In Silico Quest: Gymnema sylvestre's Chemical Arsenal Against Influenza a Virus Neuraminidase

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Influenza (flu) is a highly contagious respiratory illness that poses a significant global health threat. Frequent mutations in the influenza A virus (IAV) often reduce the effectiveness of antiviral drugs, highlighting the urgent need for new therapeutic agents. *Gymnema sylvestre*, a medicinal plant from the *Apocynaceae* family, found in Asia, Africa, and Australia, has been used in Ayurvedic and traditional medicine to treat hyperglycemia. This plant contains various phytochemicals with known anticancer, antioxidant, antiviral, anti-inflammatory, hepatoprotective, glucose-lowering, and lipid-lowering properties. In this study, we conducted an *in silico* analysis of compounds derived from *Gymnema sylvestre* against IAV neuraminidase (NA) (PDB: 3TI6). NA is crucial for the propagation and dissemination of the IAV within the host, making it a key target for antiviral drugs. From a comprehensive literature search, we identified 36 natural compounds and evaluated their absorption, distribution, metabolism, and excretion (ADME) properties using SwissADME. Following Lipinski's rule of five, we identified 19 compounds as potentially safe drug candidates. Virtual screenings of these selected compounds in 3D SDF form were conducted using PyRx 8.0, and those with a binding affinity greater than -5 kcal/mol underwent further blind docking using CB-Dock2. The results revealed four compounds—cedrane-v6, squalene, stigmasterol, and lupeol—showed higher binding affinities (-6.9, -7.1, -7.9, and -8.0 kcal/mol, respectively) to IAV NA compared to oseltamivir (-6.6 kcal/mol), a known NA inhibitor (PubChem: 65028). These compounds effectively interacted with key amino acids in the active site of IAV NA, potentially inhibiting the enzyme's function and blocking the release of viral progeny. Our findings suggest that these four compounds from *Gymnema sylvestre* could serve as effective IAV NA inhibitors. However, further *in vitro* and *in vivo* studies are needed to validate their pharmaceutical potential and protective effects against influenza.

Keywords: In Silico, Influenza, Gymnema Sylvestre, Swissadme, Neuraminidase

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