-

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sional 08, PyMOL and Molegro Molecular Viewer software programs. The protein sequences of 2019-nCoV was downloaded from GenBank.