Computational Insights into the Antiviral Potential of Longispinogenin and Sitakisogenin Against African Swine Fever Virus DNA Ligase

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African swine fever virus (ASFV) is a highly contagious and deadly virus that spreads rapidly among pigs. Recent studies have identified a few antiviral agents that can inhibit ASFV infections. However, there are currently no commercial vaccines or antiviral drugs available, highlighting the urgent need for new treatments. In this study, we conducted an *in silico* analysis of compounds derived from *Gymnema sylvestre*, a widely used herb in traditional and Ayurvedic medicine, against African Swine Fever Virus DNA Ligase (ASFVLig). ASFVLig is involved in the base excision repair (BER) process, which maintains the integrity of the viral genome during infection. We performed a comprehensive electronic search for natural compounds in *Gymnema sylvestre* using the SCOPUS, PubMed, EMBASE, Elsevier, Web of Science, ResearchGate, ScienceDirect, Google, and Google Scholar databases for studies published before April 2024. In the search, we collected 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 selected compounds in 3D SDF form were run 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 quercetin, citronellyl formate, conduritol A, gymnemanol, isophytol, longispinogenin, lupeol, nerolidol, n-hexanoic acid, paraben, stigmasterol, sitakisogenin, and squalene as potential inhibitors of ASFVLig. Notably, longispinogenin and sitakisogenin exhibited the highest potential, with a binding affinity of -7.4 kcal/mol and the ability to bind with all four amino acids Asn 153, Leu 211, Leu 402, and Gln 403 in the active site of ASFVLig. Taken together, we recommend further *in vitro* and *in vivo* investigations to confirm the effectiveness of these compounds as antiviral drugs in our fight against ASFV.

Keywords: African Swine Fever Virus, Gymnema sylvestre, ASFVLig, Antiviral, In silico

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