

Analysis of the Effectiveness of the New Coronavirus Vaccines

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Abstract: This article analyzes the effectiveness of different types of COVID-19 vaccines. Live attenuated vaccines can significantly reduce viral load and alleviate pathological damage by introducing weakened pathogens into the human body, showing potential for single-dose vaccination and nasal administration, such as the COVI-VAC vaccine in preclinical studies. mRNA vaccines have demonstrated the ability to respond quickly to sudden outbreaks with their rapid R&D and production capabilities, which can be reflected in the efficient response and protection of infected people in the Hungarian study. Inactivated vaccines inactivate pathogens chemically/physically, and are characterized by high safety and convenient storage and transportation (2-8 °C), which means they are suitable for areas with limited resources. This is reflected in studies in Chile and Pakistan, where their protection against severe illness, hospitalization, and death is over 86%. Recombinant protein vaccines express purified antigen proteins through genetic engineering. Taking Novavax as an example, it showed 89.7% protection efficacy in trials involving the elderly and people with underlying diseases, which reflects its applicability to special populations. Each type of vaccine has its own advantages in terms of technical paths, immune mechanisms and applicable scenarios, and together provide multiple options for epidemic prevention and control.

Keywords: COVID-19, coronavirus vaccines, treatment, effectiveness

1. Introduction

At the end of 2019, a highly contagious and rapidly spreading coronavirus appeared in Wuhan, Hubei, China. This coronavirus can cause a series of respiratory diseases. The World Health Organization (WHO) named the disease caused by this newly discovered virus COVID-19. The COVID-19 epidemic spread rapidly around the world in a short period of time. According to preliminary statistical analysis by the WHO, the total number of additional deaths caused directly and indirectly by COVID-19 in 2020 reached at least 3 million. The outbreak not only directly hit the medical systems of countries around the world, but also led to severe economic recession and social unrest. For example, according to the IMF's forecast in its World Economic Prospects report, the global economy will shrink by 3.5% in 2020, and the global GDP will drop from US\$87.75 trillion in 2019 to US\$84.68 trillion in 2020, a decrease of US\$3.07 trillion. Since there were no targeted drugs or treatments for COVID-19 at the time, researchers are developing targeted vaccines (new coronavirus vaccines) as the latest control and treatment strategy based on the severe symptoms and extremely fast spread of the COVID-19 virus. In 2025, various vaccines for the new coronavirus have been successfully developed, but the new coronavirus is still spreading around the world. The main reason

for this is the continuous mutation of the coronavirus, so this article wants to analyze the different types of vaccines for the new coronavirus and understand why the effectiveness of the new coronavirus vaccine is short and uncertain. According to the WHO, the types of research on known new coronavirus vaccines mainly include live attenuated vaccines, recombinant protein vaccines, mRNA vaccines, viral vector vaccines and inactivated vaccines.

Although many different types of vaccines were successfully developed at the time, they faced both objective and subjective obstacles in terms of effectiveness [1-3]. Objectively, the high mutation rate and high variation rate of the virus caused the strains of the new coronavirus to be constantly updated (such as Delta and Omicron), and the effectiveness of the original vaccines against the new variants was significantly reduced. At the same time, on a subjective level, people's hesitation about the new crown vaccine has hindered the efficiency of scientific researchers' research on the new crown vaccine. These influencing factors have posed challenges to the effectiveness of the new crown vaccine. Regarding the effectiveness of vaccines, most studies have proven the effectiveness of the vaccine in the environment at that time, but most studies lack the follow-up of the vaccine's subsequent effectiveness. More specifically, whether the effectiveness of the vaccine can remain at the original level under the premise of changes in the environment and mutations of the virus. Taking the specific new coronavirus variant Omicron as an example, initial immunization with two doses of COVID-19 vaccine provides limited protection against symptomatic Omicron variant disease, and the protective effect decreases over time. In combination with the above content, this article will mainly analyze the effectiveness of different types of COVID-19 vaccines (live attenuated vaccines, recombinant protein vaccines, mRNA vaccines and inactivated vaccines) through a review, and explore their performance at different times and environments (such as the effect against mutant strains and immune persistence). This article hopes to provide reference support for the selection of vaccine development through research and discussion.

2. Applications of different coronavirus vaccines

2.1. Live attenuated vaccines

Live attenuated vaccines refer to pathogens that have undergone various treatments, mutated, and weakened in toxicity, but still retain their immunogenicity. When inoculated into the body, they will not cause disease, but the pathogens can grow and reproduce in the body, triggering an immune response and providing long-term or lifelong protection.

The concept of live attenuated vaccines originated in the 18th century and is a practice of preventing diseases by vaccinating with weakened pathogens. After the 19th century, scientists began to cultivate attenuated pathogens in the laboratory, such as Pasteur and his colleagues attenuated anthrax and rabies viruses by exposing them to oxygen or high temperatures. In the mid-20th century, scientists discovered that attenuated strains could be selected by subculturing in cell culture systems, such as the rabies and oral polio vaccines developed [1]. Since then, scientists have successfully developed a variety of attenuated live vaccines through cell culture technology, such as polio, measles, mumps, and chickenpox vaccines. Live attenuated vaccines refer to pathogens that have undergone various treatments, mutated, and weakened in toxicity, but still retain their immunogenicity. When inoculated into the body, they will not cause disease, but the pathogens can grow and reproduce in the body, triggering an immune response and providing long-term or lifelong protection. The advantage of live attenuated vaccines over other antiviral vaccines is that they can induce a strong immune response and only require a small dose to achieve a protective effect. In addition, the application of live attenuated vaccines has been supported by actual cases. It has been successfully used to prevent a variety of viral diseases such as smallpox, polio, measles, mumps and yellow fever. At the same time, there are already a variety of new and more reliable attenuation methods for live

attenuated vaccines. Compared with empirical attenuation, new attenuation methods such as changing replication fidelity, codon deoptimization, mRNA control and ZFN control can better control viral replication and virulence, thereby improving safety. These new attenuation approaches can limit viral replication but still induce a strong immune response and may be safer even in immunosuppressed patients. For example, codon deoptimization can systemically attenuate the virus without affecting antigenicity and with a lower risk of recovery.

The working principle of live attenuated vaccines is that by vaccinating with weak strains, they can stimulate the body to produce an immune response without causing serious disease, thereby gaining protection against pathogens. The specific operation process is usually as follows: after the pathogen is treated with formaldehyde, the structure of the A subunit (toxic subunit) changes and the toxicity is weakened, but the activity of the B subunit (binding subunit) remains unchanged, causing the body's immune response to the virus, but does not cause the occurrence of the disease [2]. Based on the remarkable results achieved by live attenuated vaccines in the treatment and immunity of viruses, scientists have gradually begun to invest live attenuated vaccines in the research and development of treatments for the new coronavirus.

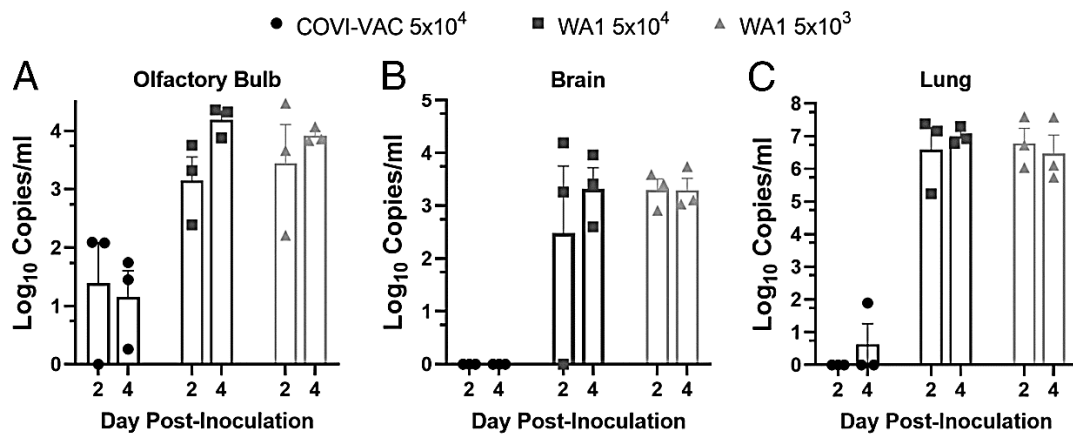


Figure 1: Attenuation of COVID-19 in the different parts of the hamsters [3]. (A) olfactory bulb. (B) brain. and (C) lungs

Given the successful use of live attenuated vaccines in preventing other viral diseases, scientists have begun to explore their potential in COVID-19 vaccine development. Regarding the application of live attenuated vaccines in the treatment of the new coronavirus, there are already vaccines in the clinical trial stage, such as COVI-VAC. COVI-VAC is an attenuated SARS-CoV-2 vaccine created using the “Synthetic Attenuated Virus Engineering (SAVE)” strategy, which involves recoding the viral genome to introduce synonymous mutations that reduce protein production and weaken the virus. In preclinical studies in Syrian golden hamsters, COVI-VAC was highly attenuated compared to wild-type SARS-CoV-2, resulting in reduced viral load (Figure 1), milder lung pathology (the average viral load of the vaccinated challenge WT WA1 was reduced by more than 50,000 times compared to the unvaccinated one), and less weight loss in vaccinated animals (Figure 2). The reason for this phenomenon is mainly because the COVI-VAC vaccine strain was prepared by synonymous codon recoding of the SARS-CoV-2 virus genome, introducing 283 silent mutations, thereby reducing the expression level of viral proteins and resulting in a high degree of virus attenuation. The COVI-VAC vaccine generated antibody and neutralization responses similar to those induced by wild-type infection and protected hamsters from weight loss and brain infection induced by the wild-type virus. COVI-VAC is a promising attenuated SARS-CoV-2 vaccine candidate that may be suitable for large-scale vaccination programs due to its scalable manufacturing and possible single-dose nasal administration [3].

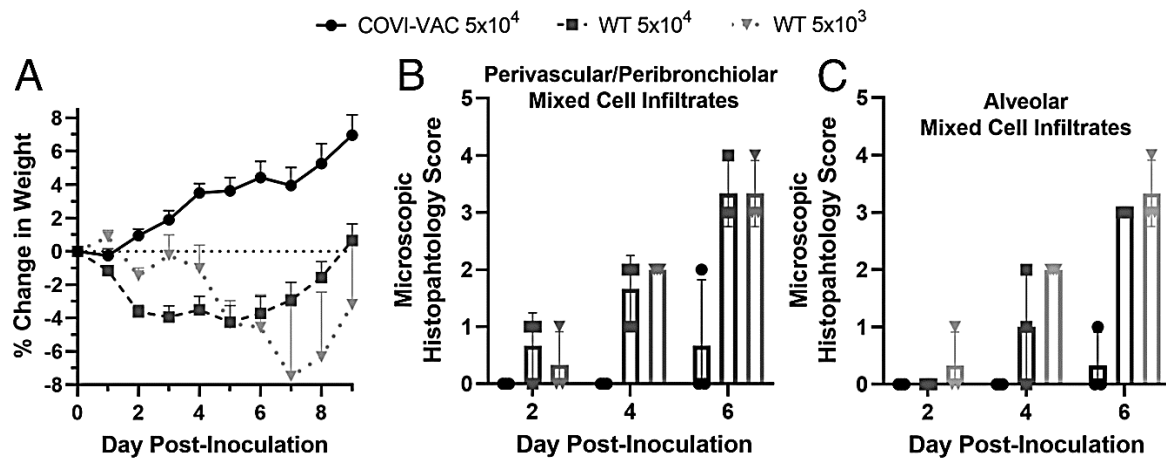


Figure 2: Safety analysis of COVID-19 vaccine [3]. (A) hamsters weight. (B) hematoxylin-stained lung sections. (C) eosin-stained lung sections

2.2. mRNA vaccines

mRNA vaccine is a new vaccine technology that uses the host cell translation mechanism to express the target protein to activate the immune response by synthesizing mRNA carrying specific antigen coding. Unlike traditional live attenuated vaccines, mRNA vaccines do not rely on intact pathogens, so their advantage over live attenuated vaccines is that they avoid the potential risk of virulence recovery of live vaccines. Its core mechanism is to deliver chemically modified mRNA into host cells to synthesize viral antigen proteins, thereby triggering a targeted immune response.

mRNA technology was discovered in the 20th century, but the key breakthrough came in 2005. Katalin Karikó and Drew Weissman found that nucleotide modification can significantly increase the stability of mRNA and reduce the recognition of the immune system [4]. In the early days of the COVID-19 outbreak in 2020, mRNA vaccines based on mRNA stability technology were successfully developed, such as Pfizer/BioNTech's BNT162b2, which became the first batch of COVID-19 vaccines on the market. The rapid development and mass production of mRNA vaccines highlight its advantages over other types of vaccines and verify its potential to respond to infectious diseases.

Compared with traditional vaccines, mRNA vaccines have many characteristics and advantages. First, the non-integrative design can ensure that it will not interfere with the host genome, thereby improving the safety of the vaccine. Second, through sequence engineering optimization (such as codon preference adjustment, UTR region modification and nucleotide modification), mRNA stability, ribosome binding efficiency and protein expression level can be simultaneously enhanced. For example, pseudouridine modification can both reduce immunogenicity and prolong half-life, and the coordinated design of the 5' cap and poly (A) tail further enhances translation efficiency, thereby improving immunogenicity and efficacy. Third, the production process is highly standardized and relies on in vitro transcription (IVT) technology, which does not require cell culture or virus inactivation steps. The production cycle can be shortened to several weeks, combining rapid response, cost control and scalability potential, making it particularly suitable for responding to virus mutations and pandemic outbreaks. The characteristics and advantages of mRNA make it different from traditional vaccines and become a more suitable and acceptable type of vaccine [4].

mRNA vaccines not only have a relatively fast production and development speed compared to other vaccines, but also can provide stable therapeutic effects. The following studies show that the new crown mRNA vaccine has no significant difference from other types of vaccines in treating new crowns. In a study of five new crown vaccines in Hungary, mRNA vaccines (such as Pfizer

BNT162b2 and Moderna mRNA-1273) showed significant advantages in preventing SARS-CoV-2 infection and COVID-19-related deaths. Studies have shown that the adjusted efficacy of mRNA vaccines against infection is 83.3% (Pfizer) and 88.7% (Moderna), significantly higher than the inactivated vaccine (Sinopharm 68.7%). The efficacy of mRNA vaccines against death is 90.6% (Pfizer) and 93.6% (Moderna), while the inactivated vaccine is 87.8%. The efficacy of adenovirus vector vaccines (such as Sputnik-V) is 85.7%, and AstraZeneca is 71.5%, but mRNA vaccines have more advantages in dealing with variants and immune persistence. The study also pointed out that the effect of mRNA vaccines in the real world is consistent with the results of clinical trials, and it still maintains a high level of protection in the chronic disease patient population [5].

2.3. Inactivated vaccines

Inactivated vaccines are a type of vaccine that completely destroys the replication ability of pathogens (such as the new coronavirus) through chemical or physical methods, inactivating the virus's genetic material (RNA/DNA), but at the same time maintaining immunity. After inactivated vaccine administration, these inactivated virus particles will be recognized by the human immune system and stimulate the body's immune protection. Inactivated vaccines are usually made by growing the virus or bacteria and then killing them by heat or chemicals (usually beta-propiolactone or formalin). Inactivated vaccines can be made of whole viruses or bacteria or split fragments of them. The concept of inactivated vaccines can be traced back to the late 19th century. Inactivated vaccines are a technology that completely inactivates pathogens by chemical or physical methods, retaining their immunogenicity to prevent diseases. In the early 20th century, a rabies vaccine through partial inactivation technology was developed. Although there were safety issues, it promoted the initial exploration of inactivated vaccines.

Compared with other types of vaccines, inactivated vaccines have the following advantages: safety, production stability, and applicability to special populations. From a safety perspective, inactivated vaccines deprive pathogens of their ability to replicate themselves, thus avoiding the risk of virulence recovery in attenuated live vaccines [6]. This is especially important for people with special immune deficiencies (HIV-infected people). The emergence of inactivated vaccines can avoid the risks posed by viruses in vaccines. In terms of production technology, inactivated vaccines usually only require conventional 2-8 °C cold chain storage, which greatly reduces the threshold for storage and transportation [7]. In contrast, the mRNA vaccine's strict requirements for ultra-low temperature storage (long-term storage at -70 °C) lead to disadvantages in its transportation.

As one of the important vaccine tools in the prevention and control of COVID-19, inactivated vaccines inactivate the virus through chemical or physical methods while retaining its immunogenicity, thereby stimulating the body to produce an immune response against the new coronavirus. This type of vaccine (such as BBIBP-CorV and Sinovac) can not only induce the production of neutralizing antibodies, but also activate T cell immunity, providing multi-level protection [8]. Clinical trials and actual application data show that inactivated vaccines are effective in preventing severe illness, hospitalization and death. For example, a study in Chile showed that Sinovac's protection rates against hospitalization and death were 87.5% and 86.3%, respectively [8]. In a comparative study in Pakistan, the inactivated vaccine was as effective as the mRNA vaccine in preventing hospitalization and death, although the recovery time was slightly longer. However, it is more suitable for use in resource-limited areas due to its relaxed storage conditions (2-8 °C) and lower production costs. The emergence of the inactivated COVID-19 vaccine has helped the spread of the COVID-19 vaccine, allowing more countries to have the ability to store vaccines and providing a reliable option for epidemic prevention and control.

2.4. Recombinant protein vaccines

A recombinant protein vaccine refers to a vaccine that uses genetic engineering technology to insert the target antigen gene of a virus or pathogen into an expression vector (such as a plasmid), then introduce the vector into host cells (such as bacteria, yeast, mammalian cells or insect cells), express the target antigen protein in large quantities under specific induction conditions, and then obtain high-purity antigens through a purification process, which is finally mixed with an adjuvant to make a vaccine.

The theoretical basis of recombinant protein vaccines comes from breakthroughs in genetic engineering technology. In 1973, Cohen et al. first achieved *in vitro* DNA molecular recombination [9]. This technological breakthrough provides a critical technical foundation for the subsequent development of recombinant protein vaccines and the operability of genes. On this basis, in 1979, Goeddel's team successfully expressed the insulin needed by humans in *E. coli* [10]. This breakthrough verified for the first time the feasibility of expressing foreign proteins in prokaryotic systems, thus promoting its application in the vaccine field [10]. The final application in the vaccine field was achieved by the Valenzuela team in 1982. In the experiment, the researchers used the yeast system to express the hepatitis B virus surface antigen (HBsAg) and form virus-like particles, thus forming the first recombinant protein vaccine (hepatitis B vaccine) [11]. These three studies explain the specific process of recombinant protein vaccines from their birth to their application in vaccines.

Compared with other types of vaccines, recombinant protein vaccines have the following advantages: safety and wide applicability. From a safety perspective, recombinant protein vaccines only contain specific antigenic components of pathogens and do not contain any genetic material or complete pathogens. There is no risk of virulence recovery like live attenuated vaccines, and the immune response caused by them is avoided. In terms of technology, the temperature required for recombinant protein vaccines (2-8 °C) is also much higher than the storage temperature required for mRNA (-70 °C for long-term storage). This storage requirement that is not demanding on temperature conditions allows the application of recombinant protein vaccines to be more extensive.

Recombinant protein vaccines have also demonstrated their unique technical advantages and clinical value in the prevention and control of COVID-19. Recombinant protein vaccines use genetic engineering technology to produce key proteins of the virus, combined with enhancers to stimulate the body's immune response to achieve the effect of inhibiting COVID-19. Taking the recombinant protein vaccine of Novavax as an example, the study included 14,039 people who met the protocol, of which 27.9% were over 65 years old and 44.6% had underlying diseases. The results showed that only 10 cases of infection were reported in the vaccination group, while there were 96 cases in the placebo group. The overall protective efficacy of the vaccine reached 89.7% (95% CI: 80.2-94.6). The data fully prove that the recombinant protein vaccine can not only effectively prevent the infection of the new coronavirus, but also has a more prominent protective effect against severe cases. It is also safe and effective in the elderly and people with underlying diseases [12].

3. Conclusion

COVID-19 has had a huge impact on the global health system and economy. In the face of this rapidly spreading epidemic, due to the lack of targeted treatment measures, the development of vaccines has become the main strategy for prevention and control in various countries. This article analyzes the four major COVID-19 vaccines, focusing on their technical characteristics and actual application effects, providing a comprehensive perspective for understanding the differences between different types of COVID-19 vaccines. In terms of vaccine types, this article focuses on four major types: live attenuated vaccines, mRNA vaccines, inactivated vaccines, and recombinant protein vaccines. Live attenuated vaccines such as COVI-VAC reduce the original toxicity of the virus through genetic

engineering technology, and its clinical data show that it can effectively reduce the viral load and lung pathological damage, but there is also a potential risk of virulence recovery. Representative mRNA vaccines are Pfizer BNT162b2 and Moderna mRNA-1273, which have demonstrated the advantages of rapid research and development and have outstanding protection against the original strain, but the protection against variants such as Omicron has been significantly reduced. Inactivated vaccines such as Sinovac CoronaVac have played an important role in resource-limited areas with their good safety and low storage requirements. Recombinant protein vaccines such as Novavax have shown an excellent balance of safety and effectiveness, and are particularly suitable for the elderly and patients with underlying diseases. The main significance of this article is that it summarizes the technical characteristics of various vaccines, providing a reference for vaccine development and selection in the context of the continuous mutation of the virus. It provides scientific basis and data support for vaccine development under different conditions.

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