Targeting SARS-COV-2 non-structural protein 16: a virtual drug repurposing study

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Non-Structural Protein 16 (nsp-16), a viral RNA methyltransferase (MTase), is one of the highly viable targets for drug discovery of coronaviruses including SARS-CoV-2. In this study, drug discovery of SARS-CoV-2 nsp-16 has been performed by a virtual drug repurposing approach. First, drug shape-based screening (among FDA approved drugs) with a known template of MTase inhibitor, sinefungin was done and best compounds with high similarity scores were selected. In addition to the selected compounds, 4 nucleoside analogs of anti-viral (Raltgravir, Maraviroc and Favipiravir) and anti-inflammatory (Prednisolone) drugs were selected for further investigations. Then, binding energies and interaction modes were found by molecular docking approaches and compouds with lower energy were selected for further investigation. After that, Molecular dynamics (MD) simulation was carried to test the potential selected compounds in a realistic environment. The results showed that Raltegravir and Maraviroc among other compounds can bind strongly to the active site of the protein compared to sinefungin, and can be potential candidates to inhibit NSP-16. Also, the MD simulation results suggested that the Maraviroc and Raltegravir are more effective drug candidates than Sinefungin for inhibiting the enzyme. It is concluded that Raltegravir and Maraviroc which may be used in the treatment of COVID-19 after Invitro and invivo studies and clinical trial for final confirmation of drug effectiveness.

Keywords: SARS-CoV-2, Drug repurposing, Molecular docking, Molecular dynamics simulation