



COVID-19 Vaccine: Review of the Mechanism of Action of Different Types of Vaccine

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Abstract

Since the discovery of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus in December 2019, it has spread rapidly affecting numerous people globally and World Health Organization (WHO) has declared a pandemic in March 2020. As cases of COVID-19 continue to rise daily, there are increasing concerns and controversies regarding the best methods to curb the coronavirus pandemic. Since there are no proven drugs that are completely effective for prevention or treatment of SARS-CoV-2, vaccines are considered to be the most favorable choice to control the spread of this disease and reduce severe morbidity and mortality from COVID-19. Therefore, this evidence-based intensive literature review aims to further identify and thoroughly understand the mechanisms of actions of the primary vaccines developed against the SARS-CoV-2, aiming to provide the latest information available on current COVID-19 vaccines, touching on the viral characteristics of SARS-CoV-2, vaccine development and platforms which may be beneficial to the advancing research of novel SARS-CoV-2 vaccines.

Subject Areas

Infectious Disease, Public Health, Global Health, Allergy & Clinical Immunology

Keywords

COVID-19, COVID-19 Vaccine, Vaccines, Immunization, Sars-CoV-2, COVID, Mechanism of Action

1. Introduction

COVID-19 is a deadly disease that has resulted in over 5 million deaths globally since December 2019. Since its discovery and rapid spread affecting countless

people throughout the world, the World Health Organization (WHO) has declared a pandemic in March 2020. This pandemic is caused by the emergence of a novel coronavirus, SARS-CoV-2, that is genetically similar to the SARS-CoV virus that was discovered in China, 2002, and also the Middle East Respiratory Syndrome coronavirus (MERS-CoV) was discovered in Saudi Arabia, 2012. However, SARS-CoV-2 is particularly contagious compared to the other epidemic-causing coronaviruses. Even prior to the onset of clinical symptoms, it is easily transmitted and the high transmissibility of SARS-CoV-2 has caused significant morbidity and mortality worldwide [1]. From epidemiological data, the discovery of SARS-CoV-2 links to the Wuhan Seafood Market in China, particularly with the western part of the Huanan Seafood Market containing positive samples of SARS-CoV-2 [2] [3]. Still, the transmission to humans is unclear and questions remain as to whether it originated from an animal source such as bats, which is the case for SARS-CoV and MERS-CoV [4]. Nonetheless, the transmission of viral particles from human-to-human is the biggest contributing factor to precipitating the spread of this disease. SARS-CoV-2 is a pneumotropic virus, mainly spread from individuals through airborne droplets, particularly in crowded settings where social distancing, usage of masks and appropriate hand hygiene is not observed [5]. Transmission can also occur via contaminated surfaces or fomites as the SARS-CoV-2 virus remains viable for up to 6 days in numerous environmental conditions, drastically potentiating its ability to infect individuals [6]. Clinically, COVID-19 can manifest in many ways ranging from vague flu-like symptoms, benign respiratory or gastrointestinal problems [7] to acute respiratory distress syndrome (ARDS), multi-organ failure and even death [8].

On 11 January 2020, the genetic sequence of SARS-CoV-2 was published, initiating an extensive global program to develop a vaccine against COVID-19 [9]. Since then, numerous vaccines were produced or are in the production process and as of 11th February, WHO states that there are 337 vaccines in development against SARS-CoV-2, all in different stages of clinical development (142 in clinical development; 195 in pre-clinical development) [10].

2. SARS-Cov-2 Viral Structure and Virulence

SARS-CoV-2 is a coronavirus belonging to the coronaviridae family with a size of ~30 kb genomes and a diameter of 50 - 200 nm [11] [12]. The virus is an enveloped, positive-sense single-stranded, non-segmented RNA virus with a helical nucleocapsid with spike-like glycoprotein projections on its surface, which resembles a crown-like or coronal appearance. SARS-CoV-2 has a double-layered lipid envelope which consists of spike (S) glycoproteins, glycoprotein membrane (M), helical nucleocapsid (N) and envelope (E) proteins. The S protein is made up of 2 subunits; S1 and S2 and two key factors affect the entry of SARS-CoV-2 into host cells *i.e.* spike protein binding to host angiotensin-converting enzyme 2 (ACE2) receptor and priming of S protein by host cell protease: transmembrane

protease serine 2 (TMPRSS2) [13]. The receptor-binding domain (RBD) on the N-terminal of the S1 subunit interacts and binds to the cellular ACE2 receptor on host cells, illustrated in **Figure 1** [12] [14] [15]. Cryo-electron microscopy has revealed that SARS-CoV-2 spike protein's binding affinity is 10 - 20× more than that of SARS-CoV, making the transmissibility of SARS-CoV-2 much greater [16], causing a massive public health concern worldwide.

On the other hand, S2 contains the fusion peptide and transmembrane domain which mediates fusion with the host cell membrane [13]. Host proteases, primarily TMPRSS2, cleave the S2 subunit on the spike protein to make required conformational changes and S protein activation to facilitate membrane fusion and subsequent entry of viral RNA into target cells [17] [18]. By binding to the ACE2 receptors on the host cell, the virus enters the host through the S protein on its surface (**Figure 2**).

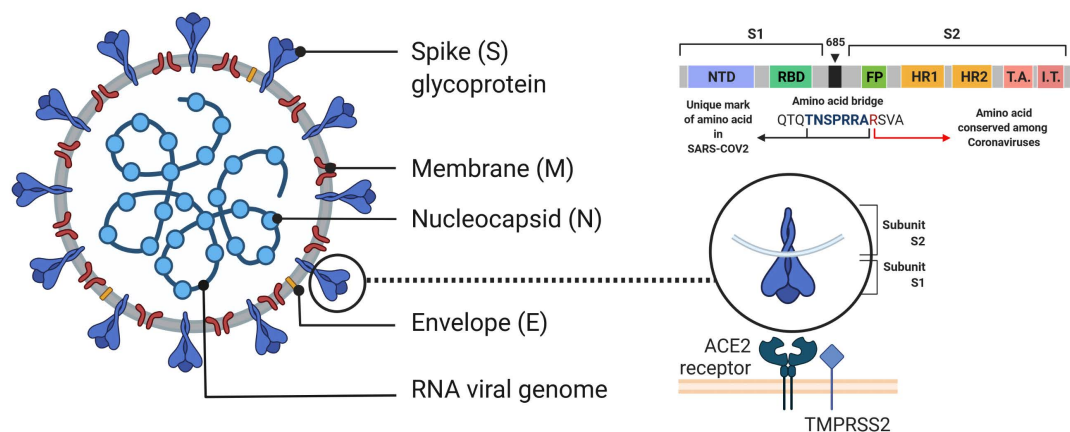


Figure 1. The SARS-CoV-2 coronavirus particle structural diagram. The S protein is mainly divided into S1 (containing the RBD), and S2 subunits. ACE2: angiotensin-converting enzyme 2; RBD: receptor-binding domain. NTD: N-Terminal Domain. Created with BioRender.com.

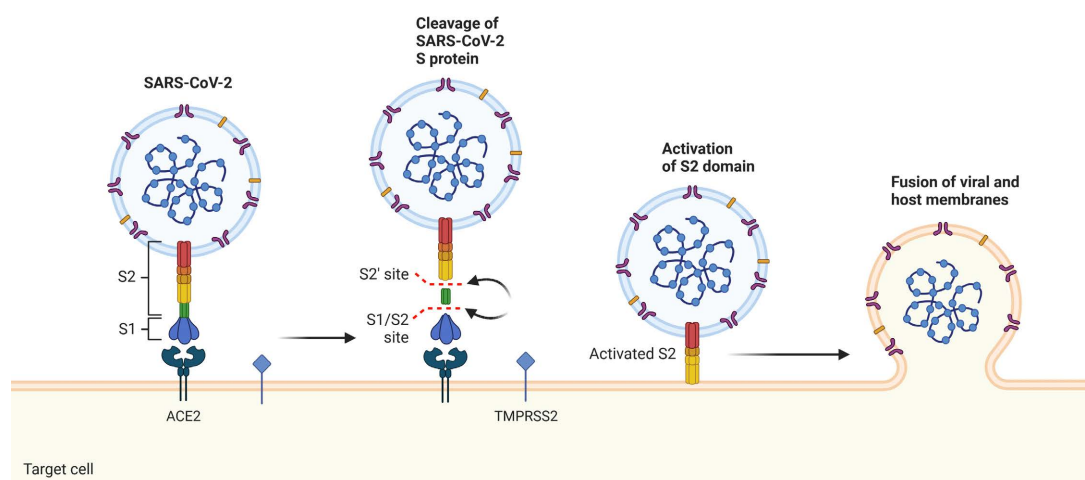


Figure 2. Mechanism of SARS-CoV-2 Viral Entry. SARS-CoV-2 S protein binds to the host ACE2 receptor and is subsequently cleaved at S1/S2 and S2' sites by TMPRSS2 protease. The S2 domain is activated and drives fusion of the viral and host membranes. Created with BioRender.com.

The most common approach for vaccine development is the use of the S protein as an antigen. The S protein which plays a major role in attachment and fusion is a major target antigen for many subunit vaccine candidates, in which not only the full-length S protein is targeted but also its antigenic fragments, S1/S2 subunit, RBD, and N-terminal domain (NTD) [19]. When injected, most of these antigens can stimulate both humoral and cell-mediated immune responses in the body [20] [21].

3. Development of the COVID-19 Vaccine

Traditionally, vaccine development takes approximately 15 years as much time is needed for undergoing different phases of clinical trials and approval in a sequential process [22], as shown in **Figure 3** and to date, the fastest vaccine produced took roughly 4 years which was for mumps in the 1960s [23], which is still double the time taken for the COVID-19 vaccine development. The sudden and unexpected COVID-19 pandemic prompted numerous developers to rapidly start developing a vaccine in a relatively short period of time, thus raising concerns from the public and anti-vaccine people. Generally, due to the high costs and risks of failure, developers tend to follow a sequential timeline, pausing in between stages for control and analysis [24].

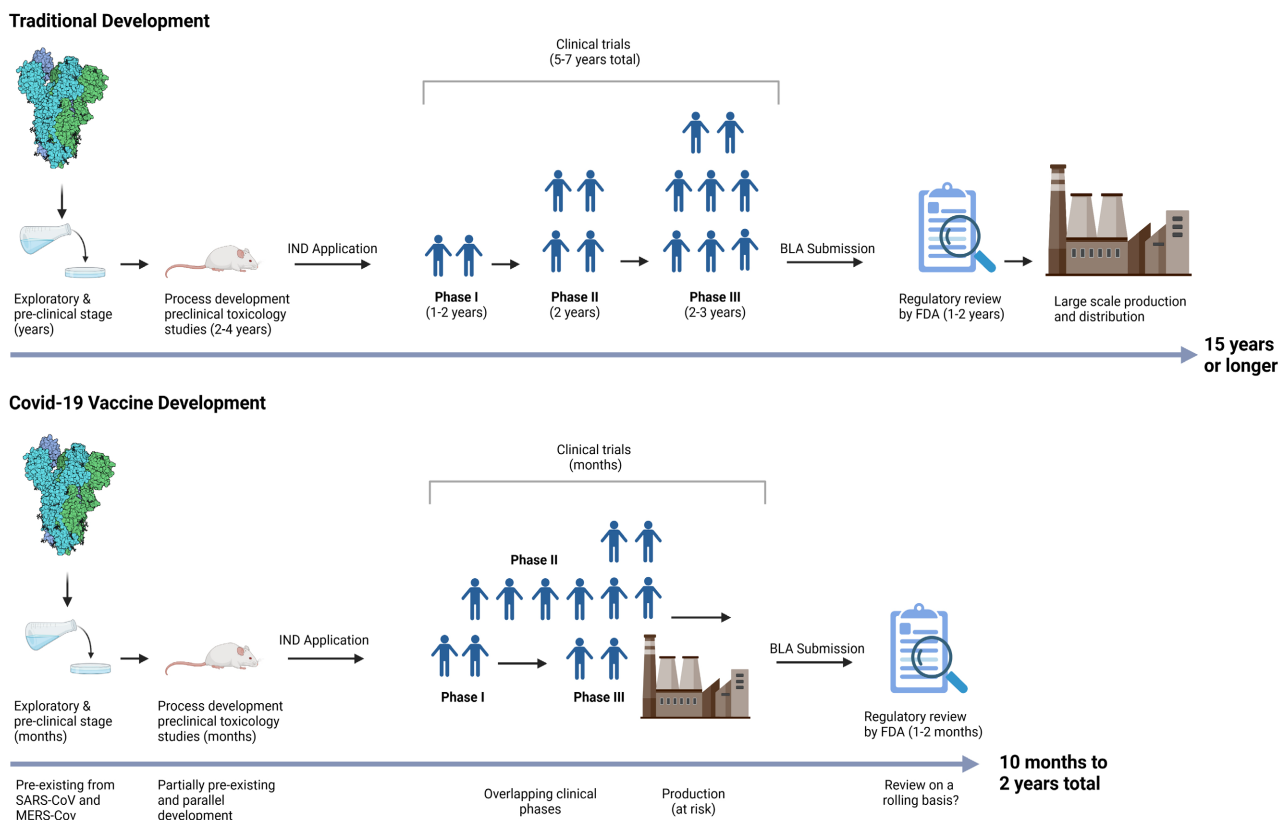


Figure 3. SARS-CoV-2 development timeline vs. the traditional vaccine development timeline. Traditional vaccine development usually takes 15 years or more compared to the COVID-19 vaccine development which takes less than 2 years. Created with Bio-Render.com.

In order to cope with the demand for a COVID-19 vaccine, developers have progressed to overlap various phases of clinical testing to accelerate the process and allocating most, if not all, of their funds towards it (something that has not been observed with other vaccines) [22] [23]. The same legal standards and safety assessment processes were still observed in the production of the vaccine [25] although some vaccines may be approved for emergency use by vulnerable groups prior to obtaining the full approval process [26]. The stages of vaccine development and aspects entailed in each stage are outlined in **Table 1**.

Table 1. Stages of vaccine development. adapted from the history of vaccines: vaccine development, testing, and regulation [27].

Stages	Processes
Exploratory Stage	<ul style="list-style-type: none"> • Basic laboratory research (~2 - 4 years) • Identify natural or synthetic antigens with possibility to prevent or treat a disease • Examples of antigens: virus-like particles, weakened viruses or bacteria, weakened bacterial toxins, or other substances derived from pathogens
Pre-clinical Stage	<ul style="list-style-type: none"> • Tissue-culture/cell-culture systems and animal testing (~1 - 2 years) • Assess safety and immunogenicity, or ability to provoke an immune response
IND Application	<ul style="list-style-type: none"> • Investigational New Drug (IND) submitted to the FDA • Describes the manufacturing and testing processes, summarizes the laboratory reports and describes the proposed study
Phase I	<ul style="list-style-type: none"> • Vaccine administered to healthy humans (small sample size <100) • Assess vaccine safety & immunogenicity
Phase II	<ul style="list-style-type: none"> • Vaccine administered to humans (moderate sample size 100 - 1000)—effect of gender, age, and ethnicity assessed • Assess vaccine's safety, immunogenicity, proposed doses, schedule of immunizations and method of delivery
Phase III	<ul style="list-style-type: none"> • Vaccine administered to humans (large sample size 1000 - 10,000) • Randomized, double blind and involve the experimental vaccine being tested against a placebo • Assess the efficacy and adverse reactions of the vaccine
Approval and Licensure	<ul style="list-style-type: none"> • Submit Biologics License Application (BLA) to FDA • Inspection of vaccine development factory and approve the labelling of vaccine • After licensure, FDA continues to monitor the production of the vaccine: inspecting facilities and reviewing the manufacturer's tests for potency, safety and purity of vaccines
Phase IV	<ul style="list-style-type: none"> • Optional studies by companies conducted after a vaccine is released • Continue to test the vaccine for safety, efficacy, and other potential uses

By far, vaccines are considered to be the most favorable option to manage the spread of COVID-19 producing herd-immunity that will decrease viral circulation within the community. It may be argued that herd immunity can be acquired solely through natural infection without a need for a vaccine. Although it is theoretically possible, the consequences to society would definitely cause devastation to any country [28]. This strategy that was observed in Sweden failed and resulted in almost three times more deaths per million people from COVID-19 compared to Germany [29].

4. Overview of Vaccine Platforms

Several vaccination platforms have been or are currently being used in the production of a SARS-CoV-2 vaccine (Figure 4). These platforms can be divided into “conventional” approaches: inactivated or live-attenuated vaccines and newer vaccine platforms such as viral vectors and recombinant proteins. Some novel platforms such as Ribonucleic Acid (RNA) or Deoxyribonucleic Acid (DNA) vaccines have not been licensed before this [22].

4.1. Live-Attenuated Vaccines

Live-attenuated vaccines (LAV) are produced by developing a genetically weakened form of the wild-type virus or using avirulent strain [30] [31]. Virus

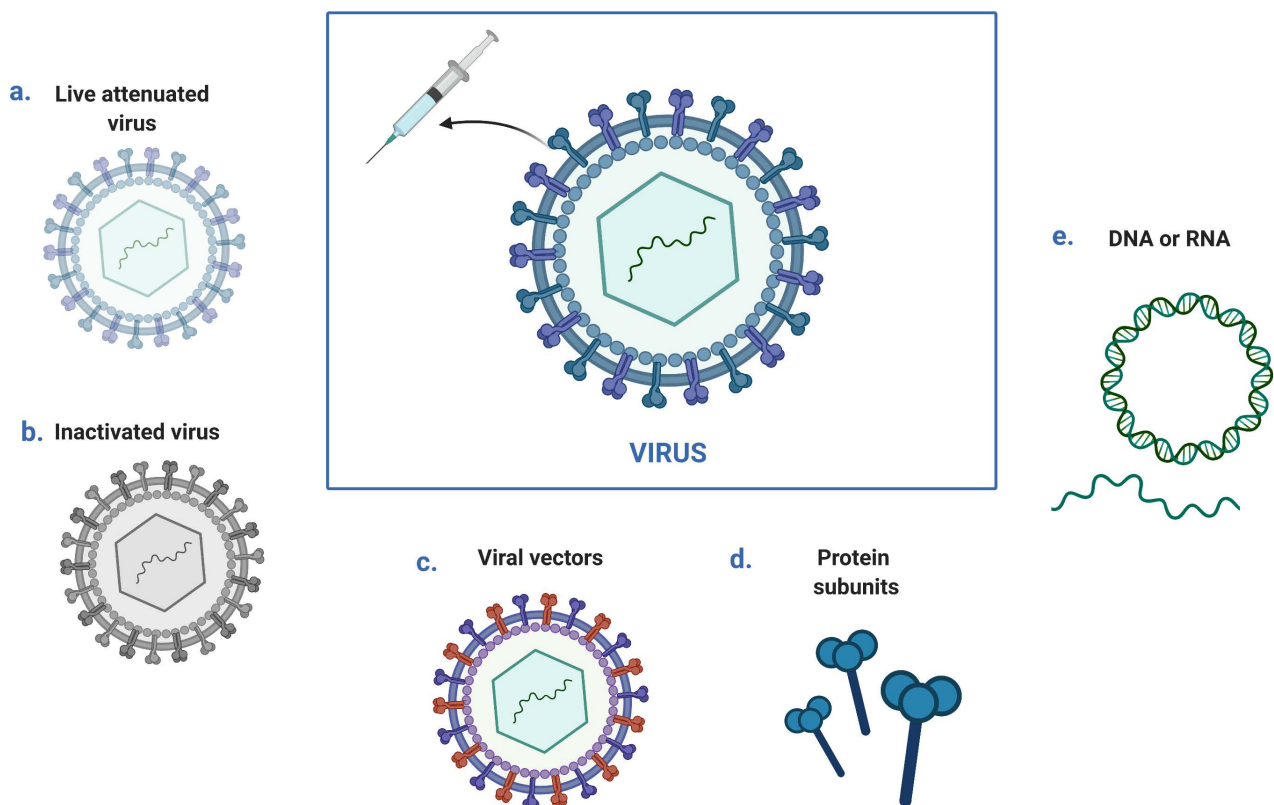


Figure 4. Vaccine platforms. (a) Live-attenuated virus. (b) Inactivated virus. (c) Viral vectors: Replicating or non-replicating viral vector. (d) Protein subunits. (e) DNA or RNA. Created with BioRender.com.

attenuation is generated by exposing the virus to adverse conditions such as low temperatures until it loses its pathogenic properties but maintaining its immunogenicity. The codon pair deoptimization strategy has also shown to be successful for viral attenuation [32] [33]. When injected, these viruses replicate in the host, eliciting an immune response, similar to when naturally infected, causing only a mild infection without actually causing the disease [34]. Some LAV currently used is chickenpox, MMR and polio vaccine.

Nonetheless, LAV may still revert to their original form and cause disease, as seen in vaccine-associated paralytic poliomyelitis associated with use of oral poliovirus vaccine (OPV) [35]. Additionally, possible errors may occur during the immunization process and due to their poor security and stability, the use of LAV is limited and those who are immunocompromised are advised against it [36]. Currently, LAV produced by Codagenix/Serum Institute of India and Meissa Vaccines, Inc are under Phase 3 and Phase 1 clinical trials respectively [10].

4.2. Inactivated Vaccines

Inactivated vaccines utilize a virus which inactivated thermally, chemically or by radiation. The preferred method is chemical inactivation (formaldehyde or alkylating agent based) as the integrity of the antigenic epitopes of the virus is better maintained and preserved when compared to the thermal inactivation [37]. The vaccine containing antigens from the inactivated viruses which are usually combined with aluminium hydroxide or another adjuvant is then injected into the body, generating an immune response [38] [39].

Inactivated vaccines have been widely used against measles, polio, influenza and other viruses in the past decades. Moreover, mass immunization programs have confirmed their safety profiles with development and evaluation standards put in place based on experience on prior usage of these vaccines. Therefore, large-scale production of inactivated vaccines is possible as manufacturing processes and methodology for development are well established [40]. However, inactivated vaccines only generate moderate immunogenicity, requiring adjuvants and several booster immunizations for an adequate immune response [41]. Moreover, many countries are still limited from performing research and independently developing the vaccines due to the need of specialized facilities like biosafety level 3 laboratories (BSL-3) [40].

For this type of vaccine, Sinovac and Sinopharm are among the manufacturers which have advanced the most in vaccine development, clearing phase 3 trials and attaining international authorizations for use [42].

4.3. Viral Vector Vaccines

Viral vector-based vaccine uses viral vector backbone bioengineered to insert viral antigen-encoding gene(s) into the host organism and is generally classified into replicating or non-replicating vectors. Some examples of replicating vectors are: measles virus and vesicular stomatitis virus (VSV) and non-replicating vec-

tors: Adenoviruses (Ad) and poxviruses [43]. This platform has been well investigated and has a reputable track performance history considering its safety, genetic malleability, absence of an adjuvant requirement and strong potential to induce cell-mediated (T cell) immunity as well as being relatively easy to design and develop [44].

Replicating vector vaccines infect target cells stimulating antigen production as well as replicate and infect new cells to also produce the vaccine antigen, triggering a more robust immune response. On the other hand, non-replicating vectors stimulate antigen production without forming new virus particles. Viral vector induces endogenous antigen production by the host, stimulating both humoral and cellular immune response [30]. Many vaccines use a non-replicating Ad vector as they are physically and genetically intact and do not integrate with the host genome. Some examples of authorized SARS-CoV-2 vaccines using viral vector platforms are AstraZeneca and Janssen/Johnson & Johnson.

One concern is that pre-existing immunity may possibly lower the immunogenicity of the vaccine [45] [46], but this issue can be avoided by using viral vectors derived from animal viruses, such as a chimpanzee adenovirus as in the Astra Zeneca vaccine [47] or using a virus uncommon in the target population (Janssen and Cansino use vectors that do not propagate in Europe and Asia respectively) [48].

4.4. Protein Subunit Vaccines

Protein subunit vaccines which include recombinant protein vaccines are based on synthetic peptides or recombinant proteins of the target pathogen, containing specific antigenic fragments without their pathogenic components which eliminates concerns of incomplete viral inactivation, virulence recovery, and pre-existing anti-vector immunity [34]. Therefore, protein subunit vaccines are regarded as relatively safe. Current notable recombinant protein vaccines in use are the HPV and Hep B vaccine. Different expression systems exist for the recombinant proteins, including insect and mammalian cells, yeast and plants [49].

Specific neutralizing antigenic epitopes can be targeted and improve immunogenicity and/or efficacy when combined with adjuvants which extends the biological half-life of the antigenic material or increase the immunomodulatory cytokine response [50] [51]. Currently, many of the SARS-CoV-2 subunit vaccines utilize the S protein and its fragments, such as the RBD as the antigen as it was shown to have numerous conformational neutralizing epitopes, which is suitable for vaccine development [52]. The RBD comprises major antigenic epitopes that elicit both neutralizing antibodies and T cell responses [43] and is demonstrated that most antibodies produced against the RBD can neutralize coronaviruses thus inhibiting its ability to attach to the host cells [53]. Some recombinant COVID-19 vaccines in development include recombinant S protein, recombinant RBD and virus-like particle (VLP) vaccines [22] and the Novavax

vaccine is also developed using this platform.

4.5. Deoxyribonucleic Acid (DNA) and Ribonucleic Acid (RNA) Vaccines

Deoxyribonucleic Acid (DNA) and Ribonucleic Acid (RNA) (nucleic acid-based) vaccines are novel platforms for vaccine development that offer great flexibility for antigen manipulation and rapid production. They are a cutting-edge vaccine development approach with huge therapeutic potential and are considered cost-effective as it eliminates the need to grow viruses or viral proteins inside live cells in tissue culture laboratory, thus making it easier for large-scale manufacturing [37] [54]. Nucleic acid vaccines are similar to viral vector vaccines in which they transmit genetic instructions (DNA or mRNA encoding disease-specific antigens), primarily for the expression of viral S protein (in COVID-19) into host cells to induce an immunogenic response [54]. DNA and RNA utilize the host cells' machinery to generate immunogens that stimulate both antibody and T-cell induction [55].

DNA vaccines use a recombinant plasmid that contains a mammalian expression promoter and a transgene encoding the antigen which undergoes a transcription-to-translational to produce the antigen. The production process is relatively simple and can produce a strong immunogenic response with a high safety margin [56] [57] [58]. Plasmid DNA vaccines have gained more attention than mRNA in the past decades due to the intrinsic stability of DNA double helixes compared to single strands of mRNA and the possible effect of degrading RNase [24]. DNA vaccines have been tested for efficacy *in vitro* and *in vivo* with some gaining approval for veterinary use [59]. Some DNA vaccines for SARS-CoV-2 currently in Phase 3 trials include ZyCoV-D (Zydus Cadila) and INO-4800 (Inovio) [10].

Similar to DNA vaccines, the mRNA vaccines are based on the induction of transient antigen (S-protein for COVID-19 vaccines) expression of host cells which can be divided into 2 categories: non-replicating mRNA and virally derived self-replicating mRNA. Conventional (non-replicating) mRNA-based vaccines encode the antigen of interest whereas the latter encodes both the antigen, as well as the viral replication machinery for intracellular mRNA amplification [60] [61]. Currently, only non-replicating mRNA vaccines are available for COVID-19. Once injected, the RNA is translated into the target protein to induce an immune response. RNA vaccines do not integrate into the host genome as it does not enter the nucleus, instead, it remains in the cell cytoplasm [62] [63]. Moreover, mRNA is degraded by ribonucleases and natural cellular processes and by using various delivery methods and modifications, its *in vivo* half-life can be regulated [60]. However, mRNA vaccines are relatively less stable compared to DNA vaccines, in which well-managed handling and storage are necessary [64] [65]. RNA vaccines were amongst the first vaccines produced for SARS-CoV-2 and some of them are Pfizer (Comirnaty/BNT162b2) and Moder-

na (mRNA-1273).

5. Mechanism of Action of Main Corona-19 Vaccines

5.1. Pfizer/BioNTech—BNT162b2 (Comirnaty)

The vaccine developed with Pfizer in collaboration with German company BioNTech is a nucleic acid vaccine with a nucleoside-modified mRNA taken from the spike (S) glycoprotein of SARS-CoV-2, formulated with lipid nanoparticles (LNP). BNT162b2 RNA encodes a full-length S protein in which the prefusion configuration is stabilized by using proline to substitute amino acids K986 and V987 (S(P2)) [66] [67], thus stabilizing the prefusion conformation of the transmembrane-anchored S protein but still allowing for cleavage of the S1 and S2 subunits [68]. The delivery methods of the mRNA vaccine are important as the mRNA molecules must penetrate lipid membranes, localize in the cytoplasm and activate the translation-to-transcription process in cells. Pfizer uses utilizes LNP encapsulation in the manufacture of the BNT162b2 vaccine [66], which has been shown to efficiently deliver mRNA *in vivo* and also protect it from degradation by nucleases [69] [70]. However, a disadvantage is that these vaccines need to be stored at -80°C [71] making it difficult to distribute to low- and medium-income countries.

After injection, internalization of mRNA occurs and is rapidly translated by antigen-presenting cells (APC) both at the injection site and in draining lymph nodes, where it is shown to initiate robust adaptive immune responses *in vivo* [72] [73], generating RBD-specific and neutralizing antibodies (nAbs) in humans [74]. A large placebo-controlled Phase III trial of over 37,000 participants showed that a two-dose regimen of BNT162b2 (30 μg per dose, given 21 days apart) was found to be safe and had 95% efficacy (95% CI 90.3 - 97.6; 8 versus 162 cases in placebo) in preventing symptomatic COVID-19 infection [74]. It also proved to generate a greater immunogenic response in children and adolescents compared to young adults [75]. It is reported that most people only experience mild local and systemic side effects such as pain at the injection site, fatigue, headache and fever which were more common after the second dose [76]. However, there have been several cases of anaphylaxis after vaccination, mostly attributed to patients with a prior history of allergies [77] [78] and rare cases of myocarditis [79]. Nonetheless, the benefits of the vaccine greatly outweigh the small increased risk of serious adverse effects.

5.2. AstraZeneca/Oxford—ChAdOx1 nCoV-19/AZD1222

ChAdOx1 nCoV-19 is a recombinant non-replicating viral vector vaccine that expresses the S protein which is synthesized based using a chimpanzee adenovirus. The sequence coding amino acids (2-1273) and tissue plasminogen activator (tPA) leader sequence at the 5' end are encapsulated in a shuttle (plasmid) vector [80]. These modified adenoviruses cannot replicate in the human body because the gene which enables virion assembly has been deleted, making it a relatively

safe way to introduce the antigenic component of SARS-CoV-2 into the host cell [54]. This strategy leads to host cells expressing the S protein thus stimulating a strong humoral and cell-mediated immune response [81] [82] [83]. Interim results from for ongoing, blinded, a multinational phase III randomized controlled trial showed 70.4% efficacy (95% CI 54.8 - 80.6) in preventing asymptomatic COVID-19 infection [84] [85].

Other than the usual mild systemic side effects, there have been several concerns regarding thrombotic events associated with thrombocytopenia [86] which some experts refer to as vaccine-associated immune thrombotic thrombocytopenia (VITT) or thrombosis with thrombocytopenia syndrome (TTS) [87] [88] [89]. A large proportion of these cases are associated with autoantibodies directed against the platelet factor 4 (PF4) antigen [90] [91], as seen in patients with autoimmune heparin-induced thrombocytopenia (HIT) [92]. A few reported cases show that thrombosis usually occurred at uncommon sites such as the cerebral venous sinuses [93], splanchnic vein, pulmonary artery and other sites [89]. Therefore, all recipients of ChAdOx1 nCoV-19 vaccines should be counselled regarding the possible risks and advised to seek immediate care for suggestive signs of thrombocytopenia. Unlike nucleic acid-based vaccines, ChAdOx1 nCoV-19 can be kept at refrigerator temperature (2°C - 8°C), making it easier for storage and distribution [94].

5.3. Sinovac—CoronaVac

CoronaVac (formerly called PiCoVacc) is based on a well-known traditional vaccine methodology, using an inactivated virus in Vero cell line culture. The SARS-CoV-2 virus (CZ02 Strain) is inoculated into African green monkey kidney cells (Vero Cell), inactivated using β -propiolactone and combined with aluminium hydroxide as an adjunct [38] [95]. When injected, antigen-presenting cells (APC) engulf the inactivated viruses, presenting different antigenic determinants which are recognised by the immune system, inducing the production of nAbs. CoronaVac can be stored at (2°C - 8°C) for years, increasing its suitability for countries with poor socioeconomic status and places with limited cold-storage capacity. Phase III trials have been conducted in several parts of the world with results of efficacy ranging from 50.7% (Brazil), 65.30% (Indonesia) and 83.5% (Turkey) [95] [96] [97]. Common adverse effects were injection-site pain and mild systemic side effects. In contrast to viral vector or nucleic acid-based vaccines, fever occurred much less after vaccination with CoronaVac [98] and was much better tolerated in adults aged 60 and above [99]. Diminishing nAbs production was noted with increased age, suggesting a need for a dosage increase for the elderly [100]. Moreover, these vaccines have a good safety profile and pose no risk of causing infection even for immunosuppressed individuals as they cannot replicate in the human body. However, they are known to be less effective compared to live-attenuated vaccines as they mainly stimulate humoral immune response with minimal cell-mediated immune response [54] [101]. Therefore, multiple doses are usually required to generate immunity. Al-

though no human studies have shown to cause antibody dependant enhancement (ADE) for CoronaVac, there is a theoretical risk that inactivated vaccines may increase the risk of developing non-neutralizing antibodies resulting in lung inflammation [102] [103], which was seen in the respiratory syncytial virus (RSV) and measles vaccine [104] [105].

6. Conclusion

In a span of just 2 years since the discovery of SARS-CoV-2, there have been tremendous technological advances worldwide in the production of a COVID-19 vaccine. Vaccines for COVID-19 have been produced at a rate that has not been witnessed before in history, some using novel platforms not used in humans prior to this pandemic. However, despite the rapid production and distribution worldwide, several new variants of concern have emerged, with threats of vaccines being ineffective in providing immunity to the population. Although this literature review highlights the different vaccination platforms, along with the mechanisms of action of some main COVID-19 vaccines, the effects of mixing different vaccines and emerging variants of concern were not addressed but it is hoped that understanding the mechanisms of action of vaccines, it can provide more insight into the advancement of research for new COVID-19 vaccines and with hopes to find more effective solutions to control this pandemic. It is postulated that around 70% of the world's population need to be vaccinated to achieve a desirable outcome of herd immunity. Each COVID-19 vaccine has its relative pros and cons with regard to its efficacy and side effects, which makes it difficult to conclude that vaccine is superior. Nonetheless, the accessibility and affordability of vaccines will be of greater importance to curb this pandemic, especially in developing nations.

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Conflicts of Interest

The authors declare no conflicts of interest.

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