

# Modern Innovations in Vaccine Development: Exploring New Trends and Technologies

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**Abstract.** Since the 18th century, vaccines have played a crucial role in preventing infectious diseases, with the earliest example being Edward Jenner's pioneering use of the cowpox vaccine to prevent smallpox in 1796. Vaccines work by inducing specific immune responses, effectively preventing the spread of various infectious diseases and protecting the health of individuals and communities. However, traditional vaccine technologies face certain limitations, such as reversion to virulence and long production cycles. In recent years, rapid advances in biotechnology have introduced new vaccine technologies, including mRNA, DNA, nanoparticle, and mosaic vaccines. These innovative technologies are expected to enhance the safety and efficacy of vaccines and accelerate development times. This review explores the latest trends and technological advancements in vaccine development, highlighting the potential applications of these new technologies. By addressing the challenges faced by traditional vaccines and emphasizing the benefits of emerging approaches, this paper aims to provide valuable insights for vaccine research and public health policy, ultimately enhancing global efforts in disease prevention and control.

**Keywords:** Vaccines, mRNA, DNA, nanoparticles, delivery systems.

## 1. Introduction

Vaccines have been a instrumental tool for preventing infectious diseases for hundreds of years. As early as 1796, Edward Jenner's pioneering use of the cowpox vaccine to prevent smallpox marked the birth of modern vaccine technology. Since then, vaccine development has undergone multiple significant phases, evolving from inactivated and live-attenuated vaccines to subunit vaccines, protein vaccines, and conjugate vaccines. These advancements have significantly contributed to the control and eradication of numerous deadly infectious diseases.

The use of vaccines has played a crucial role in public health. By inducing specific immune responses, vaccines effectively prevent the spread of various infectious diseases, protecting both individuals and communities. For example, the successful eradication of smallpox and the significant reduction in polio incidence are major achievements attributed to widespread vaccination programs [1]. Vaccines have not only saved countless lives but also reduced the economic burden and social impact of diseases.

However, traditional vaccine technologies face several challenges. Although live-attenuated vaccines can elicit strong immune responses, there is always a risk of reversion to virulence. For instance, the oral polio vaccine (OPV) can, in rare cases, cause vaccine-associated paralytic poliomyelitis (VAPP) [2]. Additionally, while inactivated vaccines and subunit vaccines have higher safety profiles, they may

not be as immunogenic as live-attenuated vaccines [3]. The lengthy production cycles of traditional vaccines also hinder rapid responses to emerging infectious disease outbreaks.

In recent years, rapid advances in biotechnology have led to the emergence of new vaccine technologies, including mRNA vaccines, DNA vaccines, nanoparticle vaccines, and virus-like particle (VLP) vaccines [4]. These innovative technologies not only show great potential for enhancing the safety and efficacy of vaccines but also accelerate the development and production processes, providing novel solutions for combating future emerging infectious diseases [5].

This paper aims to review the latest trends and technological advancements in vaccine development, exploring the application prospects of new vaccine technologies in addressing infectious diseases. By examining the challenges faced by traditional vaccines and the advantages of emerging technologies, this review seeks to provide valuable insights for vaccine research and public health policy formulation.

## **2. Development and Design of Some New Vaccines**

The development and design of new vaccines are crucial for overcoming the limitations of traditional vaccines and enhancing our ability to respond to emerging infectious diseases. While traditional vaccines have certain effectiveness, they often encounter issues such as insufficient immune response, potential reversion to virulent forms, and long production cycles. These challenges drive scientists to explore and develop new vaccine technologies.

In recent years, several innovative vaccine technologies with unique advantages have emerged. For example, mRNA vaccines demonstrated their rapid development and efficient response capabilities during the COVID-19 pandemic. DNA vaccines are gaining attention for their ability to generate stable and long-lasting immune responses. Mosaic vaccines aim to provide broad protection against multiple strains of a pathogen, while personalized vaccines tailor immune responses based on individual genetic characteristics, achieving more effective protection. These innovative vaccine technologies hold the promise of significantly enhancing our ability to prevent and control infectious diseases.

### *2.1. mRNA Vaccine*

The advent of mRNA vaccines has significantly transformed the field of immunization, particularly due to their crucial role during the COVID-19 pandemic. Compared to traditional vaccines, the mRNA vaccines developed by Pfizer-BioNTech and Moderna represent a major technological leap forward.

mRNA vaccines typically work by introducing a synthetic mRNA sequence that encodes a viral protein. In the case of SARS-CoV-2, this sequence usually encodes the spike protein. Once the mRNA is delivered into host cells, the cells' machinery translates it into the viral protein. This protein is then presented on the cell surface, triggering an immune response [6]. Notably, this process does not involve the use of live virus particles. Thus, this method not only induces a strong humoral and cellular immune response but also eliminates the risk of reversion to virulence associated with traditional live-attenuated vaccines.

Clinical trials have shown that mRNA vaccines are highly effective in preventing symptomatic COVID-19 infection. For example, the Pfizer-BioNTech vaccine demonstrated approximately 95% efficacy in phase 3 clinical trials [7]. Additionally, these vaccines have a favorable safety profile, with most adverse reactions being mild to moderate, such as injection site pain, fatigue, and headache [7].

Beyond COVID-19, mRNA vaccine technology is also being applied to other viruses. For instance, mRNA vaccines for respiratory syncytial virus (RSV) are currently under development. RSV is a common virus that can cause severe respiratory infections, particularly in infants and the elderly. Researchers are using mRNA technology to encode the fusion protein (F protein) of RSV, a key protein that allows the virus to enter host cells. By expressing this protein, mRNA vaccines can induce a strong immune response to prevent RSV infection [8].

Compared to traditional vaccines, the main advantages of mRNA vaccines lie in their rapid development and production capabilities. Traditional vaccine development can take many years, whereas for mRNA vaccines, once the genetic sequence of the pathogen is identified, they can be designed and produced within weeks. This speed was crucial during the COVID-19 pandemic, allowing

for rapid deployment to address the global crisis. Furthermore, mRNA vaccines are highly adaptable to new virus variants, which is especially important for pathogens that mutate quickly. Additionally, the production of mRNA vaccines typically does not require cell cultures or animal products, reducing the risk of contamination and simplifying the manufacturing process [5].

However, mRNA vaccines also face several challenges. For example, they require ultra-cold storage conditions, which can limit their distribution, particularly in resource-limited settings. Ongoing research aims to develop mRNA vaccines that are stable at higher temperatures. Additionally, further studies are needed to understand the long-term immunity conferred by mRNA vaccines and their effectiveness against emerging variants. In the future, mRNA technology could extend beyond infectious diseases. Researchers are exploring its application in cancer vaccines, potentially transforming treatment methods across multiple medical fields.

## 2.2. *DNA Vaccine*

DNA vaccines have garnered increasing attention in recent years due to their ability to generate stable and long-lasting immune responses. Similar to mRNA vaccines, DNA vaccines work by introducing genetic material that carries specific gene sequences from the pathogen into host cells. However, unlike mRNA vaccines, DNA vaccines introduce plasmid DNA. Once these plasmids enter host cells, they quickly move to the nucleus, where they are transcribed into mRNA. The mRNA is then translated into target antigens in the cytoplasm. Finally, these antigens are presented on the cell surface, triggering both humoral and cellular immune responses.

DNA vaccines share many advantages with mRNA vaccines, such as rapid development and the ability to adapt to emerging pathogens. However, compared to mRNA vaccines, DNA vaccines are more stable at higher temperatures, which reduces the complexity of storage and distribution. Another significant advantage is that DNA vaccines can induce a strong cellular immune response, which is particularly beneficial for combating intracellular pathogens like viruses and certain bacteria [9]. Additionally, DNA vaccines can be designed to include multiple antigens, allowing them to target multiple strains of a pathogen.

While DNA vaccines have shown promise, clinical research on them is still limited compared to mRNA vaccines. Nonetheless, some studies have demonstrated the significant immunogenicity of DNA vaccines in animal models and early human trials. For example, INOVIO Pharmaceuticals developed INO-4800, a DNA vaccine for COVID-19, which showed robust immune responses in preclinical studies and early clinical trials [10]. Furthermore, research suggests that DNA vaccines have the potential to provide long-term immune responses against chronic viral infections, such as human papillomavirus (HPV) [11].

Despite their promising outlook, DNA vaccines face several challenges. One of the main issues is the relatively low efficiency of DNA uptake by host cells, which can limit the overall effectiveness of the vaccine. To address this, researchers are exploring various delivery methods [9]. Future research will focus on improving the delivery and stability of DNA vaccines, as well as gaining a better understanding of their long-term immunity and effectiveness against different pathogens. Additionally, the potential application of DNA vaccine technology in cancer immunotherapy is being actively investigated, offering new avenues for treating various types of cancer.

## 2.3. *Mosaic Vaccine*

Mosaic vaccines are an innovative approach designed to provide broad protection against multiple strains of pathogens. By incorporating genetic sequences from various strains into a single vaccine, mosaic vaccines can induce an immune response effective against multiple variants of viruses or bacteria.

Specifically, to design a mosaic vaccine, computational methods are used to select representative epitopes from different pathogen strains. These epitopes are parts of the pathogen that are less likely to mutate and can induce a strong immune response. Next, these epitopes are integrated into a single antigen design, ensuring the antigen contains characteristics of multiple different strains. The designed antigen sequence is then inserted into a vector, such as plasmid DNA or viral vectors, and finally made

into a vaccine. These synthetic antigens can be delivered through various vaccine platforms, including DNA vaccines, viral vector vaccines, and protein subunit vaccines. When introduced into the body, host cells express these antigens, present them on the cell surface, and trigger both humoral and cellular immune responses, enabling the immune system to recognize and neutralize multiple strains of the pathogen [12].

One of the primary advantages of mosaic vaccines is their ability to provide broad-spectrum immunity. Traditional vaccines may only be effective against a single strain or a few closely related strains, whereas mosaic vaccines aim to be effective against multiple variants. This is particularly important for combating rapidly mutating viruses like HIV and influenza, which continuously circulate and evolve among different strains [13].

The clinical trials of mosaic vaccines are still in their early stages, but the initial results are promising. Studies have shown that mosaic vaccines can produce significant effects in animal models and early human trials. For example, the mosaic HIV-1 vaccine currently under development has demonstrated its ability to induce broad and potent immune responses in preclinical studies [14]. Additionally, mosaic vaccines are being explored for use against other viruses, such as influenza and coronavirus. These vaccines aim to provide comprehensive protection by including epitopes from multiple strains, thereby enhancing their effectiveness against new variants [12].

Despite their great potential, the complexity of designing and manufacturing mosaic vaccines is a major barrier to their widespread adoption. For instance, it is crucial to ensure that the selected epitopes in the vaccine design truly represent the diversity of the pathogen. Moreover, more research is needed to fully understand the long-term safety and efficacy of mosaic vaccines in different populations. Looking ahead, advancements in computational biology and vaccine technology are expected to drive the development of mosaic vaccines. Continued research investment and clinical trials will be key to unlocking the full potential of this promising vaccine design approach. Overall, the ability to quickly adjust mosaic vaccines to combat emerging infectious diseases will be critical for future public health strategies.

#### *2.4. Personalized Vaccine*

The advent of personalized vaccines marks a significant advancement in the field of immunization, aiming to tailor immune responses based on an individual's genetic characteristics. Specifically, personalized vaccines work by identifying specific antigens or epitopes that are most relevant to an individual's immune system. This requires detailed sequencing of the individual's genome before designing the vaccine to understand their unique set of immune receptors, such as human leukocyte antigen (HLA) molecules [15]. Based on this genetic information, scientists can design vaccines containing antigens that are most likely to elicit a strong immune response. This personalized approach ensures that the immune system can more effectively recognize and respond to pathogens, thereby enhancing the vaccine's effectiveness.

One of the primary advantages of personalized vaccines is their high efficacy. By tailoring the vaccine to an individual's genetic profile, these vaccines can induce a stronger and more specific immune response. This approach is particularly beneficial for diseases with high variability, such as cancer, where the vaccine can directly target tumor-specific antigens and stimulate an effective immune response [16]. Personalized vaccines also reduce the risk of adverse reactions, as the vaccine components are designed based on the individual's immune system characteristics.

Personalized vaccines are being explored in various fields, including oncology and infectious diseases. In cancer immunotherapy, personalized vaccines are designed to target neoantigens—antigens that are present on tumor cells but not on normal cells [16]. Clinical trials have shown promising results. For instance, a personalized cancer vaccine developed for melanoma patients has demonstrated significant efficacy in clinical trials. Research results indicate that this personalized vaccine can induce tumor-specific T-cell immune responses during treatment, thereby improving overall survival rates [17]. Additionally, personalized vaccines are also being developed in the field of infectious diseases. In some infectious diseases, variations in individual immune responses can affect vaccine efficacy. By

customizing vaccines based on the genetic makeup of different populations, it is possible to enhance protection against high-mutation-rate diseases such as influenza and HIV.

Despite their great potential, personalized vaccines also face several challenges. For example, the process of developing and manufacturing these vaccines is highly complex and time-consuming, requiring advanced genomic sequencing and bioinformatics tools. Additionally, the high cost of personalized vaccines is a major barrier to widespread adoption. Future research will focus on simplifying the development process and reducing costs, aiming to achieve these goals through technological and manufacturing advancements. Efforts are also being made to integrate personalized vaccines with existing healthcare infrastructure to make these vaccines more accessible. Overall, personalized vaccines hold great promise for the future of medicine. By tailoring vaccines to the unique genetic profiles of individuals, they can achieve higher efficacy and safety, paving the way for more effective prevention and treatment of various diseases.

### **3. Delivery Systems for New Vaccines**

The successful delivery of vaccines is crucial for their effectiveness in preventing diseases. Traditional vaccine delivery systems, such as intramuscular injections, have been effective for many years but also have certain limitations, such as pain at the injection site, the need for cold chain storage, lower patient compliance, and some new vaccines are not suitable for intramuscular injection. Therefore, with the development of new vaccine technologies, it has become increasingly important to explore and implement innovative vaccine delivery systems that can enhance the efficacy, stability, and accessibility of vaccines.

Specifically, new vaccine delivery systems aim to address these limitations by improving the methods of vaccine administration and ensuring more effective delivery to target sites. For example, advanced delivery methods such as liposome nanoparticles, dry powder inhalation, and soluble microneedle technology have shown potential in increasing vaccine stability and patient compliance. These new delivery systems can also promote stronger immune responses by ensuring better antigen presentation and prolonged antigen release.

#### *3.1. Liposome Nanoparticles*

Liposome nanoparticles, as an emerging vaccine delivery system, offer many unique advantages. Typically, they are spherical vesicles composed of one or more phospholipid bilayers, capable of encapsulating both hydrophilic and hydrophobic substances, making them versatile carriers for various antigens. In practice, liposome nanoparticles function by encapsulating vaccine antigens within their lipid bilayers. Upon injection, these liposomes can fuse with cell membranes, thereby facilitating the direct entry of antigens into the cytoplasm of host cells [18]. This process enhances the efficiency of antigen presentation to the immune system, leading to a robust immune response.

The primary advantage of liposome nanoparticles lies in their ability to enhance the stability of vaccines. For instance, when vaccines require cold-chain storage, liposomes can protect the encapsulated antigens from degradation, thereby extending the shelf life and stability of the vaccine. Additionally, liposomes can enhance the intensity and durability of the immune response by promoting more effective antigen presentation and prolonging antigen release. For example, in the development of COVID-19 vaccines, liposome nanoparticles were used for mRNA vaccine delivery, significantly improving the efficacy and safety of the vaccines [19]. Furthermore, liposome nanoparticles have shown great potential in the development of cancer vaccines. Researchers have used liposome nanoparticles to deliver tumor antigens to patients, inducing strong immune responses to attack and eliminate cancer cells. This application not only enhances the effectiveness of the vaccine but also reduces damage to healthy cells [20].

However, liposome nanoparticles also have certain limitations. For example, due to the complex and costly production process, which requires advanced technology and strict quality control measures, large-scale production and widespread application of liposome nanoparticles are challenging, especially in less developed regions. Additionally, although liposomes generally have good biocompatibility, they

can still trigger immune responses against the liposome components themselves, potentially affecting the efficacy and safety of the vaccine [21]. Moreover, the stability of liposomes can be affected by environmental factors such as temperature and pH, necessitating careful formulation and storage.

In conclusion, the advent of liposome nanoparticles has brought significant advancements to vaccine delivery technology. By enhancing antigen stability and promoting stronger immune responses, they provide new avenues for vaccine development. Despite some challenges, ongoing research and development are expected to further optimize the efficacy of liposome nanoparticles and overcome current limitations, paving the way for their broader application in future vaccine formulations.

### 3.2. *Dry Powder Inhalation*

Dry powder inhalation is an innovative vaccine delivery system that offers new possibilities for vaccine administration. Specifically, the mechanism of dry powder inhalation vaccines involves formulating the vaccine antigen into tiny dry powder particles, which are then delivered into the respiratory tract through an inhaler and ultimately deposited in the alveoli. There, the antigens are taken up and processed by immune cells in the lungs, thereby inducing both humoral and cellular immune responses [22]. Compared to traditional intramuscular injections, dry powder inhalation has several unique advantages. Firstly, it avoids the pain and discomfort associated with injections, thereby improving patient compliance. Secondly, since dry powder vaccines do not require cold chain storage, they greatly simplify transportation and storage conditions, which is particularly beneficial in resource-limited areas [23].

Additionally, a significant advantage of dry powder inhalation is its potential to induce mucosal immunity. Mucosal immunity is a crucial defense against respiratory viruses such as influenza and COVID-19. By activating immune responses in the lungs and respiratory tract, dry powder inhalation vaccines can provide more effective protection, preventing the initial infection and spread of the virus upon entry into the body [22]. For example, in the development of tuberculosis vaccines, researchers have found that vaccines delivered via dry powder inhalation can induce strong immune responses in animal models and are more effective than traditional injection methods [23]. Moreover, dry powder inhalation vaccines for certain strains of influenza have shown promising immunogenicity and safety in clinical trials [24].

However, dry powder inhalation technology also faces several challenges. Firstly, developing and producing dry powder vaccines requires highly specialized technology and equipment, which can increase production costs. Secondly, the size and shape of the dry powder particles must be precisely controlled to ensure they effectively reach the deep lung regions and are taken up by immune cells [23]. Additionally, since individual lung function and inhalation capacity can vary, immune responses may differ between individuals, which must be considered in future clinical trials.

### 3.3. *Soluble Microneedle Technology*

Soluble microneedle technology offers a painless and efficient method for vaccine delivery, with several types including solid, coated, dissolvable, and hollow microneedles, making it suitable for various applications. The mechanism of soluble microneedle technology involves creating a set of tiny needles, typically made from biocompatible and water-soluble materials. These microneedles are either coated with a drug layer or filled with vaccine formulations. When applied to the skin, the microneedles penetrate the outer layer (stratum corneum) and dissolve, releasing the vaccine into the epidermis and dermis. These areas are rich in immune cells, allowing the vaccine to interact directly with skin-associated lymphoid tissue (SALT), thereby eliciting a strong immune response [25].

One of the main advantages of soluble microneedle technology is its ability to provide protection against viruses with minimal discomfort. This method avoids the use of needles and syringes, reducing anxiety and pain associated with needle use and thus improving patient compliance. Additionally, the skin's immune system is highly effective at recognizing and responding to antigens, enhancing the efficacy of vaccines delivered through microneedles. For example, in the development of rabies vaccines, researchers found that using soluble microneedles significantly improved the stability and efficacy of

the vaccine, with the experimental group's average antibody titers higher than those of the control group [25]. Furthermore, microneedle delivery allows vaccines to be administered to delicate organs and tissues, such as the eyes [26]. Moreover, soluble microneedles offer practical advantages. They do not require cold chain storage, making them suitable for resource-limited areas [26]. The ease of administration means that vaccines can be delivered without the need for professional healthcare personnel, further increasing their accessibility and potential for widespread use.

However, soluble microneedle technology also faces some challenges. The manufacturing process requires precise control over the size and composition of the microneedles to ensure consistent performance. Although designed to dissolve after application, ensuring that the microneedles fully dissolve and deliver the complete vaccine dose can be challenging. Additionally, extensive clinical trials are needed to verify the safety and efficacy of this delivery method across different vaccines and populations.

#### 4. Conclusion

In conclusion, the field of vaccine development has undergone transformative changes with the advent of new technologies such as mRNA vaccines, DNA vaccines, mosaic vaccines, and personalized vaccines. These innovative technologies address some of the limitations of traditional vaccines by offering faster development, greater stability, and broader immunity. For example, during the COVID-19 pandemic, mRNA vaccines have demonstrated their efficacy and adaptability, while DNA vaccines have shown potential for long-lasting immune responses and stability under varying conditions. Mosaic vaccines are expected to provide broad-spectrum immunity against rapidly mutating pathogens, and personalized vaccines will tailor immune responses based on individual genetic characteristics (Table 1).

**Table 1.** The key features and comparisons of the new vaccine technologies.

Technology	Mechanism of Action	Advantages	Challenges
<b>mRNA Vaccines</b>	Introduces synthetic mRNA to produce antigens in host cells.	Rapid development, high efficacy, adaptable to new variants.	Requires ultra-cold storage, long-term immunity unknown.
<b>DNA Vaccines</b>	Uses plasmid DNA to produce antigens in host cells.	Stable at higher temperatures, strong cellular immunity.	Lower uptake efficiency, requires advanced delivery methods.
<b>Mosaic Vaccines</b>	Combines epitopes from multiple strains into one antigen.	Broad protection against multiple strains.	Complex design and manufacturing, long-term safety unknown.
<b>Personalized Vaccines</b>	Tailored to individual genetic profiles.	High efficacy, reduced adverse reactions.	Highly complex and costly, requires advanced genomic tools.

Additionally, advancements in vaccine delivery systems, including liposome nanoparticles, dry powder inhalation, and soluble microneedle technology, are enhancing the stability, efficacy, and patient compliance of these vaccines. These delivery methods not only improve immune responses but also simplify storage and administration, making vaccines more accessible in resource-limited areas.

Despite the need for advanced technology, high production costs, and extensive clinical trials, optimizing these new vaccine technologies and delivery systems remains a priority for the future. Future efforts will focus on refining these technologies to ensure their widespread application and effectiveness in preventing and controlling infectious diseases. Overall, the continuous evolution of vaccine technology holds great potential for public health, providing new solutions for both existing and emerging infectious diseases. By leveraging these innovations, we can enhance global vaccination efforts, improve disease prevention, and ultimately save more lives.

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