Determining the Comparative Efficacy of Adenosine Analogues in Reducing Coronavirus Replication by Interfering Viral RNA Dependent RNA Polymerase Activity

Juliano Aquilino

Advisor: Dr. Mrigendra Rajput

Introduction

Vaccines against infectious viral diseases are good in preventing those illnesses, however their application is not recommended in curing the ongoing infection. Antiviral drugs such as nucleotide analogs have been successfully used in treating various viral infections. Current study is designed to evaluate the antiviral efficacy of adenosine analogues such as Remdesivir, Galidesivir, and 2-Chloroadenosine in inhibiting the human (HOC43) replication by interfering viral RNA dependent RNA polymerase (RdRp) activity.

Materials and Methods

- RNA dependent RNA polymerase gene (RdRp) sequence for Human Coronavirus OC43 (HCoV-OC43) was obtained from National Center for Biotechnology Information (NCBI) data base.
- Molecular docking using Maestro software was performed to determine the interaction of adenosine analogues with viral RdRp.
- Invitro efficacy of adenosine analogues such as Remdesivir, Galidesivir, and 2-Chloroadenosine (Cayman Chemical, Ann Arbor, MI) in reducing HCoV-OC43 (ATCC, Manassas, VA) replication was performed in 6 cell plates using HCT-8 cells .
- After 18 hours attachment, cells were treated with adenosine analogues (10µM) for one hours. Then cells were washed and adsorbed with virus for another hour (MOI: 0.1). After one hour virus adsorption, cells were washed and cultured for 5 days in cell culture medium.
- After five days, virus titer in each well was determined by dilution method.

Results

- Molecular docking results showed that adenosine analogues such as Remdesivir, Galidesivir, and 2-Chloroadenosine efficiently interact with HCoV-OC43 RdRp (Figure 1)
- In vitro results showed that Remdesivir, Galidesivir, and 2-Chloroadenosine significate reduced HCoV-OC43 titer (log10) such as 1.00±0.00/ml, 1.33±0.57/ml and 1.33±0.57/ml respectively as compare to untreated control cells (5.00± 0.00/ml) (n=3) (Figure 2 A and 2B)

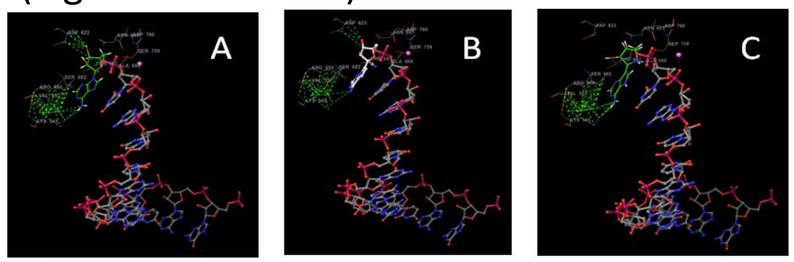

Figure 1. Molecular docking using Maestro software indicating the interaction of adenosine (A), Remdesivir (B) and Galidesivir (C) with RdRp.

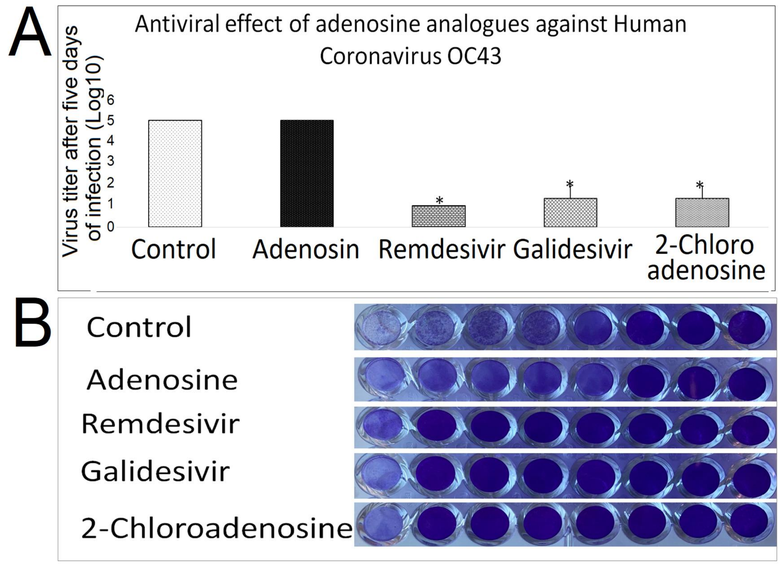

Figure 2. Adenosine analogues significantly reduced the virus titer as measured cytopathic effect under microscope (A) as well as cell staining by 1% crystal violet (B).

Conclusion and Future Directions

- All adenosine analogues used in current study significantly reduced HCoV-OC43 replication.
- Replicates the experiment for reproducibility.
- Determining lowest effect doses for each adenosine analogues in reducing HCoV-OC43 replication.
- Determining their effect on RdRp activity.

Acknowledgment

Department of Biology, University of Dayton , Dayton for providing funding for this project.