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REVIEW PAPER

Covid-19 Virus Vaccine: An Overview

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ABSTRACT

To eventually fight the emerging COVID-19 pandemic, it is very important to evolve an effective and safe vaccine against the highly infectious disease caused by the SARS-CoV-2 corna virus. The literature and clinical trial survey shows that the whole virus, along with the membrane protein, spike protein (S), and nucleocapsid protein (N), has been tested for vaccine development against MERS and SARS. Its been more than eleven month since the identification of the SARS-CoV-2 virus and along with its genome, an exceptional effort by the science community has now led to the development of more than three hundred vaccine projects. Over 60 are now in the process of clinical trial, 10 of these are in Phase-3 clinical trials, 3 of them have ended Phase-3 with positive results. Few of them are ready to approved for the emergency use. The existing data recommend that new vaccine applicants instrumental in protecting people and lowering the transmission of pandemic. The theoretical and technological platforms exploited are diverse, and it is expected that different vaccines will show to be greater suited to different groups of the human population. Because of the short time for the development, these vaccines will be deployed with several unresolved issues that only the passage of time will clarify.

Keywords: - *Covid-19, clinical trial, SARS, vaccine, pandemic.*

1. INTRODUCTION

2019 novel coronavirus causes acute respiratory disease. The first outbreak of the coronavirus first occurred in Wuhan (China). The origin of virus comes from the bat and then transmitted to the humans in China in December 2019. Because of the outbreak of the (SARS-COV) on 30th Jan, 2020 WHO (world health organization) officially declared the epidemic as a public health emergency of international concern. Corona viruses belong to the subfamily Orthocoronavirinae in family Coronaviridae, Order Nidovirales [1].

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There are four genera within the subfamily Orthocoronavirinae, namely Alphacoronavirus, Betacoronavirus, Gammacoronavirus and Deltacoronavirus. In 2002, an outbreak of SARS was firstly reported in China and then spread quickly worldwide, which resulted in hundreds of

deaths with an 11% mortality rate. In 2012, MERS first emerged in Saudi Arabia and subsequently spread to other parts of the globe, with a fatality rate of 37%.Till 1 March 2020, a total of 87,137 confirmed cases globally, 79,968 were confirmed in China and 7169 outside of China, with 2977 deaths (3.4%) had been reported by WHO [2]. Meanwhile, several independent research groups had identified that SARS-CoV-2 belongs to β-coronavirus, with highly identical genome to bat coronavirus, indicating bat as the natural source/host [3].

The novel coronavirus uses the same receptor which is angiotensin-converting enzyme 2 (ACE2) as that for SARS-CoV, and mainly spreads through the respiratory tract. Clinical symptoms of COVID-19 patients include fever, cough, fatigue and small population of patients appeared gastrointestinal infection symptoms. The elderly and also people with underlying diseases are susceptible to infection and prone to serious outcomes, which perhaps associate with acute respiratory distress syndrome (ARDS) [4].

1.2 Structure of corona virus:

The **corona virus** are organized with long Ribo Nucleic Acid polymers and are tightly packed into the center of the particle, and surrounded by a protective capsid, which is a lattice of repeated protein molecules referred to as coat or capsid proteins. In **corona virus**, these proteins are called nucleocapsid (N). The corona virus core particle is further surrounded by an outer membrane envelope made of lipids (fats) with proteins inserted. These membranes derive from the cells in which the virus was last assembled but are modified to contain specific viral proteins, including the spike (S), membrane (M), and the envelope (E) proteins [5].

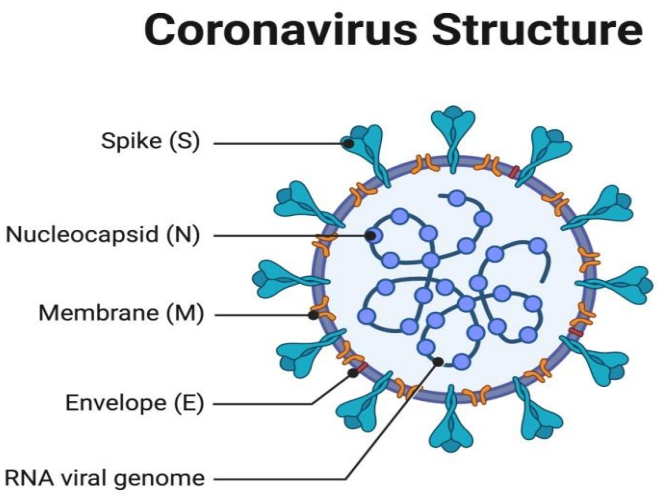


FIGURE 1: Structure of corona virus.

Symptoms of corona virus

Fever, Dry cough, Tiredness, Loss of taste or smell, Aches or pain, Sore throat, Difficulty breathing or shortness of breathing, Lack of movement, Chest pain, Headache, Congestion, Coughing, Nausea, Diarrhea, Chills with shaking and Fatigue.

How does coronavirus infect someone?

It begins with the "spike" that gives coronaviruses their name.A corona virus is surrounded by a fatty outer layer ("envelope") and on the surface of this layer is the "corona" (crown) of spikes made of protein. On the surface of human cells is an enzyme called ACE2, which acts as the receptor that enables SARS-CoV2 to launch its attack [6]. The virus's spike protein binds to the receptor, then fuses with the cell surface, and releases its genetic material (RNA in the case of SARS-CoV2) into the cell. The coronavirus that causes SARS, called SARS-CoV, uses the same ACE2 receptor to invade a cell [7]. Once inside, the virus replicates itself by using the cell's molecular mechanism. All these stages involve various interactions between virus proteins and human proteins. Any treatment being developed or researched will look to inhibit these activities at one stage or the other [8].

All about vaccine

Vaccine is a mild form of particular disease which is injected in order to protect from the particular disease. It triggers the immune response to recognize and fight from the disease causing microorganisms. The sudden outbreak of covid-19 forced scientist around the world to design the SARS-Cov-2 vaccine. In case of corona virus it is very urgent to develop the more effective vaccine to get rid of the virus along with its variants [9]. The COVID-19 vaccines are under development for providing more efficacy or some of them have been approved and are expected to provide more and more protection against the virus and its different variants because these vaccines elicit a broad immune response involving a range of antibodies and cells. Therefore, changes or mutations in the virus should not make vaccines completely ineffective. In the event that any of these vaccines prove to be less effective against one or more variants, it will be possible to change the composition of the vaccines to protect against these variants.Data are collected and and ready to be analysed on new variants of the COVID-19 virus. And it is shocking that we are still learning about the virus. All we need to do is to stop the spread of virus and for that we need to prevent the mutations among the virus which may reduce the efficacy of existing vaccines [10].

List of vaccines discovered(according to WHO)

- Pfizer/ BioNtech
- SII/ Covishield
- AstraZeneca/AZD1222
- Janssen/Ad26.COV2.S

- Moderna COVID-19 vaccine(m-RNA 1273)
- Sinopharm
- Sinovac-coronavac

Working of Vaccine

A pathogen is microorganisms that may cause disease in the body. Pathogen are made up of different sub-parts, usually unique to that particular pathogen and the disease it cause. The sub-part of a pathogen that is responsible for the formation of antibodies is called an antigen. The antibodies produced in response to the pathogen's antigen are an important part of the immune system. Antibodies are considered as the soldiers in body's defense system. Antibody/ soldier, in the body is trained to recognize one specific antigen. There are thousands of different antibodies are present in the body [11]. When the human body is exposed to an antigen for the first time, it takes time for the immune system to respond and produce antibodies specific to that antigen. In the meantime, the person is susceptible to becoming ill. Once the antigen-specific antibodies are produced, they work with the rest of the immune system to destroy the pathogen and cure the disease. Antibody of one pathogen generally don't protect against another pathogen [12]. It only protects when two pathogens are very similar to each other. Once the body starts to produce antibody in its primary response to an antigen, it also creates antibody-producing memory cells, which remain alive even after the pathogen is overcome by the antibody. If the body is exposed to the same pathogen more than once, the antibody response is much faster and more effective than the first time around because the memory cells are at the ready to pump out antibodies against that antigen [13]. It means next time if the person is exposed to the dangerous pathogen their immune system will be able to respond immediately protecting against the disease.

How vaccines help?

Vaccines contains mild or inactive particles of a particular microorganism pathogen (antigen) that trigger an immune response within the body. Newly discovered vaccines contain the blueprint for producing antigens rather than the antigen itself. Regardless of whether the vaccine is made up of the antigen itself or the blueprint so that the body will produce the antigen, this mild or weaker version will not cause the disease in the person receiving the vaccine, but it will boost their immune system to respond much as it would have on its first reaction to the actual pathogen [14].

Covid-19 vaccines require multiple doses that is given months apart. This is sometimes needed to allow for the production of long-lived antibodies and development of memory cells. In this way, the body is trained to fight the specific Covid-19-causing organism, building up memory of the pathogen so as to rapidly fight it if and when exposed in the future [15].

2.5 Herd immunity

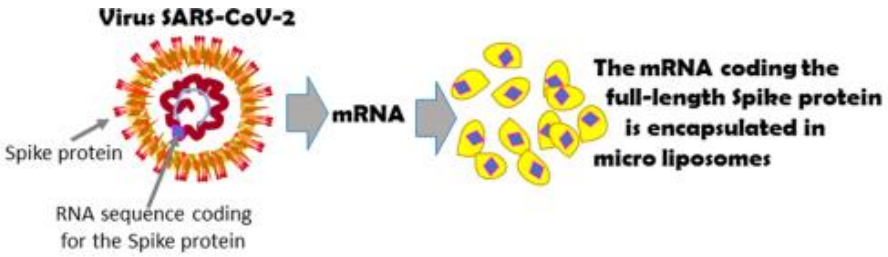
When anyone receives the vaccine, they are likely to be protected against the targeted disease. But not everyone can be vaccinated. Person with severe health conditions that weaken their immune systems (such as cancer or HIV) or who already have severe allergies to some vaccine components may not be able to receive vaccine. These people are still protected if they live amongst others who vaccinated. When a lot of people in a community are vaccinated the pathogen has a hard time circulating because most of the people it encounters are immune. So the more that others are vaccinated, the less likely people who are unable to be protected by

Vaccines are at risk of even being exposed to the harmful pathogens. This is called herd immunity. This is especially important for those people who not only can't be vaccinated but may be more susceptible to the diseases we vaccinate against. No single vaccine provides 100% protection, and herd immunity does not provide full protection to those who cannot safely be vaccinated. But with herd immunity, these people will have substantial protection, thanks to those around them being vaccinated. Vaccinating not only protects yourself, but also protects those in the community who are unable to be vaccinated. If you are able to, get vaccinated [16]. Throughout history, humans have successfully developed vaccines for a number of life-threatening diseases, including meningitis, tetanus, measles and wild polio

1. **m-RNA vaccines**

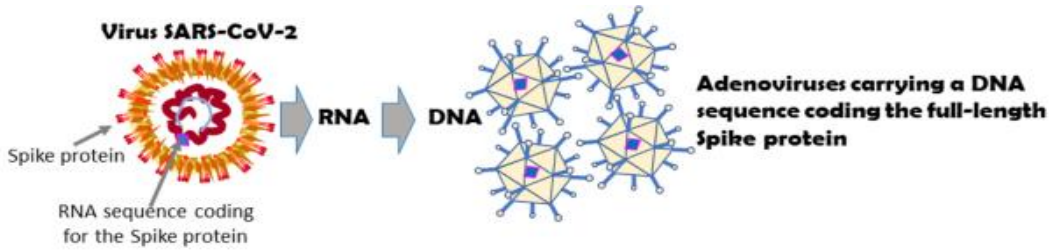
Moderna and Pfizer both utilize lipid nanoparticles to encapsulate m-RNA payload. It also encodes for the spike protein of SARS CoV-2 which binds with the ACE-2 receptor. Direct cytoplasmic delivery and increased specificity towards antigen presenting cell was made possible because of the use of lipid nano-particles as a carrier. The nano-particle used by Pfizer are known as to be slightly cationic.

2. Viral vector vaccines: Adenoviruses are simple non-enveloped viruses that contain a linear double-stranded DNA genome and are responsible for a variety of illnesses including cold-like symptoms. Adenovirus vectors are used in vaccines to express foreign antigens and thus stimulate an immune response, achieved by replacing sections of DNA within the adenovirus. The Oxford-AstraZeneca vaccine (ChAdOx1) utilizes an adenovirus vector derived from the chimpanzee, incorporating genetic sequences that instruct cellular machinery to produce the full-length spike protein of SARS-CoV-2. Some changes were made to the genetic sequence that would prevent replication and improve translation, specifically by deleting E1 and E3 and incorporating a tissue plasminogen activator leader sequence.



Company and country	Vaccine name	Number of doses	Approval and registration
Pfizer, USA and BioNTech, Germany	BNT162b2	2	Final results of the Phase III trial enrolling 45 539 participants demonstrated BNT162b2 vaccine to be 95% effective. Pfizer has obtained emergency vaccine registration in UK and USA; a conditional marketing authorization is under evaluation by the EU regulatory agency (EMA).
Moderna, USA and US Governement	mRNA-1273	2	Final results of the Phase III trial in the US enrolling 30 000 people showed 94% vaccine efficacy; Nobody who was vaccinated with mRNA-1273 developed severe COVID-19. A rolling review of trial data by US, UK and EU regulatory agencies is ongoing.

Figure2: Pfizer and Moderna Covid-19 mRNA vaccines

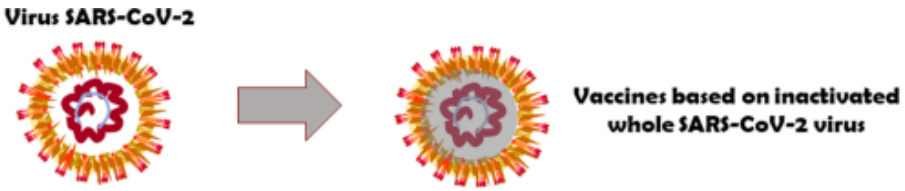


Company and country	Vaccine name	Number of doses	Approval and registration
CanSino Biologicals	Ad5-nCoV	1	This vaccine is based on the human adenovirus Ad5 carrying the mRNA for the Spike protein is approved for administration to Chinese health care workers and and soldiers ahead of the end of Phase III trial.
Gamaleya Res Inst, Russia	Sputnik V	2	This vaccine based on two human adenoviruses (Ad5 and Ad26) carrying the mRNA for the Spike protein administered sequentially was approved for limited use ahead of the end of Phase III trial.
Johnson&Johnson, USA	Ad26COVs1	1	The Phase III trial based on a human adenovirus Ad26 carrying the mRNA for the Spike protein with up to 60 000 participants is expected to finish by the end of 2020. A second Phase III trial was launched to observe the effects of two doses of the vaccine.
AstraZeneca, Sweden- UK Univ. Oxford, UK	ChAdOx1	2	The Phase III trial on this vaccine is based on a chimpanzee adenovirus carrying the mRNA for the Spike protein led only to 62 percent efficacy. However, when ChAdOx1 was given first half dose, followed by a full dose, the protection climbed to 90%. Additional studies are underway to determine the efficacy of this vaccine.

Figure3: Viral vector vaccines

3. Attenuated SARS-CoV-2 virus vaccine:

This vaccine is based on living microbe (pathogens) that has been weakned so that it doesn't cause disease. Attenuated microbes have the ability to retain 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 (17).



Company and country	Vaccine name	Number of doses	Approval and registration
Sinovac Biotech, China	---	2	Ahead of Phase II trial it is offered to essential workers and other high-risk people of the Chinese town of Jiaxing for about 30 €/dose
Beijing Institute of Biological Products and Sinopharm, China	BBIBP-CorV	2	Limited approval for Chinese health care workers and ahead of Phase III trial. This vaccine has been approved by United Arab Emirates on the basis of preliminary data showing that it is 86% effective.
Wuhan Institute of Biological Products, and Sinopharm, China	---	2	Limited approval for Chinese health care workers and soldiers ahead of Phase III trial.
Bharat Biotech, India	COVAXIN	2	The Phase III trial with 26 000 volunteers is expected to close in February 2021.

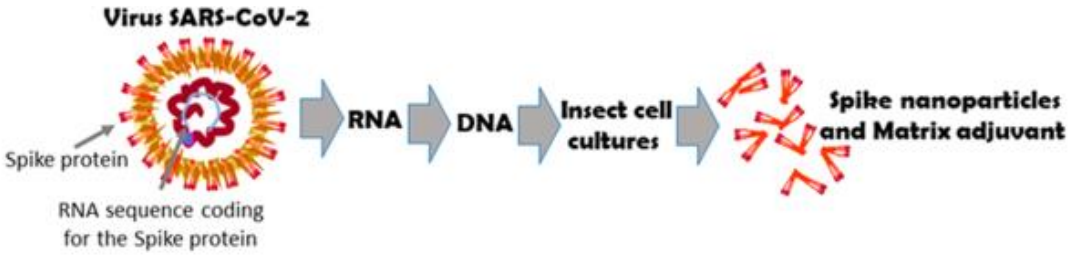
Figure4: Attenuated SARS-CoV-2 virus vaccine

4. Inactivated SARS CoV-2 virus vaccine:

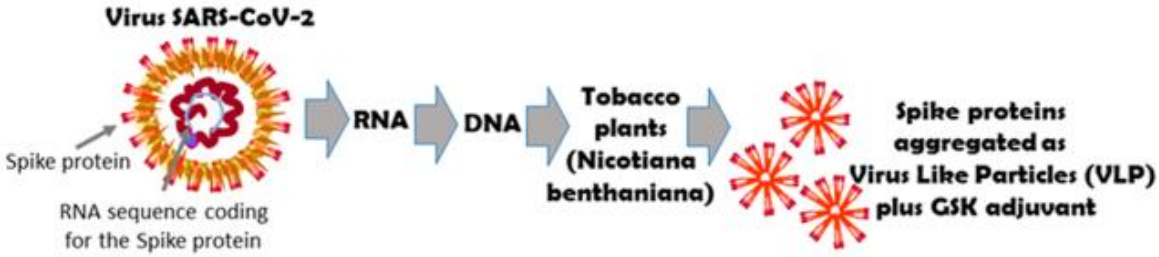
Vaccines based on killed microorganisms (inactivated vaccines) belong to a very traditional technological platform that has led to numerous vaccines. The vaccines produced using this method are more stable than live attenuated vaccines but their limit is mainly related to the short duration of immune 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 (18).

5 Protein vaccine: There are several human vaccines based on proteins present on the surface of microbes [1]. Initially, these proteins were purified from the microbes while today, in most of the cases, they are produced in vitro exploiting the recombinant DNA technology (19).

6 Viral vector vaccines: The DNA coding for the Spike protein can be conveyed into the cells by viral vectors. By inserting the DNA in a virus, it is possible to exploit the virus's great ability to infect and deliver the mRNA into the human cells (20).



Company and country	Vaccine name	Number of doses	Approval and registration
Novavax, US	NVX-CoV2373	2	A first Phase III trial of 15 000 volunteers was launched in the UK. A second Phase III is enrolling 30 000 volunteers in the US and Mexico.



Company and country	Vaccine name	Number of doses	Approval and registration
Medicago, Canada and GSK, Italy	Co-VLP	2	A Phase III trial is enrolling in over 30 000 subjects in North America, Latin America and Europe

Figure5: Viral vector vaccines

Conclusion:

Covid-19 is a major health challenge throughout the world. Expert and authorities are working to develop and enact other preventative measures. Scientific research does not support that the vaccination is unsafe. Vaccine do not contain toxins in level that are unsafe to human body. Vaccines have proven to be effective against the SARS CoV-2 virus in preventing serious illness and death. In an article published in Nature Medicine on June 9, an analysis of data from the United Kingdom, gathered between December 1, 2020 and April 30, 2021 when alpha variant was predominant, showed that the AstraZensca vaccine had an effecrivness of 64% after one dose and 79% after two doses, in protecting against severe illness and death. In the same article, the authors also found that a previous infection with SARS CoV-2 had a significant protective effect against reinfection.

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