XXIX Symposium on Bioinformatics and Computer-Aided Drug Discovery

Polytechnic University of the Philippines
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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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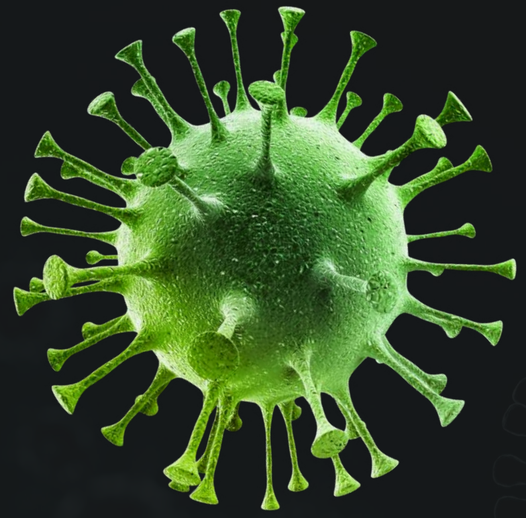
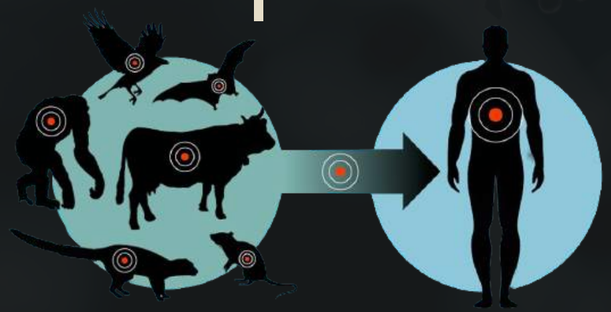
NIPAH VIRUS

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



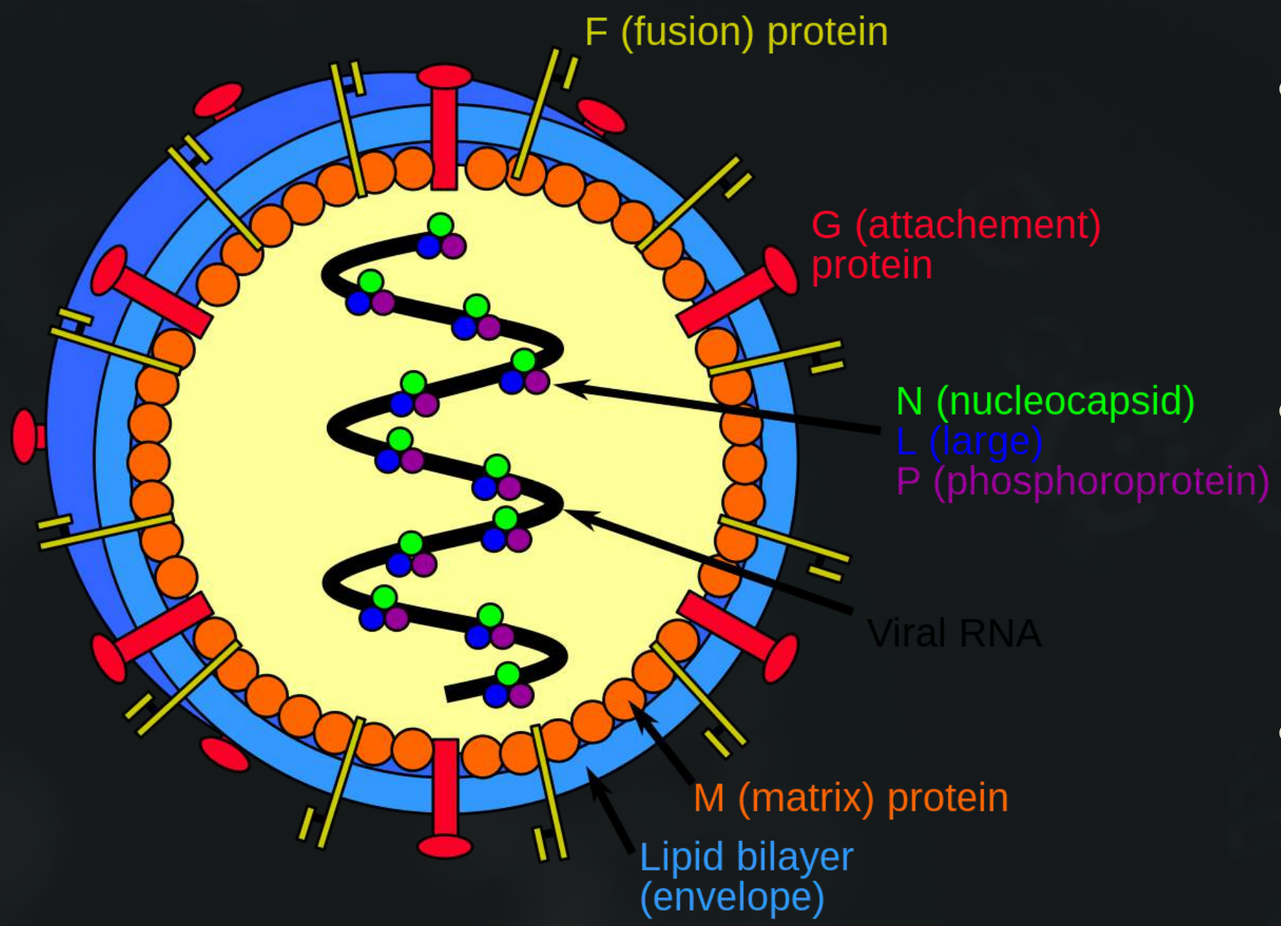
ZOONOTIC

NO VACCINE AVAILABLE

HIGH PRIORITY PATHOGEN

(Epstein et. al, 2022; CDC, 2020; WHO, 2018, Tigabu et. al, 2014)

NIPAH VIRUS–STRUCTURAL CHARACTERISTICS



- The virus mainly enters cells through the fusion of the virus' cell membrane on the hosts' plasma membrane.
- The **F and G proteins** works 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

1

- Glycoprotein
- Fusion Protein
- Phosphoprotein

National Center for Biotechnology Information

Ligand Selection and Preparation

2

- 49 Fungal secondary metabolites
- 14 antiretroviral drugs

Molecular Docking Simulation

3

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

Post-Dock Analysis

4

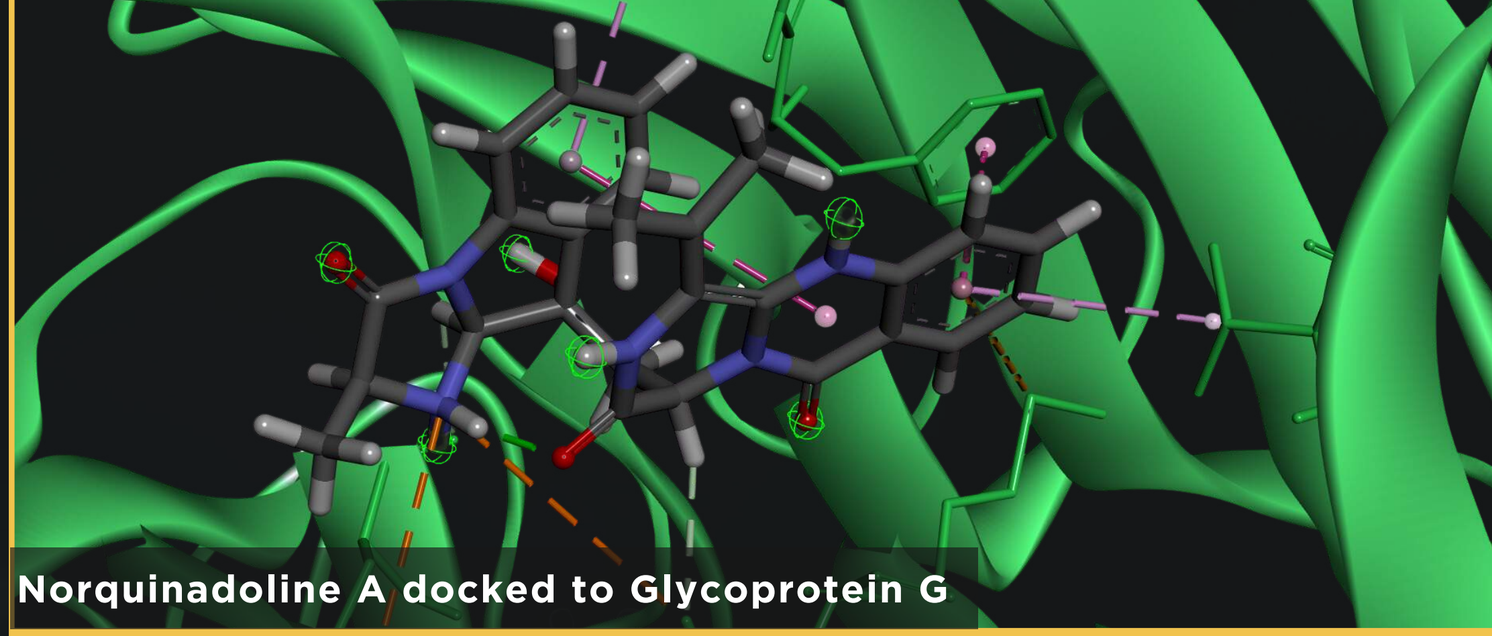
The docking poses with the prime affinity represent the set and are subjected to the post-dock analysis

Highest affinity protein-ligand complexes

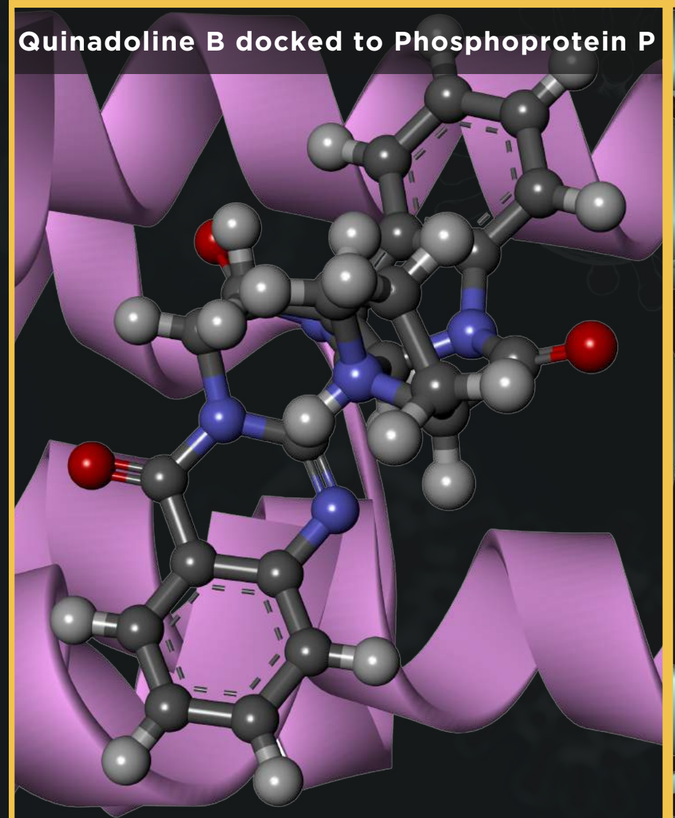
5

RESULTS

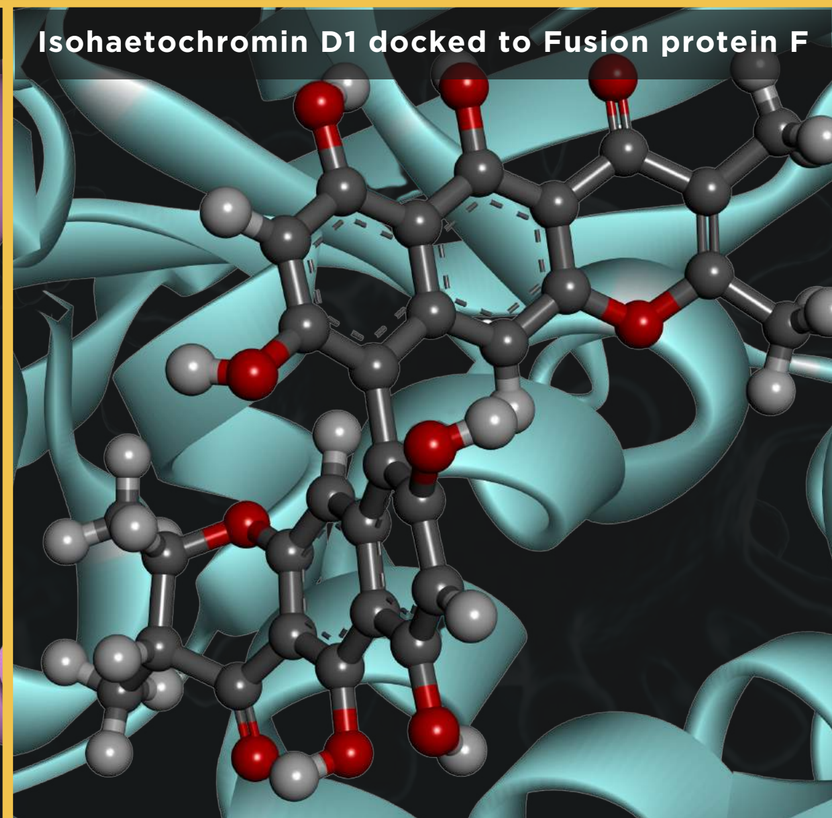
Alkaloids norquinadoline A and quinadoline B, and polyketide isochaetochromin D1 showed the highest binding affinity on the glycoprotein G, fusion protein F, and phosphoprotein P of NiV.



Norquinadoline A docked to Glycoprotein G

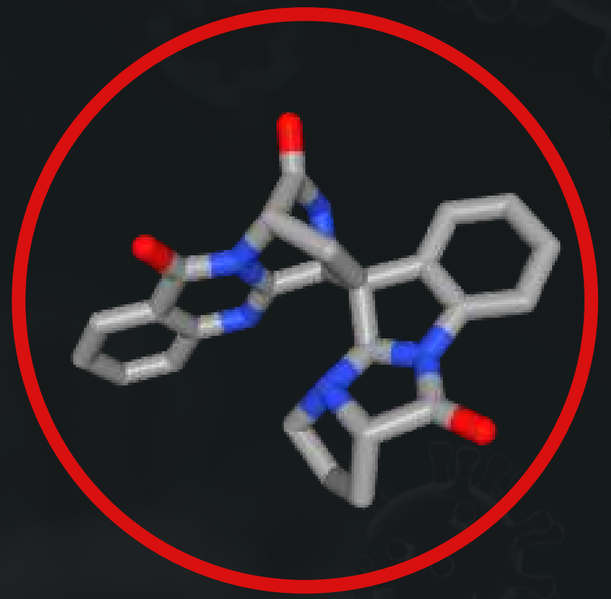


Quinadoline B docked to Phosphoprotein P



Isohaetochromin D1 docked to Fusion protein F

RESULTS



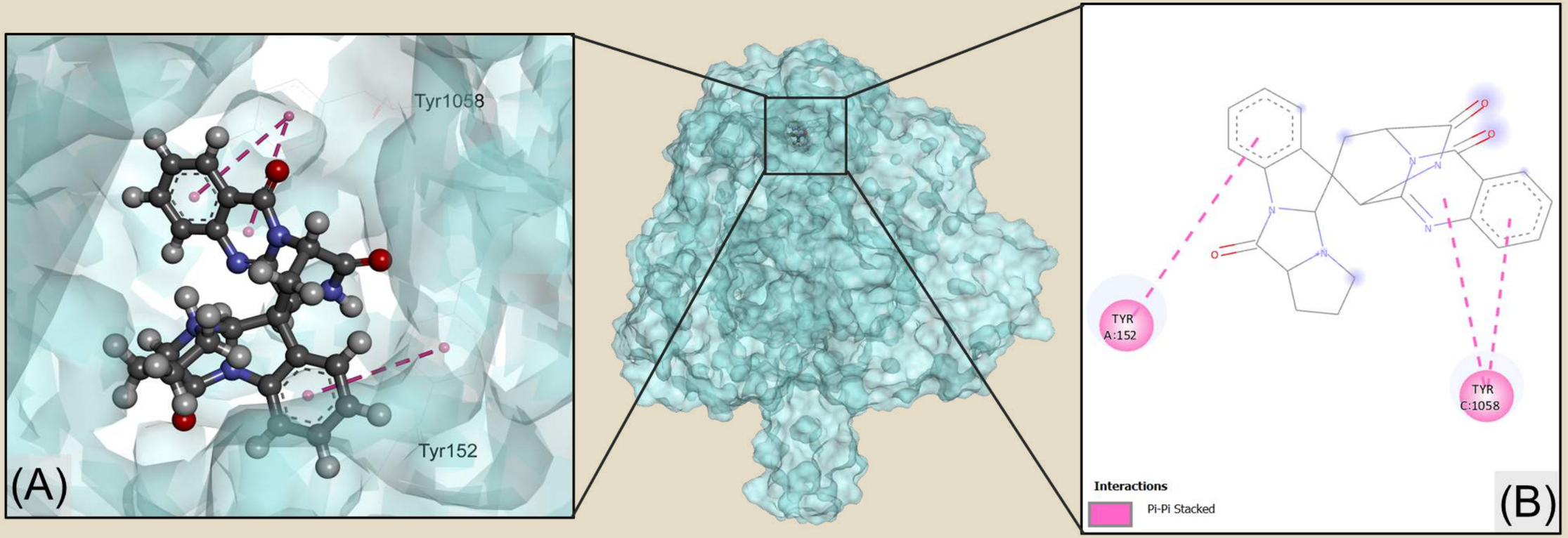
QUINADOLINE B

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

Target Viral Protein	Ligand Against NiV Viral Proteins	Binding Energy (kcal/mol)
Fusion Protein	Quinadoline B	-10.4
Phosphoprotein P	Quinadoline B	-9.1

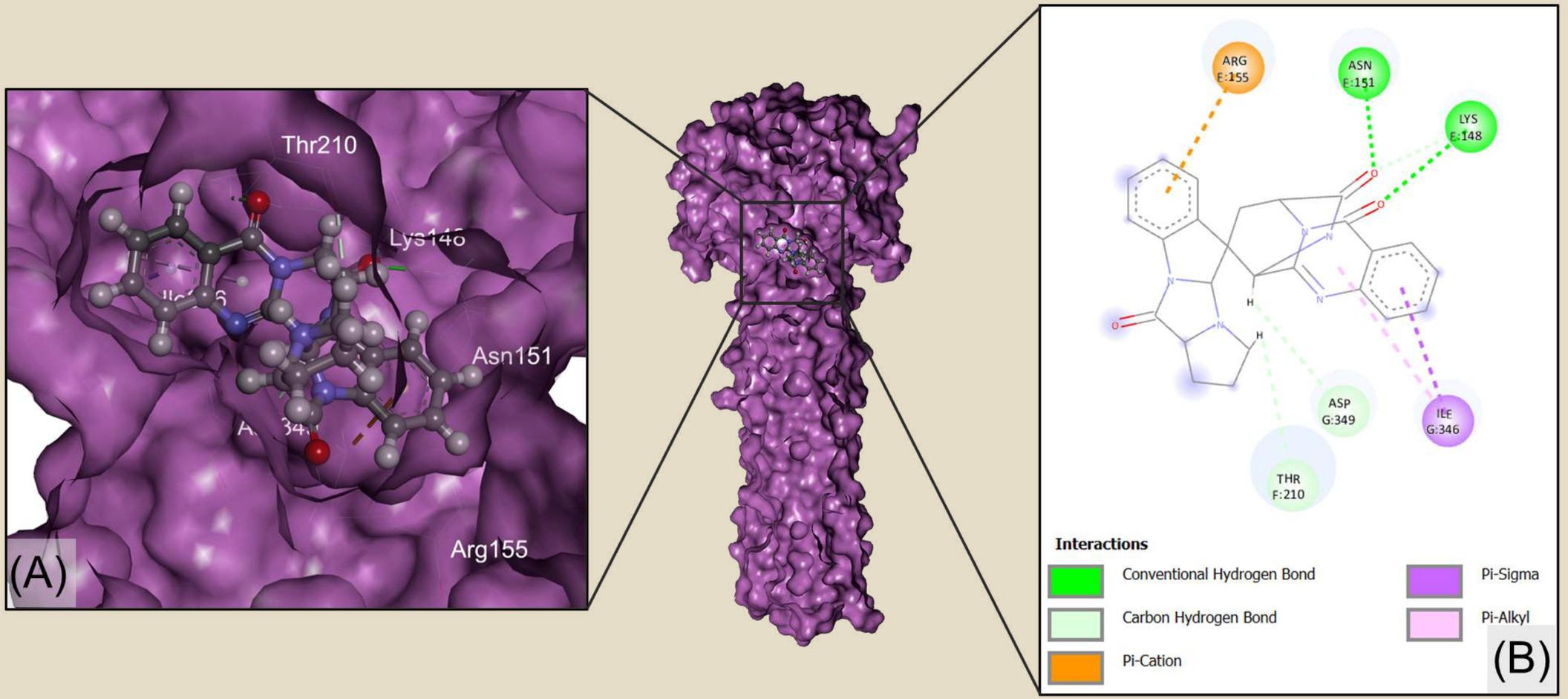
(Quimque et al., 2020)

RESULTS



Docked pose of quinadoline B against fusion protein F of NiV showing molecular interactions on (A) molecular surface and (B) 2D representation.

RESULTS



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.

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THANK YOU!