

## **Fighting SARS-CoV-2 with Nanomedicine**

2021-08-02

A new review paper explores the potential role of nanomedicine to fight the ongoing COVID-19 (coronavirus disease 2019) pandemic.

Published in the [Journal of Controlled Release](#), researchers from the [German University in Cairo](#), and the [University of Cologne](#), looked into nano-reformulation of repurposed antiviral and immune-modulating drugs for inhalation therapy against COVID-19. In addition, they focused on how nanomedicine could address the limitations of current therapeutics, enhancing the efficacy, specificity, and safety of such drugs.

### **SARS-CoV-2 structure & pathogenicity**

The researchers briefly describe severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) origins, structure, and pathogenicity. After entering the host, SARS-CoV-2 hijacks the cell translational machinery to translate viral polyproteins that are subsequently cleaved into functional proteins.

The researchers discuss the pivotal host cell proteins as well as the viral proteins that are active in the pathogenesis and immune suppression - all these proteins serve as suitable targets for antiviral therapy.

### **Reformulation of repurposed drugs**

Addressing how to tackle SARS-CoV-2 using drugs, the researchers explain how they fall into two broad classes, drugs targeting viral components and drugs acting on host cell components.

The researchers have tabulated a long list of immunomodulatory drugs clinically evaluated against COVID-19, presenting the method and route of administration, and the clinical trials, including the side effects of the drugs.

The inhalation of drugs was only considered until recently as opposed to systemic administration (delivery directly into the bloodstream).

In some cases, systemic administration of the anti-SARS-CoV-2 medications may present adverse effects, especially when combined with other preexisting conditions that require additional medication.

Unlike virus-targeting drugs, the target in host-cell targeting drugs is large and wide (also aimed at non-targeted organs). Therefore, these drugs cause undesired side effects in COVID-19 patients.

“Although, currently, little is known about the effective drug concentration required to inhibit SARS-CoV2 replication, the exposure of the virus to a low drug concentration in-vivo is a plausible reason for the clinical ineffectiveness observed with antiviral drugs.”

Citing on the advantages of targeted local delivery - higher drug concentrations to the site of action, minimize toxicity (due to off-target distribution), and possibly reducing the administered dose; the researchers looked at how the micro-and nanoparticles can play a role here.

COVID-19 usually being confined to conducting airways of the lungs, the researchers discussed how the SARS-CoV-2 infection progresses and how antiviral drug inhalation may help alleviate the progression. They discussed relevant drug targeting approaches within the respiratory system, extrapolating effective nano-reformulation possibilities.

They also presented another table with the properties of the immunomodulatory drug with

the reported nano-formulations, including exhaustive references.

The review also provided examples from literature by which the deposition of small nanoparticles on the lungs was enhanced by nebulization or through the incorporation into larger particles for administration in dry form for local drug delivery to the lung.

Additionally, the review provided a list of drugs, their molecular targets, and reported side effects that act on tackling the enraged immune system (hyper inflammation and cytokine storm).

The researchers supported the use of nano-reformulation of the immunomodulatory drugs for inhalation therapy as a viable approach to enhance the drug efficacy (high specific surface area in nanocarriers or nanosized capsules). "This is backed up by the urgent appeal from the International Society for Aerosols in Medicine (ISAM), urging governments and decision-makers to consider the inhaled route for therapy of COVID-19," the researchers informed.

## **Perspectives and conclusions**

Sharing in a noteworthy perspective, the researchers added that in some cases, the systemic administration of the nano-drugs might be warranted, even in the case of inhalation therapy.

Fingolimod, a drug currently under investigation in COVID-19 therapy, can ameliorate the cytokine storm via the action of fingolimod in lung endothelial cells. Because fingolimod could also stabilize the pulmonary endothelial barrier (central orchestrators of cytokine amplification), it also decreases inflammatory infiltrate and subsequent ARDS (Acute respiratory distress syndrome). "Delivery of fingolimod loaded NPs to lung endothelial cells following intravenous administration might be warranted," the researchers said.

Discussing the effect of the excipients used in the drug formulation, the researchers highlighted that these are not necessarily inert, especially when in the nanoscopic range.

Citing examples, they emphasized that care has to be taken so that the excipients provide synergistic effects rather than opposing actions.

“Nanoformulation of drugs represent a promising resource to unify the progress in nanotechnology and understanding of surface chemistry with known drug-delivery mechanisms to enhance the sitespecific delivery.”

Playing with the idea of an intelligent nano-robot that would also impressively function in vivo, the researchers questioned the feasibility, cost, and possibility of such a system.

Foreboding recurrent spillovers of CoVs in humans and future zoonotic transmission events, the researchers concluded that “the presence of an inhaled carrier system capable of delivering antiviral or immunomodulatory drugs should be available as part of the repertoire in the fight against future outbreaks.”

Read the [original article](#) on News Medical.