Deciphering Inhibitory Activity of Natural Compound Against SARS-Cov-2 Main Protease of Omicron Variant (B.1.1.529): By Using Molecular Docking and Molecular Dynamics Simulations study.

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**Abstract**

A pandemic of coronavirus disease-19 (COVID-19) brought on by the novel corona virus (nCoV) has resulted in a disaster for global health. Following that, mutations in COVID-19 have made treating and preventing SARS-COV-2 extremely difficult. The primary characteristics of mutations are the generation of novel variants with high tensile strength, disruption of viral fitness, and acceleration of virus reproduction. The Delta variant (B.1.617.2), which was initially discovered in India, is one of the varieties that have lately come to light. A more vicious mutant, also known as omicron (B.1.1.529), first appeared in South Africa in November 2021. In this study, we applied a computational approach for identifying new corona virus-targeted antiviral drugs from natural compounds as potential SARS-CoV-2 Main protease (SARS-CoV-2 Mpro) inhibitors. SARS-CoV-2 Mpro a novel corona virus major protease enzyme is a target for drug discovery since it plays a significant role in the spread of the corona virus infection.

Molecular docking study done by using AutoDock-4.2. Top hits based on their highest binding affinity were analysed. Carnosol interacted strongly and stably with the amino acid residues found on the SARS-CoV-2 Mpro active site, with the highest binding affinity (-8.85 Kcal/mol). Arjunglucoside-I (-8.25 Kcal/mol) and Rosmanol (-8.12 Kcal/mol) additionally showed strong and stable affinity for binding along with having optimistic ADME characteristics. These natural compounds exhibit significant hydrogen-bonding interactions with the SARS-CoV-2 Mpro active site residue in Molecular Dynamics simulations (MDS) for 50 ns and are stable inside the active site. These chemical compounds may be employed as possible inhibitors against SARS-CoV-2 Mpro, according to our virtual screening results, which may also have an antiviral effect against omicron. To assert that these inhibitors of the SARS-CoV-2 main protease are appropriate for further validation and investigation and clinical trials are required.

**Keywords:** Omicron variant (B.1.1.529), SARS-CoV-2 Mpro, ADME, AutoDock-4.2, MDS.