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Chemistry of selected drugs for SARS-CoV-2 inhibition: Tested *in vitro* and approved by the FDA

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A B S T R A C T

Coronavirus belongs to many species of viruses that cause multiple diseases for mankind and different animals. Several coronaviruses are well-known to cause respiratory tract infection in human beings, starting from common colds with effective infection. COVID-19 is a contagious disease caused by a recently discovered coronavirus (SARS-CoV-2019), which mainly attacks the respiratory system. In this research, we are focusing on the up-to-date used medications to treat COVID-19. The presented medications were approved by many governmental administrations and also tested in many trails.

Capsule Summary: The chemistry of the suggested drugs that could help to treat COVID-19 patents and methods of protection were discussed.

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INTRODUCTION

There was no previous knowledge about the presence of the SARS-CoV-19 virus, that caused COVID-19 disease, before its spreading in China, essentially in Wuhan city in December 2019 (Alsayed et al., 2020a). The World Health Organization (WHO) officially announced the COVID-19 as a pandemic on 12 March 2019 where COVID-19 cases were confirmed in 139 countries worldwide. On March 13, the total cases were 145,369 and total deaths were 5429 (Hadi et al., 2020a). Therefore, the world response to the COVID-19 outbreak was by monitoring and containing the cases to control the infection during the pandemics. China has listed the biosafety and infectious disease prevention guidelines after the epidemic of SARS in 2003, where a direct network reporting

system for infectious diseases was set. In July 2004, the national program to monitor infectious diseases was released with the earlier diagnosis; besides, the national program had many responding plans that played an important role in response to the recent outbreak (Aldoori et al., 2021). Since SARS-CoV-2 was identified by the Chinese researchers in Wuhan/Hubei Province, there were attempts to prevent spreading the disease in the next 10 days. Unfortunately, these attempts were unsuccessful and the source of the outbreak kept unknown. COVID-19 is difficult to detect because only a minor portion of patients reveals the symptoms, while others were without pneumonia symptoms or fever. On February 19th, 2020, Iran reports about COVID-19 emerged, sending fear about a pandemic that began in Qom. On the first of March, the cases in Iran became 593 cases with 43 deaths (Alsayed et al., 2020b). Later, Latin America published the first report of coronavirus, which synchronized with a carnival that attracts international visitors with millions of Brazilians; the first case of infection came from Italy (Rodriguez-Morales, 2020; Franco-Paredes, 2020).

Iraq and many Arab countries gained COVID-19 disease because of some citizens who visited Iran and came back home. However, the first case was detected in Iraq at Al-Najaf city in February 2020 for an Iranian student. On March 13, 2020, the Iraqi Health Ministry declared that 101 confirmed cases and 9 deaths recorded in 14 out of 18 Iraqi provinces due to COVID-19 (Al-mashhadani et al., 2020).

In Italy, on the 20th of February in the Northern area, two large outbreaks have spread, then all over the country. The disease spreading was very rapid and a remarkable increase occurred in a few weeks as total cases 86.498, positive cases 66.414, fatalities 9.134 and recoveries 10.950 (INMH, 2020). A similar situation took place in France, On March 27, more than 30,000 cases were reported and nearly 2000 have died (Dong et al., 2020).

Many clinical trials are ongoing to test possible therapies now, Ivermectin has a broad spectrum of antiviral activity in vitro with an inhibition of the SARS-CoV-2. The Food and Drug Administration (FDA) approved Ivermectin as anti-parasitic previously, though it needs further investigation to obtain the maximum possible benefits in humans (Calya et al., 2020).

Similarly, hydroxychloroquine showed good efficiency on SARS-CoV-2, and its effect is improved with azithromycin in treating the COVID-19 cases (Molina, J., et al., 2020). Recently, the French Ministry of Health allowed the use of hydroxychloroquine to cure COVID-19 although the results of current clinical trials are still pending (Gautret et al., 2020; Toumi et al., 2020). Also, colchicine was used as an unselective inhibition of NLRP3 inflammasome, which could prevent the COVID-19 (Deftereos et al., 2020).

The psychological situation of an individual has a high impact on people's health and immunity. Information about the COVID-19 epidemic on the internet may not be accurate and uncontrolled, thus people feel depressed, despaired, and anger especially during the isolation period. However, free psychological consultation played an important role in supporting the medical staff and people to successfully overcome mental disorders. This may be used as a reference to pass this crisis by governments across the world (Dan, 2020). Another way of treatment, which is free, available, and simple to apply is the exposure to direct sunlight (ultraviolet radiation). It was found that 7-14 min exposure to sunlight can kill the virus (Ratnesar-Shumate, 2020).

Chemistry of drug

Antimalarial drugs like hydroxychloroquine and chloroquine are classes of drugs known as 4-aminoquinolines. These are used in the treatment of

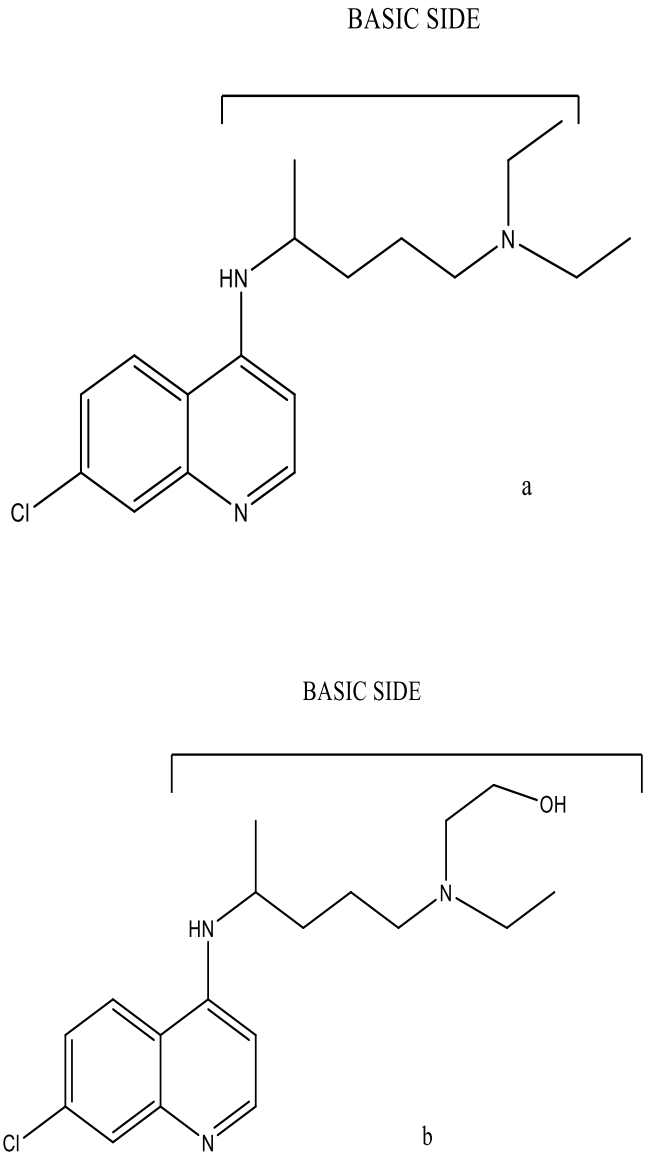

Fig. 1: The chemical structure of (a) Chloroquine and (b)

rheumatoid arthritis, systemic lupus, and inflammatory rheumatic diseases, Figure 1 shows the structure of these components. Both drugs have an aromatic ring that is classified as weak bases due to the presence of a basic ring, these drugs interfere with the lysosomal activity and autophagy. The basic side of the chain interacts with the nucleic acids through the membrane, which alters signaling pathways and transcriptional activity modulation of costimulatory molecules (Schrezenmeier and Dörner 2020). The interaction of lysosomal activity may help in cytokine production (Mauthe et al., 2018). Different countries recommend different types of drugs; China reports found that chloroquine inhibits the *COVID-19 in vitro* in humans. While France found hydroxychloroquine to be a good drug to treat the disease (Owens, B., 2020). The US FDA also declared the use of hydroxychloroquine in SARS-CoV-2 treatment. It is good to mention that hydroxychloroquine drug was used as an antiviral for the past 40 years (Cyranoski, 2020).

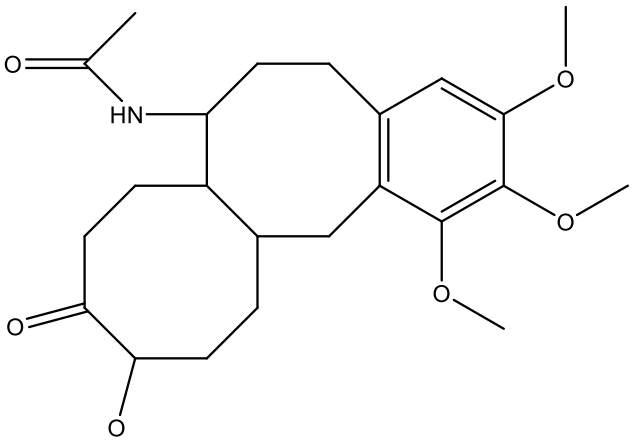

Fig. 2. The chemical structure of Colchicine

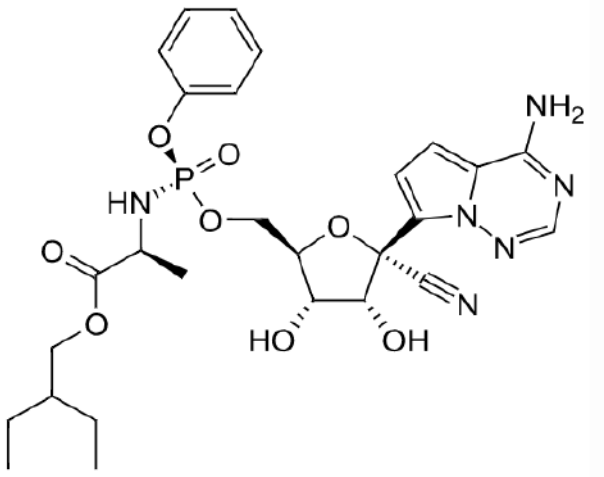

Fig. 3: The chemical structure of Remdesivir

Colchicine is approved by the FDA, it is a drug used for years in various cases showing a safety profile and promising results. In the United States, since 1969, it was utilized for Mediterranean fever and gout treatment (Adler, Y., et al., 2015; Tardif, J.C., et al., 2019). In its recent use, it can reduce the inflammatory cause of COVID-19 and improve the immunity system. As a result, pneumonia, system failure, and death are decreasing (Rabbani, A. B., et al., 2020). The antiviral medication is among the first medicines prescribed for treating SARS-CoV-2. The University of Chicago Medicine had a study on 125 volunteers with SARS-CoV-2, where 113 had severe conditions (Feuerstein, A., et al., 2020). Only two cases faced death and all others were discharged with good health. However, Remdesivir was originally developed against the EBOLA virus (Nili et al., 2020; Amirian and Levy, 2020).

Preventive measures

Wash hands with soap and water constantly for 20 seconds. Avoid handshaking and kissing in meetings. Cover the mouth and nose when coughing and sneezing. Get rid of used napkins in a safe manner. Avoid direct contact with any suspected or confirmed case. Avoid contact with the eyes, nose, and mouth by hand after contact with surfaces. Eat healthy foods, rich with vitamin C to strengthen your immune system. Avoid using the same cup or bowl for more than one person.

The common symptoms are high temperature, tiredness, and dry cough. A few patients may suffer pain, headaches, nasal congestion, cool, laryngitis, or diarrhoeal. The disease can be transferred from the patient to another person by a small spray that is dispersed from the nose and mouth when the patient coughs and sneezes. The spray of coughs or sneezes falls on the surfaces, and other people can get infected when they touch the contaminated surfaces and then touch their faces. People can also become infected if they breathe the spray of coughs or sneezes from the infected person.

Therefore, it is important to stay away from patients for more than two meters. The main mode of transmission is the respiratory residual that a person generates when coughing. The risk of COVID-19 spreading is reduced by a person who has no symptoms but the opportunity is still presenting, especially in the early phases of the disease. Statistics indicate that older people and people with chronic illnesses are the most affected class (Hadi et al., 2020b). As a domestic way to treat or decrease the hard breathing associated with COVID-19, we recommend breathing the boiled eucalyptus vapor. This practice with drugs could help patients to overcome the disease (Marzano et al., 2021; Núñez-Gil et al., 2021; Repullo, 2021; Rizzetto et al., 2021).

CONCLUSIONS

The chemistry of some medications that were suggested as COVID-19 treaters were discussed. These drugs are suggested due to their medical history and benign effect. Clinical trials were conducted on patents and good results were obtained. Antimalarial drugs, colchicine and antivirals showed good impact in curing from COVID-19. Decreasing the symptoms of COVID-19 could help saving lives, in addition to other infection prevention methods. Also, protecting the body from the cytokine storm is an important way of treatment.

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