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Review Article

AN OVERVIEW ON HYDROXYCHLOROQUINE AND COVID -19

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ABSTRACT

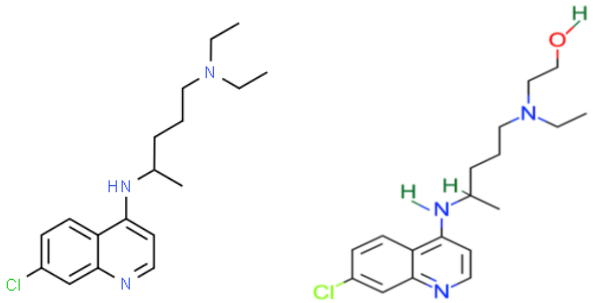
Recently, a novel coronavirus (2019-nCoV), officially known as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), emerged in China. Despite drastic containment measures, the spread of this virus is ongoing. SARS-CoV-2 is the aetiological agent of coronavirus disease 2019 (COVID-19) characterized by pulmonary infection in humans. Preliminary trials of chloroquine repurposing in the treatment of COVID-19 in China have been encouraging, leading to several new trials. Here we discuss the possible mechanisms of chloroquine interference with the SARS-CoV-2 replication cycle. There is a long trail of research studies testing the in vitro and in vivo efficacy of chloroquine and its derivatives in treating and preventing infection by various coronavirus species. More recent findings have highlighted the possibility of treating patients infected with the 2019 novel coronavirus, SARS-CoV-2. This review describes About COVID-19 and Hydroxychloroquine and mechanism of action of chloroquine, and summarizes the available literature highlighting the efficacy of chloroquine as an anti-coronavirus agent.

Keywords: COVID-19, Hydroxychloroquine, SARS-COV-2, China, Preliminary trials

1. INTRODUCTION

The outbreak of coronavirus disease 2019 (COVID-19) caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2/2019-nCoV) poses a serious threat to global public health and local economies. As of March 3, 2020, over 80,000 cases have been confirmed in China, including 2946 deaths as well as over 10,566 confirmed cases in 72 other countries. Such huge numbers of infected and dead people call for an urgent demand of effective, available, and affordable drugs to control and diminish the epidemic [1].

Retinopathy is a dose-limiting adverse effect of hydroxychloroquine, and a safe daily dose appears to correspond to 6.5 mg/kg of ideal body weight and 5.0 mg/kg of actual body weight. Although there are more clinical data on the anti-corona viral activity of chloroquine than that of hydroxychloroquine, both of these agents are theoretically similar in their antiviral activity. Moreover, chloroquine is not as widely available as hydroxychloroquine in some countries. In addition, chloroquine is associated with greater adverse effects than hydroxychloroquine. For example, in patients with COVID-19, chloroquine can interact with lopinavir/ritonavir, resulting in prolongation of the QT interval. Hence, it is necessary to consider hydroxychloroquine instead of chloroquine when the latter is not available for treating patients with COVID-19. For example, in Iran, there is a serious shortage of chloroquine and hydroxychloroquine can be recommended instead. Other therapeutic agents for COVID-19, such as antiviral agents (oseltamivir, lopinavir/ritonavir, ribavirin, etc.), interferons and intravenous immunoglobulins that do not interfere with hydroxychloroquine, are currently under investigation [2].



(a) (b)

Fig. 1: Structure of (a) Chloroquine, (b) Hydroxy -chloroquine

2. USES OF HYDROXYCHLOROQUINE

2.1. Used to treat systemic lupus erythematosus

2.2. Used in rheumatic disorders

2.3. Used to treat Fever and Malaria
2.4. Also gives activity against COVID -19

3. SIDE EFFECTS

In short term maleria

3.1. Abdominal cramps
3.2. Cramps
3.3. Diarrhea
3.4. Heart problems
3.5. Reduced appetite
3.6. Headache
3.7. Vomiting

Table 1: Properties of Hydroxychloroquine and Chloroquine

Term	Hydroxychloroquine	Chloroquine
Formula	C18H26ClN3O	C18H26ClN3
Molar mass ($g \cdot mol^{-1}$)	335.872	319.872
Bioavailability	Variable	Variable
Protein Binding	45%	46-74%
Half life	32-50 days	1-2 months
Metabolism	Liver	Liver
Excretion	Mostly kidney	Mostly kidney

4. MECHANISM OF HYDROXYCHLOROQUINE

Hydroxychloroquine (HCQ), sold under the brand name Plaquenil among others, is a medication used to prevent and treat malaria in areas where malaria remains sensitive to chloroquine. Other uses include treatment of rheumatoid arthritis, lupus, and porphyria cutaneatarda. It is taken by mouth. It is also being studied as a treatment for coronavirus disease 2019 (COVID-19) [3, 4].

5. POTENTIAL ANTIVIRAL EFFECT OF CHLOROQUINE AGAINST SARS-COV-2

Because of its broad spectrum of action against viruses, including most coronaviruses and particularly its close relative SARS-CoV-1, and because coronavirus cell entry occurs through the endolysosomal pathway, it made sense in a situation of a public-health emergency and the absence of any known efficient therapy to investigate the possible effect of chloroquine against SARS-CoV. A recent paper reported that both chloroquine and the antiviral drug remdesivir inhibited SARS-CoV-2 in vitro and suggested these drugs be assessed in human patients suffering from COVID-19 [5]. Recently, the China National Center for Biotechnology Development indicated that chloroquine is one of the three drugs with a promising profile against the new SARS-CoV-2 coronavirus that causes COVID-19. Chloroquine repurposing was investigated in hospitals in Beijing, in central China's Hunan Province and South China's Guangdong Province. According to preliminary reports from the Chinese authorities suggesting that approximately 100 infected patients treated with chloroquine experienced a more rapid decline in fever and improvement of lung computed tomography (CT) images and required a shorter time to recover compared with control groups, with no obvious serious adverse effects, the Chinese medical advisory board has suggested chloroquine inclusion in the SARS-CoV-2 treatment guidelines. As a result, chloroquine is probably the first molecule to be used in China and abroad on the front line for the treatment of severe SARS-CoV-2 infections. Although the long use of this drug in malaria therapy demonstrates the safety of acute chloroquine administration to humans, one cannot ignore the minor risk of macular retinopathy, which depends on the

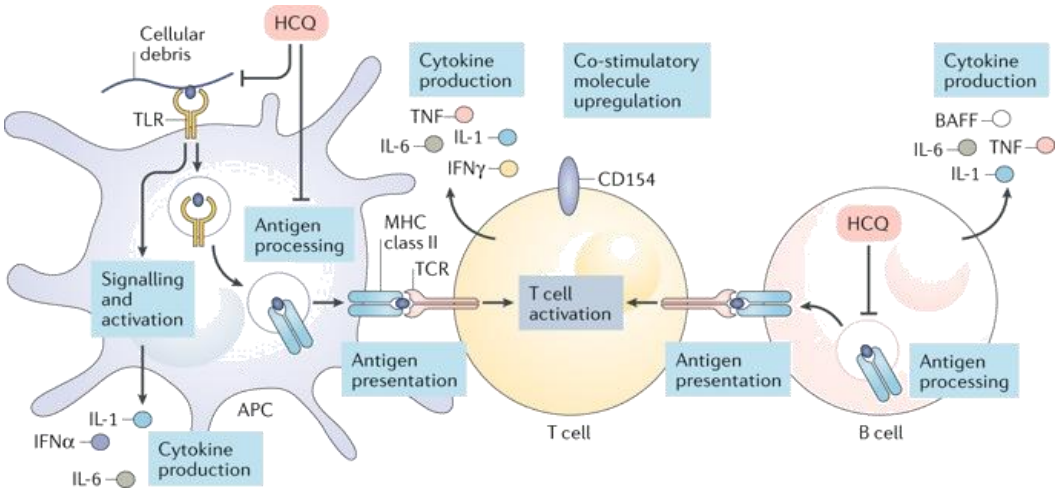


Fig. 2: Mechanism of action of Hydroxychloroquine

cumulative dose and the existence of some reports on cardiomyopathy as a severe adverse effect caused by chloroquine [6]. A survey of SARS-CoV-2-infected patients for adverse effects of chloroquine therapy remains to be performed. However, chloroquine is currently among the best available candidates to impact the severity of SARS-CoV-2infections in humans. Currently, at least ten clinical trials are testing chloroquine as an anti-COVID-19 therapy [7, 8].

6. ABOUT HYDROXYCHLOROQUINE RESEARCH AGAINST COVID -19

As of 3 April 2020, there is limited evidence to support the use of hydroxychloroquine for coronavirus disease 2019 (COVID-19). Studies are ongoing with the benefits versus harms of treatment being unclear. While its use is not approved by the FDA for COVID-19 as of 7 April 2020, there is an Emergency Use Authorization for such use.Some are also using it off label for the disease [9].

In April 2020, the US National Institutes of Health (NIH) began a trial to assess whether hydroxychloroquine is safe and effective to treat COVID-19. A small randomized trial in China of 30 patients did not show a demonstrable effect with hydroxychloroquine [10].

7. CONCLUSION

In our review article description the MOA of Hydroxychloroquine and information about it's and Chloroquine. Chloroquine, a relatively safe, effective and cheap drug used for treating many human diseases including malaria, amoebiosis and human immunodeficiency virus is effective in inhibiting the infection and spread of SARS CoV in cell culture. The fact that the drug has significant inhibitory antiviral effect when the susceptible cells were treated either prior to or after infection suggests a possible prophylactic and therapeutic use.

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