

Vaccines for COVID-19

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Abstract

Coronavirus disease 2019 (COVID-19) was initially reported in December 2019 in China and cause an acute respiratory disease. Since then, no specific therapy or vaccine is being available for the treatment or prevention of the disease. Teams of scientists around the world are racing to develop a treatment to end the COVID-19 pandemic. Extensive clinical trial data are required to identify safe and effective treatments for COVID-19. In this review, we aim to provide an overview of antiviral drugs, their pharmacological features, and their outcome against the disease based on the available data. We have discussed their mechanism of action, doses, and adverse effects in detail. In addition, a close review of vaccines that are in the developmental state has also been discussed.

Introduction

The symptoms of COVID-19 infection vary widely, from mild fever and headache to pneumonia and life-threatening complications, such as respiratory distress syndrome, organ failure, sepsis, and death [1-3]. These symptoms become aggravated in older patients and those with preexisting cardiovascular or respiratory conditions and are at the greatest risk. [2, 3] To prevent COVID-19, social distancing is the most common and effective method. Besides, hand hygiene and face coverings in public settings are also recommended [4]. COVID-19 patients with mild symptoms are suggested to self-isolate and can take acetaminophen to reduce fever [5]. However, some studies have shown that NSAIDs like naproxen and ibuprofen can worsen COVID-19 symptoms [6]. In the savior cases of COVID-19, especially in the elderly with previous health conditions, hospitalizations with proper medical attention is required. Unfortunately, the Food and Drug Administration has not approved any drugs for the treatment of COVID-19 till date. Teams of scientists around the world are racing to develop a treatment to end the COVID-19 pandemic. Extensive clinical trial data are required to identify safe and effective treatments for COVID-19. In this review, we aim to provide an overview of antiviral drugs, their pharmacological features, and their outcome against the disease based on the available data. We have discussed their mechanism of action, doses, and adverse effects in detail. In addition, a close review of vaccines that are in the developmental state has also been discussed.

Vaccines for COVID-19

During this pandemic period vaccination is being considered as one of the most effective strategies against the COVID-19 disease and will be extremely helpful in restricting the spread of the disease. Usually, the development of vaccines takes years of testing and production, however, scientists are expecting to produce a vaccine within 12 to 18 months. Researchers and companies all-round the globe are working around the globe to develop vaccines against the disease with more than 170 candidate vaccines now tracked by the World Health Organization (WHO). In this review, we will be discussing the vaccines which are at a later phase of their development, Table 2. The vaccines are designed to teach the immune system how to fight with a certain kind of disease. These are several different types of vaccines:

Genetic vaccines

In genetic vaccination, the genetically engineered plasmid (containing DNA or RNA) of the Coronavirus is injected. The genetic material can encode the antigen against which an immune response can be formed by the host cells. Presently, no DNA vaccines have been permitted for human use. Some of the adverse effects of the vaccine are the risk of affecting genes controlling cell growth. Some of the adverse effects of the vaccine are the risk of affecting genes controlling cell growth and the likelihood of making antibody production against DNA. Less risk of infection, easy to develop, storage stability, and cost-effectiveness are some of the advantages of DNA vaccines

Viral vector vaccines

Viral vectors are tools used to transfer genetic material into cells. In viral vector vaccines, the Coronavirus genes (coding the surface proteins) are inserted into the cell which will provoke an immune response against the disease. Some of the challenges of this method are a limited number of viral vectors available for use. If the pre-existing immunity is present in the patient, then the therapy can get ineffective.

Protein-based vaccines: Similar to the viral vector proteins, in these vaccines the Coronavirus protein or a protein fragment is used to provoke the immune response. A common example is the hepatitis B vaccine, containing the surface antigen of the hepatitis B virus [7].

Whole-virus vaccines

In these types of vaccines a weakened/inactivated version of the virus is injected to provoke an immune response in the host body. A famous example is a polio vaccine in which an inactivated and a weakened poliovirus is given to prevent poliomyelitis (polio) [8].

Repurposed vaccines

Repurposed vaccines are the vaccines that are already available in the market and is used in other diseases that may also be used in COVID-19. This approach is being used in Murdoch Children's Research Institute in Australia by using BCG vaccines against COVID-19.

The Pfizer–BioNTech COVID 19 vaccine, sold under the brand name Comirnaty, is developed by collaboration of American company Pfizer, German company BioNTech and Chinese company Fosun. The mRNA-based COVID-19 vaccine whose foundation was laid by Kariko and coworkers is given via intra-muscular injection and requires two doses given three weeks apart [10]. The vaccine is composed of nucleoside-modified mRNA (modRNA) encoding a mutated form of the Spike proteins (S proteins), which are encapsulated in lipid nanoparticles [10]. This vaccine has shown an efficacy of 95% with some side effects, i.e., mild to moderate pain at the injection site, fatigue, and headache. To date, reports of serious side effects or adverse drug or allergic reactions, have been very rare, with no long-term complications [9, 11]. Similar to the Pfizer-BioNTech COVID 19 vaccine, the Moderna COVID 19 vaccine (mRNA-1273) also contains nucleoside-modified mRNA which encoded a mutated form of the S protein [12]. However, unlike the Pfizer vaccine it is administered intra-muscularly with two shots four weeks apart. The vaccine developed by the collaborative work of Biomedical Advanced Research and Development Authority (BARDA), National Institute of Allergy and Infectious Diseases (NIAID), and Moderna [13]. Some of the side effects reported so far for this vaccine is little more in magnitude compared to Pfizer's one. Some common symptoms include pain, swelling, and redness throughout the body, chills, tiredness, and headache [14, 15]. These side effects usually start within a day or two after the vaccine is injected. The vaccine has shown an efficacy of 94.1%, which is similar to the mRNA based vaccine developed by Pfizer and has been authorized for the emergency purpose in the USA [13]. Another subclass of genetic material based vaccine which utilizes a viral-vector is developed by AstraZeneca in collaboration with University of Oxford in England. Interesting fact about viral vector vaccines are that they are deprived of antigens but they use recipient cells to generate it. Thus, leading to large memory induced effect even after degrading from the body. This vaccine is sold under the brand names of Covishield and Vaxzevria (codename AZD1222). It is a replicating viral vector vaccine given by intramuscular injection [16]. The modified chimpanzee adenovirus ChAdOx1 is used as a non-replicating vector for this vaccine [17]. Interestingly, among genetic based vaccine a lower

efficacy of 81.3% was observed for replicating viral vector vaccine (Covishield) in comparison to mRNA based vaccines developed by Pfizer and Moderna. Second dose of vaccine is given after 12 weeks, which leads to delay in completion of immunization in comparison to mRNA based vaccines [17]. Higher level of side effects in comparison to mRNA based vaccines has been reported so far and some of the symptoms include injection-site pain, headache, and nausea [18]. Very few cases of anaphylaxis and increased risk of blood clots in combination with low levels of blood platelets has been reported so far [19, 20]. Viral vector vaccines can be divided in two sub categories, where first category include use of replicating vectors and lead to the development of Covishield, as they have the ability to make new viral particles as they infect new cells makes it a very promising drug candidate to fight mutant variant [21]. Whereas second sub-category is non-replicating vectors, i.e., adenovirus vectors (which cannot replicate within cells). As the name non-replicating vaccine suggest this vaccine only make antigens of vaccines, they cannot make new particles. The Johnson & Johnson COVID-19 vaccine falls into latter category, with an efficacy of 66.9%, which is lower than replicating viral vector vaccines. This vaccine uses human adenovirus that has been modified to contain the gene for making the spike protein of the SARS-CoV-2 virus and lead to immune respons and produce antibodies against COVID-19 virus. Advantage of this vaccine is that it requires only single dose, making vaccination quick and as it is based on stable DNA molecules it does not require ultracold storage as required by making it easier to handle and distribute.8. Recent studies have shown that it is 66% effective in a one-dose regimen in preventing symptomatic COVID-19, with an 85% efficacy in preventing severe COVID-19, and 100% efficacy in preventing hospitalization or death caused by the disease. The Sputnik V viral vector vaccine was developed by the Gamaleya Research Institute of Epidemiology and Microbiology, Russia [22-25]. It is a viral two-vector vaccine based on two human adenoviruses - a common cold virus - containing the gene that encodes the full-length spike protein (S) of SARS-CoV-2 to stimulate an immune response.22 The vaccine has shown an efficacy of 91.6% efficacy. However, little is known about the side effects of the vaccine.

CoronaVac, is vaccine that falls under the viral vaccine's category, where virus is killed by chemical and physical therapy or attenuated virus are used (virus that are harmless and non-replicative in humans, through frequent passages in a non-human cells). This inactivated virus COVID-19 vaccine developed by the Chinese company Sinovac Biotech11 relies on traditional technology similar to BBIBP-CorV and BBV152. One of the demerits of this class of vaccines are they required proper 4 phase clinical trials and like other inactivated-virus COVID-19 vaccines this vaccine is in Phase III clinical trials [13, 26]. Phase III results from Brazil submitted to Lancet showed 50.7% efficacy at preventing symptomatic infections, 83.7% effective in preventing mild cases and needs treatment. Covaxin (also known as BBV152) is another example of inactivated virus-based COVID-19. It has been developed in collaboration between Indian Council of Medical Research and Bharat Biotech.12 Studies have shown that it is has a 65.7% efficacy in preventing moderate symptoms of COVID-19, and 91% efficacy in preventing severe disease. Some of the adverse event was pain at the injection site, followed by headache, fatigue, and fever [27, 28].

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