**In Silico Molecular Docking Analysis For Repurposing Ribavirin Antiviral Drugs Against Tumour Activity**

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**Introduction and Objective**

# The growing cost of medical care worldwide, particularly in oncology, has incentivized researchers and physicians to repurpose clinically used drugs to alleviate the financial burden of drug development and offer potential new therapeutics. Present works have explain anticancer properties of the FDA-approved drug Ribavirin antiviral molecule used over the past four decades for the treatment of antiviral1. Eukaryotic translation initiation. Further more ribavirin has shown to be safe and effective to enhance anticancer activity .The extensive work carried out in this study is to examine the interaction of the cancer protein and different antiviral drug ligands to inhibit the cancer protein main protease.the most robust preclinical docking suggest that ribavirin principal target in serveral cancer is eIF4E,modulated via direct binding and competiitive inhibition. The results from this in silico molecular docking study enhance the use of ribavirin for as potential candidate drugs for the treatment of cancer because the drug expressed their highest docking scores.

# Methods

Since its advent as an antiviral therapy over 40 years ago, a growing body of work has shown evidence for ribavirin as an anticancer agent. In particular, the elucidation of its antagonism toward the oncogenic eukaryotic translation initiation factor Eukaryotic translation initiation factor -4E (eIF4E)1 has led to promising preclinical and clinical results in monotherapy and combination therapy for several cancers. Moreover, several clinical trials have examined the safety and efficacy of ribavirin in malignancies and have validated its use as an antineoplastic agent, particularly in combination therapies2.

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# 3D Structure of Ribavarin

# C:\Users\Lenovo\Desktop\3d ribavarin.jpg

**STEP: I**

The main virus protease was collected from a Protein Data Bank

#### Protein Target: 3D Structures of protein were procured from PDB. The protein structures were cleaned (water molecules and other heteroatoms removed), prepared and minimized before docking.

**Ligand preparation.**

Preparation of ligand is also done because of some reasons,

* A reasonable 3D structure is needed as starting point.

Protonation state and tautomeric form of a particular ligand could influence its hydrogen bonding ability.

**STEP: II**

Docked with a sequence of selected approved antiviral drugs, and based on the binding energy score, we suggest that these compounds can be tested against virus and used to develop effective antiviral drugs.

**Define binding site**

After the protein and ligand preparation, next step is to define binding site for docking.

Receptor ligand interaction → Define & Edit binding site [In Define site, there are 3 options: – From Receptor Cavities, From PDB Site Records, and From Current Selection].

**Docking:** Docking module Schrodinger using Mastero13.2 was used to study interaction between the Protein and ligand molecules.

**Result**

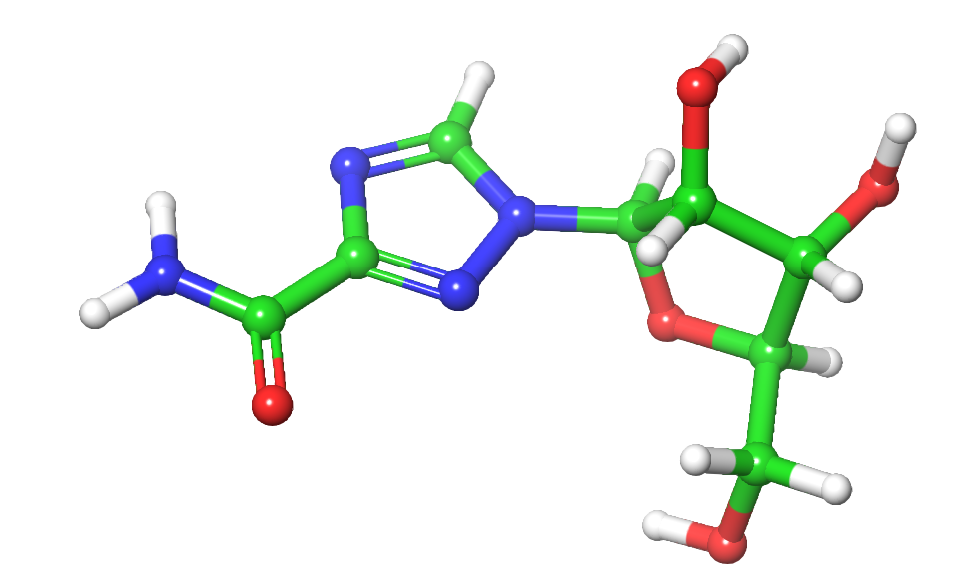
**Protein Preparation**

Mastero13.2- Protein Preparation-PDB import structure(eIF4E)- Review structure-entry clearance-Run



**Ligand Preparation**

Mastero13.2-File-Import structure in SDF format-Ligprep-workspace format-default setting-Run

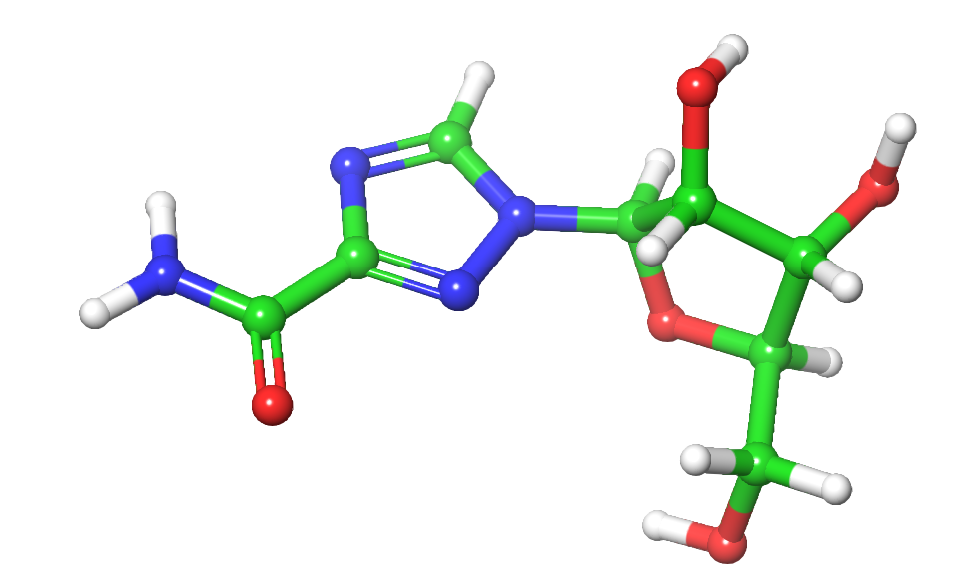
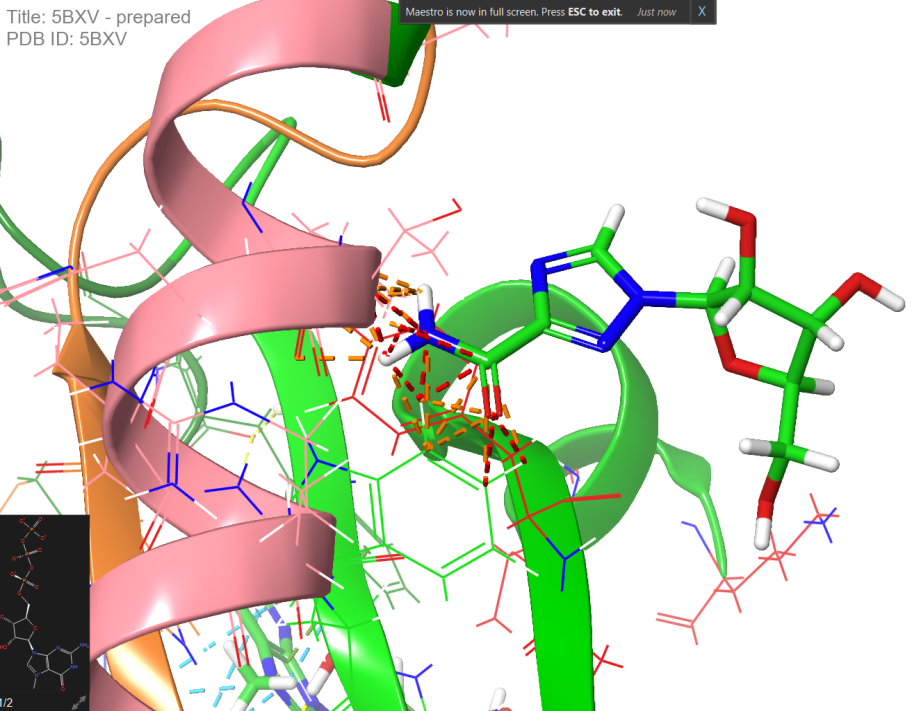


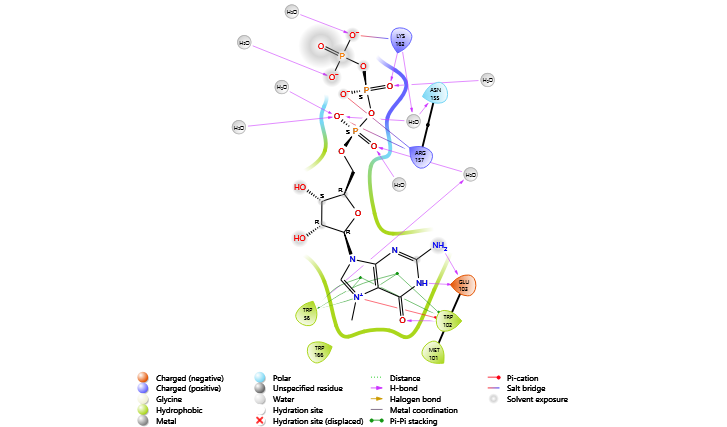
**Glide preparation**

Mastero13.2- prepared protein- Entry point selection-Glide browser-Receptor Grid generation- select entry point- Default setting – Run

**Docking**

Maestro 13.2- Ligand docking- Glide prepared protein maestro format- Prepared Ligand- Run

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**Protein-Ligand intraction with molecular docking of ribavirin**

**Docking analyis of ribavirin**

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| --- | --- | --- | --- | --- |
| **S.no** | **Ligand** | **Docking scores** | **Total no of hydrogen in protein (polar and non polar)** | **RMSD=Root mean square deviation** |
| **1.** | Ribavirin | -1258.833 | H-3227(non-polar-1752 )and (polar-927) | 0.600 |

# Conclusions

Eukaryotic translation initiation factor -4E (eIF4E) main protease inhibitor is a key to reduce the spread of the cancer infection and repurposing approved antiviral drugs is a fast approach in finding the safest treatment for the novel anticancer treatment.Further more ribavirin has shown to be safe and effective to enhance anticancer activity .The extensive work carried out in this study is to examine the interaction of the cancer protein and different antiviral drug ligands to inhibit the cancer protein main protease, the most robust preclinical docking suggest that ribavirin principal target in serveral cancer is eIF4E,modulated via direct binding and competiitive inhibition. The results from this in silico molecular docking study enhance the use of ribavirin for as potential candidate drugs for the treatment of cancer because the drug expressed their highest docking scores.

**References**

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2. Jones G, Wilett P, Glein RC, Leach AR, Taylor R. Development and Validation of Genetic Algorithm and an Empirical Binding Free Energy Function. J Mol Biol. 1997; 267: 727-748.