Investigating the Therapeutic Potential of Epigallocatechin Gallate and Theaflavin-3, 3'-digallate on Inhibiting ACE2-Spike Protein Binding and Mitigating Induced-Cellular Death by SARS-CoV-2

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As of April 2022, there have been 500 million cases and 6.18 million deaths from COVID-19 worldwide. Current treatments are limited, thus necessitating the development of an effective therapeutic to combat infection and cell death. Epigallocatechingallate (EGCG) and Theaflavin-3,3'-digallate (TF3), catechins found in tea, have been recognized by biochemists for their antiviral properties. The COVID-19 spike protein binds to human angiotensin-converting enzyme-2 (ACE2) cell-surface receptors, thus making it a target for potential preventative treatments. The primary objectives of this study were to investigate the abilities of EGCG and TF3 to prevent spike receptor-binding-domain (RBD)-ACE2 binding and to improve metabolic activity in infected cells. Molecular docking identified binding affinities of ligands with the ACE2-receptor and spike-RBDs of COVID-19 variants. Cell survival, attachment, and caspase-3 assays were conducted with EGCG and TF3 to measure changes in cell viability and spike-RBD attachment in human U937 monocytic and SW1573 lung cells; both present ACE2-receptors on their surface. Results showed that EGCG and TF3 displayed the highest binding affinities amongst tested ligands to ACE2 and spike proteins. 50 µM EGCG and 5 µM TF3 significantly decreased cellular attachment mediated by the spike protein (p-value<.01), suggesting abilities to prevent infection. 5 µM EGCG/TF3 treatments increased cellular viability and decreased caspase-3 activity significantly, suggesting therapeutic effects in infected cells (p-value<.05). These results suggest EGCG and TF3 as preventative threapeutics for the SARS-CoV-2 virus. Future clinical studies involving ingestion of these compounds should be conducted to determine viability of treatment in-vivo.

Awards Won: Fourth Award of \$500