IN SILICO ANALYSIS OF VARIOUS FUNGAL SECONDARY METABOLITES AND ANTIRETROVIRAL DRUGS ON ITS MOLECULAR BINDING TO NIPAH VIRUS PROTEINS INVOLVED IN CELLULAR ATTACHMENT, FUSION, AND REPLICATION

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Nipah virus (NiV) is a biosafety level 4 (BSL-4) pathogen that causes extreme respiratory illness and encephalitis among infected patients.

- It is an *enveloped virus* containing a single layer of surface protrusions.
- NiV genome contains *six transcription units* that encodes the main structural proteins of the virus.

**ZOONOTIC**

**NO VACCINE AVAILABLE**

**HIGH PRIORITY PATHOGEN**

*Epstein et. al, 2022; CDC, 2020; WHO, 2018, Tigabu et. al, 2014*
The virus mainly enters cells through the fusion of the virus' cell membrane on the hosts' plasma membrane.

- The F and G proteins work in high coordination allowing the viral entry of the virus.
- The P protein is responsible for the viral replication of the nipah virus.
METHODOLOGY

Target Protein Preparation
- Glycoprotein
- Fusion Protein
- Phosphoprotein

Molecular Docking Simulation
- The three-dimensional molecular structure of the target proteins is added to the docking platform as PDB formats

Ligand Selection and Preparation
- 49 Fungal secondary metabolites
- 14 antiretroviral drugs

Post-Dock Analysis
- The docking poses with the prime affinity represent the set and are subjected to the post-dock analysis

Highest affinity protein-ligand complexes
RESULTS

Alkaloids norquinadoline A and quinadoline B, and polyketide isochaetochromin D1 showed the highest binding affinity on the glycoprotein G, fusion protein F, and phosphoprotein P of NiV.
RESULTS

QUINADOLINE B

- Fumiquinazoline alkaloid previously reported to have anti-influenza (H1N1) properties.

<table>
<thead>
<tr>
<th>Target Viral Protein</th>
<th>Ligand Against NiV Viral Proteins</th>
<th>Binding Energy (kcal/mol)</th>
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</thead>
<tbody>
<tr>
<td>Fusion Protein</td>
<td>Quinadoline B</td>
<td>-10.4</td>
</tr>
<tr>
<td>Phosphoprotein P</td>
<td>Quinadoline B</td>
<td>-9.1</td>
</tr>
</tbody>
</table>

(Quimque et al., 2020)
Docked pose of quinadoline B against fusion protein F of NiV showing molecular interactions on (A) molecular surface and (B) 2D representation.
Docked pose of quinadoline B against phosphoprotein P of NiV showing molecular interactions on (A) molecular surface and (B) 2D representation.
CONCLUSION

- Fungal-derived secondary metabolites yielded the highest binding energy scores on the glycoprotein, fusion protein, and phosphoprotein of NiV involved in cellular attachment, fusion, and replication.

- Quinadoline B showed multi-target characteristics due to its favorable binding scores with proteins F and P

- strong favorable binding interactions are predominantly charged and hydrophobic interactions conferring stable protein-ligand complexes.

- It is recommended to explore the application of the top-ranked ligands about their antiviral activity against NiV in vitro.
REFERENCES


THANK YOU!