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# THE SCIENCE OF HOPE: A COMPREHENSIVE REVIEW OF COVID-19 VACCINE PROGRESS

Ashish Srivastava <sup>1</sup>\*, Versha Chaturvedi <sup>2</sup>, Pranay Wal<sup>3</sup>, Parul Srivastava<sup>4</sup>, Ankita Wal<sup>5</sup>, Anil Yadav<sup>6</sup>

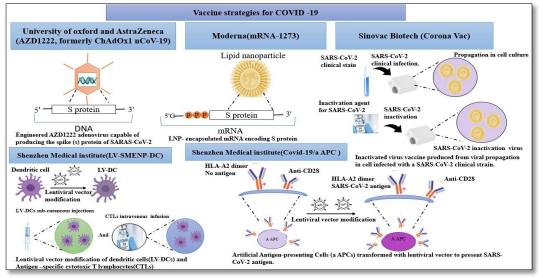
<sup>1\*</sup>,<sup>2,3,4,5,6</sup>PSIT-Pranveer Singh Institute of Technology (Pharmacy) Kanpur, Kanpur-Agra -Delhi NH-19, Bhauti, Kanpur, Uttar Pradesh, India

\*Corresponding author :Dr. Ashish Srivastava \*Department of Pharmaceutical Chemistry, PSIT- Pranveer Singh Institute of Technology, Kanpur E-mail address: srivastava457@gmail.com

#### Abstract

It is expected that the SARS-CoV-2 (severe acute respiratory syndrome-CoV-2) virus started a pandemic in 2020 that had affected the health of people everywhere in the world. Scientists are still trying to find COVID-19 vaccines and medicines that work. In this review article the study on the COVID-19 candidates for the vaccine that are currently going through clinical trials, in addition to the top candidates that are going through pre-clinical development and research at the moment. Five main bases were used to make these candidates There is a live-attenuated vaccine, an mRNA-based vaccine, DNA vaccines, an inactivated virus, and a viral-vector-based vaccine. Making a fast vaccine against other coronaviruses like SARS-CoV and MERS-CoV are similar to SARS-CoV-2 is dangerous for many reasons. The most important things that need to be done quickly are finding out how dangerous a new virus is and if it might have an antigen, choosing the best experimental models and delivery methods for the vaccine, doing the immune response study, setting up the clinical trials, and figuring out if the vaccine is safe and effective.

#### **GRAPHICAL ABSTRACT**



#### **KEYWORD**: SARS-CoV-2 and COVID-19, coronavirus, vaccine.

#### **1.INTRODUCTION**

Catrin Sohrabi *et al.* (April 2020) identified that COVID-19 was identified as the causative agent of an unprecedented outbreak of pneumonia in Wuhan City. The COVID-19 pandemic, caused by the novel coronavirus SARS-CoV-2, has had a profound impact on global health and the economy since it was first identified in December 2019 in Wuhan, China.<sup>[1]</sup> It is caused by a beta coronavirus named SARS-CoV-2 that affects the lower respiratory tract and manifests as pneumonia in humans.

Muhammad Ghafoor Ali *et al.* (2020) studied that the spread of disease as a pandemic occurred due to movement of carriers outside China. The virus has rapidly spread to every corner of the world, resulting in millions of confirmed cases and hundreds of thousands of deaths.<sup>[2]</sup> The outbreak has been declared a pandemic by the World Health Organization (WHO), and has triggered a global public health emergency response.<sup>[3]</sup>

COVID-19 is primarily spread through respiratory droplets when an infected person talks, coughs, or sneezes. The virus can also be transmitted through contact with contaminated surfaces and objects.<sup>[4]</sup> Jitian Li *et al.* (2020) identified that the symptoms of COVID-19 vary from mild to severe and can include fever, cough, fatigue, and difficulty breathing, headache, diarrhoea, rhinorrhoea, stuffed nose, nausea, vomiting, muscle or joint ache.<sup>[5]</sup> The elderly and those with underlying medical conditions are at a higher risk of developing severe complications, such as pneumonia and acute respiratory distress syndrome (ARDS).<sup>[6]</sup>

Efforts to contain the spread of the virus have included measures such as social distancing, maskwearing, and quarantine.<sup>[7]</sup> Devin Skoll *et al.* (2021) studied that the COVID-19 pandemic is unique in its ability to be spread by asymptomatic and pre-symptomatic patients, and countries have implemented digital solutions to combat it. The U.S. must develop a framework to curb the viral spread by rapidly developing a framework implementing both enhanced tracing and testing strategies balancing the needs of public health while respecting individual liberties. Governments and public health organizations around the world have also implemented widespread testing and contact tracing, and have invested heavily in the development and distribution of COVID-19 vaccines.<sup>[8]</sup>

Despite these efforts, the pandemic continues to pose a significant threat to public health and the global economy. The emergence of new variants of the virus has further complicated efforts to control its spread.<sup>[9]</sup> Saima Hamid *et al.* (2020) studied that coronavirus disease (COVID-19) is highly pathogenic viral infection caused by SARS-CoV-2. Currently, COVID-19 has caused global health concern. It is assumed that COVID-19 has zoonotic origin based on the large number of infected people who were exposed to the wet market in Wuhan City, China. The transmission of COVID-19 infection from one person to another resulted in the isolation of patients who were subsequently given a variety of treatments. To monitor the current outbreak, robust steps have been taken around the globe to reduce the transmission of COVID-19 infection particularly banning international and domestic flights, inducting lockdowns in vulnerable areas, social distancing etc as such, it is crucial that researchers continue to study COVID-19 to better understand its mechanisms of transmission, pathogenesis, and potential treatments.<sup>[10]</sup>

In this article, we will review the current state of knowledge on COVID-19, including its origins, transmission, clinical presentation, and management.<sup>[11]</sup> Annoor Awadasseid *et al.* (2021) tell that Coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Vaccination is considered as one of the greatest successes in medical history. Based on prior experience with the development of SARS-CoV vaccines, all COVID-19 vaccines must be subjected to the tests for protective effects and harmful risks derived from antibody-dependent enhancement that may contribute to augmented infectivity and/or eosinophilic infiltration and will also discuss the impact of the pandemic on public health and the global economy, and outline ongoing efforts to develop effective treatments and vaccines.<sup>[12]</sup>

#### 2. THE RESPONSES OF THE IMMUNE SYSTEM TO THE SARS-COV-2 INFECTION

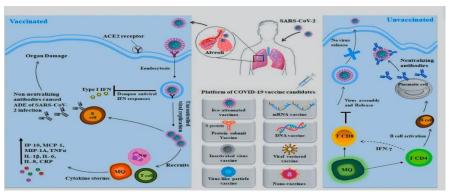
Chih-Cheng Lai et al. (2019) studied that the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) previously provisionally named 2019 novel coronavirus or 2019-nCoV) disease (COVID-19). The end of 2019 has caused a large global outbreak and is a major public health issue. As of 11 February 2020, data from the World Health Organization (WHO) have shown that more than 43 000 confirmed cases have been identified in 28 countries/regions, with >99% of cases being detected in China. On 30 January 2020, the WHO declared COVID-19 as the sixth public health emergency of international concern. It is spread by human-to-human transmission via droplets or direct contact, and infection has been estimated to have mean incubation period of 6.4 days and a basic reproduction number of 2.24–3.58. <sup>[13]</sup> When the virus enters the human body, the immune system is activated to recognize and eliminate the virus<sup>[14]</sup> Rita Carsett *et al.* (2020) performed a longitudinal follow-up, flow-cytometric and serological analysis of innate and adaptive immunity in 64 adults with a spectrum of clinical presentations: 28 healthy SARS-CoV-2- negative contacts of COVID-19 cases; 20 asymptomatic SARS-CoV-2-infected cases; eight patients with Mild COVID-19 disease and eight cases of Severe COVID-19 disease. The wide spectrum of clinical expression of SARS-CoV-2 illness suggests that individual immune response to SARS-CoV-2 infection involves both innate and adaptive immunity.<sup>[15]</sup>

Innate immunity is the first line of defence against invading pathogens <sup>[16].</sup> When SARS-CoV-2 enters the body, it is recognized by various innate immune cells such as dendritic cells, macrophages, and natural killer cells<sup>[17]</sup> These immune cells release cytokines, which are signalling molecules that recruit more immune cells to the site of infection<sup>[18]</sup> In some cases, the immune response can lead to excessive cytokine production, leading to a cytokine storm, which can cause severe damage to the body's tissues<sup>[19]</sup>

Adaptive immunity involves the production of antibodies and activation of specific immune cells, such as T cells and B cells, that target the virus<sup>[20]</sup> B cells produce antibodies that bind to the virus and mark it for destruction by other immune cells<sup>[21]</sup> T cells, on the other hand, directly target and kill infected cells. The adaptive immune response takes several days to develop and is critical for long-term protection against the virus.<sup>[22]</sup>

In some cases, the immune response to SARS-CoV-2 infection can be insufficient, leading to persistent viral replication and disease progression<sup>[23]</sup> This is particularly true in people who are immunocompromised, such as those with HIV/AIDS, cancer, or who have received organ transplants<sup>.[24]</sup> In these individuals, the virus can replicate unchecked, leading to severe disease and potentially death<sup>.[25]</sup>

Overall, the immune response to SARS-CoV-2 infection is complex and can vary widely between individuals<sup>[26]</sup> While some people may develop mild or asymptomatic infections, others can develop severe disease and even die<sup>[27]</sup> Ongoing research is focused on understanding the factors that contribute to these differences and developing effective treatments and vaccines to prevent and treat COVID-19<sup>[28]</sup> (Figure 1).



**Figure 1.** When the mass is infected with severe acute respiratory syndrome-CoV-2 (SARS-CoV-2) or is vaccinated, the immune system reacts in different ways. Aerosolized SARS-CoV-2 is taken in

by alveolar type 2 cells and other cells with receptors for angiotensin-converting enzyme 2 (ACE2).

Then, these cells get sick. The virus might stop the body from making antiviral interferon (IFN) type I, which means that the virus can't be stopped from spreading. When neutrophils, monocytes, and macrophages were called in, cytokine storms happened. This means that too many cytokines and chemokines that cause inflammation were made. Also, non-deactivating antibodies made by B-cells could make the severe acute respiratory syndrome-CoV-2 (SARS-CoV2) impurity worse by increasing organ damage complete a process known as antibody-dependent enhancement (ADE). In a healthy immune response to a vaccine, the early irritation sends CD8+ T-cells and CD4+ T-cells to the place where the infection is, where they kill the infected cells before the virus can spread.

These people have antibodies that stop viruses from spreading.

#### 2.1. INNATE IMMUNITY

Innate immunity is the first line of defence against invading pathogens, including the SARS-CoV-2 virus<sup>[29]</sup> The innate immune response is a rapid, non-specific response that occurs within hours of infection.<sup>[30]</sup> It involves various cells and molecules in the body, including epithelial cells, phagocytes, natural killer cells, and complement proteins.<sup>[31]</sup>

When the SARS-CoV-2 virus enters the body, it is recognized by the innate immune cells, such as dendritic cells, macrophages, and natural killer cells.<sup>[32]</sup> These cells have receptors on their surface that can bind to specific structures on the virus, such as the spike protein.<sup>[33]</sup> Once the virus is recognized, these cells release cytokines and chemokines, which are signalling molecules that recruit more immune cells to the site of infection.<sup>[34]</sup>

Phagocytes, such as neutrophils and macrophages, are important innate immune cells that engulf and destroy invading pathogens<sup>[35]</sup> When they encounter the SARS-CoV-2 virus, they engulf it and break it down inside their own cells.<sup>[36]</sup> They also release cytokines and chemokines that help recruit other immune cells to the site of infection<sup>.[37]</sup>

Natural killer (NK) cells are another important innate immune cell that can recognize and kill infected cells.<sup>[38]</sup> NK cells can detect changes in the surface of infected cells and release toxic molecules that cause the infected cells to die<sup>.[39]</sup> This helps limit the spread of the virus to other cells in the body.<sup>[40]</sup> Complement proteins are a group of proteins that help the innate immune system to recognize and destroy pathogens.<sup>[41]</sup> They can directly kill the virus by punching holes in the viral membrane or by marking it for destruction by phagocytes.<sup>[42]</sup>

While the innate immune response is critical for controlling the initial stages of SARS-CoV-2 infection, it is not always sufficient to eliminate the virus<sup>[43]</sup> In some cases, the virus can evade the innate immune response or even exploit it to promote its own replication<sup>[44]</sup> This can lead to a more severe infection and an overproduction of cytokines, which can cause tissue damage and inflammation.<sup>[45]</sup>

Overall, the innate immune response to SARS-CoV-2 infection is a complex process involving multiple cells and molecules<sup>.[46]</sup> Understanding the innate immune response to SARS-CoV-2 is crucial for developing effective treatments and vaccines to prevent and treat COVID-19.<sup>[47]</sup>

#### **2.2. B-CELL RESPONSE**

B cells are a type of white blood cell that play a critical role in the adaptive immune response to viral infections such as SARS-CoV-2.<sup>[48]</sup> B cells produce specialized proteins called antibodies that can bind to specific structures on the surface of the virus, known as antigens.<sup>[49]</sup> This binding marks the virus for destruction by other immune cells, such as phagocytes.<sup>[50]</sup>

In response to SARS-CoV-2 infection, B cells are activated and begin to produce antibodies that are specific to the virus.<sup>[51]</sup> The antibodies produced by B cells can neutralize the virus and prevent it from entering and infecting host cells.<sup>[52]</sup> These antibodies can also help to clear the virus from the body.<sup>[53]</sup>

Studies have shown that people who have recovered from COVID-19 have high levels of SARS-CoV-2-specific antibodies in their blood<sup>.[54]</sup> This suggests that the B cell response to SARS-CoV-2 infection is an important part of the immune response to the virus.<sup>[55]</sup>

However, there is still much that is not known about the B cell response to SARS-CoV-2. For example, it is not yet clear how long the antibody response to the virus lasts<sup>,[56]</sup> or whether people who have recovered from COVID-19 are protected from reinfection.

Recent research has also suggested that new variants of the virus, such as the Delta variant, may be able to evade the B cell response to some extent.<sup>[57]</sup> This highlights the importance of ongoing research into the B cell response to SARS-CoV-2 and the development of effective vaccines that can protect against emerging variants of the virus.<sup>[58]</sup>

In addition to producing antibodies, B cells also play a role in the activation of other immune cells, such as T cells, which can directly kill infected cells<sup>[59]</sup> The interactions between B cells and other immune cells are complex and not yet fully understood, but are critical for the effective control of SARS-CoV-2 and other viral infections<sup>[60]</sup>

Overall, the B cell response to SARS-CoV-2 is an important part of the immune response to the virus<sup>[61]</sup> On-going research is focused on understanding the B cell response to the virus and developing effective treatments and vaccines to prevent and treat COVID-19.<sup>[62]</sup>

# 2.3. T-CELL RESPONSE

T cells are another type of white blood cell that play a key role in the immune response to SARS-CoV-2, the virus responsible for COVID-19.<sup>[63]</sup> T cells are divided into two main types: CD4+ T cells and CD8+ T cells, both of which contribute to the immune response against the virus.<sup>[64]</sup>

CD4+ T cells, also known as helper T cells, are responsible for coordinating the immune response against the virus<sup>.[65]</sup> When a person is infected with SARS-CoV-2, CD4+ T cells recognize fragments of the virus that are presented on the surface of infected cells<sup>.[66]</sup> This recognition activates the CD4+ T cells, which then release cytokines and other immune signalling molecules that help to recruit and activate other immune cells, including B cells and CD8+ T cells.<sup>[67]</sup>

CD8+ T cells, also known as cytotoxic T cells, are responsible for directly killing infected cells.<sup>[68]</sup> When a CD8+ T cell recognizes a cell that is infected with SARS-CoV-2, it releases perform and granzymes, which can cause the infected cell to undergo programmed cell death<sup>.[69]</sup> This process not only eliminates the infected cell but also helps to prevent the virus from spreading to other cells in the body.<sup>[70]</sup>

T cells also play a role in the development of immunological memory, similar to B cells.<sup>[71]</sup> Memory T cells are long-lived cells that can quickly recognize and respond to the virus upon re-exposure.<sup>[72]</sup> This rapid response is critical for preventing severe illness and reducing the spread of the virus in the population.[<sup>73]</sup>

The T cell response to SARS-CoV-2 is complex and multifaceted, with different subsets of T cells playing different roles in the immune response.<sup>[74]</sup> Recent studies have shown that individuals who recover from COVID-19 often have robust T cell responses, including both CD4+ and CD8+ T cells, suggesting that T cells may play an important role in the development of immunity to the virus.<sup>[75]</sup>

Overall, the T cell response to SARS-CoV-2 is an essential component of the immune response against the virus.<sup>[76]</sup> By coordinating the immune response and directly killing infected cells, T cells contribute to the elimination of the virus and the development of immunological memory.<sup>[77]</sup>

# **3-CORONAVIRUS VACCINE DEVELOPMENT STRATEGIES**

The development of safe and effective vaccines is a critical component of the global response to the COVID-19 pandemic.<sup>[78]</sup> Scientists and researchers around the world have been working tirelessly to develop vaccines against the novel coronavirus, using a variety of different strategies.<sup>[79]</sup>

One of the most widely used approaches for developing COVID-19 vaccines involves the use of messenger RNA (mRNA) technology.<sup>[80]</sup> This strategy involves creating a synthetic piece of RNA that codes for a specific antigen, or protein, found on the surface of the virus.<sup>[81]</sup> When the mRNA vaccine is injected into the body, it prompts the immune system to produce antibodies against the virus. Two mRNA vaccines,<sup>[82]</sup> produced by Pfizer-BioNTech and Moderna, have been granted emergency use authorization by regulatory agencies around the world.<sup>[83]</sup>

Another approach to COVID-19 vaccine development involves the use of viral vector technology.<sup>[84]</sup> This strategy involves using a harmless virus, such as an adenovirus, to deliver a piece of the SARS-CoV-2 virus to the body's cells.<sup>[85]</sup> This triggers an immune response, which can protect against future infection. Several viral vector vaccines, including those produced by AstraZeneca and Johnson & Johnson, have been authorized for emergency use.<sup>[86]</sup>

A third approach to vaccine development involves the use of inactivated or killed virus particles.<sup>[87]</sup> This strategy involves growing large quantities of the virus in a lab, then inactivating or killing the virus so that it cannot cause disease.<sup>[88]</sup> When this vaccine is injected into the body, it prompts an immune response without causing infection.<sup>[89]</sup> Several inactivated virus vaccines, including those produced by Sinovac and Bharat Biotech, have been authorized for use in some countries.<sup>[90]</sup>

Other strategies for COVID-19 vaccine development include protein subunit vaccines, which use a piece of the virus's surface protein to prompt an immune response, and DNA vaccines, which use a small piece of the virus's DNA to prompt an immune response.<sup>[91]</sup> These strategies are still being studied in clinical trials.<sup>[92]</sup>

In summary, there are a variety of different strategies being used for the development of COVID-19 vaccines, including mRNA technology, viral vector technology, inactivated or killed virus particles, protein subunit vaccines, and DNA vaccines.<sup>[93]</sup> Each approach has its own strengths and weaknesses, and ongoing research is needed to determine which strategies are the most effective and safe for preventing COVID-19.<sup>[94]</sup> **table 1** shows.

Vaccine Stage	Coronavirus	Report	Clinical trial	How the immune system
v accine Stage	Coronavirus	Report	Chinical trial	is activated
		SARS-CoV packet point protein recombinant weakened infection virus.	preclinical	antibody-based immune response
Live Attenuated injection	SARS-CoV	Attenuated vesicular stomatitis virus (VSV) that produces SARS-CoV spike protein.	Preclinical	Immune reactions based on antibodies
		Live attenuated with the E protein and other proteins taken out	Preclinical	Getting T cells and antibodies to respond
inactivated injection	SARS-CoV	-propiolactone was used to kill the SARS-CoV virus. ARS-CoV can be turned off by UV light with or without an adjuvant	Preclinical	Immune responses based on antibodies Make T-cells respond and make cytokines like IFN-, TNF-, IL-5, IL-4, and IL-2.
Vector-based injection	SARS-CoV	duovirus with SARS-CoV N- terminal segment of S1 gene	Preclinical	Make humoral replies
Nucleic acid injection	SARS-CoV,	duovirus-vectored are made up of full-length spike glycoprotein MERS-CoV (ChAdOx1 MERS Full spike (S) glycoprotein or fragments	Preclinical	Activate the immune system and cells Certain responses from CD4+ and CD8+ T-cells and neutralising antibodies

**Table 1.** Platforms for making injections for MERS-CoV and SARS-CoV.

# **3.1. FIRST-GENERATION VACCINES (LIVE-ATTENUATED AND INACTIVATED VACCINES)**

The first generation of COVID-19 vaccines includes two types of vaccines: live attenuated vaccines and inactivated vaccines<sup>[95]</sup> Both types of vaccines have been widely used in the past to prevent infectious diseases, and they have been adapted to target the SARS-CoV-2 virus responsible for COVID-19<sup>[96]</sup> Live attenuated vaccines contain a weakened form of the virus that causes COVID-19.<sup>[97]</sup> The weakened virus is unable to cause disease, but it can still stimulate the immune system to produce a response <sup>[98]</sup> The immune response generated by the vaccine can then provide protection against future infections.<sup>[99]</sup> However, there are some potential risks associated with live attenuated vaccines, such as the possibility of the virus reverting to its original, more virulent form.<sup>[100]</sup> Inactivated vaccines, on the other hand, contain a killed version of the virus that causes COVID-19.<sup>[101]</sup> Because the virus is no longer able to replicate, it cannot cause disease<sup>.[102]</sup> However, the immune system can still recognize the viral antigens and mount a response, thereby providing protection against future infections<sup>[103]</sup> Inactivated vaccines are considered safer than live attenuated vaccines, but they may require booster doses to maintain protection over time<sup>[104].</sup> Both types of vaccines have been developed and used successfully in the past to prevent a range of infectious diseases, including polio, measles, and influenza<sup>.[105]</sup> However, there are some challenges associated with developing effective vaccines for COVID-19<sup>[106]</sup> The SARS-CoV-2 virus is highly infectious, and there is a risk of vaccine-induced disease enhancement, which occurs when the vaccine stimulates an immune response that actually enhances the severity of the disease upon infection.<sup>[107]</sup> Despite these challenges, live attenuated and inactivated vaccines have shown promising results in clinical trials for COVID-19.[108] Several countries, including China and India, have already approved inactivated vaccines for emergency use<sup>[109]</sup> Live attenuated vaccines are also being developed, but they are still in the early stages of clinical trials<sup>[110]</sup>

In conclusion, the first generation of COVID-19 vaccines includes live attenuated and inactivated vaccines<sup>[111]</sup> Both types of vaccines have been used successfully in the past to prevent infectious diseases, and they have shown promising results in clinical trials for COVID-19<sup>[112]</sup> While there are some challenges associated with developing effective vaccines for COVID-19, ongoing research and development efforts continue to offer hope for controlling the pandemic<sup>[113]</sup>

# **3.2. SECOND-GENERATION VACCINES (PROTEIN SUBUNIT AND VECTOR-BASED** VACCINES)

Protein-based vaccines are a type of vaccine that work by presenting a protein antigen from the pathogen to the immune system<sup>[114]</sup> The immune system then generates an immune response against the protein, which can provide protection against future infections.<sup>[115]</sup> There are two types of proteinbased vaccines: subunit vaccines and vector-based vaccines.<sup>[116]</sup> Subunit vaccines contain only a portion of the pathogen's protein, rather than the entire pathogen<sup>[117]</sup> This means that the vaccine is less likely to cause side effects and is safer to use than other types of vaccines.<sup>[118]</sup> Subunit vaccines are also highly specific, meaning that they can be designed to target a particular protein on the pathogen that is important for causing disease<sup>[119]</sup> However, subunit vaccines may require the use of adjuvants, which are substances that enhance the immune response, to generate a strong immune response<sup>[120]</sup> Vector-based vaccines use a harmless virus or bacterium as a carrier, or vector, to deliver the protein antigen to the immune system<sup>[121]</sup> The vector is modified to contain the genetic material that codes for the protein antigen<sup>[122].</sup> Once the vector enters the body, it infects cells and causes them to produce the protein antigen, which stimulates an immune response <sup>[123]</sup> Vector-based vaccines have been used successfully in the past to prevent diseases such as Ebola and Zika virus<sup>.[124]</sup> However, there is a risk of the vector causing an immune response that can interfere with the effectiveness of the vaccine<sup>[125]</sup> Protein-based vaccines have been developed for COVID-19, with the most widely used being the subunit vaccine developed by Novavax, which includes the spike protein of the SARS-CoV-2 virus<sup>[126]</sup> Early clinical trials have shown promising results, with the vaccine demonstrating high levels of efficacy and safety Vector-based COVID-19 vaccines have also been developed, such as the Oxford/AstraZeneca vaccine, which uses a modified adenovirus vector to deliver the spike protein antigen.<sup>[127]</sup> The Johnson & Johnson vaccine also uses an adenovirus vector to deliver the genetic material that codes for the spike protein antigen.<sup>[128]</sup>

In conclusion, protein-based vaccines, including subunit and vector-based vaccines, have shown promise in the prevention of COVID-19<sup>[129]</sup> These vaccines offer specific and safe immune stimulation against the SARS-CoV-2 virus, and ongoing research and development efforts continue to explore their potential for controlling the pandemic<sup>[130]</sup>

# **3.3. THIRD-GENERATION VACCINES (NUCLEIC ACID AND NANO-MATERIAL-BASED VACCINES)**

Third generation vaccines, also known as nucleic acid and nanomaterial-based vaccines, represent a cutting-edge technology in the field of immunization<sup>.[131]</sup> These vaccines use genetic material, such as DNA or RNA, to stimulate an immune response against a specific pathogen<sup>[132]</sup> The genetic material is often delivered using nanomaterials, which protect the fragile nucleic acid molecules and help them reach their target cells<sup>[133]</sup> One of the key advantages of third generation vaccines is their flexibility.<sup>[134]</sup> Unlike traditional vaccines, which require the cultivation of live or inactivated pathogens, nucleic acid vaccines can be designed and produced in a matter of weeks<sup>[135]</sup> This makes them particularly useful in the context of emerging infectious diseases or rapidly evolving pathogens.<sup>[136]</sup> Another advantage of third generation vaccines is their safety profile.<sup>[137]</sup> Since they only contain genetic material and not the entire pathogen, the risk of adverse reactions is low.<sup>[138]</sup> Furthermore, nucleic acid vaccines do not integrate into the host genome, reducing the risk of longterm side effects<sup>[139]</sup> Several nucleic acid and nanomaterial-based vaccines have already been developed and are in use or undergoing clinical trials.<sup>[140]</sup> For example, the Pfizer-BioNTech and Moderna COVID-19 vaccines are both mRNA-based vaccines that have demonstrated high efficacy in preventing COVID-19 infections<sup>[141]</sup> In addition to their potential as prophylactic vaccines, third generation vaccines also hold promise in the field of therapeutic vaccines.<sup>[142]</sup> By delivering genetic material that encodes for specific proteins or antigens, these vaccines can stimulate an immune response against cancer cells or other diseases<sup>[143]</sup> Overall, third generation vaccines represent an exciting new direction in the field of immunization.<sup>[144]</sup> As the technology continues to evolve, we can expect to see more advanced and effective nucleic acid and nanomaterial-based vaccines developed for a range of infectious and non-infectious diseases<sup>[145]</sup>

# 4. COVID-19 VACCINE CANDIDATES IN CLINICAL TRIALS

The COVID-19 pandemic has prompted an unprecedented global effort to develop vaccines against the SARS-CoV-2 virus, which causes COVID-19.<sup>[146]</sup> As of April 2023, several COVID-19 vaccine candidates have been authorized for emergency use or full approval by regulatory agencies around the world<sup>[147]</sup> However, many more vaccine candidates are still in various stages of clinical development<sup>[148]</sup> One of the most widely used COVID-19 vaccines is the Pfizer-BioNTech vaccine, which is based on messenger RNA (mRNA) technology<sup>[149]</sup> The vaccine uses a small piece of genetic material from the SARS-CoV-2 virus to stimulate an immune response<sup>[150]</sup> Another mRNA-based vaccine, Moderna, has also been authorized for emergency use.[151] Other COVID-19 vaccine candidates in clinical trials include vaccines based on viral vectors, such as the Johnson & Johnson vaccine, which uses a modified adenovirus to deliver a piece of the SARS-CoV-2 virus into cells to stimulate an immune response<sup>.[152]</sup> The AstraZeneca vaccine, which uses a similar approach, has been authorized for emergency use in many countries but has faced some regulatory challenges due to reports of rare blood clotting disorders.<sup>[153]</sup> Several protein-based COVID-19 vaccines are also in clinical trials, including the Novavax vaccine, which uses a protein from the SARS-CoV-2 virus to stimulate an immune response<sup>[154]</sup> The protein is produced in insect cells and then purified for use in the vaccine.<sup>[155]</sup> Another protein-based vaccine candidate is the Sanofi/GSK vaccine, which uses an adjuvant to enhance the immune response to a protein from the SARS-CoV-2 virus<sup>[156]</sup> In addition to these vaccine candidates, there are also several others that are in earlier stages of clinical development<sup>.[157]</sup> These include vaccines based on DNA or live attenuated viruses, as well as vaccines that use novel approaches like nanoparticles or virus-like particles. Overall, the COVID-19 vaccine development effort has been an extraordinary feat of scientific collaboration and innovation<sup>.[158]</sup> While many challenges remain, the availability of multiple safe and effective vaccines is a major milestone in the global fight against COVID-19<sup>.[159]</sup>

Platform	applicant	report	clinical	how the immune	company
			trail	system is triggered	
Live attenuated	BCG vaccine	The BCG live attenuated vaccine will be used for COVID-19.	Phase II/ III	Activating the body's natural immune system; making cytokines that cause inflammation (IL-1, TNF, and IL-6)	Netherlands Research Group
	BCG vaccine	The BRACE trial was done to see if the BCG live-attenuated vaccine could be used to treat SARS-CoV- 2.	Phase IV	Activating the body's natural immune system; making cytokines that cause inflammation (IL-1, TNF, and IL-6)	The Murdoch Children's Research Institute
	mRNA-1273	Lipid nanoparticle (LNP)-encapsulated mRNA vaccine	Phase I	Cause responses from CD4 T cells and a Th1-skewed	Moderna
mRNA vaccine	BNT162	Synthetic strand of mRNA made to get the immune system to react.	Phase I/ II	IgG and T cell responses should last for a long time.	Pfizer and BioNTech
	ARCT-021	In a lipid nanoparticle, mRNA that codes for the 2019-nCoV prefusion spike protein and can copy itself (LNP)	Phase I/ II	Neutralizing antibodies cause strong CD8+ T-cells and Th1 cells to grow.	The company Arcturus Therapeutics, Inc.
	CVnCoV Vaccine (CV07050101 )	Synthetic strand of mRNA made to get the immune system to react.	Phase I	Get neutralising antibodies to react	Curevac
DNA vaccine	INO-4800	Plasmid DNA that makes the SARS- CoV-2 spike protein antigenic	Phase I/ II	Induces cellular and humoral immune reply	Inovio Pharmaceuticals is a company that makes drugs.
	GX-19	The SARS-CoV-2 S- protein antigen was made into a DNA vaccine.	Phase I/ IIa	Immune responses based on antibodies	Genexine, Inc
	AG0301	The SARS-Co. V -2 S-protein antigen was made into a DNA vaccine.	Phase I/ II	Immune responses based on antibodies	Osaka University/Ange's/Takar a Bio
Inactivated virus	Sinopharm	A vaccine made from dead SARS-Co. V-2 virus to get the body's immune system to work.	Phase I/ II	Immune responses based on antibodies	The Wuhan Institute of Virology and Sinopharm

**Table 2.** COVID-19 vaccine candidates tested in clinical trials.

	Sinovac Academy of Medical Sciences in China	Formalin-inactivated and alum-enhanced COVID-19 candidate vaccine SARS-CoV-2 vaccine that has been killed	Phase I Phase Ib/IIb	Immune responses based on antibodies Immune responses based on antibodies	Sinovac The Chinese Academy of Medical Sciences Institute of Medical Biology
Viral vectored	Ad5-nCoV ChAdOx1	Adenovirus type 5 viral vectors that don't replicate can express SARS-CoV- 2 spike protein The RNA gets into	Phase I Phase I/	trigger immune responses based on antibodies Activate anti-spike	CanSino Bio College of Oxford
	nCoV19 (AZD1222)	the cells through the nonreplicating chimpanzee adenovirus vaccine vector (ChAdOx1).	II	IgG responses and spike-specific T-cell responses	Conege of Oxford
	LV-SMENP- DC	The minigenes of Covid-19 are expressed by a dendritic cell that has been changed with the efficient lentiviral vector system (NHP/TYF).	Phase I/ II	Activate cytotoxic T cells	Shenzhen Geno- Immune Medical Institute

#### **Table 3.** Studies on possible COVID-19 vaccines are nearing their end.

Platform	Applicant	Report	Clinical trial	Company
mRNA vaccine	SA RNA	RNA vaccine that grows on its own	Start Phase I in summer 2020	Imperial College London
DNA vaccine	Bac TRL- Spike Linear Rx	Bifidobacterial monovalent SARS-CoV-2 DNA vaccine COVID-19 can be stopped with a Linear DNA vaccine made with LineaRx's PCR-based production platform.	Animal results will be released in May 2020, and Phase I will begin in the fall of 2020.	Sy vivo Takis Biotech
Live attenuated	TNX-1800	Live modified horsepox virus vaccine to be given through the skin to prevent COVID-19.	Pre-clinical	Southern Research and Tonix Pharmaceuticals Holding Corp.
Inactivated coronavirus	Dynavax	Coronavirus vaccine with CpG 1018 TM adjuvant that has been killed	Phase I will begin in July 2020.	Dynavax and Sinovac

#### 4.1. LIVE-ATTENUATED VACCINE 4.1.1. BCG VACCINE

The Bacillus Calmette-Guérin (BCG) vaccine is a vaccine that was originally designed to prevent tuberculosis (TB).<sup>[160]</sup> However, there has been recent interest in the potential of the BCG vaccine to provide some level of protection against COVID-19, the disease caused by the SARS-CoV-2 virus<sup>[161]</sup> Several studies have suggested that countries with high rates of BCG vaccination have lower COVID-19 mortality rates, leading some scientists to hypothesize that the BCG vaccine may provide some level of protection against COVID-19<sup>[162]</sup> However, it is important to note that these observations do not prove causality, and other factors could be at play.<sup>[163]</sup> There have also been several clinical trials investigating the potential of the BCG vaccine to prevent COVID-19 or reduce its severity<sup>[164]</sup> Some early studies have suggested that the BCG vaccine may be effective against COVID-19, but larger and more rigorous studies are needed to confirm these findings.<sup>[165]</sup> One proposed mechanism for how the BCG vaccine may provide some level of protection against COVID-19 is through its ability to stimulate the immune system in a non-specific way, a phenomenon known as "trained immunity".[166] This could potentially enhance the immune response to the SARS-CoV-2 virus, although the exact mechanisms are not yet fully understood.<sup>[167]</sup>While the potential of the BCG vaccine to provide some level of protection against COVID-19 is an interesting area of research, it is important to note that the vaccine is not a substitute for other preventative measures like social distancing, mask-wearing, and vaccination with specific COVID-19 vaccines.<sup>[168]</sup> People should always follow public health guidelines and consult with their healthcare provider regarding any potential medical interventions.<sup>[169]</sup>

#### 4.1.2. TNX-1800

TNX-1800 is a novel monoclonal antibody treatment that has shown promising results in the fight against COVID-19<sup>[170]</sup> The drug, developed by biopharmaceutical company Tonix Pharmaceuticals, is designed to target the spike protein of the SARS-CoV-2 virus, which is responsible for its ability to infect human cells.<sup>[171]</sup> In preclinical studies, TNX-1800 demonstrated potent neutralizing activity against the original strain of the SARS-CoV-2 virus as well as against the B.1.1.7 (UK) and B.1.351 (South Africa) variants<sup>[172]</sup> The drug was also found to be effective in reducing viral loads in animal models of COVID-19.<sup>[173]</sup> Tonix Pharmaceuticals has initiated a phase 1 clinical trial to evaluate the safety and immunogenicity of TNX-1800 in healthy volunteers.<sup>[174]</sup> The trial will enrol up to 72 participants and will evaluate various doses of the drug administered either alone or in combination with other monoclonal antibodies<sup>[175]</sup> If the clinical trial is successful, TNX-1800 could potentially be used as a treatment for COVID-19 patients, particularly those who are at high risk of developing severe disease.<sup>[176]</sup> Monoclonal antibody treatments have been shown to be effective in reducing the risk of hospitalization and death in COVID-19 patients, and TNX-1800 could be a valuable addition to the existing arsenal of treatments.<sup>[177]</sup> However, it is important to note that TNX-1800 is still in the early stages of development, and more research is needed to fully understand its safety and efficacy.<sup>[178]</sup> The ongoing clinical trial will provide important data on the drug's potential as a COVID-19 treatment, and additional studies will be needed before it can be approved for widespread use<sup>[179]</sup> In summary, TNX-1800 is a promising new monoclonal antibody treatment for COVID-19 that has shown potent neutralizing activity against the SARS-CoV-2 virus and is currently being evaluated in a phase 1 clinical trial<sup>.[180]</sup> If successful, TNX-1800 could be a valuable addition to the existing treatments for COVID-19 and could help to reduce the burden of the disease on healthcare systems around the world.[181]

# 5. M-RNA VACCINE

# 5.1. M-RNA-1273

M-RNA-1273 is a vaccine developed by Moderna, a biotechnology company based in Massachusetts, USA.<sup>[182]</sup> The vaccine is designed to prevent COVID-19, the infectious disease caused by the coronavirus SARS-CoV-2. M-RNA-1273 is based on a messenger RNA (mRNA) technology, a novel

approach to vaccine development that has shown great promise in the fight against COVID-19<sup>.[183]</sup> M-RNA-1273 works by instructing cells in the body to produce a piece of the spike protein found on the surface of the SARS-CoV-2 virus.<sup>[184]</sup> This spike protein is then recognized by the immune system as foreign, triggering an immune response that produces antibodies and other immune cells that can recognize and attack the virus if it enters the body.<sup>[185]</sup> Clinical trials of mRNA-1273 have shown it to be highly effective in preventing COVID-19<sup>.[186]</sup> In a phase III trial involving over 30,000 participants, the vaccine was found to be 94.1% effective at preventing symptomatic COVID-19, and 100% effective at preventing severe COVID-19<sup>[187]</sup> The vaccine was also found to be safe and welltolerated, with side effects generally mild and short-lived. M-RNA-1273 has been authorized for emergency use by regulatory agencies in several countries, including the United States, European Union, and Canada<sup>[188]</sup> The vaccine is administered as a two-dose series, with the second dose given 28 days after the first<sup>.[189]</sup> The vaccine can be stored at standard freezer temperatures (-20°C) for up to six months, making it easier to distribute and administer than some other COVID-19 vaccines<sup>[190]</sup> Overall, M-RNA-1273 represents a significant breakthrough in the fight against COVID-19<sup>[191]</sup> Its high efficacy and safety profile make it one of the most promising vaccines available and it has already played a key role in helping to bring the COVID-19 pandemic under control in many parts of the world<sup>[192]</sup> As research into mRNA technology continues, it is likely that other mRNA-based vaccines will be developed for a range of other infectious diseases, offering new hope for the prevention and treatment of these conditions.<sup>[193]</sup>

#### 5.1.1. BNT162 (3 LNP-MRNAS)

BNT162 is a vaccine candidate developed by Pfizer and BioNTech to combat the COVID-19 pandemic.<sup>[194]</sup> The vaccine is an mRNA vaccine, which means it uses a small piece of genetic material from the virus to instruct cells in the body to produce a protein that triggers an immune response<sup>.[195]</sup> This immune response allows the body to recognize and fight the virus if it encounters it in the future<sup>[196]</sup> Clinical trials of BNT162 have shown promising results in terms of its ability to protect against COVID-19. In a large-scale phase 3 clinical trial, the vaccine demonstrated an efficacy rate of 95%, which is higher than many experts had anticipated <sup>[197]</sup> The vaccine has also been shown to be safe, with only mild to moderate side effects reported.<sup>[198]</sup> BNT162 has been authorized for emergency use in many countries, including the United States, the United Kingdom, and the European Union<sup>[199]</sup> The vaccine is a crucial tool in the global effort to control the spread of COVID-19 and protect public health<sup>.[200]</sup> However, the emergence of new variants of the virus has raised questions about the effectiveness of existing COVID-19 vaccines, including BNT162<sup>.[201]</sup> Pfizer and BioNTech have stated that they are monitoring the situation closely and are prepared to adapt the vaccine if necessary to ensure continued protection against the virus<sup>.[202]</sup> Overall, BNT162 is a promising vaccine candidate that has shown strong efficacy and safety in clinical trials.<sup>[203]</sup> Its authorization for emergency use represents a significant step forward in the fight against COVID-19<sup>[204]</sup>

#### 5.1.2. ARCT-021

ARCT-021 is an investigational RNA-based therapeutic developed by Arcturus Therapeutics to treat COVID-19<sup>.[205]</sup> The therapy uses messenger RNA (mRNA) technology to deliver a small piece of genetic material that instructs cells to produce a specific protein, which helps the immune system fight the virus.<sup>[206]</sup> ARCT-021 has shown promising results in preclinical studies and has entered phase 1/2 clinical trials. In a phase 1 study, the therapy was well-tolerated and showed a dose-dependent increase in the production of the target protein<sup>.[207]</sup> In a phase 1b/2a study, ARCT-021 was shown to be safe and well-tolerated, and demonstrated a significant reduction in viral load in patients with COVID-19<sup>.[208]</sup> One of the unique features of ARCT-021 is its ability to be administered as a single, low-dose intranasal spray, which could make it more convenient and accessible than other COVID-19 therapies that require intravenous infusion<sup>.[209]</sup> ARCT-021 is still in the early stages of development, and more research is needed to determine its safety and efficacy<sup>.[210]</sup> However, the results from early clinical trials are promising, and the therapy has the potential to be an important

tool in the fight against COVID-19, especially if it proves effective against emerging variants of the virus<sup>.[211]</sup> Overall, ARCT-021 represents a novel approach to treating COVID-19, and its development is an important step forward in the search for effective therapies to combat the pandemic<sup>.[212]</sup>

# 5.1.3. CVNCOV VACCINE (CV07050101)

CVnCoV is a vaccine candidate developed by CureVac to combat the COVID-19 pandemic<sup>[213]</sup> The vaccine uses messenger RNA (mRNA) technology to instruct cells in the body to produce a protein that triggers an immune response <sup>[214]</sup> This immune response allows the body to recognize and fight the virus if it encounters it in the future Clinical trials of CVnCoV have shown promising results in terms of its ability to protect against COVID-19. In a large-scale phase 2b/3 clinical trial, the vaccine demonstrated an overall efficacy rate of 48%, which is lower than some other COVID-19 vaccines currently in use.<sup>[215]</sup> However, the vaccine showed higher efficacy rates in younger age groups and in those without pre-existing medical conditions<sup>.[216]</sup> CVnCoV has been authorized for emergency use in some countries, including the European Union<sup>.[217]</sup> However, the lower efficacy rate has led some experts to express caution about the vaccine's use, especially in areas where more effective vaccines are available<sup>.[218]</sup> CureVac is continuing to study CVnCoV and is working to improve the vaccine's efficacy<sup>[219]</sup> The company is also investigating the use of the vaccine as a booster shot for individuals who have already received other COVID-19 vaccines<sup>[220]</sup> Overall, CVnCoV is a vaccine candidate that has shown some promise in clinical trials, but its lower efficacy rate has raised some concerns<sup>[221]</sup> Further research is needed to fully evaluate the vaccine's safety and effectiveness, and to determine its role in the global effort to control the spread of COVID-19.<sup>[222]</sup>

# 6. DNA VACCINES

#### 6.1. INO-4800

The new DNA vaccine for SARS-CoV-2 was made by Inovio Pharmaceuticals.<sup>[223]</sup> It is called INO-4800. This candidate got the drug through the skin with the help of a CELLECTRA electroporation device.<sup>[224]</sup> This device sends out a small amount of electricity to make it easier for DNA molecules to enter human cells.<sup>[225]</sup> It was planned to test In a non-randomized, open-label Phase I trial with 40 healthy people in Philadelphia, PA, and Kansas City, MO, the safety, tolerability, and immunogenicity of INO-4800 against COVID-19 were tested. [226] The helpers got one or two 1.0mg intradermic doses of INO-4800 at the start of the study and again after 4 weeks<sup>.[227]</sup> After that, electroporation (EP) was done with the CELLECTRA® 2000 machine (NCT04336410). <sup>[228]</sup> On June 25, 2020, A phase I/IIa trial was going to be started by the Coalition for Epidemic Preparedness Innovations and Inovio Pharmaceuticals<sup>[229]</sup> INO-4800 has the plasmid pGX9501, which contains the entire SARS-CoV-2 spike glycoprotein<sup>.[230]</sup> The main goal of this trial is to find out how well INO-4800 is tolerated, how safe it is, and how well it makes people immune to it when it is injected intradermally (ID) and then subcutaneously (EP) into healthy adults ages 19 to 64.[231] (The parts A and B) Part-A is made up of two parts, 1 and 2. On day 0 or week 4, 20 people in each group got an IV injection of INO-4800 at either 1 mg/dose or 2 mg/dose + EP with CELLECTRA® 2000<sup>[232]</sup> Part B has 90 and 30 people in Groups III and IV, which are the placebo groups<sup>[233]</sup> Part B involved injecting 1 or 2 mg/dose of INO-4800 + EP with CELLECTRA® 2000 into the muscle (IM) (dosing at day 0 and week 4).<sup>[234]</sup> (NCT04447781). Also, the International Vaccine Institute (IVI) and the Korean National Institute of Health (KNIH) planned for a Phase I/II trial of this vaccine to take place in South Korea at the same time as the trial in the U.S. <sup>[235]</sup> This vaccine was made by Inovio in the same way that CEPI paid for experimental vaccines for Lassa and MERS. INO-4800 had plasmid DNA, which, when given to a host, makes the host's cells make the harmful SARS-CoV-2 spike protein<sup>.[236]</sup>

# 6.2. VACCINE BASED ON SANOFI'S RECOMBINANT DNA PLATFORM

The action is a shot that hasn't been given a name yet<sup>.[237]</sup> The vaccine was made possible by Sanofi's recombinant DNA platform.<sup>[238]</sup> The platform is built to make a certain set of genetic proteins that are

on the outside of the virus.<sup>[239]</sup> This shot has a lot of antigens from the coronavirus, which can help your immune system work improved<sup>.[240]</sup> In order to do this, the antigen's DNA sequence will be added to the DNA of the platform for baculovirus expression.<sup>[241]</sup> Sanofi wants to speed up the process of making a COVID-19 vaccine by collaborating with the Biomedical Advanced Research and Development Authority (BARDA).<sup>[242]</sup>

# 6.3. LINEAR RX

Linear, which is part of Practical DNA Sciences, is working on a linear DNA inoculation for COVID-19.<sup>[243]</sup> They do this with the help of Linear Rx's production platform based on The polymerase chain reaction (PCR).<sup>[244]</sup> The Italian Ministry of Health gave Takis Biotech permission to start a test of a possible COVID-19 vaccine before it is used on people. We should see the first results in April 2020<sup>.[245]</sup>

# 6.4. GX-19

The GX-19 DNA vaccine is made by Genexine Inc. It contains the S-protein antigen of the SARS-CoV-2 virus. After the shot, the DNA will be taken up by the host cells, which will then make the protein<sup>[246]</sup> This will cause the immune system to respond by making antibodies that stop the wild-type virus from spreading and keep the person from getting sick<sup>.[247]</sup> On June 17, 2020, 210 healthy adults between the ages of 19 and 50 took part in a Phase I/IIa trial to check for safety, tolerability, and immune response<sup>.[248]</sup>

# 6.5. AG0301

The DNA vaccine AG0301-COVID19 was made by Ange's Inc., Japan Agency for Medical Research and Development (JAMRD) and Osaka University (Osaka University).<sup>[249]</sup> It has the SARS-CoV-2 S-protein antigen in it.<sup>[250]</sup> A non-randomized, open-label, non-controlled Phase I/II study was done with 30 healthy volunteers between the ages of 20 and 65 in June 2020<sup>.[251]</sup> All of the people who took part in this study had 1 mg and 2 mg of AG0301-COVID19 injected into their muscles so that the safety and immunogenicity could be tested. By July 2021, we should know what the study found (NCT04463472).<sup>[252]</sup>

#### 7. INACTIVATED VIRUS 7.1. SINOPHARM

Researchers at the China National Pharmaceutical Group's Beijing Institute of Biological Products and Wuhan Institute of Biological Products have made a new inactivated COVID-19 vaccine candidate (Sinopharm).<sup>[253]</sup> This new inactivated vaccine is being tested on healthy people over the age of 6 in a Phase I/II randomised, double-blind, placebo-controlled trial to see how well it works<sup>.[254]</sup> The goal is to find out if it is safe and how well it works (ChiCTR2000031809).<sup>[255]</sup> In The Nan, Shangqiu, China, there will be another Randomized, double-blind, placebo-controlled, parallel-group phase I/II clinical trial in healthy people over the age of 3 to test the safety and immunogenicity<sup>[256]</sup> of the inactivated SARS-CoV-2 vaccine (Vero cells) (ChiCTR2000032459).

# 7.2. SINOVAC

Sinovac has made a possible COVID-19 vaccine that uses formalin to kill the virus and aluminium to make it stronger<sup>.[257]</sup> This candidate can get the immune system to make antibodies that stop SARS-CoV-2 from spreading<sup>.[258]</sup> After the SARS pandemic in 2003, the company Sinovac made the vaccine<sup>.[259]</sup> A randomised, controlled Phase I trial was started to find out if this new SARS-CoV-2 inactivated vaccine is safe and works (NCT04352608). <sup>[260]</sup> 144 healthy people between the ages of 18 and 59 took this test<sup>.[261]</sup> They either got two different doses of the vaccine or a sugar pill instead<sup>.[262]</sup> In a randomised, double-blind, placebo-controlled Phase I/II study, healthy adults younger than 60 years old were given the inactivated SARS-CoV-2 vaccine made by Sinovac Research & Development Co., Ltd.<sup>[263]</sup> This was done to find out if the vaccine was safe and if it

would make people immune. <sup>[264]</sup> There will be a total of 422 people, 72 in the first phase and 350 in the second.<sup>[265]</sup>

# 7.3. DYNAVAX

Dynavax and Sinovac remain working together to make an injection for COVID-19. <sup>[266]</sup> The candidate vaccine is a coronavirus vaccine that uses an advanced adjuvant made by Dynavax called CpG 1018 TM<sup>.[267]</sup> This candidate is an adjuvant that is used in the FDA-approved HEPLISAV-B® vaccine for adults (Hepatitis B Vaccine, Recombinant, Adjuvanted).<sup>[268]</sup> The HEPLISAV-B study showed that CpG 1018 can make the immune system react better to vaccinations<sup>.[269]</sup> Also, this candidate was made with a process that was very automated, reliable, and scalable<sup>.[270]</sup> This could speed up the process of making a lot of this possible vaccine. <sup>[271]</sup> Dynavax says that the Phase I clinical trial for this candidate could begin as early as July 2020<sup>.[272]</sup>

#### 7.4. CHINESE ACADEMY OF MEDICAL SCIENCES

The Chinese Academy of Medical Sciences and the Institute of Medical Biology made a dead SARS-CoV-2 vaccine<sup>-[273]</sup> On June 2, 2020, a phase IA/IIa trial was set up to see how safe and effective different doses of the inactivated SARS-CoV-2 vaccine were at making people immune to the virus.<sup>[274]</sup> This trial included 942 people between the ages of 18 and 59. In Phase IA, 192 people were given 50 U/0.5 ml candidate vaccines every 14 or 28 days<sup>-[275]</sup> In Phase IIa, 750 people got 100 u/0.5 ml of this vaccine every 14 or 28 days<sup>-[276]</sup> This study should be done by September 20, 2021<sup>-[277]</sup> (NCT04412538). On July 14, 2020, a phase Ib/IIb trial will start to see how safe and effective different doses of the inactivated SARS-CoV-2 vaccine are at making people immune. <sup>[278]</sup> The trial will be random, double-blind, and controlled by a placebo<sup>-[279]</sup> In all, 471 people over 60 will take part in the study<sup>-[280]</sup> There will be 96 people in phase Ib and 375 people in phase IIb.<sup>[281]</sup>

# 8. BUILDING PUBLIC TRUST: A RESPONSE TO COVID-19 VACCINE HESITANCY PREDICAMENT

Vaccines to stop and get rid of the Novel Corona Virus are coming out faster than ever.<sup>[282]</sup> These vaccines are the result of a lot of research by experts and government officials.<sup>[283]</sup> Some people still don't believe in the vaccine, even though it's said to be backed by science and provide an immediate solution to the global health crisis<sup>[284]</sup> In a short report that was just published in this journal, it was found that almost a quarter of the US medical students who took part did not know if they should get the COVID-19 vaccine.<sup>[285]</sup> Also, doctors still don't want to take part in programmes that the government wants them to do<sup>[286]</sup> Some people didn't trust the COVID-19 vaccine and didn't want to get it because of things like language barriers and bad feelings like fear and anxiety, according to research published in this journal<sup>[287]</sup> So, these studies seem to show that clear and effective strategic communication is the best way to sell the idea of vaccination.<sup>[288]</sup> But people in charge of public health will have a harder time dealing with the postmodern problem of too much information and the question of how objective the truth is<sup>.[289]</sup> The World Health Organization (WHO) has actually warned people that the world is facing a "information epidemic" that spreads fake news, wrong information, and false scientific claims<sup>.[290]</sup> Studies also show that Michel Foucault's idea of "biopolitics," in which a government has the power to decide whether or not a population lives or dies, is coming true<sup>[291]</sup> This makes people, especially minorities, more afraid, anxious, and unsure. <sup>[292]</sup> People are losing faith in COVID-19 vaccines, which will make it hard for the government to make everyone get vaccinated<sup>[293]</sup> Recently, a number of authorities and businesses have said they want to require vaccinations from the people they work with to keep the environment safe and healthy.<sup>[294]</sup> Also, airlines are thinking about making international travellers show that they have been vaccinated by using a health passport or vaccine passport. [295] But before forcing people to get vaccinated, governments or businesses might want to think about how to earn the public's trust <sup>[296]</sup> WHO found that trust is based on six things: being knowledgeable, being fair, being consistent, being honest, and having faith<sup>[297]</sup> All of these things must be taught in public schools.<sup>[298]</sup> Studies have also shown that people will trust vaccinations and the government more if public education is better, more effective, more localised, and more specific. <sup>[299]</sup> To make sure it is relevant, strategic communication should include an explanation of all the pros and cons of vaccinations<sup>.[300]</sup> This needs to be shortened and changed to fit a certain group<sup>.[301]</sup> Unfortunately, 98 scientists have said that researchers are not being honest enough about the vaccines they are making<sup>.[302]</sup> Since this is the case, it's not surprising that some minority groups still have doubts about vaccines<sup>.[303]</sup> Even though they are experts and have power, people who work in public health and for the government should try to show that they can be trusted and are honest<sup>.[304]</sup> A study says that people who work in public health can't just assume that patients and the general public will "trust" them because of their position in society or years of training. <sup>[305]</sup> The UK and the USA recently gave the first COVID-19 shots<sup>.[306]</sup> Some people who got the shots were medical experts and heads of state<sup>.[307]</sup> People are more likely to trust leaders who get vaccinated on their own because it shows that they care about the safety of the vaccine<sup>.[308]</sup>

# 9.CONCLUSION

The severe acute respiratory syndrome-CoV-2 (SARS-CoV-2) virus, which is also called COVID-19, affects people of all nationalities, religions, creeds, and colours, just like every other pandemic in history. But the COVID-19 epidemic is dissimilar because it moves around the world quickly. The first case was found in Wuhan, China, in December 2019. So far, COVID-19 has been found in 213 countries and territories. This virus spread quickly because it is easy to move around in the 21st century and people at first didn't care how dangerous it was. To stop the COVID-19 pandemic from hurting health care systems, social and economic balances, and the futures of some countries, everyone needs to work together and act as one. Because of recent progress in virology, molecular biology, and pharmacology, we were able to quickly figure out the COVID-19-causing virus's structure, functions, life cycle, and pathophysiological features.

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