

# Review of Clinical Therapies of Coronavirus Disease 2019 (COVID-19) During Worldwide Pandemic Outbreak

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## Abstract

Coronavirus disease 2019 (COVID-19) is a respiratory tract infection caused by a novel coronavirus now called severe acute respiratory syndrome coronavirus 2 (2019-nCoV), which was first identified in Wuhan City, Hubei Province, China on December 2019. It rapidly spread, resulting in an epidemic throughout China, followed by an increasing number of cases in other countries throughout the world.

Transmission of COVID-19 is believed to occur via respiratory droplets from sneezing, coughing and if any one touches an infected surface and then touches his or her eyes, nose, or mouth.

According to the WHO, the CDC, and the FDA, there are currently no medications or vaccines proven to be effective for the treatment or prevention of COVID-19. For any drug therapy efficacy has not been proved.

In this review, we summarized the pharmacotherapy of COVID-19, and discussed the current treatment and scientific advancements to combat the world wide pandemic novel coronavirus. Even though, studies exploring prevention and control measures have begun to gradually increase, most studies that have been published was focused on the epidemiology and potential causes. All scope of the Studies are needed to minimize the impact of this world wide pandemic outbreak.

**Keywords:** Obesity • Endocrinology • Human Genome • Inflammatory Factors • Mental Disorder • Metabolic Disorders

## Abbreviations

ACE2: Angiotensin converting enzyme

CDC: Center for Disease Control

CoV: Coronavirus

COVID19: Coronavirus disease 2019

IFN: Interferon

IL: Interleukin

LPV: Lopinavir

RT-PCR: reverse-transcription polymerase chain reaction

RTV: Ritonavir

WHO: World Health Organization

## Introduction

### Background

A 2019 global pandemic outbreak of COVID-19 was first identified as the cause of a cluster of pneumonia cases in Wuhan, as city in the Hubei Province of China. It rapidly spread, resulting in an epidemic throughout China, followed by an increasing number of cases in other countries throughout the world [1, 2].

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It was initially reported to the WHO on December 31, 2019. On January 30, 2020, the WHO declared the COVID-19 outbreak a global health emergency [3, 4]. On March 11, 2020, the WHO declared COVID-19 a global pandemic [5].

The result of this study would provide the evidence of early findings on the pharmacotherapy of COVID-19 (introduction, epidemiology, pathophysiology, etiology, diagnosis, prevention and treatment) in early stages of this outbreak. The finding of this study will help as a secondary data for subsequent research that deal with COVID-19 and may support government decision making on strategies to handle this public health emergency. In this review, we summarized the pharmacotherapy of COVID-19, and discussed the current treatment and scientific advancements to combat the word wide pandemic novel coronavirus.

## Methods and Materials

### Study design

Studies are conducted according to the following steps:

- a) Identifying objective,
- b) Identifying relevant articles,
- c) Selection of articles,
- d) Extraction of data, and
- e) Analyzing, summarizing, discussing and reporting the results [6].

## Study period

A scoping review was conducted from February 20 to April 5

## Study identification

We identified Literature by searching online from bioRxiv, medRxiv, Google scholar, PubMed and EMBASE databases.

## Summarizing result

The studies included full-text articles, guidelines and abstracts published by various specialists. A total of 50 documents referring to Clinical therapies of COVID-19 during worldwide pandemic outbreak was reviewed.

## Scope of the study

**Definition:** COVID-19 is a respiratory tract infection caused by a novel coronavirus now called severe acute respiratory syndrome coronavirus 2 (2019-nCoV), which was first identified in Wuhan City, Hubei Province, China [7]. The WHO announced that the official name of the 2019 novel coronavirus is COVID-19 [8].

**Epidemiology:** As of April 2, 2020, COVID-19 has been confirmed in more than one million individuals worldwide and has resulted in more than 51,000 deaths. More than 180 countries have reported laboratory-confirmed cases of COVID-19 on all continents except Antarctica [9]. In the United States, 236,339 cases of COVID-19 have been confirmed [10,11].

**Etiology:** COVID-19 is caused by a novel coronavirus that named SARS-CoV-2 [13]. SARS-CoV-2 is a single-stranded RNA virus [14].

## Route of Transmission

Transmission of COVID-19 is believed to occur via respiratory droplets from sneezing, coughing and if any one touches an infected surface and then touches his or her eyes, nose, or mouth [15,16]. Transmission of novel corona virus from asymptomatic individuals has also been described [17,18].

## Clinical presentation

The most common clinical symptoms of COVID-19 at the onset of illness were; Myalgia's Anorexia, Fever, Dyspnea, Fatigue, Dry cough and Sputum production [19]. The development of the Symptoms may take two days to two weeks following exposure to the virus [20].

The study led by Prof. Nan-Shan Zhong's team, by sampling 1099 laboratory-confirmed cases, found that the common clinical symptoms included fever (88.7%), cough (67.8%), fatigue (38.1%), and sputum production (33.4%), shortness of breath (18.6%), sore throat (13.9%), and headache (13.6%) [21].

Complications of infection included severe pneumonia, septic shock, acute respiratory distress syndrome, and multiorgan failure resulting in death [22].

## Diagnosis

Patients with suspected COVID-19 should be diagnosed in a private room with the door closed and asked to wear a surgical mask. All other standard contact and airborne precautions should be observed [23]. Then perform RT-PCR to detect the positive nucleic acid of SARS-CoV-2 in the lower respiratory tract samples, throat swabs and sputum [24, 25].

If initial testing is negative but the suspicion for COVID-19 remains, the WHO recommends resampling and testing from multiple respiratory

tract sites [26]. Serologic tests identify patients who have either current or previous infection but a negative PCR test [27]. The diagnostic sensitivity of radiologic is limited, so it is necessary to verify with clinical symptoms and virus RNA detections [28].

## Prevention and Treatment of coronavirus disease 2019 (COVID-19)

According to the WHO, the CDC, and the FDA, there are currently no medications or vaccines proven to be effective for the treatment or prevention of COVID-19. For any drug therapy efficacy has not been proved [29].

General measures for prevention include; Handwashing with soap and water for at least 20 seconds. An alcohol-based hand sanitizer may be used if soap and water are unavailable. Avoid touching eyes, nose, and mouth with unwashed hands. Avoid close contact with sick people. Coughs and sneezes should be covered with a tissue, followed by disposal of the tissue in the trash. Frequently touched objects and surfaces should be cleaned and disinfected regularly [30].

## Investigational Drugs with potential activity against SARS-CoV-2:

### Hydroxychloroquine and chloroquine

Hydroxychloroquine and chloroquine are widely used antimalarial drugs. As inhibitors of heme polymerase, they are also believed to have additional antiviral activity. Both have been reported to inhibit SARS-CoV-2 in vitro, although hydroxychloroquine appears to have more potent antiviral activity. The pharmacological activity of chloroquine and hydroxychloroquine was tested using SARS-CoV-2 infected Vero cells. Physiologically-based pharmacokinetic models (PBPK) were implemented for both drugs separately by integrating their in vitro data [31].

Optimal dosing is uncertain; various regimens are being used; 400 mg twice daily on day 1 then daily for five days, 400 mg twice daily on day 1 then 200 mg twice daily for four days, and 600 mg twice daily on day 1 then 400 mg daily for four days [32].

Side effect: cardiac arrhythmias and retinal damage; Caution in patients with G6PD deficiency and in diabetics [33, 34].

### Lopinavir; Ritonavir:

This combined protease inhibitor, which has primarily been used for HIV infection, has in vitro activity against the SARS-CoV [35]. But, according to Cao B, Wang Y, Wen D, et al randomized trial, there was no difference in clinical improvement or mortality between those who received lopinavir-ritonavir (400/100 mg) twice daily for 14 days in addition to standard care and those who received standard of care alone [36].

Therapeutic LPV/RTV plus interferon beta (IFNb) improved pulmonary function but did not reduce virus replication or severe lung pathology [37].

**Side effect:** cardiac arrhythmias, Caution in patients with hepatic disease or hepatitis [34, 38].

### Remdesivir

An in vitro study showed that the antiviral activity of remdesivir plus interferon beta (IFNb) was superior to that of lopinavir/ritonavir. Prophylactic and therapeutic remdesivir improved pulmonary function and reduced lung viral loads and severe lung pathology in mice, whereas LPV/RTV-IFNb slightly reduced viral loads without affecting other disease parameters [37].

### Adjunctive/Supportive therapy:

### Azithromycin

In an open-label study of 36 patients with COVID-19, the use of azithromycin in combination with hydroxychloroquine appeared to have additional benefit, but there are methodological concerns about the control

**Table 1:** Summary of Investigational Drugs and Adjunctive/Supportive therapy For COVID-19

Investigational Drugs with potential activity against SARS-CoV-2	Adjunctive/Supportive therapy
Remdesivir	Azithromycin
Lopinavir; Ritonavir	Tocilizumab
Hydroxychloroquine	COVID-19 Convalescent Plasma
Chloroquine	Corticosteroids

groups for the study, and the biologic basis for using azithromycin in this setting is unclear [39]. In other small open-label study of hydroxychloroquine in France included azithromycin in 6 patients for potential bacterial Superinfection. These patients were reported to have 100% clearance of SARS-CoV-2 [40].

Side effect: cardiac arrhythmias [34, 41].

### Tocilizumab

Tocilizumab inhibits IL-6-mediated signaling. IL-6 is a pro inflammatory cytokine that is involved in diverse physiological processes such as T-cell activation, differentiation stimulation, immunoglobulin secretion induction, and hepatic acute-phase protein synthesis initiation [42].

Cytokine release syndrome may be a component of severe disease in COVID-19 patients [43].

Treatment guidelines from China's National Health Commission include the IL-6 inhibitor tocilizumab for patients with severe COVID-19 and elevated IL-6 levels; the agent is being evaluated in a clinical trial [44].

Side effect: GI perforation and Risk of hepatotoxicity [42].

### COVID-19 Convalescent Plasma

COVID-19 Convalescent Plasma is a Plasma collected from persons who have recovered from COVID-19 that may contain antibodies to SARS-CoV-2 [45]. The FDA is facilitating access to convalescent plasma, antibody-rich products that are collected from eligible donors who have recovered from COVID-19. Use of this product in patients with serious or immediately life-threatening COVID-19 may shorten the duration or severity of illness [46].

### Corticosteroids

The WHO and CDC recommend glucocorticoids in patients with COVID-19 pneumonia only when there are other indications such as exacerbation of chronic obstructive pulmonary disease [47,48]. Corticosteroids are not generally recommended for treatment of COVID-19 or any viral pneumonia [49]. The benefit of corticosteroids in septic shock results from tempering the host immune response to bacterial toxin release in below Table 1 [50].

For COVID-19.

Investigational Drugs with potential activity against SARS-CoV-2. Adjunctive/Supportive therapy

- Remdesivir, Azithromycin
- Lopinavir; Ritonavir: Tocilizumab

Hydroxychloroquine, COVID-19 Convalescent Plasma

- Chloroquine, Corticosteroids

## Conclusion

As of 2 April 2020, the pandemic outbreak of coronavirus disease 2019(COVID-19) has spread to more than 180 countries and has been confirmed in more than one million individuals worldwide and has resulted in more than 51,000 deaths. The WHO issued a public health emergency

of international concern on 30 January 2020, at the moment there is no vaccine and no specific treatment for COVID-19. Scientists have made progress in the characterization of the novel coronavirus and are working extensively on the therapies and vaccines against the virus.

This review summarizes the current research in response to the world wide pandemic outbreak of coronavirus disease 2019(COVID-19) along with the prevention and treatment. All scope of the Studies are needed to minimize the impact of this world wide pandemic outbreak. We recommend that the scholarly community conduct further research on improving the accuracy of early diagnostic tests, developing the vaccine and identifying effective drugs to control this world wide pandemic emergency.

### Quotes on COVID-19

"Pandemic is not a word to use lightly or carelessly. It is a word that, if misused, can cause unreasonable fear, or unjustified acceptance that the fight is over, leading to unnecessary suffering and death." Dr. Tedros Adhanom Ghebreyesus

"If you're gonna ring a bell, you'd better have a way to unring it.... I don't see anybody right now elaborating on, well, what happens if [COVID-19] cases go up four-fold in a two-week period? Will we reestablish these measures that we've had in place?"

WGBH, May 15, 2020

"Ultimately, the greatest lesson that COVID-19 can teach humanity is that we are all in this together." Kiran Mazumdar-Shaw

"There is a large body of data right now showing how easily this is transmitted just in the air by breathing. You can literally just walk into a room, where someone with the virus is breathing, and their virus will be floating in the air.... It doesn't mean wherever I walk I'm going to get infected. But if you're close to someone who is infected, you have a good chance of getting infected yourself."

WCCO, Apr 29, 2020

"Widespread testing would be extremely helpful in many states to better understand the degree of community spread, which can alert public health and medical professionals of high numbers of infected people in a region (city, county, etc). Alcohol-based sanitizers are useful when soap and running water are not available or out of convenience when you need to clean your hands quickly. Alcohol-based hand wipes can also help remove viruses from hands but need to be used carefully to cover all the hand/finger surfaces."

Dr. Louis Mansky, Professor and Director, Institute for Molecular Virology, University of Minnesota.

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