Identification of pyrazole derivatives of Usnic Acid as Novel Inhibitor of SARS-CoV-2 main protease through virtual screening approaches

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ABSTRACT

The infection produced by the SARS-CoV-2 virus remains a significant health crisis worldwide. The lack of specific medications for COVID-19 necessitates a concerted effort to find the much-desired therapies for this condition. The main protease (M^{pro}) of SARS-CoV-2 is a promising target, vital for virus replication and transcription. In this study, fifty pyrazole derivatives were tested for their pharmacokinetics and drugability, resulting in eight hit compounds. Subsequent molecular docking simulations on SARS-CoV-2 main protease afforded two lead compounds with strong affinity at the active site. Additionally, the molecular dynamics (MD) simulations of lead compounds (17 and 39), along with binding free energy calculations, were accomplished to validate the stability of the docked complexes and the binding poses achieved in docking experiments. Based on these findings, compound 17 and 39, with their favorable projected pharmacokinetics and pharmacological characteristics, are the proposed potential antiviral candidates which require further investigation to be used as anti-SARS-CoV-2 medication.

KEYWORDS

ADMET; Docking; Drug-likeness; Molecular dynamics simulation; Pyrazole derivatives of Usnic acid; SARS-CoV-2

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