

Broad-spectrum Antiviral Inhibits SARS-CoV-2

ORALLY BIOAVAILABLE BROAD-SPECTRUM ANTIVIRAL INHIBITS SARS-CoV-2

Abstract
Orally bioavailable nucleoside analog with broad-spectrum antiviral activity against various unsegmented RNA viruses is effective against SARS-CoV-2.

Background
NHC exerts potent, broad-spectrum activity against SARS-CoV, MERS-CoV, and their related bat-CoV in primary human airway epithelial cell cultures.

Results
NHC is generally antiviral against the newly emerging SARS-CoV-2 as well as against coronavirus bearing resistance mutations to the potent nucleoside analog inhibitor, remdesivir (RDV). Both prophylactic and therapeutic administration (EIDD-2801, an oral NHC prodrug (β-D-N4-hydroxycytidine-5'-isopropyl ester)) improved pulmonary function, reduced virus titer and animal mortality in SARS- and MERS-CoV infected mice.

Conclusions
Mechanism appears to be through lethal when deleterious transition mutations accumulate in viral RNA.

AN ORALLY BIOAVAILABLE BROAD-SPECTRUM ANTIVIRAL INHIBITS SARS-CoV-2

Sheahan et al, bioRxiv
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Purpose
Address whether β-D-N4-hydroxycytidine (NHC), an orally bioavailable nucleoside analog with broad-spectrum antiviral activity against various unsegmented RNA viruses is effective against SARS-CoV-2.

Results in a nutshell

- The analyses show that NHC exerts potent, broad-spectrum activity against SARS-CoV, MERS-CoV, and their related bat-CoV in primary human airway epithelial cell cultures.
- They also show that NHC is generally antiviral against the newly emerging SARS-CoV-2 as well as against coronavirus bearing resistance mutations to the potent nucleoside analog inhibitor, remdesivir (RDV).
- Both prophylactic and therapeutic administration (EIDD-2801, an oral NHC prodrug (β-D-N4-hydroxycytidine-5'-isopropyl ester)) improved pulmonary function, reduced virus titer and animal mortality in SARS- and MERS-CoV infected mice.
- Mechanism appears to be through lethal when deleterious transition mutations accumulate in viral RNA.

Source: [Efra Rivera-Serrano, PhD](#) [Twitter](#) [Handle @NakedCapsid](#)

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SARS-CoV-2 is a zoonotic virus which causes the disease COVID-19 and there are currently no approved therapies. Sheahan et al recently pre-published a paper that states that ribonucleoside analog β-D-N4-hydroxycytidine (NHC, EIDD-1931) has broad spectrum antiviral activity against SARS-CoV 2, MERS-CoV, SARS-CoV, and related zoonotic group 2b or 2c Bat-CoV. The researchers also stated that there is an increased potency against a coronavirus bearing resistance mutations to another nucleoside analog inhibitor.

EIDD-2801, an orally bioavailable NHC-prodrug (β-D-N4-

hydroxycytidine-5'-isopropyl ester) was also shown to improve pulmonary function and reduce virus titre in mice infected with SARS-CoV or MERS-CoV. NHC/EIDD-2801 was shown to be potent against multiple coronaviruses and therapeutically effective which highlights its potential as an effective antiviral against SARS-CoV-2 and other future zoonotic coronaviruses.

Journal Article: [BioRxiv – Sheahan, T.P. et al. An orally bioavailable broad-spectrum antiviral inhibits SARS-CoV-2 and multiple endemic, epidemic and bat coronavirus](#)

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