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Details of the Collaborative Activity

2020-21

Name of the Collaborating Institute: Department of Zoology, Central University of Jammu, Jammu & Kashmir, India

Name of the Collaborating Department: Yenepoya Research Center

Joint Research Publication

1. Yadav R, Parihar RD, Dhiman, U, Dhamija P, Upadhyay SK, Imran M, **Behera SK, Prasad TSK.** Docking of FDA Approved Drugs Targeting NSP-16, N-Protein and Main Protease of SARS-CoV-2 as Dual Inhibitors. *Biointerface Research in Applied Chemistry*. 2021; 11(3): 9848 - 61

ATTESTED

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Biointerface Research in Applied Chemistry
Platinum Open Access Journal (ISSN: 2069-5837)

Article
Volume 11, Issue 3, 2021, 9848 - 9861
https://doi.org/10.33263/BRIAC113.98489861

Docking of FDA Approved Drugs Targeting NSP-16, N-Protein and Main Protease of SARS-CoV-2 as Dual Inhibitors

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Received: 2.09.2020; Revised: 19.09.2020; Accepted: 20.09.2020; Published: 22.09.2020

Abstract: At present world is lurching under the spread of new SARS-CoV-2 infection. The treatment is still elusive despite the relentless effort by the scientists against various viral structures. Whereas the 3-Chymotrypsin-like proteases cleave polyproteins and structural proteins help in viral replication. At the same time, non-structural proteins stimulate mRNA cap methylation to evade the immune response. The present study aims to identify novel dual inhibitor compounds with potential hits simultaneously against any of these three targets, including 3C-like proteases, N-protein, and NSP16 through virtual screening, molecular docking approach, and molecular dynamics. Such dual inhibitors may provide the necessary treatment to alleviate the current pandemic. We screened 265 FDA approved infectious disease drugs against three types of Covid-19 targets, i.e., 3C-like proteinase (6w63), N-protein (6vyo), and Non-structural protein 16 (6w4h) using a computer-assisted drug repurposing approach in this study. The Schrodinger suite 2019 is employed for high throughput screening, molecular docking, and binding free energy through the Glide module. We sorted 27 drugs, out of which the best common three drugs were suggested based on their virtual statistics parameters. We found three drugs that belonged to two main categories as dual inhibitors. The Plazomicin (Aminoglycoside) and Cefiderocol (Cephalosporins) are an antibiotic group of drugs, and the Vanganciclovir is antiviral. The molecular dynamics simulation studies over 30000ps for Plazomicin against NSP16 was conducted based on their promising docking scores profile. The RMSD parameter remained stable at 2.5Å for ligands for 30000ps. Thus these three compounds can be validated as a SARS-CoV-2 therapy through clinical trials.

Keywords: SARS-CoV-2; dual inhibitors; NSP-16; main protease; COVID-19.
Abbreviations: CoV: Coronavirus; MERS: Middle East Respiratory Syndrome; SARS: Severe Acute Respiratory Syndrome; MD: Molecular Dynamics; COVID–19: Coronavirus Disease 2019; RNA: Ribonucleic acid; PDB: Protein Data Bank; HTVS: High throughput virtual screening; FDA: Food and Drug Administration; WHO: World Health Organization; NSP: Non-Structural Proteins; 3CP: 3' Chymotrypsin-like protease.

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