

An overview of some drugs: Lopinavir, Ritonavir, Chloroquine, Hydroxy chloroquine and Interferon as a effective treatment against COVID-19

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ABSTRACT

Lopinavir, Ritonavir and Interferon (IFN) are anti-viral drugs mainly used in the treatment of HIV infection by protease inhibitors. Chloroquine and Hydroxychloroquine are used in the treatment of malarial, causing infection such as Plasmodium falciparum and also autoimmune condition such as rheumatoid arthritis. Chloroquine makes toxic for the parasite to digest its host haemoglobin and disrupting the virus ability to enter the cell. The anti-viral and anti-malarial drugs are used in the first-line drug therapy for the treatment of COVID-19. This therapy aims to minimize the symptoms and shortens the duration of illness.

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INTRODUCTION

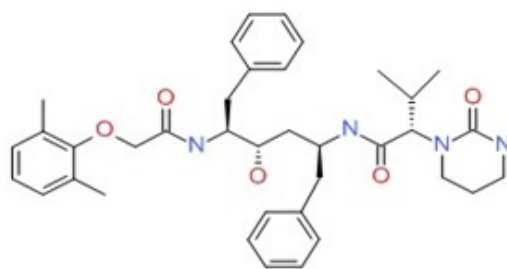
There are different types of viruses that affect humans, birds and animals, some causing severe illness. New species of the human virus are still being identified. The severity of these viruses differs in their ranging from mild to severe illness.

The coronavirus is a kind of positive-chain single-stranded RNA virus with a diameter of 80-120 nm, which can be classified as a, b, d, and g type. It spreads only when the person is in close contact with the infected person or inhalation of small droplets of the infected person, so social distanc-

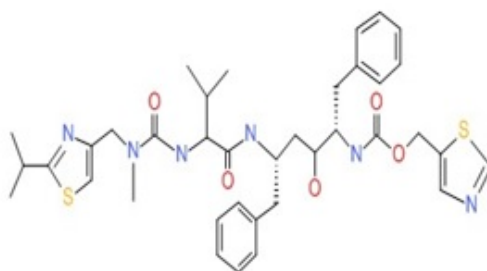
ing is the only way to prevent the spread of diseases. Coronavirus has the characteristics of various strains, wide distribution, and cross-species newly identified human virus in the sense that they have recently started to infect humans called as specialist human pathogens some are SARS (Severe Acute Respiratory Syndrome- horseshoe bats) and Human coronavirus OC43. Such viruses are easily transmitted between humans to cause significant outbreaks and become pandemic in the human population [1].

Viruses are obligate, intracellular parasites, challenging to find out the drug target site that interferes in the viral replication without affecting the host cell. Coronavirus is one among the contagious diseases that affect humans, animals and birds it causes upper respiratory tract infection may be mild to lethal those who have weakened immune system or those who have medical conditions including asthma, heart, lung or liver diseases, severe obesity, kidney diseases and diabetes, there is no specific treatment for COVID-19. So several studies focused on the anti-viral medication like Lopinavir, Ritonavir and interferon & Anti-malarial drugs like chloroquine and Hydroxychloroquine [2].

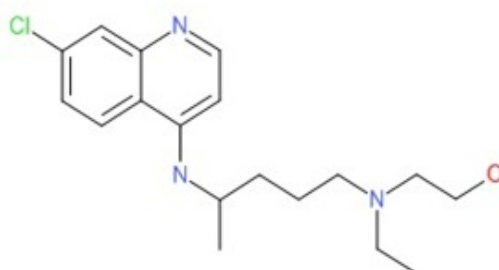
To inhibit the viral action, there are the number of



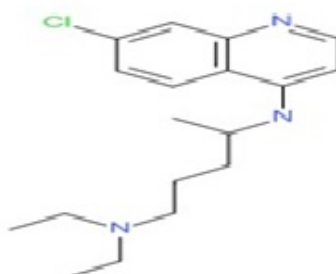
A.Lopinavir



B.Ritonavir



C.Hydroxychloroquine



D.Chloroquine

Figure 1: Structure of anti-viral drugs

Table 1: Mechanism, clinical uses and adverse effect

Sl.No	Drug	Mechanism of action	Clinical uses	Side effect
1	Lopinavir	Protease inhibitor	* Anti-viral drug * Anti-Retroviral agent * Enzyme inhibitors * Experimentally unapproved treatment for COVID-19 [3]	liver problems–loss of appetite, stomach pain, itching, dark urine, Hyperglycemia Polydipsia increased urination
2	Ritonavir	Protease inhibitor	* Anti-Retroviral agent for the treatment of HIV infection * Experimentally unapproved treatment for COVID-19 [4]	nausea, vomiting, diarrhoea high cholesterol or changes in the shape or location of body fat (especially in your arms, legs, face, neck, breasts, and waist).
3	Chloroquine	It inhibits viral replication in the membrane by pH-dependent	* Anti-Malarial drug * 2 nd line agent in the treatment of rheumatoid arthritis * Anti-inflammatory response * Immunomodulatory response * Anti-viral drug * Inhibit early-stage replication in COVID-19	chest discomfort or pain chills cold sweats confusion continuing ringing or buzzing or other unexplained noise in the ears cough dark urine
4	HCQ	Increase pH within intracellular vacuoles and alter processes such as protein degradation by acidic hydrolases in the lysosome, assembly of macromolecules in the endosomes, and posttranslational modification of proteins in the Golgi apparatus.	*Immunosuppressants * Anti-malarial agent * Anti-infective agent [5]	headache dizziness diarrhoea stomach cramps vomiting
5	Interferon	Protease inhibitor	* Anti-viral agents *Immunosuppressive agents [6]	Fever Chills Headache Muscle aches Pains Malaise

anti-viral drugs used, anti-viral drugs (LOPINAVIR, RITONAVIR and INTERFERON) inhibit the protein that contributes one or several steps in viral replication. There are four classes of anti-viral drugs [7].

PROTEASE INHIBITOR

- Neutralizing antibodies
- Protein-based fusion inhibitors

- Neuraminidase inhibitors

Chloroquine- Inhibit the degradation of haemoglobin ingested by the parasite by raising the pH of the food vacuole of the parasite.

Hydroxychloroquine (HCQ) –Impair or inhibit lysosomal and autophagosome function and activate the immune system.

Interferon (IFN)- Inhibit the viral replication at the early stage but failed to inhibit at a later stage. IFN

is safe and comfortable to upscale treatment against COVID-19 in the early stage of infection. IFN produce a protective effect on the respiratory tract. IFN in combination with Lopinavir, Ritonavir and Hydroxychloroquine and Remdesivir in the first clinical trial in the WHO [8].

Pathology and drug target of COVID-19

Once COVID-19 enters the alveolus, it begins to infect type II alveolar cells and replicate, infected type II alveolar cells release pro-inflammatory cytokines, which reduces the immune system activity and produce symptoms such as cough, fever and body aches. Neutrophils release reactive oxygen species and proteinases, which destroy infected cells. These dead cells combine with the plasma to form a protein-rich fluid that accumulates within the alveolus, causing shortness of breath and pneumonia. Accumulation of fluid and dilution of surfactant lining the alveolus causes alveolar collapse, which decreases gas exchange and can lead to hypoxaemia and acute respiratory distress syndrome. If the immune system goes into overdrive, inflammation can spread throughout the circulatory system, leading to systemic inflammatory response syndrome, also known as a cytokine storm. This systemic inflammation can cause septic shock, where blood pressure drops dangerously low, and organs can no longer be perfused, leading to multi-organ failure and death [9].

Contraindication of Chloroquine and Hydroxychloroquine

Some precautions will be needed while using these drugs that include frequent monitoring of haematological parameters (RBC, WBC and platelet counts) Chloroquine and HCQ should not be used concurrently with lopinavir/ritonavir and remdesivir for QTC prolongation [10]. Use of HCQ in patients with diabetes in India where it is already approved for treatment. All clinicians using these drugs must know contraindication to both these compounds; hypersensitivity to these agents, retinopathy, porphyria, epilepsy, preexisting maculopathy, G6PD deficiency, recent myocardial infarction [10, 11].

The anti-viral activity of chloroquine and HCQ have been identified in the in-vitro studies and the growth of many different viruses have been inhibited in the cell culture line by both the agents, including the SARS COVID.

Lopinavir and Ritonavir are contraindicated to some patients, which shows hypersensitivity and hepatic impairment [12].

CONCLUSION

Many clinical trials are underway to explore new medication to treat COVID-19. Lopinavir, Ritonavir, interferons, Chloroquine and Hydroxychloroquine, are used for the treatment regimen for COVID-19. Further novel drug discovery and development for COVID-19 remains for future studies. Several trials are currently underway with both chloroquine and HCQ in patients with COVID-19 at different doses. Research for resistance to drugs in already mutating virus strains We still do not know whether these compounds can be useful to prevent the transmission of the virus, especially for healthcare workers. Recently drug repurposing is the only way to treat the COVID-19. There is no specific vaccination for preventing the spread of COVID. Researches are still in progress to find out the new molecule for the treatment of COVID 19 pandemic.

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CONFLICT OF INTEREST

None declared

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