



NOVEL CORONA VIRUS AND ITS IMPACT: A REVIEW

Steffy P Raju¹, Sreejith. M^{1*}, Akash Marathakam²

¹Nazareth College of Pharmacy, Othera P.O Thiruvalla, Kerala, India

²National College of Pharmacy, Manassery P.O Calicut, Kerala, India

*Corresponding author E -mail: sreejithmadavankutty@gmail.com

ARTICLE INFO

ABSTRACT

Key Words

Coronavirus,
SARS,
MERS, antiviral drugs

Access this article online

Website:

<https://www.jgtps.com/>

Quick Response Code:



Coronaviruses are enveloped RNA viruses and they are related to the family Corona viridae, and it can be observed in humans and other mammals. In December 2019, many pneumonia cases were reported by patients with unknown causes and observed that the demand of marine and wet animals in Wuhan, China has mainly been linked, and viral pneumonia clinically has resembled. Coronaviruses are a huge family of viruses and they can cause various diseases such as common cold to very serious illnesses. They are like the Middle East Respiratory Syndrome (MERS-CoV) and Severe Acute Respiratory Syndrome (SARS-CoV). Novel coronavirus (nCoV) is a different strain and it is newly discovered in humans. The several known coronaviruses circulate in animals not yet infected by humans. It is a zoonotic virus and they are spread between animals and then to humans. The studies showed that SARS-CoV was transmitted to humans by civet cats and MERS-CoV by dromedary camels. The common signs of infections are Respiratory symptoms, fever, cough, shortness of breath, and difficulty in breathing. This review article focuses on some of the points regarding COVID-19 like structure of virus, pathophysiology, transmission of virus, diagnosis, precautions, treatments etc published by WHO and other health officials.

INTRODUCTION

The Coronavirus disease 2019 (COVID 19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).¹ Coronaviruses can infect animals and can sometimes be spread to humans.² The current outbreak was first reported in Wuhan, China, in December 2019,³ declared to be a Public Health Emergency of International Concern on 30 January 2020, and recognized as a pandemic by the World Health Organization on 11 March 2020.⁴ Novel Coronavirus disease (COVID-19) will cause mild to moderate respiratory illness and they will recover without requiring special treatment. Older people and those people with underlying medical problems like cardiovascular disease, diabetes, chronic

respiratory disease, and cancer are more likely to develop serious illness.⁵ The name "coronavirus" is derived from the Latin word Corona and the Greek word korónē, which means crown. While observing through electron microscopy, it reveals the presence of Virions (the virus infectious form), which have a wide fringe, reminiscent of either royal crown or a solar corona. Before the 2003 SARS outbreak, only 19 coronaviruses were identified, which includes 2 humans, 4 avian, and 13 mammalian coronaviruses. More than 20 additional novel coronaviruses with full genome sequences have been identified after the SARS epidemic and as on date, 7 human coronaviruses were identified including the

recent 2019 novel coronavirus. The best way to prevent and slow down transmission is to be well informed about the COVID-19 virus, the disease it causes, and how it spreads and strictly complies with the instructions of health care providers. The COVID-19 virus spreads primarily through droplets of saliva or discharge from the nose when an infected person coughs or sneezes, so we must practice respiratory etiquette by coughing into a flexed elbow.⁶ The first COVID-19 vaccine in China is expected to be ready for clinical trials by the end of April and several pharmaceutical companies are involved in developing coronavirus drugs/vaccines.⁷

DESCRIPTION OF VIRUS:

SARS-CoV-2 is a coronavirus that causes coronavirus disease 2019 (COVID-19). Coronaviruses, in general, are a family of viruses that target and affect mammals respiratory systems. According to their specific characteristics, there are four main genera of coronaviruses, which are called alpha, beta, delta, and gamma. Mostly these genera can affect only animals, but a few can also pass to humans. The genera that are transmissible to humans are alpha and beta.⁸ There have been two major global outbreaks caused by coronaviruses. The first of these was the SARS coronavirus responsible for severe acute respiratory syndrome (SARS) which first started spreading back in 2002 in China. The SARS virus epidemic primarily affected the populations of mainland China and Hong Kong, and it died off in 2003. Severe acute respiratory syndrome (Sars) and Middle Eastern respiratory syndrome (Mers) are both caused by coronaviruses that came from animals. In 2002, Sars spread virtually unchecked to 37 countries, causing global panic, infecting more than 8,000 people and killing more than 750. Mers appears to be less easily passed from human to human, but has greater lethality, killing 35% of about 2,500 people who have been infected.⁹

HOW HUMANS GOT INFECTED?

Studies on the receptor recognition by SARS-CoV have identified the key interactions

between SARS-CoV spike protein and its host receptor angiotensin-converting enzyme 2 (ACE2), which regulate both the cross-species and human-to-human transmissions of SARS-CoV.¹⁰ Humans do become infected with a coronavirus, typically happens via contact with an infected animal. Some of the most common carriers are bats, although they do not transmit coronaviruses directly to humans. The transmission might occur via an intermediary animal, which will usually not always be a domestic one. The SARS coronavirus spread to humans via civet cats, while the MERS virus spread via dromedaries. However, it is difficult to determine the animal from which a coronavirus infection first starts spreading. The new coronavirus is a respiratory virus that spreads primarily through contact with an infected person through respiratory droplets when the affected individual coughs or sneezes, or through saliva droplets or nose discharge. Everyone should practice good respiratory hygiene like sneeze or cough into a flexed elbow or use a tissue and immediately discharge it into a closed bin. It is also very important for people to regularly wash their hands with either alcohol-based hand rub or soap and water.

In the case of the new coronavirus outbreak, initial reports from China tied the outbreak to a seafood market in central Wuhan. As a result, local authorities closed down the market on January 1st. While it is likely originated in animals, the transmission of the new coronavirus from person to person can occur, even though some questions about its transmission remain unanswered. According to the WHO spokesperson, researchers are still studying the exact parameters of human-to-human transmission. The transmission of coronaviruses is through the respiratory route, which means that the virus is concentrated in the airways and it can pass to another person via droplets from their nose or mouth. WHO states that the risk of catching COVID-19 from someone with no symptoms at all is very low. However, many people with COVID-19 experience only mild symptoms. It is therefore possible to catch COVID-19 from someone who has, just a mild cough and does not feel ill. That is, the virus likely takes about 5–6 days to

give rise to symptoms once it has infected a person. WHO note that experts estimate that the new virus's incubation period may last anywhere between 1 and 14 days.¹¹

STRUCTURE OF CORONA VIRUS

Researchers from Chinese institutions were able to use state-of-the-art genome sequencing tools to identify the DNA structure of the novel coronavirus. It has emerged that SARS-CoV-2 is most similar to two bat coronaviruses known as bat-SL-CoVZC45 and bat-SL-CoVZXC21 and its genomic sequence is 88% the same as theirs. The same study shows that the new virus's DNA is about 79% the same as that of the SARS coronavirus and approximately 50% like that of the MERS virus. Recently, a study by researchers in China suggested that pangolins may have been the initial propagators of SARS-CoV-2, as its genomic sequence appeared to be 99% like that of a coronavirus specific to these animals. Since then, however, other specialists have cast doubts over this idea, citing inconclusive evidence.¹¹

PATHOPHYSIOLOGY OF CORONA VIRUS

The SARS-CoV-2 virus, like the closely-related MERS and SARS coronaviruses, affects its cellular entry via attachment of its virion spike protein (a.k.a. S protein) to the angiotensin-converting enzyme 2 (ACE 2) receptor. This receptor is commonly found on alveolar cells of the lung epithelium, underlying the development of respiratory symptoms as the commonest presentation of COVID-19. It is thought that the mediation of the less common cardiovascular effects is also via the same ACE-2 receptor, which is also commonly expressed on the cells of the cardiovascular system.¹²

SYMPTOMS OF CORONA VIRUS DISEASE

According to the WHO, the most common symptoms of Covid-19 are fever, tiredness, and a dry cough. Some patients may

also have a runny nose, sore throat, nasal congestion and aches and pains or diarrhea. Some people report losing their sense of taste and/or smell. About 80% of people who get Covid-19 experience a mild case about as serious as a regular cold and recover without needing any special treatment.¹³ About one in six people, the WHO says, become seriously ill. The elderly and people with underlying medical problems such as high blood pressure, heart problems or diabetes, or chronic respiratory conditions, are at a greater risk of serious illness from Covid-19.

WHAT ARE THE PRECAUTIONS TO BE TAKEN?

Wash your hands frequently:

Regularly and thoroughly clean your hands with an alcohol-based hand rub or wash them with soap and water. Washing your hands with soap and water or using alcohol-based hand rub kills viruses that may be on your hands.

Maintain social distancing:

Maintain at least 1 meter (3 feet) distance between yourself and anyone who is coughing or sneezing. When someone coughs or sneezes they spray small liquid droplets from their nose or mouth which may contain viruses. If you are too close, you can breathe in the droplets, including the COVID-19 virus if the person coughing has the disease.

Avoid touching eyes, nose and mouth

Hands touch many surfaces and can pick up viruses. Once contaminated, hands can transfer the virus to your eyes, nose or mouth. From there, the virus can enter your body and can make you sick.

Practice respiratory hygiene

Make sure you, and the people around you, follow good respiratory hygiene. This means covering your mouth and nose with your bent elbow or tissue when you cough or sneeze. Then dispose of the used tissue immediately. Droplets spread virus. By following good

respiratory hygiene you protect the people around you from viruses such as cold, flu and COVID-19.

If you have fever, cough and difficulty breathing, seek medical care early

Stay home if you feel unwell. If you have a fever, cough and difficulty breathing, seek medical attention and call in advance. Follow the directions of your local health authority. National and local authorities will have the most up to date information on the situation in your area. Calling in advance will allow your health care provider to quickly direct you to the right health facility. This will also protect you and help prevent spread of viruses and other infections.

Stay informed and follow advice given by your healthcare provider

Stay informed on the latest developments about COVID-19. Follow advice given by your healthcare provider, your national and local public health authority or your employer on how to protect yourself and others from COVID-19. National and local authorities will have the most up to date information on whether COVID-19 is spreading in your area. They are best placed to advise on what people in your area should be doing to protect themselves.¹⁴

IMPACT OF CORONA VIRUS

The WHO officially changed their classification of COVID-19 from a public health emergency of international concern to a pandemic on March 11. The global implications have become severe. Many countries have closed schools and are recommending that people work from home where they can. Some international borders have been completely locked down and in many places travel is being discouraged unless it is deemed essential. According to recent assessments, SARS-CoV-2 seems to be more infectious than other coronaviruses such as those that cause SARS and MERS but less likely to lead to death. Some estimates suggest that the death rate of the new coronavirus is in

the range of 2–3%, but there are no official numbers in this regard, as it is hard to tell how the outbreak will develop. **The WHO reports that the two groups most at risk of experiencing severe illness due to a SARS-CoV-2 infection are older adults, defined as “over 60 years old”, and individuals who have other health conditions that compromise their immune system.** The report also notes that the risk of severe disease gradually increases with age starting from around 40 years. Other reports note that very few children have become infected with the new coronavirus. Among adults, some reports suggest that men might be more at risk than women. Pregnant women experience immunologic and physiologic changes which might make them more susceptible to viral respiratory infections, including COVID-19. The CDC also recommend that infants born to mothers with suspected or confirmed COVID-19 are placed in isolation as a “person under investigation.” There are no currently published scientific reports on pregnant women. The WHO reports that pregnant women with COVID-19 symptoms should receive priority access to diagnostic tests.¹⁵

DIAGNOSIS AND MARKERS

The definitive test for SARS-CoV-2 is the real-time reverse transcriptase-polymerase chain reaction (RT-PCR) test. It is believed to be highly specific, but with sensitivity reported as low as 60-70%¹⁶ and as high as 95-97%.¹⁷ Thus, false negatives are a real clinical problem, and several negative tests might be required in a single case to be confident about excluding the disease. Multiple radiological organizations have come forward to state that CT should not be relied upon as a primary diagnostic/screening tool for COVID-19. On 16 March 2020, an American-Singaporean panel published that CT findings were not part of the diagnostic criteria for COVID-19.^{18,19} However, CT findings have been used as a surrogate diagnostic test by some studies.^{20,21}

Markers

The most common ancillary laboratory findings in a study of 138 hospitalized patients were the following.²²

- lymphopenia
- increased prothrombin time (PT)
- increased lactate dehydrogenase

Mild elevations of inflammatory markers (CRP and ESR) and D-dimer are also seen.²³

TREATMENT: There currently isn't a vaccine against developing COVID-19. Antibiotics are also ineffective because COVID-19 is a viral infection and not bacterial. If the symptoms are more severe, supportive treatments may be given by the doctor or at a hospital. This type of treatment may involve:²⁴

- Fluids to reduce the risk of dehydration
- Medication to reduce a fever
- Supplemental oxygen in more severe cases

People who have hard time breathing on their own due to COVID-19 may need a respirator. COVID-19 vaccines and treatment options are being researched worldwide. There is some evidence that certain drugs can be effective in preventing disease or in treating COVID-19 symptoms. However, researchers need to perform randomized controlled trials trusted Source in humans before potential vaccines and other treatments become available. This may take several months or longer. Here are some treatment options that are currently being investigated for protection against SARS-CoV-2 and treatment of COVID-19 symptoms.

1. Chloroquine

Chloroquine and hydroxychloroquine is a clinically approved drug effective against malaria, and it is known to show antiviral effects against several viruses, including human immunodeficiency virus type 1, hepatitis B virus, and herpes simplex virus type 1.²⁵ Scientist Savarino and his colleagues hypothesized that chloroquine might be of some use for the clinical management of SARS.²⁶ Moreover, chloroquine was reported to inhibit the replication of HCoV-229E and

SARS-CoV in vitro. In a study, it showed that the 50% effective concentration (EC₅₀) of chloroquine ($8.8 \pm 1.2 \mu\text{M}$) for the inhibition of SARS-CoV in vitro was significantly lower than its cytostatic activity ($261.3 \pm 14.5 \mu\text{M}$), yielding a selectivity index of 30, and that this EC₅₀ approximates the plasma concentrations of chloroquine reached during treatment of acute malaria. The addition of chloroquine to infected cultures could be delayed for up to 5 h postinfection without a significant drop in antiviral activity.²⁷ The antiviral effects of chloroquine against human immunodeficiency virus type 1 replication are currently being tested in clinical trials. Chloroquine is a weak base that increases the pH of acidic vesicles. When added extracellularly, the nonprotonated portion of chloroquine enters the cell, where it becomes protonated and concentrated in acidic, low-pH organelles, such as endosomes, Golgi vesicles, and lysosomes. Chloroquine can affect virus infection in many ways, and the antiviral effect depends in part on the extent to which the virus utilizes endosomes for entry. Besides having a direct antiviral effect, chloroquine is endowed with an immunomodulatory activity, suppressing the production and release of tumor necrosis factor alpha and interleukin 6, which mediate the inflammatory complications of several viral diseases.²⁸

2. Lopinavir and ritonavir

Lopinavir and ritonavir are sold under the name Kaletra and are designed to treat HIV. In South Korea, a 54-year-old man was given a combination of these two drugs and had a significant reduction Trusted Source in his levels of the coronavirus. According to the World Health Organization (WHO), there could be benefits to using Kaletra in combination with other drugs. The clinical response of patients with severe acute respiratory syndrome (SARS) to a combination of lopinavir/ritonavir and ribavirin was examined after establishing the in vitro antiviral susceptibility of the SARS associated coronavirus to a panel of antiviral agents. The in vitro susceptibility of the prototype of SARS associated coronavirus to a panel of nucleoside analogs and protease inhibitors currently

licensed for clinical use was studied. Forty-one patients with SARS followed for 3 weeks were treated with a combination of lopinavir/ritonavir and ribavirin. The clinical progress and virological outcomes were monitored and compared with 111 patients treated with ribavirin only who served as historical controls. In vitro antiviral activity against SARS associated coronavirus was demonstrated for lopinavir and ribavirin at concentrations of 4 micro g/ml and 50 micro g/ml, respectively, only at 48 hours. The adverse clinical outcome (ARDS or death) was significantly lower in the treatment group than in the historical controls (2.4% v 28.8%, $p < 0.001$) at day 21 after the onset of symptoms. The adverse outcome remained significantly lower in the treatment group than in the controls-both those diagnosed early ($p < 0.001$) and those diagnosed later in the course of the epidemic ($p = 0.002$)-but there was no significant difference in adverse outcome rates between the two time periods ($p = 0.548$). No time related difference in outcome was observed in the control groups. A reduction in steroid usage and nosocomial infections was seen in patients initially treated with lopinavir/ritonavir, and these patients had a decreasing viral load and rising peripheral lymphocyte count. Multivariate analysis showed that age, hepatitis B carrier status, and lack of treatment with this antiviral combination were independent predictors of an adverse outcome. Lopinavir/ritonavir treatment was associated with a better outcome even when adjusted for baseline lactate dehydrogenase level. The apparent favourable clinical response with lopinavir/ritonavir and ribavirin supports further randomised placebo controlled trials in patients with SARS.²⁹

3. APN01

A clinical trial is set to start soon in China to examine the potential of a drug called APN01 to fight the novel coronavirus. The scientists who first developed APN01 in the early 2000s discovered that a certain protein called ACE2 is involved in SARS infections. This protein also helped protect the lungs from injury due to respiratory distress. From recent research, it turns out that

the 2019 coronavirus, like SARS, also uses the ACE2 protein to infect cells in humans. The randomized, dual-arm trial will look at the effect of the medication on 24 patients for 1 week. Half of the participants in the trial will receive the APN01 drug, and the other half will be given a placebo. If results are encouraging, larger clinical trials will be done. APN01 is the recombinant form of the human angiotensin-converting enzyme 2 (rhACE2), and has the potential to block the infection of cells by the novel SARS-CoV-2 virus (COVID-, and reduce lung injury. The Phase II trial aims to treat 200 severely infected COVID-19 patients, and the first patients are expected to be dosed shortly. The novel coronavirus strain SARS-CoV-2 is a very close relative of the first SARS-CoV virus, which emerged globally in 2002. APN01 has a unique dual mode of action. APN01 imitates the human enzyme ACE2, which is used by the virus to enter cells. The virus binds to soluble ACE2/APN01, instead of ACE2 on the cell surface, which means that the virus can no longer infect the cells. At the same time, APN01 reduces the harmful inflammatory reactions in the lungs and protects against acute lung injury (ALI/acute respiratory distress syndrome (ARDS)).³⁰

4. Favilavir: China has approved the use of the antiviral drug favilavir to treat symptoms of COVID-19. The drug was initially developed to treat inflammation in the nose and throat. Although the results of the study haven't been released yet, the drug has supposedly shown to be effective in treating COVID-19 symptoms in a clinical trial of 70 people.³¹

CONCLUSION:

Viral diseases can be devastating like COVID-19, and they can cause both social and economic issues. National and international protocols for the prevention of infection should be stringent, well-coordinated, planned, and scheduled. To avoid the severity of the corona outbreak, hospitals should be prepared for the treatment of cases with control measures and protocols. Several clinical trials and

experiments are needed to find effective medicines and vaccines to treat COVID-19.

REFERENCES

1. <https://Www.Mayoclinic.Org/Diseases-Conditions/Coronavirus/Symptoms-Causes/Syc-20479963>, Retrieved April 17,2020
2. To KK, Hung IF, Chan JF, Yuen KY. From SARS Coronavirus To Novel Animal And Human Coronaviruses. *Journal Of Thoracic Disease*. 2013 Aug;5(Suppl 2):S103.
3. <https://Www.Who.Int/Csr/Don/12-January-2020-Novel-Coronavirus-China/En> Retrieved April 17,2020.
4. [https://Www.Who.Int/News-Room/Detail/30-01-2020-Statement-On-The-Second-Meeting-Of-The-International-Health-Regulations-\(2005\)-Emergency-Committee-Regarding-The-Outbreak-Of-Novel-Coronavirus-\(2019-Ncov\)](https://Www.Who.Int/News-Room/Detail/30-01-2020-Statement-On-The-Second-Meeting-Of-The-International-Health-Regulations-(2005)-Emergency-Committee-Regarding-The-Outbreak-Of-Novel-Coronavirus-(2019-Ncov)) Retrieved April 17,2020.
5. https://Www.Who.Int/Health-Topics/Coronavirus#Tab=Tab_1 (Last Accessed 08/04/2020)
6. Bourouiba L. Turbulent Gas Clouds And Respiratory Pathogen Emissions: Potential Implications For Reducing Transmission Of COVID-19. *JAMA*. 2020 Mar 26
7. <https://Www.Clinicaltrialsarena.Com/Analysis/Coronavirus-Mers-Cov-Drugs/> Retrieved April 17,2020
8. Ramalingam Kothai, Balasubramanian Arul. 2019 Novel Coronavirus: A Mysterious Threat From Wuhan, China—A Current Review; *Int. J. Res. Pharm. Sci.*, 2020, 11(SPL)(1), 7-15
9. *The Guardian.Com*, January 26, 2020.
10. Wan Y, Shang J, Graham R, Baric RS, Li F. Receptor Recognition By The Novel Coronavirus From Wuhan: An Analysis Based On Decade-Long Structural Studies Of SARS Coronavirus. *Journal Of Virology*. 2020 Mar 17;94(7).
11. <https://Www.Medicalnewstoday.Com/Articles/Novel-Coronavirus-Your-Questions-Answered#1.-What-Is-The-New-Virus?> (Last Accessed 07/04/2020)
12. Zheng YY, Ma YT, Zhang JY, Xie X. COVID-19 And The Cardiovascular System. (2020) *Nature Reviews. Cardiology*. Doi:10.1038/S41569-020-0360-5 - Pubmed.
13. Www.Theguardian.Com/World/2020/Apr/07(Last Accessed 07/04/2020).
14. <https://Www.Who.Int/Emergencies/Diseases/Novel-Coronavirus-2019/Advice-For-Public-Precautions>(Last Accessed 07/04/2020).
15. <https://Www.Medicalnewstoday.Com/Articles/Novel-Coronavirus-Your-Questions-Answered#6.-What-Is-Its-Impact?> (Last Accessed 07/04/2020).
16. Jeffrey P Kanne, Brent P Little, Jonathan H Chung, Brett M Elicker, Loren H Ketai. Essentials For Radiologists On COVID-19: An Update—Radiology Scientific Expert Panel. (2020) *Radiology*. Doi:10.1148/Radiol.2020200527 - Pubmed.
17. Mahmud Mossa-Basha, Carolyn C Meltzer, Danny C Kim, Michael J Tuite, K Pallav Kolli, Bien Soo Tan. Radiology Department Preparedness For COVID-19: Radiology Scientific Expert Panel. (2020) *Radiology*. Doi:10.1148/Radiol.2020200988 - Pubmed
18. ACR Recommendations For The Use Of Chest Radiography And Computed Tomography (CT) For Suspected COVID-19 Infection.” *American College Of Radiology*, 11 Mar. 2020, ACR [Accessed 16 March 2020]
19. COVID-19 Updates”. *Ranzcr.Com*, 2020. [Link].
20. Another Decade, Another Coronavirus. (2020) *New England Journal Of Medicine*. Doi:10.1056/Nejme2001126 - Pubmed
21. Jeffrey P Kanne, Brent P Little, Jonathan H Chung, Brett M Elicker, Loren H Ketai. Essentials For Radiologists On COVID-19: An Update—Radiology Scientific Expert Panel. (2020) *Radiology*. Doi:10.1148/Radiol.2020200527 - Pubmed
22. Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, Wang B, Xiang H, Cheng Z, Xiong Y, Zhao Y, Li Y, Wang X, Peng Z. Clinical Characteristics Of 138 Hospitalized Patients With 2019 Novel

- Coronavirus-Infected Pneumonia In Wuhan, China. (2020) JAMA. Doi:10.1001/Jama.2020.1585 - Pubmed
23. Rodrigues, J.C.L. Et Al. An Update On COVID-19 For The Radiologist - A British Society Of Thoracic Imaging Statement. (2020) Clinical Radiology.
 24. <https://doi.org/10.1016/j.crad.2020.03.003>
 25. <https://www.healthline.com/health/coronavirus-treatment#bottom-line> (Last Accessed 08/04/2020)
 26. Els Keyaerts, Sandra Li, Leen Vijgen, Evelien Rysman, Jannick Verbeeck, Marc Van Ranst,* And Piet Maes. antimicrobial agents and chemotherapy, Aug. 2009, P. 3416–3421
 27. Savarino, A., J. R. Boelaert, A. Cassone, G. Majori, And R. Cauda. 2003. Effects Of Chloroquine On Viral Infections: An Old Drug Against Today's Diseases? Lancet Infect. Dis. 3:722–727
 28. Keyaerts, E., L. Vijgen, P. Maes, J. Neyts, And M. Van Rans. 2004. In Vitro Inhibition Of Severe Acute Respiratory Syndrome Coronavirus By Chloroquine. Biochem. Biophys. Res. Commun. 323:264–268.
 29. Singh AK, Singh A, Shaikh A, Singh R, Misra A. Chloroquine And Hydroxychloroquine In The Treatment Of COVID-19 With Or Without Diabetes: A Systematic Search And A Narrative Review With A Special Reference To India And Other Developing Countries. Diabetes & Metabolic Syndrome: Clinical Research & Reviews. 2020 Mar 26.
 30. Chu CM, Cheng VC, Hung IF, Wong MM, Chan KH, Chan KS, Kao RY, Poon LL, Wong CL, Guan Y, Peiris JS, Yuen KY; HKU/UCH SARS Study Group. Thorax. 2004 Mar;59(3):252-6.
 31. <https://www.thepharmaletter.com/article/apieron-biologics-moves-forward-with-apn01-for-treatment-of-covid-19>
 32. <https://www.clinicaltrialsarena.com/news/china-favilavir-testing-approval/>