

Title: Phytoconstituents of Citrus limon (Lemon) as Potential Inhibitors Against Multi Targets of SARS-CoV-2 by Use of Molecular Modelling and In Vitro Determination Approaches

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Abstract: In the present work, phytoconstituents from Citrus limon are computationally tested against SARS-CoV-2 target protein such as Mpro - (5R82.pdb), Spike - (6YZ5.pdb) & RdRp - (7BTF.pdb) for COVID-19. Docking was done by glide model, QikProp was performed by in silico ADMET screening & Prime MM-GB/SA modules were used to define binding energy. When compared with approved COVID-19 drugs such as Remdesivir, Ritonavir, Lopinavir, and Hydroxychloroquine, plant-based constituents such as Quercetin, Rutoside, Naringin, Eriocitrin, and Hesperidin. bind with significant G-scores to the active SARS-CoV-2 place. The constituents Rutoside and Eriocitrin were studied in each MD simulation in 100 ns against 3 proteins 5R82.pdb, 6YZ5.pdb and 7BTF.pdb. We performed an assay with significant natural compounds from contacts and in silico results (Rutin, Eriocitrin, Naringin, Hesperidin) using 3CL protease assay kit (B.11529 Omicron variant). This kit contained 3CL inhibitor GC376 as Control. The IC₅₀ value of the test compound was found to be Rutin –17.50 μ M, Eriocitrin–37.91 μ M, Naringin–39.58 μ M, Hesperidine–140.20 μ M, the standard inhibitory concentration of GC376 was 38.64 μ M. The phytoconstituents showed important interactions with SARS-CoV-2 targets, and potential modifications could be beneficial for future development.

Keywords: Eriocitrin, Naringin, Hesperidin, Molecular dynamics (MD) simulation, Molecular docking, ADMET (QikProp)

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