INTERNATIONAL JOURNAL OF ADVANCED RESEARCH
International Peer-Reviewed Research Journal
ISSN (Online): 3106-7980 | ISSN (Print): 3106-7972
Volume 3 • Issue 5 • September 2026

EFFICACY OF CHLOROQUINE AND HYDROXYCHLOROQUINE IN THE TREATMENT AND PREVENTION OF CORONA VIRUS INFECTION.

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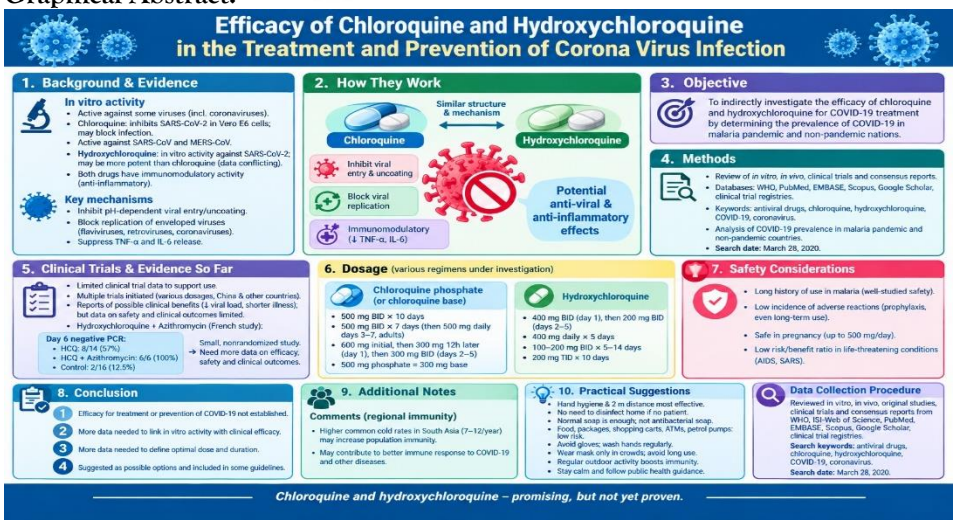
DOI: https://doi.org/10.5281/zenodo.23082571

Keywords

Article History
Received: 01 June 2026
Accepted: 23 August 2026
Published: 25 September 2026

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Graphical Abstract:



Abstract

Coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), emerged as a major global public health challenge and prompted an urgent search for effective antiviral therapies. Chloroquine and hydroxychloroquine attracted considerable attention because of their established antimalarial activity, immunomodulatory properties, and reported in vitro antiviral activity against several viruses, including coronaviruses. This review aimed to evaluate the potential antiviral

activity, clinical evidence, safety, and proposed mechanisms of action of chloroquine and hydroxychloroquine against COVID-19. Relevant in vitro and in vivo studies, clinical trials, original research articles, and consensus reports were identified through databases and sources including PubMed, Web of Science, EMBASE, Scopus, Google Scholar, the World Health Organization, and clinical trial registries. The literature search focused on terms including chloroquine, hydroxychloroquine, antiviral drugs, COVID-19, SARS-CoV-2, and coronavirus treatment. Evidence from laboratory studies demonstrated inhibition of SARS-CoV-2 replication, while proposed mechanisms included interference with pH-dependent viral entry and replication and modulation of inflammatory responses. Early clinical reports suggested possible reductions in viral load and disease duration; however, these findings were based largely on small or non-randomized studies, and subsequent evidence did not establish consistent clinical efficacy. The combination of hydroxychloroquine with azithromycin was also investigated, but the available early evidence was insufficient to establish its effectiveness and raised concerns regarding safety. Although chloroquine and hydroxychloroquine possess established pharmacological properties and demonstrated antiviral activity in vitro, clinical efficacy for the treatment or prevention of COVID-19 was not established. Further well-designed clinical studies were therefore required to determine their therapeutic value, optimal dosage, duration of treatment, and safety profile.

International Journal of Advanced Research

INTRODUCTION:

COVID-19, a highly contagious disease caused by 2019nCOV, still lacks effective treatment modalities. Researchers are in struggle to find suitable medications for its treatment and produce. Vaccines for prevention against COVID-19 to save lives, however, developing vaccines for COVID-19 will take a long time (Ibrar et al.). From the 3rd of January 2020 to the 8th of September 2021, there were 1,186,234 confirmed cases of COVID-19 in Pakistan, with a total of 26,330 deaths reported to WHOhttps://covid19.who.int/region/emro/country /pk)Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) was discovered as the unique coronavirus that causes the Coronavirus Disease 2019 (COVID-19) pandemic. COVID-19 has spread worldwide since its emergence, with the World Health Organization reporting over 71 million confirmed cases and 1.6 million deaths (WHO) (Khan et al., 2024).The following are evidence-based studies about the use of chloroquine and hydroxychloroquine in the treatment and prevention of In vitro activity against some viruses, including coronaviruses.(D. E. N. Khan et al., 2026; Wang et al.)

Chloroquine: In vitro activity against SARS-CoV-2 in infected Vero E6 cells reported; some evidence it may block infection in Vero E6 cells exposed to (SARS-CoV-2). (Cortegiani et al.; Wang et al.) Chloroquine: Active in vitro against (SARS-CoV and MERS-CoV). (Devaux et al., 2020; Keyaerts et al., 2004) Hydroxychloroquine: In vitro activity against SARS-CoV-2 in infected Vero 6 cells reported; may be more potent than chloroquine in vitro, but some data are conflicting and additional study needed. (Siddiq et al., 2026; Vickers, 2017) Both drugs have immuno-modulatory activity that theoretically could contribute to an anti-inflammatory response in patients with viral infections (Devaux et al., 2020; Wang et al.)

Objective:

The novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), also called COVID-19, has caused a pandemic which has swiftly involved the entire world and raised great public health concerns. The scientific community is actively exploring treatments that would

potentially be effective in combating COVID-19. Hydroxychloroquine has been demonstrated to limit the replication of SARS-CoV-2 virus in vitro. In malarial pandemic countries, chloroquine is widely used to treat malaria. In malarial non-pandemic nations, chloroquine is not widely used. Chloroquine and hydroxychloroquine share similar chemical structures and mechanisms of action. The aim of this study was to indirectly investigate the efficacy of chloroquine and hydroxychloroquine for the treatment of COVID-19 by determining the prevalence of COVID-19 in malaria pandemic and non-pandemic nations. (Feng et al., 2020)

Operational definition:
Since 1934, Chloroquine is a well-known antimalarial 9-aminoquinoline with interesting biochemical properties that might be used against some viral infections. Chloroquine directly inhibiting pH-dependent steps of the replication of most of viruses including members of the flaviviruses, retroviruses, and coronaviruses. Chloroquine effects are those against HIV/AIDS replication, which are being tested in clinical trials. Chloroquine has immunomodulatory effects by suppressing the release of tumor necrotizing factor α and interleukin 6, resulting mediate the inflammatory complications of several viral diseases. Numerous studies are available, the effects of chloroquine on viral infections, but the question is whether this old drug may be effective in the treatment of viral diseases such as severe acute respiratory syndrome (SARS), which affect the whole mankind in the era of globalization. (Touret & de Lamballerie, 2020)

Viral inhibition by chloroquine:
Chloroquine has been shown to inhibit different viruses requiring a pH-dependent step for entry by suppressing the release of tumor necrotizing factor α, interleukin 6, like in the Borna disease virus, the minute virus of mice MVMp, and the avian leucosis virus. Of particular interest for hu man pathology is the report that chloroquine inhibits uncoating of the hepatitis A virus, thus blocking its entire replication.(Devaux et al., 2020; Pirzada et al., 2025)

Replication of enveloped viruses' interaction:
Chloroquine induces to accumulate of non-infectious diseases herpes simplex viruses 1 particles in the TGN by inhibiting budding of Mayaro virus particles. Chloroquine inhibits the replication of the Flaviviridae viruses with the avian reticulo-endotheliosis viruses REV, A, and HIV, 1, The mechanism of action to affect the normal proteolytic process of flavivirus prim protein to M and impaired viral infectivity(Aamir et al., 2025). Chloroquine also produces of non-infectious retrovirus particles to inhibit of glycosylation of the envelope glycoproteins. (Devaux et al., 2020; Shahab et al.)

Effects of chloroquine on the immune system:
Chloroquine accumulate in lymphocytes and macrophages, seems to have anti-inflammatory properties led to its clinical uses in the treatment of auto-immune diseases i.e., rheumatoid arthritis, SLE, sarcoidosis(Abdullah et al., 2022). Thus reduces the secretion of TNFα and proinflammatory cytokines in the cell line of a macrophage and in the primary cells of the peritoneal macrophage in mouse, human whole blood cells and mononuclear cells of the peripheral blood.(Ahmad et al., 2026; Ratikan et al., 2013)

Safety considerations:
Chloroquine seems to have in-vitro antiviral, anti-inflammatory and immune activation properties associated in those viral infections, the risk/benefit ratio is to estimate the safety criteria. Chloroquine has been uses since more than 50 years in the treatment and prevention of malaria, demonstrate the safety of the drug but also has a high and well-studied toxicity profile in human being(Ghufran et al., 2023) . Chloroquine has been showed low incidence of adverse reactions as uses in the prophylaxis of antimalaria even chronic administration of the drug for periods of up to many years(M. Khan et al., 2026).

Recent studies are encouraging the uses of this drug even in pregnancy showed safety profile of a high dosage (up to 500 mg of chloroquine base per day).

So, the administration and uses of this old drug, chloroquine showed low risk ratio with high benefit and well preventable toxicity in human being when administered in life threatening condition such as AIDS, SARS, both these serious infectious diseases are caused by enveloped RNA viruses. (Devaux et al., 2020)

Materials And Methods:

We reviewed in vitro studies, in vivo studies, original studies, clinical trials, and consensus reports that were conducted to evaluate the antiviral activities of chloroquine and hydroxychloroquine. The studies on "COVID-19 and its allied treatment were found from World Health Organization (WHO), ISI-Web of Science, PubMed, EMBASE, Scopus, Google Scholar, and clinical trial registries. The search was based on keywords: antiviral drugs, chloroquine, hydroxychloroquine, COVID-19, COVID-19 treatment modalities, and coronavirus. In addition, we analysed the prevalence of COVID-19 in malaria pandemic and non-pandemic countries. The review and analyses were performed on March 28, 2020.(Feng et al., 2020)

The following trials have been done so far.

- Only limited clinical trial data available to date to support use of chloroquine or hydroxychloroquine for treatment or prevention of COVID-19.(Chowdhury et al., 2020).
- Multiple clinical trials initiated using various dosages in patients with COVID-19 in China and other countries. (3)
- Clinical experience in patients with COVID-19 accumulating; reports of possible clinical benefits, including decrease in viral load and duration of illness, only limited data available to date to support efficacy and identify possible safety concerns in patients with COVID-19. (Cortegiani et al.)
- Hydroxychloroquine with Azithromycin: Preliminary data from an ongoing study in France in hospitalized patients with confirmed COVID-19 was used to assess efficacy of hydroxychloroquine used alone or with azithromycin; un-treated patients were used as a negative control. The primary end point was negative PCR results in nasopharyngeal samples at day 6. Data from 14 patients treated with hydroxychloroquine (200 mg 3 times daily for 10 days),(Kapoor & Kapoor, 2020) Patients treated with hydroxychloroquine and azithromycin (500 mg on day 1, then 250 mg daily on days 2-5), and 16 patients in the control group were analysed. At day 6, 8/14 (57%) in the hydroxychloroquine group, 6/6 (100%) in the hydroxychloroquine and azithromycin group, and 2/16 (12.5%) in the control group had negative PCR results. At day 8, a positive PCR was reported in a patient treated with both drugs who had tested negative at day 6. This was a small nonrandomized study that didn't appear to be designed to compare hydroxychloroquine vs hydroxychloroquine and azithromycin (patients received antibiotics to prevent bacterial super-infection based on clinical judgment). Data on disease severity was unclear (some asymptomatic patients were included when study initiated) and information on disease progression and clinical outcomes was not presented. Although it provides some evidence of the effects of hydroxychloroquine in patients with COVID-19, additional data needed before any conclusions can be made regarding possible benefits of using hydroxychloroquine with azithromycin. (Esposito et al., 2020; Rabaan et al., 2020)

Dosage:

Various dosages recommended or being investigated.

- Oral chloroquine phosphate: 500 mg twice daily for 10 days. (4)
- Oral chloroquine phosphate: 500 mg twice daily for 7 days (adults 18-65 years weighing (50 kg), 500 mg twice daily on days 1 and 2, then 500 mg once

daily on days 3-7 (adults weighing 50 kg). (Kapoor & Kapoor, 2020)

- Oral chloroquine phosphate: Initial dose of 600 mg (of chloroquine) followed by 300mg (of chloroquine) 12 hours later on day 1, then 300 mg (of chloroquine) twice daily on (days 2-5). (Kapoor & Kapoor, 2020)
- Consider: 500 mg of chloroquine phosphate is equivalent to 300 mg of chloroquine base.(Singh et al., 2020)
- Oral hydroxychloroquine: 400 mg twice daily on day 1, then 200 mg twice daily on days 2-5. (Cortegiani et al., 2020)
- Oral hydroxychloroquine: 400 mg daily for 5 days. (4)
- Oral hydroxychloroquine: 100-200 mg twice daily for 5-14 days. (4)
- Oral hydroxychloroquine: 200 mg 3 times daily for 10 days. (Cortegiani et al., 2020)

Conclusion:

1- Efficacy of chloroquine or hydroxychloroquine for treatment or prevention of COVID-19 not established.

2- Additional data needed to determine whether in vitro activity against SARS-CoV-2 corresponds with clinical efficacy for treatment or prevention of COVID-19.

3- Additional data needed to substantiate initial reports of efficacy and identify optimal dose and duration.

4- Chloroquine and hydroxychloroquine are suggested as possible options and are included in some guidelines for treatment of COVID-19.

Comments:

Common cold viruses are being addressed differently in different regions. People of the subcontinent including Pakistan, India, Bangladesh, Afghanistan, probably due to the dirty atmosphere have the common cold at an average of 7 to 12 attacks per year as compared to European countries. This may have been a blessing in disguise as this may have increased the immunity of the population in these areas. To my knowledge we have better immune response to COVID-19 & other diseases as compare to others i.e., west countries.

Suggestion:

Finally, something practical and honest from the Head of the infectious Disease Clinic, University of Maryland, USA. (Park et al., 2016)

- We may have to live with C-19 viruses for months or many years, let us learn to live with this fact and do not make our lives useless.
- You cannot destroy C19 viruses that have penetrated cell walls, drinking gallons of hot water – you just go to the bathroom more often.
- Washing hands and maintaining at least 2 meters of distance is the best method of protection.
- If you do not have a C19 patient at home, there is no need to disinfect the surfaces around at your home.
- Lugged, packages of cargo, petrol and gas pumps, shopping carts and ATMs do not cause infection.
- C19 is not a food infection, and there is no demonstrated risk that C19 is transmitted by ordering food. It is associated with drops of infection like the flue.
- You can also lose your senses of smells with a lot of allergies and others viral infections. This is only a non-specific symptom of C19.
- 0nce at home, you do not need to change your clothes and go shower.
- The C19 viruses does not hanging in the air. This is a respiratory droplet infection that requires close contacts with each-others.
- The air is clean, you can walk through the parks and gardens, and just keeping your physical protection distance through garden or park.
- It is enough to use normal soap against C19 and do not use antibacterial soap. This is a virus not bacteria.
- You do not have to worry about your food orders. But you can heat it all up in the microwave if you wish.

- The chances of bringing C19 home with your shoes is like being struck by lightning twice in a day, infection do not spread like that!
- You cannot be protected from the virus by taking vinegar, sugarcane juice and ginger! These are for immunity not a cure.
- Wearing a mask for long periods interferes with your breathing and oxygen levels. Wear it only in crowds.
- Wearing of gloves is also not a good idea, if you touch your face through contaminated gloves the viruses can be easily transmitted, better just to wash your hands regularly.
- Immunity is greatly weakened by always staying in a sterile environment. Even if you eat immunity boosting foods, please go out of your house regularly to any park/beach. Immunity is increased by EXPOSURE TO PATHOGENS, not by sitting at home and consuming fried/spicy/sugary food and aerated drinks. We must learn to live with C19.

Data collection procedure:

We reviewed in vitro studies, in vivo studies, original studies, clinical trials, and consensus reports, that were conducted to evaluate the antiviral activities of chloroquine and hydroxychloroquine. The studies on "COVID-19 and its allied treatment were found from World Health Organization (WHO), ISI-Web of Science, PubMed, EMBASE, Scopus, Google Scholar, and clinical trial registries. The search was based on keywords: antiviral drugs, chloroquine, hydroxychloroquine, COVID-19, COVID-19 treatment modalities, and coronavirus. In addition, we analysed the prevalence of COVID-19 in malaria pandemic and non-pandemic countries. The review and analyses were performed on March 28, 2020.(Feng et al., 2020)

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