# Guanosine as RNA Replication Blocker for Therapeutic Treatment of COVID 19

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## Abstract

This theoretical paper presents Guanosine as a therapeutic intervention in treating COVID-19 through interruption of the SARS CoV2 pathogenesis in the host cell, by blocking the metal ions at the viral RNA dependent RNA Polymerases' active site.


## Introduction

Given the current understanding of the SARS-COV2 virus, one of the therapeutic interventions that can be considered in treating COVID-19 is to block RNA synthesis through inhibition of RNA dependent RNA Polymerase (RdRP) activity[1].

There are several methods that are being actively considered, which are designed to employ nucleotide analogues to interrupt RNA replication or protein translation from the viral +ssRNA.

However, SARS-CoV2 has exhibited high level of recombination, and mutation[2], which can overcome errors in transcription or replication. An alternate method of blocking replication is to block the divalent metal ions at the RNA polymerase's active site[3], which will reduce proliferation of the virus in the host cells.

In this short communication, the author examines the possibility of using nucleosides as a therapeutic intervention in blocking RdRP replication of the positive sense single stranded RNA (+ssRNA)[4] by using nucleotides to bind to the metal ions at the RdPR's active site.

## Methods and Materials

Based on the author's earlier investigations[5] on the origin of bacterial mutations that enabled drug-resistance, it was discovered that bacterial mutation was enhanced by addition of extra cellular magnesium in the form of magnesium sulphate, and supressed by the addition of adenosine.

The efficacy of adenosine in suppressing mutation could be overcome by the addition of extracellular magnesium. This indicates that the magnesium bound to cellular adenosine triphosphate (MgATP) is the active component in promoting mutation during DNA replication due to its role in the active sites of both ribosomes and polymerases.

## Results

This also indicates that addition of adenosine may bind to the cellular magnesium, especially in the active site at the DNA Polymerase and in the ribosomes, thereby blocking both replication and translation.

Assuming that magnesium has a role similar to its catalytic role in the DNA replication process in the SARS-CoV-2's RdRP's RNA replication process, introduction of extracellular nucleobases may block the RdRP thereby terminating the SARS CoV-2's RNA replication process.

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## Discussion

While the author had initially considered adenosine as a candidate for blocking RNA replication by binding to magnesium ions, adenosine also functions in cellular signalling pathways and is considered an antiarrhythmic agent. Adenosine may be excluded as a therapeutic intervention, as the observed adverse effects [6] can exacerbate morbidity of patients suffering from COVID-19.

The closest candidates among the other three Nucleosides is Guanosine, which like Adenosine, is a Purine nucleoside. Guanosine does not cause bronchoconstriction[7] when inhaled, in both normal and asthmatic subjects and has minimal side effects[8].

The author suggests that administration of guanosine may result in reduction of cellular magnesium levels, either by through conversion to MgGTP, or Mg-Guanosine, or by forcing an ATP-GTP imbalance, resulting in conversion of AMP/ADP conversion to MgATP, thereby reducing the availability of Magnesium ion for the RdRP driven RNA synthesis.

In addition, addition of guanosine may block GTPase activity on EF-2, preventing viral RNA synthesis[9].

## Conclusions

Nasal administration of guanosine may be used to reach the viruses' target cells, such as pneumocyte type II cells.

The administered extracellular guanosine may bind to the cellular magnesium, through which the translation and transcription processes of the viruses' genetic material may be blocked.

This will also ensure that that both mutation and recombination are avoided, and thereby preventing the pathogenesis of the virion.


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## Financial Relationship

There are no financial relationships to disclose