Review Article

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Various types of drug treatment for covid19 pandemic disease

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Abstract

The leading theme of the article is the naming of newly discovered coronavirus drugs, for the 2019 virus, Severe acute respiratory syndrome coronavirus(SARS-Cov-2).SARS-Cov-2 is the 3rd zoonotic coronavirus after SARS-Cov and MERS-Cov. The first human coronavirus (HCoV) appeared in reports in the mid-1960s and was isolated from persons with the common cold. Two species were first detected: HCoV-229E and subsequently, then, more species were discovered. Human coronavirus 229E (HCoV-229E) is one of the first coronavirus strains being identified in Wuhan, which is creating a hectic boom globally.. Coronavirus disease was first discovered in humans in the 1930s. The virus, human coronavirus 229E was first isolated in 1965. (HCOV-229E). A new corona virus was identified in 2012 with a SARS-like illness, called middle east respiratory syndrome (MERS) COV resulted in a limited number of outbreaks, mostly in Saudi Arabia. In December 2019, a novel coronavirus (nCOV) was identified in Wuhan, China, which was isolated on 7 January 2020. Current clinical management includes infection prevention and control measures and supportive care including supplemental oxygen and mechanical ventilatory support. Currently, Antiviral agents Remdesivir, Hydrochloroquine, Chloroquine, Lopinavir, Umifenovir, Favipiravir, Oseltavir, and supporting agents like Ascorbic acid, Azithromycin, Corticosteroids, Nitric oxide, IL-6 Antagonist are using against virus. Evolving research and clinical data regarding the virologic SARS-CoV-2 suggest a potential list of repurposed drugs with appropriate pharmacological effects and therapeutic efficacies in treating COVID-19 patients. In this review, we will update and summarize the most common and plausible drugs for the treatment of COVID-19 patients. We hope that this review will provide useful and most updated therapeutic drugs to prevent, control, and treat COVID-19 patients until the approval of vaccines and specific drugs targeting SARS-CoV-2.

Keywords: Hcov-229E, SARS, MERS, nCov, pandemic, plausible drugs, vaccine...

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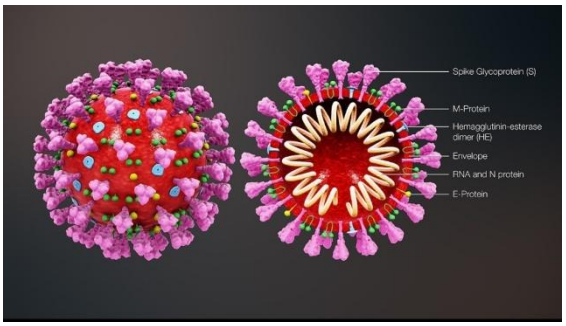
Introduction

Structure And Function of Sars-Cov-2



Coronaviruses are large, roughly spherical particles with bulbous surface projections. The average diameter of the virus particles is around 125 nm.. The diameter of the envelope is 85 nm and the spikes are 20 nm long. The envelope of the virus in electron micrographs appears as a distinct pair of electron-dense shells (shells that are relatively opaque to the electron beam used to scan the virus particle).

The viral envelope consists of a lipid bilayer, in which the membrane (M), envelope (E) and spike (S) structural proteins are anchored.The ratio of E:S:M in the lipid bilayer is approximately 1:20:300.On average a coronavirus particle has 74 surface spikes.A subset of coronaviruses (specifically the members of

betacoronavirus subgroup A) also have a shorter spike-like surface protein called hemagglutinin esterase (HE).

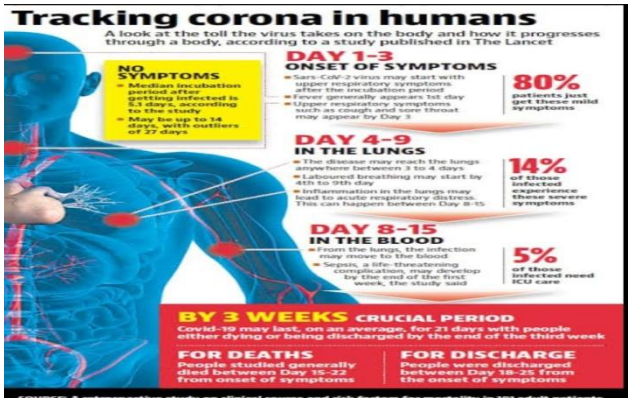
The coronavirus surface spikes are homotrimers of the S protein, which is composed of an S1 and S2 subunit. The homotrimeric S protein is a class I fusion protein which mediates the receptor binding and membrane fusion between the virus and host cell. The S1 subunit forms the head of the spike and has the receptor binding domain (RBD). The S2 subunit forms the stem which anchors the spike in the viral envelope and on protease activation enables fusion. The E and M protein are important in forming the viral envelope and maintaining its structural shape.

Inside the envelope, there is the nucleocapsid, which is formed from multiple copies of the nucleocapsid (N) protein, which are bound to the positive-sense single-stranded RNA genome in a continuous beads-on-a-string type conformation. The lipid bilayer envelope, membrane proteins, and nucleocapsid protect the virus when it is outside the host cell [1].

FUNCTION OF VIRUS IN HUMAN BODY

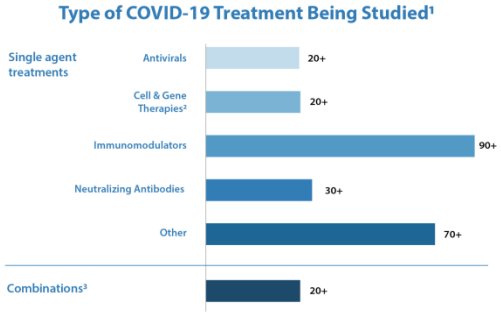
ACE2 and TNPRSS2 are two proteins that the novel coronavirus uses to enter a person's body cells. External body organs with a high density of these proteins are particularly vulnerable to the novel coronavirus, and thus can become entry gates for Covid-19.

- At first SARS-COV-2 anchors to ACE2 through spike protein.
- TNPRSS2activates entry of virus into body cell.
- attaches to goblet and ciliated cells in nose.
- virus starts replication.
- huge number of virus are produced leads to the inflammation of the mucous membrane and damage the air sacs.
- inflammation hampers the lung ability to oxygenate the blood.
- Infected cells come out of the body in the form of droplets or spit due to coughing or sneezing.
- Which will survives in the external environment for hours to few days.



CORONAVIRUS TREATMENT ACCELERATION PROGRAM (CTAP) :

FDA has created a special emergency program for possible coronavirus therapies, the Coronavirus Treatment Acceleration Program (CTAP). The program uses every available method to move new treatments to patients as quickly as possible, while at the same time finding out whether they are helpful or harmful. We continue to support clinical trials that are testing new treatments for COVID so that we gain valuable knowledge about their safety and effectiveness.



The categories in this bar chart span a number of categories :

- Antiviral drugs keep viruses from multiplying and are used to treat many viral infections (such as HIV, Herpes, Hepatitis C, and influenza).
- Immunomodulators are aimed at tamping down the body's own immune reaction to the virus, in cases where the body's reaction basically goes overboard and starts attacking the patient's own organs.
- Neutralizing antibody therapies may help individuals fight the virus and include manufactured antibodies, animal-sourced antibody therapies, and blood-derived products such as convalescent plasma and hyperimmune globulin, which contain

antibodies taken from people who have previously had COVID-19.

- Cell therapy products include cellular immunotherapies and other types of both autologous and allogeneic cells, such as stem cells, and related products.
- Gene therapy products seek to modify or manipulate the expression of a gene or to alter the biological properties of living cells for therapeutic use.

The diversity of therapeutic approaches being investigated is important because it rapidly expands our understanding of the effect of different categories of potential treatments.

Currently, there is no vaccine and/or specific therapeutic drugs targeting the SARS-CoV-2. Hence, it remains a major challenge to decide what potential therapeutic regimens to prevent and treat the severely sick COVID-19 patients. Effective vaccines are essential to combat against the extremely contagious SARS-CoV-2. At present, a lot of research efforts have been invested to develop vaccines around the world. Until we have specific vaccines or therapeutic drugs targeting SARS-CoV-2, "repurposed" drugs that have been approved by the FDA in the USA for other indications have been used to treat COVID-19 patients. This review will summarize the most current pharmacotherapeutics prescribed in the treatment of severe cases of COVID-19 patients. These include antiviral therapy, antibiotics, systemic corticosteroids and anti-inflammatory drugs (including anti-arthritis drugs), neuraminidase inhibitors, RNA synthesis inhibitors, convalescent plasma, and traditional herbal medicines [1].

COVID DRUG UPDATES

The Covid-19 pandemic is one of the greatest challenges modern medicine has ever faced. Doctors and scientists are scrambling to find treatments and drugs that can save the lives of infected people and perhaps even prevent them from getting sick in the first place.

There is no cure yet for Covid-19. And even the most promising treatments to date only help certain groups of patients and await validation from further trials. The F.D.A. has not fully licensed any treatment specifically for the coronavirus. Although it has granted emergency use authorization to some treatments, their effectiveness against Covid-19 has yet to be demonstrated in large-scale, randomized clinical trials [2].

Remdesivir

Remdesivir, made by Gilead Sciences, was the first drug to get emergency authorization from the F.D.A. for use on Covid-19. It stops viruses from replicating by inserting itself into new viral genes. Remdesivir was originally tested as an antiviral against Ebola and Hepatitis C, only to deliver lackluster results. But preliminary data from trials that began this spring suggested the drug can reduce the recovery time of people hospitalized with Covid-19 from 15 to 11 days. (The study defined recovery as "either discharge from the hospital or hospitalization for infection-control purposes only.") These early results did not show any effect on mortality, though retrospective data released in July hints that the drug might reduce death rates among those who are very ill [2].

FAVIPIRAVIR

Originally designed to beat back influenza, favipiravir blocks a virus's ability to copy its genetic material. A small study in March indicated the drug might help purge the coronavirus from the airway, but results from larger, well-designed clinical trials are still pending.

MK-4482 :

Another antiviral originally designed to fight the flu, MK-4482 (previously known as EIDD-2801) has had promising results against the new coronavirus in studies in cells and on animals. Merck, which has been running clinical trials on the drug this summer, has announced it will launch a large Phase III trial in September.

RECOMBINANT ACE -2 :

To enter cells, the coronavirus must first unlock them — a feat it accomplishes by latching onto a human protein called ACE-2. Scientists have created artificial ACE-2 proteins which might be able to act as decoys, luring the coronavirus away from vulnerable cells. Recombinant ACE-2 proteins have shown promising results in experiments on cells, but not yet in animals or people.

Lopinavir and ritonavir :

Twenty years ago, the F.D.A. approved this combination of drugs to treat H.I.V. Recently, researchers tried them out on the new coronavirus and found that they stopped the virus from replicating. But clinical trials in patients proved disappointing. In early July, the World Health Organization suspended trials on patients hospitalized for Covid-19. They didn't rule out studies to see if the drugs could help patients not sick enough to be hospitalized, or to prevent people exposed to the new coronavirus from falling ill. The drug could also still have a role to play in certain combination treatments.

Hydroxychloroquine and chloroquine

German chemists synthesized chloroquine in the 1930s as a drug against malaria. A less toxic version, called hydroxychloroquine, was invented in 1946, and later

was approved for other diseases such as lupus and rheumatoid arthritis. At the start of the Covid-19 pandemic, researchers discovered that both drugs could stop the coronavirus from replicating in cells.Since then, they've had a tumultuous ride. A few small studies on patients offered some hope that hydroxychloroquine could treat Covid-19.

A study on monkeys found that hydroxychloroquine didn't prevent the animals from getting infected and didn't clear the virus once they got sick. Randomized clinical trials found that hydroxychloroquine didn't help people with Covid-19 get better or prevent healthy people from contracting the coronavirus. Another randomized clinical trial found that giving hydroxychloroquine to people right after being diagnosed with Covid-19 didn't reduce the severity of their disease.

Mimicking the Immune System

Most people who get Covid-19 successfully fight off the virus with a strong immune response. Drugs might help people who can't mount an adequate defense [3].

Convalescent plasma

A century ago, doctors filtered plasma from the blood of recovered flu patients. So-called convalescent plasma, rich with antibodies, helped people sick with flu fight their illness. Now researchers are trying out this strategy on Covid-19. In May, the F.D.A. designated convalescent plasma an "investigational product." That means that despite not yet being shown as safe and effective, plasma can be used in clinical trials and given to some patients who are seriously ill with Covid-19. Tens of thousands of patients in the U.S. have received plasma through a program launched by the Mayo Clinic and the federal government.

Monoclonal antibodies

Convalescent plasma from people who recover from Covid-19 contains a mix of different antibodies. Some of the molecules can attack the coronavirus, but many are directed at other pathogens. Researchers have sifted through this slurry to find the most potent antibodies against Covid-19. They have then manufactured synthetic copies of these molecules, known as monoclonal antibodies. Researchers have begun investigating them as a treatment for Covid-19, either individually or in cocktails.Since the start of the pandemic, researchers have found dozens of monoclonal antibodies that show promise against Covid-19 in preclinical studies on cells and animals. Companies like Eli Lilly and Regeneron recently began clinical trials studying monoclonal antibodies.

Dexamethasone

This cheap and widely available steroid blunts many types of immune responses. Doctors have long used it to treat allergies, asthma and inflammation. In June, it became the first drug shown to reduce Covid-19 deaths.It may be less likely to help — and may even harm — patients who are at an earlier stage of Covid-19 infections, however. In its Covid-19 treatment guidelines, the National Institutes of Health recommends only using dexamethasone in patients with COVID-19 who are on a ventilator or are receiving supplemental oxygen.(3).

Ivermectin:

Old FDA approved drug for parasitic infection.

The trails have proved that the drug Ivermectin reduces the number of cell associated viral DNA by 99.8% in 24hrs,it was an invitro study.

It is currently used to treat parasitic infection..such as intestinal worms.lice.mites.

Recently ivermectin has also been studies to treat a range of viruses...

MOA: At first virus should enter body cell nucleus where the virus makes heaps of copies of itself so it can spread. There is a protein called cargo transporter by which the virus enters into human body cells. The function of ivermectin is to block the corgo transporter ,by this the virus. Cannot enter into the nucleus and replicate .By this it stops the virus count from increasing and stops the infection getting worse [4].

Ascorbic acid:

1 In the absence of a specific treatment for SARS, the possibility that vitamin C may show non-specific effects on severe viral respiratory tract infections should be considered. There are numerous reports indicating that vitamin C may affect the immune system,2,3 for example the function of phagocytes, transformation of T lymphocytes and production of interferon. In particular, vitamin C increased the resistance of chick embryo tracheal organ cultures to infection caused by an avian coronavirus.4 Studies in animals found that vitamin C modifies susceptibility to various bacterial and viral infections,3 for example protecting broiler chicks against an avian coronavirus.5 Placebo-controlled trials have shown quite consistently that the duration and severity of common cold episodes are reduced in the vitamin C groups,3 indicating that viral respiratory infections in humans are affected by vitamin C levels. There is also evidence indicating that vitamin C may affect pneumonia.3 In particular, three controlled trials with human subjects reported a significantly lower incidence

of pneumonia in vitamin C-supplemented groups,6 suggesting that vitamin C may affect susceptibility to lower respiratory tract infections under certain conditions. The possibility that vitamin C affects severe viral respiratory tract infections would seem to warrant further study, especially in light of the recent SARS epidemic.

ARBIDOL (Umifenovir)

The sequence and structural similarities between the Arbidol binding sites for SARS-CoV-2 spike glycoprotein and H3N2 HA seem promising and suggest that Arbidol may have efficacy to treat COVID-19. Molecular dynamics and structural analysis showed that SARS-CoV-2 spike glycoprotein is the drug target for Arbidol, and suggested the potential drug binding mode with key interacting residues and mechanism of action, whereby Arbidol can effectively block or impede the trimerization of SARS-CoV-2 spike glycoprotein, which is key to cell adherence and entry [9]. Blocking the trimerization of SARS-CoV-2 spike glycoprotein also leads to the formation of naked or immature virus which is less infectious. This study has significant implications, but the efficacy and safety of Arbidol against SARS-CoV-2 still require clinical investigation. Although current drug options are mainly focused on ACE2 inhibitors and viral RNA polymerase, potential drugs to impede the trimerization of SARS-CoV-2 spike glycoprotein are equally essential as a combination of drugs may have a profound effect on the battle against SARS-CoV-2. It is hoped that knowledge of the potential drug target and mechanism of action of Arbidol will help in the development of new therapeutics for SARS-CoV-2.

The better solution is to widely inoculate people with COVID-19 vaccines when available, and reserve antibody treatments for people who have the disease or were recently exposed to it [5, 6].

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