Acta Scientific Pharmaceutical Sciences (ISSN: 2581-5423)

Volume 4 Issue 9 September 2020

Editorial

# Pharmacological Treatments and Development of SARS-CoV-2

**Zaharaddeen Umar Na'abba and Abhishek Kumar Verma***

*Department of Life Sciences, School of Science and Technology, Mewar University, Gangrar, Chittorgarh Rajasthan, India*

***Corresponding Author:** Abhishek Kumar Verma, Assistant Professor, Department of Life Sciences, School of Science and Technology, Mewar University, Gangrar, Chittorgarh, Rajasthan, India. **E-mail:** abhishekbairwa913@gmail.com

**Received:** July 26, 2020

**Published:** August 01, 2020



Currently, the FDA for the treatment of COVID-19 pneumonia has approved no drugs or therapeutics vaccines. Some pharmacological treatment has gained emergency use authorization from FDA based on preliminary data displaying a faster time to recovery of hospitalized patients with severe COVID-19 infection. In this editorial, different pharmacological treatment that have been adopted for the management and treatment of COVID-19 pneumonia.

Remdesivir is a nucleoside analog prodrug that can competitively incorporates with viral RNA dependent RNA polymerase (RdRp), resulting in RNA synthesis inhibition. Remdesivir binds to RNA-dependent RNA polymerase and acts as an RNA-chain terminator and it displays potent *in vitro* activity against SARS-CoV-2 with an $EC_{50}$ at 48 hours of 0.77 μM in Vero E6 cell. The drug also displays a high genetic barrier to resistance in coronaviruses and has a long intracellular half-life that allows for once daily dosing. Several clinical trials have conducted some are on progress to examine the efficacy and safety of Remdesivir in management and treatment of COVID-19 infection and have yielded a promising result.

Chloroquine is an antimalarial agent with anti-inflammatory and immunomodulatory activities that has gained significant interest as a potential therapeutic choice for the management of COVID-19 pneumonia. Chloroquine and hydroxychloroquine appear to block viral entry into cells by inhibiting glycosylation of host receptors, proteolytic processing, and endosomal acidification. These agents also have immunomodulatory effects through attenuation of cytokine production and inhibition of autophagy and lysosomal activity in host cells. Chloroquine has an immunomodulatory activity by suppressing the production and release of tumor necrosis factor (TNF) and interleukin 6 (IL-6), which mediate the inflammatory complications of several viral diseases. Several clinical trials have been conducted to evaluate the efficacy of Chloroquine and hydroxychloroquine in management of COVID-19 and has produced a positive result.

Lopinavir/ritonavir can inhibit the SARS-CoV-2, 3C-like protease (3CLpro) *in vitro* (IC50 50 μM) resulting in termination of viral replication. Efficacy and safety of lopinavir in combination with ritonavir have examine and promising results have being achieved. Lopinavir/ritonavir has demonstrated *in vitro* activity against other novel coronaviruses via inhibition of 3- chymotrypsin-like protease. *In vitro* antiviral activity against SARS-CoV-2 associated coronavirus was demonstrated for lopinavir and ribavirin at concentrations of 4 μg/ml and 50 μg/ml, respectively, only at 48 hours. The adverse clinical outcome (ARDS or death) was significantly lower in the treatment group than in the historical controls (2.4% *v* 28.8%, $p < 0.001$) at day 21 after the onset of symptoms. The adverse outcome remained significantly lower in the treatment group than in the controls-both those diagnosed early ($p < 0.001$) and those diagnosed later in the course of the epidemic ($p = 0.002$).

Favipiravir is an antiviral agent that selectively and potently inhibits the RNA-dependent RNA polymerase (RdRp) of RNA viruses. Favipiravir is Guanosine nucleotide analogue, prodrug, RdRp inhibitor developed and approved for the treatment of influenza viruses in Japan. Favipiravir inhibits *in vitro* replication of wide range of influenza viruses and many other RNA viruses including arenaviruses, bunyaviruses, flaviviruses, alphaviruses, paramyxoviruses, and norovirus family. The antiviral efficiency of favipiravir have being evaluated against a clinical isolate of SARS-CoV-2 *in vitro*.

Ribavirin is a guanine analogue that inhibits viral RNA-dependent RNA polymerase. Its activity against other nCoVs makes it a candidate for COVID-19 treatment. Ribavirin interferes with the replication of RNA and DNA viruses. However, the antiviral activity of ribavirin is not limited to interference with polymerases; it also interferes with RNA capping that relies on natural guanosine to prevent RNA degradation. Moreover, to further promote the destabilization of viral RNA, ribavirin inhibits natural guanosine generation by directly inhibiting inosine monophosphate dehydrogenase in a pathway that is vital for the production of the guanine precursor to guanosine. Several clinical trials of ribavirin or in combination with other drugs have examine for its efficacy and safety in management of COVID-19 infection and has produced promising results.

Ivermectin is an FDA-approved broad-spectrum anti parasitic agent that in recent year has shown to have antiviral activity against a broad range of viruses *in vitro*. Ivermectin have shown to inhibit the nuclear import of host and viral proteins. It has also demonstrated to limit infection by some RNA viruses including influenza, dengue and West Nile viruses. Ivermectin has similarly been shown to be effective against the DNA virus pseudorabies virus (PRV) both *in vitro* and *in vivo*, with ivermectin treatment shown to increase survival in PRV-infected mice.

Although specific treatments, including vaccines, have not yet been developed for COVID-19, effective prevention methods are now recommended on a global scale. Accordingly, to overcome this pandemic, developing specific inhibitors for viral entry and replication, as well as drug repositioning, will be necessary. As above, several clinical trials and drug repositioning studies are currently ongoing and drug repurposing ongoing clinical trials should be based on the specific guidelines and Specific regimen for therapeutic efficacy of the drugs.