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A Comprehensive Study of Corona Virus, it's Diagnostic Tests, Treatment and Therapy

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➢ ABSTRACT

Following the emergence of Severe Acute Respiratory Syndrome (SARS) in 2002 and Middle East Respiratory Syndrome (MERS) in 2012, the world is now combating third large scale outbreak caused by coronavirus, the Coronavirus Disease 2019(COVID-19). Since Dec 2019, the global pandemic caused by highly infected novel coronavirus 2019(COVID-19) has been rapidly spreading. In this review we summarize the current diagnostic tools and therapeutic strategies for covid-19.

➢ KEYWORDS

COVID-19, Severe Acute Respiratory Syndrome Corona Virus 2(SARS CoV-2), Diagnosis, Treatment, Vaccines.

➢ INTRODUCTION

Emerging and re-emerging pathogens are global public health challenges.[1] Coronaviruses are non-segmented, enveloped, positive RNA viruses belonging to the family Coronaviridae and the order Nidovirales and are widely distributed in humans and other mammals.[2] The coronavirus of severe acute respiratory syndrome 2 (SARS-CoV-2), the most recently discovered, which causes COVID-19, has spread rapidly in several countries. [3-11] Since the first identification of human cases with symptom onset in December 2019 in Wuhan, China, severe acute respiratory syndrome (SARS)-coronavirus (CoV)-2 has spread rapidly across the globe, infected more than 30 million people in 212 countries and territories, and caused 950 000 deaths as of September 2020.[14-16] The coronavirus disease 2019 (COVID-19) has created an onerous burden on the global health care system and has led to an unusual increase in demand for intensive care units (ICUs).[17-19] In addition to the clinical implications and public health concerns, the COVID-19 pandemic has greatly affected the social fabric of nations and has caused severe global macroeconomic impacts.[20-22] SARS-CoV-2 is the seventh species of coronavirus that is pathogenic to humans and transmittable between people.[23,24]

➢ Coronavirus and Respiratory Diseases

The respiratory illnesses caused by coronavirus (SARS-CoV and MERS-CoV) are highlighted and comparable to COVID-19.

• SARS

SARS-CoV is a member of the Coronavirus genus in the Coronaviridae family and is characterized by the presence of a large positive-sense RNA genome (27.9 kb).[25] The outbreak of SARS was initially identified in Foshan, China, in November 2002 and emerged in mainland China by February 2003. The outbreak spread to North America and Europe (encompassing 29 countries) by infected international travellers. SARS was contained by July 2003 with 8096 reported cases and 774 deaths during the outbreak period. [26-28] SARS-CoV is mainly transmitted through close person-toperson contact and the exchange of respiratory droplets formed through coughing or sneezing, or by touching contaminated surfaces. [29, 30]

• MERS

MERS is a viral respiratory disease caused by the coronavirus MERS-CoV, which emerged in 2012, 10 years after the outbreak of SARS-CoV. [31] The first case of MERS was reported in Saudi Arabia, where MERS-CoV was discovered in the sputum of a deceased patient with acute pneumonia and subsequent renal failure.[31] MERS-CoV was then spread from the Arabian Peninsula by infected international travellers and resulted in person-to-person nosocomial transmission (Figure 1). As of January 2020, MERS-CoV cases were reported in 27 countries with 2519 confirmed cases and 866 fatalities [32]. Since bats are known reservoirs of different types of coronavirus, initial studies focused on bats as the reservoir of MERS-CoV.[33]

• SARS-CoV-2

SARS-CoV-2 first emerged in Wuhan, China, and rapidly spread on an international scale. SARS-CoV-2 is one of the most aggressive forms of coronavirus, having infected ≈30 million people and having caused over 950 000 deaths, worldwide.[14-16,34] Symptoms typically associated with COVID-19 include tussis, fever or chills, and shortness of breath.[35] The prevalence of pre-existing medical conditions such as hypertension, obesity, diabetes, asthma, and cardiovascular disease are confounding factors linked to COVID-19 fatalities.[35] SARS-CoV-2 has a bat origin and is transmitted to humans through an intermediate host, potentially pangolins.[23,36,37] SARS-CoV-2 shares 96% genomic sequence identity with the bat coronavirus RaTG13, and 79% and 50% sequence identity with SARS-CoV and MERS-CoV, respectively.[23] Viral strains detected in pangolins have a similar spike protein amino acid sequence as SARS-CoV-2, which binds to the human ACE2 receptor,[23,36,37] leading to the theory of pangolins as an intermediate species.

Other important epidemiological aspects of the disease include the incubation period, transmission rate, infectious period, and pathogenesis. Lauer et al. found that the median incubation period was 5.1 days and that 97.5% of infected patients displayed symptoms within 11.5 days.[38] Several studies found similar incubation periods for SARS-CoV-2.[39-41] The transmission rate of SARS-CoV-2 has been estimated by multiple sources to be 2.2.[39,42,43] The infectious period for those afflicted with the SARS-CoV-2 virus is still being debated, however, He et al. developed a model showing that infectiousness begins 2–3 days prior to the development of symptoms and diminishes after a week with symptoms.[44] A brief case study by Zou et al. confirmed infection by asymptomatic patients[45] while another case study by Rothe et al. has identified viral transmission while the patient was in the incubation period.[46] The evidence points to increased transmissibility of the virus in the early stages of infection.

Once infection has taken place, the COVID-19 disease progresses with the initial common symptoms of fever, cough, fatigue, and muscle aches.[47] Symptoms then progress to shortness of breath and difficulty breathing, before developing into acute pneumonia.[47] Chest CT scans showed ground glass opacities in the lungs that became worse as the disease progressed.[48] Lastly, cardiovascular injury was observed in some patients, while elevated cytokine levels (including some proinflammatory cytokines) were detected in the patient's blood.[47]

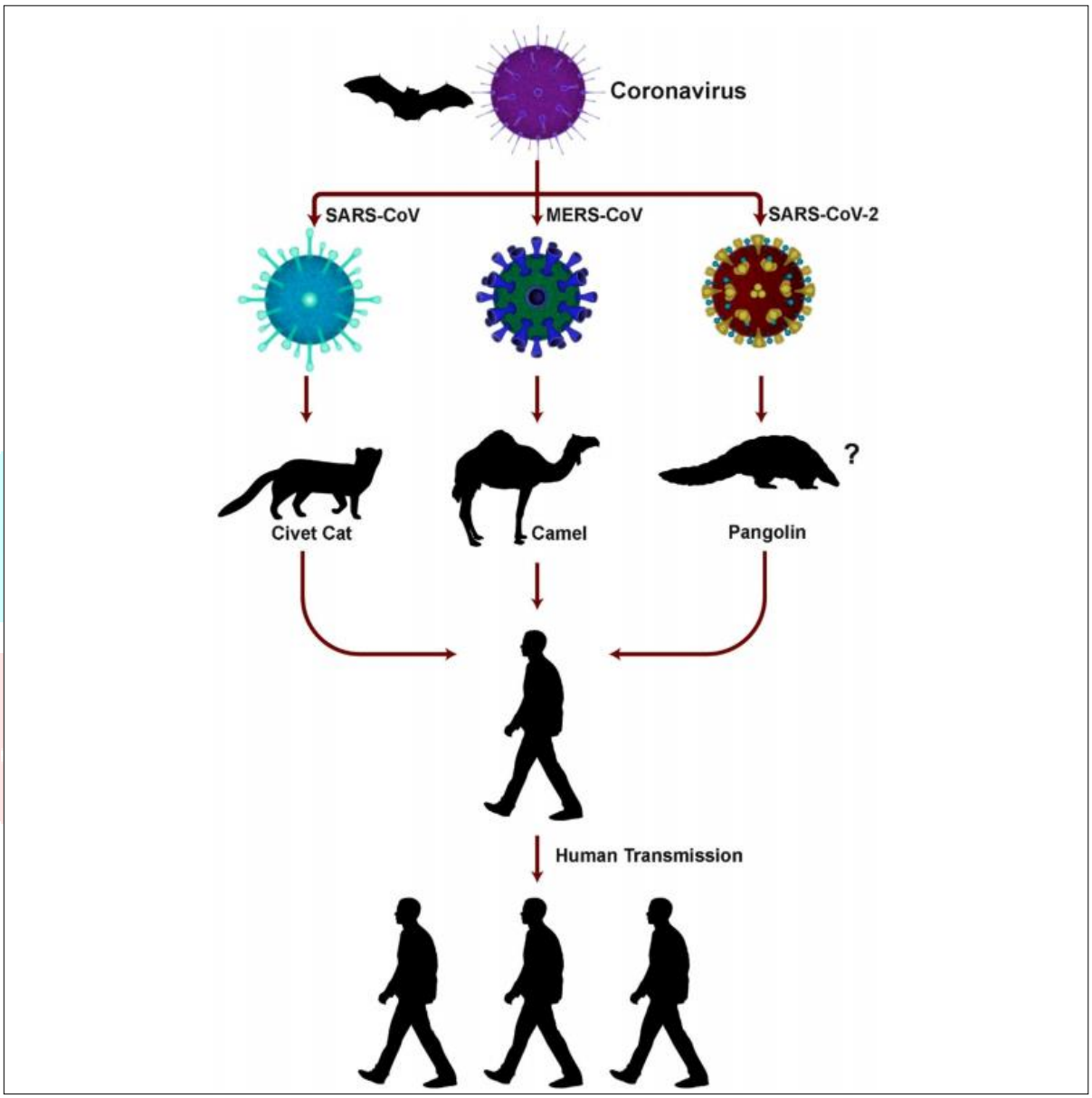


Figure 1. Schematic illustrating the transmission of SARS, MERS, and COVID-19 Pangolins have been suggested as the intermediate carriers, however, the real source is still unknown, according to WHO [49]

➢ DIAGNOSTIC TESTS

Fast and accurate diagnostic tests are needed to confirm COVID-19 infection, trace its origin, and suppress its transmission [50,51]. The current diagnostic strategies for COVID-19 include both clinical and laboratory diagnosis.

- Clinical diagnosis

The symptoms of COVID-19 patients may develop gradually over one week or longer, first with mild symptoms, and then (in some cases) progress to dyspnea and even shock [52]. Common symptoms at disease onset are fever (98%), cough (76%), and fatigue or myalgia (44%); while less-common symptoms are sputum production (28%), headache (8%), hemoptysis (5%), and diarrhea (3%) [52]. Guan et al. [53] investigated the clinical features of COVID-19 patients by extracting the data of 1099 cases with laboratory confirmed COVID-19 from 552 hospitals. Patients' median age was 47 years and the median incubation period was estimated at four days. Their most common symptom was fever, followed by cough (67.8%), whereas their least common symptoms were vomiting or nausea (5.0%) and diarrhea (3.8%). Moreover, Zhou and co-workers [54] assessed the clinical features of 191 patients with COVID-19. Approximately half of these patients had comorbidities, of which hypertension, diabetes and coronary heart disease were the most frequent. Multivariable regression indicated the increased risk of in-hospital mortality was probably attributed to the older age.

The main method currently used to clinically diagnose COVID-19 is chest imaging, including chest X-ray and computed tomography (CT) scans. This method is also essential for diagnosing pneumonia and assessing its severity. Most patients with COVID-19 have abnormalities in chest imaging, usually with bilateral lung involvement, ranging from a ground-glass shadow at the recovery stage in patients with mild symptoms to a consolidation of lung lobes in patients with severe symptoms [55-58].

Chest X-ray examination typically shows interstitial alterations and multiple patchy shadows [52], which are remarkable in the lung periphery [58] of pneumonia cases at the early stage. Patients with severe symptoms may present with multiple ground-glass opacities (GGOs), infiltrative shadows and pulmonary consolidation, together with pleural effusions [59]. Chest CT images of patients with COVID-19 show multi lobar ground glass opacities with a peripheral distribution [60].

Thus, the combined application of chest imaging with laboratory and clinical findings can facilitate the early diagnosis of COVID-19 pneumonia.

Overall, CT scans seem to be more sensitive [61] and clearer than X-ray examinations for the diagnosis of COVID-19, but normal CT manifestations may not be able to distinguish COVID-19 [62]. An investigation of the CT scans of COVID-19 patients revealed that three (14%) patients presented with normal CT scans, twelve (57%) presented with GGOs only, and six (29%) presented with GGOs and consolidation [63]. Another study of CT scans found pure GGOs in 77% of cases, GGOs with interlobular and/or interstitial septal thickening in 75% of cases, and GGOs with consolidation in 59% of cases [64]. Furthermore, the GGOs were bilateral in 88% of cases, involved the posterior lungs in 82% of cases, and the peripheral lungs in 85% of cases. [64] The imaging characteristics of COVID-19 patients were comparable to those of patients infected with MERS or SARS, which is not surprising since they all belong to CoVs.

- Laboratory diagnosis
  - Nucleic acid testing

Nucleic acid testing, including reverse-transcription polymerase chain reaction (RT-PCR), RT loop-mediated isothermal amplification (RT-LAMP) and real-time RT-PCR (rRT-PCR), is currently the most effective and accurate method for diagnosing COVID-19. [65-67] Many RT-PCR assays have been designed and prepared for detecting SARS-CoV-2 genetically. The first step in RT-PCR is the conversion of SARS-CoV-2 RNA into single-strand complementary DNA (cDNA) through retroviral DNA polymerases, followed by PCR amplification of the target cDNA regions. [68, 69] The protocol generally involves two major steps: (I) multiple sequence alignment and primer/probe design, and (ii) optimization and validation of RT-PCR assays. [70] Laboratory testing that involves oropharyngeal and nasopharyngeal

swab tests has become a standard procedure for the diagnosis of patients infected with COVID-19 based on the latest diagnostic criteria reported by the China National Health Commission.

- Protein testing

The detection of viral protein antigens and antibodies produced during SARS-CoV-2 infection plays a major role in the diagnosis of COVID-19. The variation of viral load in the infected patients may make it difficult to detect viral proteins. However, antibody tests can be used for the effective surveillance of COVID-19 patients because the antibodies formed in response to viral proteins can provide a large window of opportunity [70]. Research on serology testing for COVID-19 has been recently undertaken by Zhang et al. [71]. The authors analysed immunoglobulin G (IgG) and immunoglobulin M (IgM) in the serum samples of COVID-19 patients using an ELISA kit. Rp3 nucleocapsid protein is employed as an antigen, which has more than 90% amino acid identical to that of other related coronaviruses. They found that the positive rate of IgM was increased from 50% to 81%, while that of IgG was increased from 81% to 100%. Protein testing is beneficial to the diagnosis of COVID19 after recovery, as opposed to nucleic acid testing. This allows clinicians to trace both infected and recovered cases in order to estimate the accumulated number of SARS-CoV-2 infections.

- Point-of-care testing

In the absence of laboratory infrastructure, point-of-care testing can be applied to diagnose patients more simply and quickly. A typical detection [70] uses a paper-like membrane strip coated with 2 lines. One line is conjugated with antibody-gold nanoparticles and the other line captures antibodies. The patient's sample is dropped onto the membrane, and the targets are drawn up by capillary action into all the strips. When the sample moves along the first line, the proteins (antigens) may bind to antibody-gold nanoparticle conjugates, and the resulting complex will flow to and fuse with the membrane. When the complex reaches the second line, the complex is captured by the immobilized antibodies, and a blue or red line is visualized. The dispersed gold nanoparticle is red in colour, while the aggregated gold nanoparticle is blue because of the coupling of the plasmon band. Unfortunately, a major obstacle for this test is the need to improve its sensitivity.

Another strategy to be used at the point-of-care is Fluorescence based biosensors. Elledge et al. [72] developed the split luciferase antibody biosensors for a fast and low-cost detection of antibodies in whole blood, plasma, serum, and saliva. This point-of-care strategy, which obtained quantitative results within 5 min, greatly reduced the complexity and improved the scalability of COVID-19 diagnostic testing. Point-of-care testing can serve as an inexpensive, easy-to-use, and handheld technique for diagnosing COVID-19 patients at areas outside a centralized facility, such as community centres, in order to reduce the burden of COVID-19 on clinical laboratories

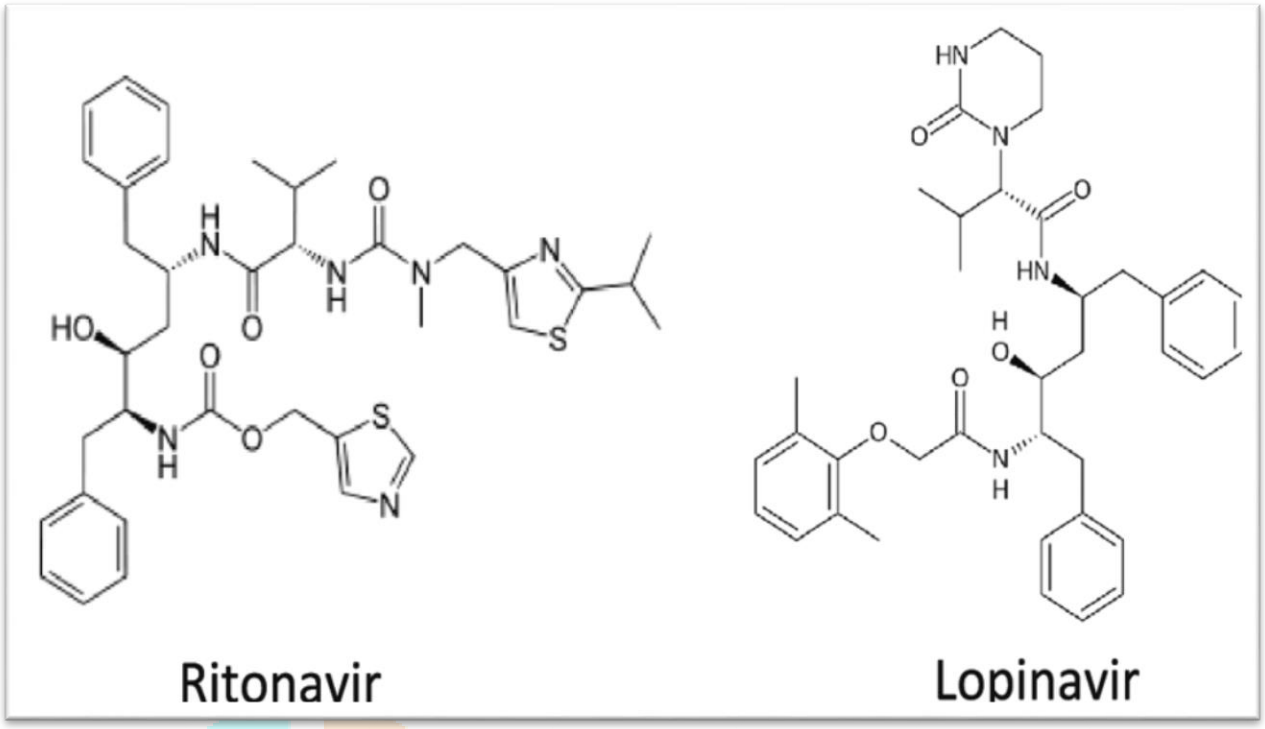
➢ Treatments for COVID-19

- Antiviral agents

Currently, no specific anti-SARS-CoV-2 agent has been approved for treating COVID-19 patients. With only in vitro findings (for the SARS-CoV-2 and/or related viruses) and a lack of clinical experiences, several antiviral agents have been used under the "compassionate use" principle in the United States as they undergo testing in clinical trials.

- Lopinavir and ritonavir

✓ Chemical Structure:



✓ Mechanism of Action:

The SARS-CoV-2 virus is a single stranded RNA beta-coronavirus, similar to SARS-CoV and MERS-CoV. These viruses enter host cell and replicate, producing strands that contain multiple copies of the viral genetic material (RNA-Riboneuclic Acid). The strands of genetic material accumulate at the periphery of the cell, ready to be cleaved, packaged and prepared for released from the host cell. The enzyme 3-chymotrypsin-like protease ($3CL^{pro}$) plays the crucial role in processing the viral RNA. As lopinavir is a protease inhibitor, it may inhibit the action of $3CL^{pro}$, thereby disrupting the process of viral replication and release from host cell.

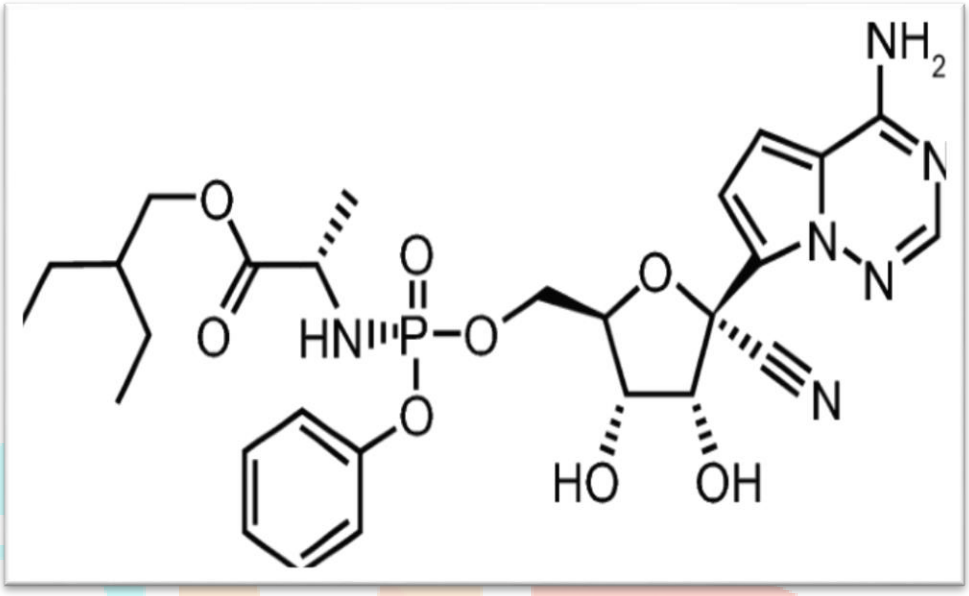
Lopinavir and ritonavir have been approved by the U.S. Food and Drug Administration (FDA) for treating human immunodeficiency virus (HIV) infection [73,74]. The agents have also been used in the empirical treatment of SARS [75], and they are currently under study for the treatment of MERS [76] because lopinavir is a promising agent that suppresses the protease activities of CoVs in vitro. In China, these two antiviral agents have been used to treat some COVID-19 patients in concomitant with alpha interferon [77]. Han and co-workers [78] reported a case study of a 47-year-old man with a 1-week history of cough, fever, and bosom frowsty. The patient had a history of stage two hypertension and type II diabetes. To resolve phlegm, relieve asthma and suppress virus replication, this patient was treated with 800 mg of lopinavir, 200 mg of ritonavir, 10 million IU of interferon alfa-2b recombinant, 400 mg of moxifloxacin hydrochloride, 60 mg of ambroxol hydrochloride, and 40 mg of methylprednisolone each day. The next day, the patient had low-grade intermittent fevers ($36^0Ce37.2^0Ce$). Moreover, many symptoms such as cough with production of phlegm/mucus, runny or stuffy nose, fatigue and vertigo were considerably alleviated. Due to the repeated negative testing results on days six and seven and in addition to the partial absorption of lung lesions, the patient was no longer infectious and discharged from hospital on day 10, suggesting that the treatment strategy could be effective. A recent review [79] found that the anti-CoV effect of lopinavir/ritonavir combination therapy mainly occurred with early treatment window and included the reduction of patient fatality and glucocorticoid administration. However, if the ideal window was missed, the treatment might have no significant effects on patient outcomes. Therefore, further studies that explore the clinical effects of the early use of lopinavir/ritonavir combination therapy for treating SARS-CoV-2 pneumonia are needed

✓ Side Effects:

Abdominal pain, weakness, nausea, diarrhea, vomiting, headache and insomnia.

o Remdesivir

✓ Chemical Structure:



✓ Mechanism of Action:

Remdesivir is a monophosphoramidate nucleoside prodrug that undergoes intracellular metabolic conversion to its active metabolite nucleoside triphosphate (NTP). As described for several other direct-acting antivirals, the active metabolite of remdesivir (remdesivir triphosphate [remdesivir-TP] or GS-443902) subsequently targets the machinery responsible for the replication of the viral RNA genome, a highly conserved element of the viral life cycle. Nucleoside analogues are synthetic compounds that work by competition with endogenous natural nucleoside pools for incorporation into replicating viral RNA. While these compounds mimic their physiological counterparts, the incorporation of the analogue molecule disrupts subsequent molecular processes. The drug target and the exact processes that lead to the inhibition of viral replication.

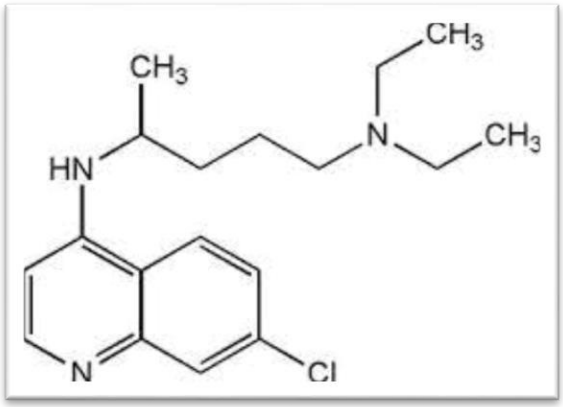
Remdesivir, a monophosphoramidate prodrug of C-adenosine nucleoside analogue, can be incorporated into viral RNA chains and thereby initiate the premature termination of RNA replication [80]. It displays a significant anti-CoV activity in vitro [80]. Previous studies [81-83] showed that remdesivir could inhibit the replication of SARS-CoV, MERS-CoV, and bat CoV strains in primary human airway epithelial cells and regulate cell entry through hACE2 receptor. Remdesivir acts during early-stage infection and dose dependently reduces RNA levels, which parallels a decrease in virus titers [84]. Remdesivir displays an EC90 (90% effective concentration) value of 1.76 mM towards SARS-CoV-2 in Vero E6 cells, indicating that it is effective in non-human primates [85]. Besides, it is noted that SARS-CoV-2 requires RdRp gene to replicate, which can be covalently bound to remdesivir, hence terminating chain elongation [86]. Moreover, remdesivir also suppresses virus infection in human liver cancer Huh-7 cells, a cell line that is susceptible to SARS-CoV-2 [85]. Furthermore, remdesivir has been given on a compassionate use basis to COVID-19 patients [87], and the results indicated that a 10-day course of the antiviral drug (200 mg on day 1, followed by 100 mg daily for 9 days), might exhibit potential clinical benefits for these patients.

Side Effects:

Increased liver enzyme levels that may indicate possible liver damage, Nausea, Vomiting, etc.

- Chloroquine

✓ Chemical Structure:



✓ Mechanism of Action:

Its mechanism of action (MOA) includes the interference in the endocytic pathway, blockade of sialic acid receptors, restriction of pH mediated spike (S) protein cleavage at the angiotensin-converting enzyme 2 (ACE2) binding site and prevention of cytokine storm.

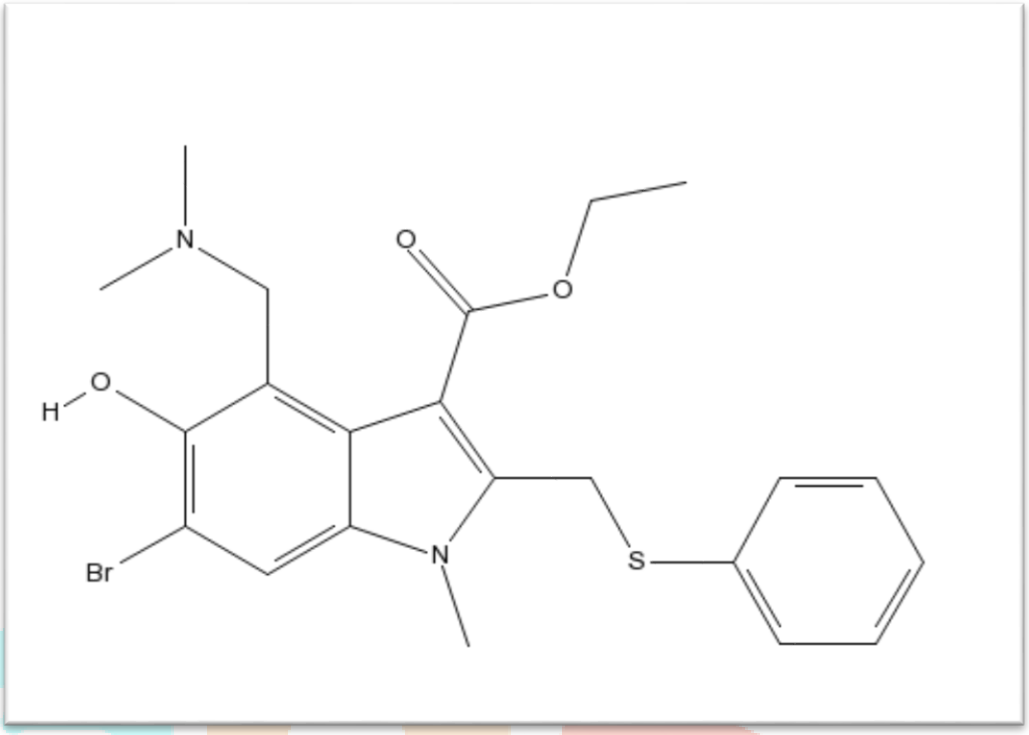
Chloroquine, a potent broad-spectrum antiviral agent, is commonly utilized as an auto-immune disease or anti-malarial agent [88-90]. Chloroquine may stop a virus infection by elevating the endosomal pH necessary for virus-cell fusion and disrupting the terminal glycosylation of hACE2 receptor [91]. Recent work has shown that chloroquine inhibits SARS-CoV-2 infection at entry and post-entry stages in a Vero E6 cell line [85]. After oral administration, chloroquine is distributed throughout the body, especially in the lungs. Apart from its antiviral activity, chloroquine also exhibits immunomodulatory activities, which in turn leads to a synergistic enhancement of its antiviral effect in vivo [85]. Chloroquine has been considered as a potential drug for the treatment and prevention of COVID-19 pneumonia [92, 93]. However, a recent study has found that chloroquine is ineffective for the treatment of COVID-19 [94]. Given the controversy about the effectiveness of this antiviral agent, it is important to determine whether chloroquine has potential applicability for SARS-CoV-2 treatment and prevention.

✓ Side Effects:

Gastrointestinal (GI) upset along with nausea and vomiting [105,106]. GI symptoms basically include dyspepsia, abdominal cramps also includes cases of rashes, itching, headaches, etc.

- Arbidol

✓ Chemical Structure:



✓ Mechanism of Action:

Arbidol is a broad-spectrum antiviral agent that blocks influenza A and B viruses by inhibiting virus-cell membrane fusion [95].

Low level evidence shows that arbidol taken alone or concomitantly with other antiviral drugs produces therapeutic benefits for COVID-19 pneumonia [96-98]. In China, many randomized control trials are currently under way to assess the efficacy of arbidol on COVID-19 pneumonia. Zhang et al. [99] performed a retrospective cohort trial on healthcare workers and family members who have been exposed to a confirmed case of COVID-19. The authors found that arbidol could decrease the risk of SARS-CoV-2 infection in both hospital-care and family care settings. Zhu et al. [100] compared the efficacy of arbidol and lopinavir/ritonavir in 50 patients with laboratory-confirmed COVID-19, and the results demonstrated that COVID-19 patients treated with arbidol recovered more rapidly than those treated with lopinavir/ritonavir.

✓ Side Effects: Nausea, Vomiting

- Immunity-based therapy

Immunity-based therapy, including convalescent plasma therapy and immunoglobulin therapy, is also an important strategy in the treatment of COVID-19. Convalescent plasma therapy is one of the classic adaptive immunotherapies used for the treatment and prevention of numerous infectious diseases such as SARS and MERS. Because of the similarity of clinical and virological characteristics among COVID-19, MERS and SARS, convalescent plasma therapy has emerged as a choice of rescue for COVID-19 patients [101]. Duan and co-workers [102] investigated the effectiveness of convalescent plasma therapy against COVID-19. All symptoms (e.g., cough, fever and difficulty breathing) of the 10 patients with COVID-19 disappeared or largely improved within one-to-three days of convalescent plasma therapy. Furthermore, all of the patients displayed varying degrees of absorption of pulmonary lesions after convalescent plasma

transfusion. Among the convalescent plasma samples of 40 recovered COVID-19 cases, 39 demonstrated high antibody titres of more than 1:160, and only one exhibited a lower antibody titre of 1:32. Thus, these results indicate that convalescent plasma therapy is well tolerated and can enhance the health outcomes of patients with severe COVID-19 by neutralizing viremia.

Immunoglobulin is also being investigated as a possible therapeutic option for COVID-19 patients. Cao and co-workers [103] published a case study of the treatment of severe COVID-19 using high-dose intravenous immunoglobulin (IVIg). A 34-year-old male patient from Jinyintan Hospital reported a fever of up to 38.5 ^{0}C and a dry cough, and subsequently was diagnosed with severe COVID-19. The patient was treated with 25 g/day of IVIg for five days, and became afebrile on the second day of treatment, with a progressive alleviation of breathlessness. He was discharged

- Vaccines :

As of Feb 2021, just few months after the definition of the SARS-CoV-2 genome, there are over 150 official vaccine projects [107,108]. About fifty of them have already reached human experimentation and a few of these are currently administered to some sectors of the general population. By exploiting different technologies, these anti-SARS-CoV-2 candidate vaccines are targeting the whole SARS-CoV-2, molecules or fragments of molecules expressed on this virus surface. These different candidate vaccines can be grouped based on the technological platform exploited to elicit a protective immune response.

- Vaccines based on attenuated SARS-CoV-2 viruses

The history of vaccination begins with vaccines based on a living microbe that has been weakened so it can not cause disease. Since attenuated microbes retain the ability to replicate in vivo giving rise to a limited disease, they are very effective in stimulating the immune system and inducing a strong and persistent immune memory that is efficacious in preventing infection. Hundreds of millions of people have been protected from disabling and fatal diseases by using attenuated vaccines [109].

✓ Strategy

This is the most traditional technology exploited in the construction of vaccines. Live attenuated vaccines can be obtained by growing the virus in unfavourable conditions or by generating a genetically weakened version of the virus. However, the attenuation of trillions of viruses is complex and delicate and can be associated with major biosafety risks [110]. Once produced, their storage and handling require carefully observed procedures. The experience with attenuated virus vaccines shows that rare but significant side effects could be expected since attenuated viruses cause disease, even if this is a minor one. The oral route (as in the case of the Sabin polio vaccine) and the intranasal route could induce a mucosal immunity based on secretory IgA and IgM.

✓ Frontrunners

Only three projects of attenuated SARS-CoV-2 vaccines are in active preclinical development at the following institutions:

- The Serum Inst of India, India, in collaboration with Codagenix, a New York private biotech;
- Indian Immunologicals Ltd, India, in collaboration with the Griffith University, Australia;
- Mehmet Ali Aydunar Univ, Turkey.

None of these vaccine projects have yet reached the stage of clinical trials.

- Vaccines based on the inactivated SARS-CoV-2 viruses

Vaccines based on killed microorganisms (inactivated vaccines) belong to a very traditional technological platform that has led to numerous vaccines. The vaccines produced using this method are more stable than

live attenuated vaccines but their limit is mainly related to the short duration of immune memory which demands inoculation of higher amounts of vaccine or the association of the inactivated microorganism with an adjuvant. The immune response elicited is directed not only against the Spike protein but also against many other SARS-CoV-2 antigens. While the induced response is generally weaker concerning that induced by attenuated viruses, the vaccine is more easily handled, less expensive, and much safer.

✓ Strategy

The SARS-CoV-2 is inactivated by exploiting different chemical techniques. All these candidate vaccines are injected intramuscularly.

✓ Frontrunners

Seven vaccine candidates based on variously inactivated SARS-CoV-2 virions are in clinical trials, four of which in

Phase III trials and already approved for limited use. When available, reports from Phase II trials suggest that the vaccine is safe and induces a high titer of antibodies. The seven clinical trials are run by:

- Sinovac Biotech, China, this vaccine called CoronaVac is in late-stage Phase III trial and interim results are expected in late November. Meanwhile, CoronaVac has already been approved for limited use among the general population
- Sinopharm, China, two of its distinct projects are approved for limited use in the general population
- Wuhan Inst Biol Products, China, this vaccine has been approvedfor limited use in the general population
- Chinese Acad Med Sci, China;
- Bharat Biotech, India, this vaccine, called Covaxin, is in late stage Phase III trial;
- RIBSP, Kazakhstan.

➢ Conclusions:

Currently, SARS-CoV-2 has spread to more than 240 countries worldwide, which causes illness ranging from the common cold to lung pneumonia, making it a very serious public-health threat. From the initial outbreak of COVID-19, the United States has greatly surpassed China as the country with the largest number of confirmed COVID-19 cases globally.In the fight against COVID-19, there are still many problems to be solved, such as the origin, transmission route and structures of SARS-CoV-2. Although bat has been identified as a natural reservoir and vector for the transmission of CoVs, the origin and transmission routes of SARS-CoV-2 are still under investigation. SARS-CoV-2 has typical features that are distinguishable from the CoV family. It may be transmitted from human to human via respiratory droplets or mucous membranes in the eye, nose and mouth. However, the spread mechanism of SARS CoV-2 is still uncertain and knowledge about human-to-human transmission is mainly derived from similar CoVs. Arguably, the greatest challenge for COVID-19 is the lack of availability of effective antiviral drugs. To date, there is still no effective drug to treat SARS-CoV-2. Clinical treatment of COVID-19 is mainly symptomatic treatment. From the current clinical cases, the SARS-CoV-2 is more dangerous to the elderly and patients with other diseases. In COVID-19 prevention, wearing masks and reducing crowd aggregation is the most cost and effective approach. Fortunately, many scientists and enterprises are stepping up the development of antiviral agents and vaccines, some of which have begun clinical trials. We believe that in a short period of time, effective scientific measures will prevent the infectious spread of COVID-19.

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