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Full Length Research Article

The Transformative Role of Biotechnology In Vaccine Development

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Abstract

Vaccines are biological substances that stimulate the body's immune system and is-one of the most effective public health tools for preventing infectious diseases. Biotechnology has improved vaccine development by transforming the field from traditional, empirical approaches to rational, antigen-specific design. This review evaluates the historical, traditional and the fundamental role of modern vaccine development, which have provided speed, scalability, and enhanced safety in combating infectious diseases. The key biotechnological innovations, which include recombinant subunit technology, mRNA vaccines, viral vectors systems, peptide-based vaccines, and nanoparticle delivery system have been analyzed for their mechanism, production efficiency, and capacity to induce strong immune response. These innovations enhance vaccine design, production, storage, and delivery. This paper further discusses biotechnology's role in addressing global health emergencies, the challenges faced in implementation, and future trends such as Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR) -based gene editing and AI-driven vaccine development through in silico antigen optimization. Finally, the force of the impact of biotechnology on vaccine development requires continued investment in research, fostering global collaboration to ensure these life-saving innovations are universally accessible and remain the cornerstone of improved global public health security.

Keywords: Biotechnology; CRISPR; mRNA; Nanotechnology; Recombinant DNA; Vaccine development.

Introduction

Vaccines are one of the most effective public health tools for preventing infectious diseases. They are biological substances that stimulate the body immune systems when either a killed or attenuated disease causing-organism or surface protein is introduced in a healthy body (Frazer, 2014 and Rai *et al.*, 2024). The traditional methods such as live-attenuated and inactivated vaccines have been successful (Plotkin, 2018). The advent of vaccine campaigns has eradicated diseases such as small pox and have significantly reduced the prevalence of others like polio and measles (Reidel, 2005). However, the traditional methods are often time consuming, labor intensive and carry safety concerns especially for immunocompromised individuals

The advent of biotechnology has transformed vaccine development, offering new techniques that are faster, safer, and more efficient (Rappuoli *et al.,* 2019). Biotechnology employs the fields of molecular biology, genetics and bioinformatics to create innovative solutions in vaccine design and production. For example, the development of recombinant DNA technology and mRNA vaccines has enabled the creation of vaccines that are highly specific and adaptable to emerging pathogens (Pardi *et al.*, 2018).

The introduction of novel vaccine technologies such as recombinant DNA, mRNA vaccines, and viral vectors has not only improved the effectiveness and safety profiles of vaccines but has also reduced the time required for their development and mass production (Poria *et al*., 2023; Tushar, 2024). Additionally, advances in computational biology allow researchers to be able to design vaccine candidates in silico before physical testing begins.

This review traces the evolution of vaccine technology through the lens of biotechnology, with a critical analysis of how biotechnology has revolutionized vaccine discovery and development. We highlighted the key technologies, their applications, advantages, and challenges associated with these modern vaccine technologies as well as emerging innovations and their roles in combating recent global health emergencies and accelerating vaccine development.

Historical Perspective on Vaccine Development

The history of vaccines development dates back to the late 18th century when Edward Jenner developed the first smallpox vaccine by using material from cowpox lesions. This breakthrough laid the foundation for the concept of immunization, which involves exposing the immune system to weakened or inactive forms of pathogens to build immunity (Riedel, 2005; Hsu, 2013). Jenner's discovery demonstrated that intentional exposure to a harmless version of a pathogen could provide protection against a more severe disease, paving the way for modern immunization practices (Greenwood, 2014).

Following Jenner's work, Louis Pasteur expanded vaccine research in the late 19th century, introducing vaccines against rabies and anthrax. Pasteur's germ theory of disease reinforced the scientific basis of vaccination, leading to further advancements in infectious disease control (Hussein *et al.*, 2015; Plotkin, 2018). The eradication of smallpox in 1980, led by global vaccination efforts, remains one of the greatest public health achievements (WHO, 2020).

Traditional vaccines use live-attenuated or inactivated pathogens but carry safety risks for immunocompromised individuals. Additionally, this method also depended heavily on basic microbiology techniques and often some times lacked the precision that is demanded by emerging public health challenges (Chavda *et al*., 2024). The biotechnological advancements such as recombinant DNA and mRNA vaccines emerged in order to overcome these limitations.

The 20th century has also witnessed the introduction of inactivated and subunit vaccines, which improved safety by using only specific parts of a pathogen rather than the whole organism (Tenorio *et al*., 2022). The advent of biotechnology, by the introduction of recombinant DNA technology in the late 20th century marked a significant shift in vaccine development (Montero *et al*., 2024). This enabled scientists to be able to engineer specific antigens without the use of the whole pathogen, which resulted in vaccines that were safer and easier to produce at large scale. Notable examples include the recombinant hepatitis B vaccine and the human papillomavirus (HPV) vaccine.

The COVID-19 outbreak further displayed the importance of biotechnology, as mRNA-based vaccines were developed and deployed into the market within a shorter time frame (Chavda *et al.,*

2024). These developments represent a new era in vaccinology, one where biotechnology enhances rapid, precise, and scalable responses to emerging infectious diseases. This historical evolution shows the critical role of global collaboration in combating health threats through vaccination.

Traditional Perspective on Vaccine Development

Traditional vaccines rely primarily on two strategies (live-attenuated or inactivated vaccines) for rendering a pathogen safe while retaining its immunogenicity.

1. Live-attenuated Vaccines: These vaccines that use pathogen forms that are weakened and, that cannot cause disease in healthy individuals but still provoke an immune response. An example of such vaccines is measles, mumps, and rubella (MMR) vaccine (Kusters and Almond, 2008).
2. Inactivated Vaccines: These are produced by killing the pathogen, ensuring it cannot replicate, and requires booster doses for sustained immunity. Examples include the polio vaccine (inactivated polio vaccine) (Roldão *et al.,* 2010).

While effective, these methods come with challenges: The production process is time consuming, requiring extensive safety testing to ensure the pathogen does not regain virulence. Live-attenuated vaccines are unsuitable for immunocompromised individuals due to the small risk of reactivation while inactivated vaccines often require booster doses to maintain immunity (Plotkin , 2018; Rappuoli *et al.*, 2019).

Core Biotechnological Approaches in Vaccine Development

Biotechnology has revolutionized vaccines development, making it faster, and safer (Rappuoli *et al*., 2019). Modern techniques utilize cutting-edge molecular biology tools, enabling the production of vaccines tailored to specific pathogens. The modern biotechnological methods have significantly advanced vaccine development, enabling the creation of vaccines that are more effective and faster to produce using the following:

i. **Cell-Culture Technology**: This uses the insect or mammalian cells for vaccines production, moving away from traditional methods involving chicken eggs.

ii. **Adjuvants:** These are substances which enhance the immune response when added to vaccine.

iii. **Research Focus**: The development of novel adjuvants to improve the effectiveness and longevity of immune responses allowed the vaccine development to be focused and safe time. This has been seen during Covid 19 vaccine development.

iv. **Reverse Vaccinology**: This involves the use of genomic information to identify potential vaccine targets without pathogens being cultured.

v. **Structural Biology and Computational Approaches**: Theses techniques use cryo-electron microscopy and computational modeling which help researchers to understand the three dimensional structures of pathogens which facilitate the design of targeted vaccines (Tushar,2024)

The following highlight key biotechnological approaches and their applications in vaccine development:

Recombinant DNA vaccine Technology: This technique produces antigens that mimic components of pathogens in order to stimulate the immune response and is done through DNA recombination or manipulation, which eliminates the need to handle live pathogens. The hepatitis B and human papilloma virus (HPV) vaccines are prime examples of this advancements (WHO, 2021 and Kailaje, 2024). The hepatitis B vaccine was the first recombinant vaccine licensed for human use. It uses a recombinant form of the hepatitis B surface antigen (HBsAg) produced in yeast cells (WHO, 2021).

The mechanisms involved are as follows:

i. The gene encoding the target antigen is identified and isolated from the pathogen.
ii. This gene is inserted into a bacterial or yeast plasmid using restriction enzymes and ligases.
iii. The recombinant plasmid is introduced into host cells (e.g., *E. coli* or yeast) to produce the antigen.
iv. The antigen is purified and used to formulate the vaccine.

Its advantages include limiting the needs to handle life viruses and reducing the biosafety risks, enabling high-yield and scalable; as well as

the production of highly purified and specific antigens with limited side effects.

Messenger RNA (mRNA) Vaccines Technology: Messenger RNA (mRNA) vaccines use synthetic mRNA sequences that instruct cells to produce a pathogen-specific protein. The immune system then recognizes this protein as foreign and generates a response (Pardi *et al*., 2018). The Moderna COVID-19 was one of the first mRNA vaccines approved for widespread use, and research is still ongoing for mRNA-based vaccines for influenza, zika virus, and HIV (Moderna, 2024). The COVID-19 mRNA vaccines (Moderna, Pfizer) demonstrated rapid development and high efficacy (Philippon, 2023).

The Processes of mRNA Vaccines Development include:

i. Identification of the genetic sequence encoding the antigen.
ii. Synthesis of mRNA encoding the antigen.
iii. Encapsulation of the mRNA in lipid nanoparticles for delivery.
iv. Injection of the vaccine, leading to antigen expression and immune activation.

Its advantages includes rapid development (mRNA vaccines were developed within months for COVID, high efficacy and adaptability (mRNA sequences can be easily modified to target emerging variants) and no need for live pathogens, ensuring safety. However, the requirement for ultra-cold storage, making distribution complex and high production costs in the initial stages are challenges.

Viral Vector-Based Vaccines: Viral vector vaccines use harmless viruses (vectors) used to deliver genetic material encoding an antigen. The host cells produce the antigen, triggering an immune response (Voysey *et al.*, 2021). Vectors like adenovirus serve as delivery particles for genetic material that code for antigens (Francis, 2017). They are used in Johnson & Johnson, AstraZeneca, and Ebola vaccines. The Process of Viral Vector Vaccine Development include:

i. Selection of a non-replicating viral vector (e.g., adenovirus).
ii. Insertion of the antigen's gene into the viral genome.
iii. Injection of the vaccine, allowing cells to produce the antigen.

Peptide-Based and Subunit Vaccines (Epitome vaccines): Peptide-based and subunit vaccines use purified protein fragments of a pathogen rather than whole viruses or bacteria. These fragments are sufficient to stimulate an immune response without causing disease. The peptides mimic the epitopes of the antigen that triggers direct or potent immune responses (Plotkin, 2018). Synthetic peptides have considerably attracted attention as a basis for subunit vaccine design. The synthetic peptides play some critical roles to determine the specificity and magnitude of cell-mediated (T-cells) and humoral (antibody) immunity and can contain the minimal sequences necessary for immuno-modulation. The delivering of correct peptides harboring B- or T-cell receptor epitopes are sufficient to elicit effective immune responses. Additionally, to stimulate a protective response against a particular pathogen, peptide-based immuno-therapy can be used for the treatment of other chronic ailments such as cancer or be developed for immune suppression for autoimmune diseases. Its advantages is that it can be easily be synthesized and characterized, and are generally more stable than whole pathogens or full-length proteins

However, peptides when used alone as vaccines, are typically poorly immunogenic. Their delivery is dependent on potent immunostimulatory adjuvants to effectively activate the adaptive and innate arms of the immune system. A lot of vaccine adjuvants have been available since 1970s, but up to date, only a few have been approved for human use, consequently slowing the development of synthetic peptide vaccines (O'Hagan and De Gregorio, 2009). The significant advancement in the engineering of adjuvants such as novel particulate delivery systems and Toll-like receptor (TLR) agonists in the past decade, have made peptide-based vaccines a viable option for modern immunotherapy.

The processes of subunit vaccine development include:

i. Identification of immunogenic peptides or proteins.
ii. Recombinant expression of these proteins in host cells.
iii. Purification and formulation of the vaccines.

The Novavax COVID-19 vaccine is a subunit vaccine based on recombinant spike proteins, also, the Pertussis vaccine (whooping cough) is another example (CDC, 2019; CDC, 2023). Its advantages includes: fewer side effects due to the absence of live pathogens, suitability for immunocompromised individuals and highly specific immune responses. However, its challenges are that it often requires adjuvants to enhance immune responses and may need multiple doses or boosters.

Cell Culture Techniques in Vaccine Production: This is produced using cell lines instead of embryonated eggs, allowing for more consistent and scalable production (Rappuoli *et al*., 2019; Bublot, 2023). For example, the influenza vaccine is now produced in cell cultures instead of eggs and the rabies vaccine uses Vero cells for virus propagation. The process of cell culture-based vaccine development includes:

i. Selection of a suitable cell line (e.g., Vero cells, CHO cells).
ii. Cultivation of viruses or recombinant proteins in the cells.
iii. Purification and formulation of the vaccine.

Its advantages include: overcoming supply chain issues related to egg-based vaccine production and allowing for more rapid scaling and consistency in vaccine quality. However, high costs of setting up cell culture facilities and the requirement of specialized expertise for maintenance and quality control are the two major challenges

Nanoparticles-mediated delivery and vaccine Delivery: Nanoparticles such as lipids based and virus-like particles aid in the improvement of stability, delivery, and immune response. For example: Lipid nanoparticles (LNPs), Improve mRNA delivery and enhance antigen expression. Virus-like nanoparticles (VLPs), Mimic natural infections, improving immune response without using live viruses; and Polymeric nanoparticles which allow slow and sustained antigen release for longer-lasting immunity. Nanotechnology-based vaccines are being explored for HIV, tuberculosis, and cancer immunotherapy (Zhao *et al.*, 2014; Zhang *et al.*, 2022).

Advantages of Biotechnology in Vaccine Development

Biotechnology has significantly improved vaccine development by enabling faster production, enhanced safety, and improved efficacy (Rappuoli *et al.*, 2019). This section explores the key advantages of biotechnological approaches in vaccine research, design, and manufacturing.

1. **Rapid vaccine development and pandemic response:** Traditional vaccine development typically takes 10-15 years, involving extensive research, preclinical studies, and clinical trials (Plotkin, 2018). However, biotechnology has drastically reduced this timeline. For example, The Pfizer-BioNTech and Moderna COVID-19 vaccines were developed in less than a year using mRNA technology (Morderna, 2024). Recombinant DNA techniques allowed for rapid production of the Ebola vaccine, which was deployed within five years of an outbreak.
2. **Safety and reduced risk of infections:** Traditional vaccines, particularly live-attenuated vaccines, pose risks to immunocompromised individuals. For example, the Hepatitis B vaccine, developed using recombinant DNA technology, completely avoids the risks associated with using blood-derived antigens (Rappuoli *et al.,* 2019). Biotechnology-based vaccines improve safety in several ways, such as:

i. No live pathogens: Recombinant DNA and mRNA vaccines eliminate the risk of reversion to virulence.
ii. Precise antigen targeting: Subunit and peptide-based vaccines reduce the likelihood of adverse reactions.
iii. Standardized production: Bioreactor-based cell culture vaccines provide greater consistency compared to egg-based methods. Bioreactors were widely used in cell culture-based viral vaccine production, especially during the coronavirus disease in 2019 (COVID-19) pandemic. The development and application of bioreactors provided more efficient and cost-effective vaccine production to meet the global vaccine demand (Zhongbiao *et al*., 2022)

3. Scalability and mass Production: Biotechnology has made vaccine manufacturing more scalable, allowing for rapid distribution during global health crises. Cell culture techniques eliminate dependence on embryonated eggs, ensuring higher yield and better quality control. Bioreactor systems allow for large-scale

protein and viral antigen production, significantly increasing vaccine output. Also, mRNA vaccine production does not require live virus handling, allowing for rapid up scaling. During the COVID-19 pandemic, mRNA and viral vector platforms enabled the production of billions of doses in under a year, highlighting the scalability advantage of biotechnology-based vaccines (Pardi *et al.,* 2018).

4. High efficacy and long-lasting Immunity: Biotechnology enables vaccines to be designed with improved immunogenicity, enhancing their effectiveness. The advent of mRNA vaccines has led to the production of strong cellular and humoral immune responses, often providing longer-lasting immunity. Viral vector vaccines mimic natural infections, generating a robust immune response. Adjuvants (e.g., MF59, AS03) also enhance antigen presentation, leading to stronger protection with lower doses. For example, the HPV vaccine, developed using recombinant virus-like particles (VLPs), has shown nearly 100% efficacy in preventing cervical cancer-related infections (WHO, 2021).

5. Customization and adaptability: Biotechnological advancements allow for rapid modification of vaccines to address emerging diseases and mutations (WHO, 2021). mRNA vaccines can be quickly updated to target new virus strains (e.g., COVID-19 variants). Recombinant DNA methods allow for quick substitution of antigen-coding genes in response to new threats. For example, influenza vaccines are reformulated annually using recombinant and cell-based technologies, ensuring effective protection against evolving strains.

6 Cost effectiveness and reduced dependency on animal models: Traditional vaccine production often required animal-derived components, leading to high costs and ethical concerns but, modern biotechnology-based vaccines rely on synthetic biology and cell culture methods as alternative, reducing dependency on animals (Rappuoli *et al.*, 2019). For Instance, the switch from egg-based Influenza vaccines to cell culture-based production has led to fewer supply chain disruptions and increased efficiency (McLean *et al.*, 2016). Additionally, high-yield plant-based expression systems, such as those used in Medicago's COVID-19 vaccine, as well as low-infrastructural synthesis provide a scalable and cost-effective alternative to traditional vaccine manufacturing (Ward *et al.*, 2021). The adoption of single-use bioreactor systems has also minimized infrastructure costs, making vaccine production more flexible and responsive to emerging Infectious diseases (Crommelin *et al.*, 2021).

7. Overcoming stability challenges: Some biotechnological advancements have focused on enhancing vaccine stability, particularly for distribution in remote regions (Kowalzik *et al.,* 2021). This can be seen in:

i. Lipid nanoparticles (LNPs) in mRNA vaccines, it protect the fragile genetic material.
ii. Lyophilization (freeze-drying) that extends shelf-life and simplifies transportation.
iii. Plant-based vaccine technology (e.g., Medicago's COVID-19 vaccine) that offers temperature-stable alternatives.
iv. Absence of ultra-cold storage required in early mRNA vaccines, unlike in newer formulations that aim to overcome this limitation for broader accessibility.

Challenges and Limitations of Biotechnology In Vaccine Development

Despite its numerous advantages, biotechnology-driven vaccine development faces several challenges, including production costs, regulatory hurdles, and public acceptance (Rappuoli *et al*., 2019). Understanding these limitations is crucial for optimizing vaccine strategies and ensuring widespread accessibility. These challenges are discussed below:

1. High production and research costs

Developing biotechnological vaccines involves significant financial investment (Plotkin, 2018) due to advanced technology requirements (e.g mRNA synthesis, bioreactor systems), specialized personnel training in molecular biology and bioinformatics, and high costs of clinical trials, which require thousands of participants. For instance, mRNA vaccines were expensive to develop initially due to the need for specialized lipid nanoparticles (Pardi *et al.*, 2018). However, costs may decrease with improved production methods.

2. Cold Chain and Storage Challenges

Many biotechnology-based vaccines require strict temperature control, making distribution difficult in low-resource settings (Wang *et al.,* 2021); mRNA vaccines (Pfizer, Moderna) initially

required storage at -70°C, limiting availability in rural areas. Some recombinant protein vaccines require cold storage, and increasing logistical cost.

3. Manufacturing and scalability issues

While biotechnology allows for rapid vaccine design, large-scale production remains complex due to:

Limited global production capacity, especially in low-income countries, and Supply chain disruptions affecting raw material availability (e.g., lipid nanoparticles for mRNA vaccines). For example, COVID-19 vaccine production was initially hindered by raw material shortages (WHO, 2021).

4 Regulatory and approval barriers

Vaccine approval involves strict regulatory assessments to ensure safety and efficacy, which can delay roll out, this can be seen in long clinical trial phases (Preclinical → Phase I → Phase II → Phase III → Post-market surveillance). These phases are as explained below:

Preclinical Phase: This stage involves laboratory research and animal testing to evaluate the vaccine's safety, immunogenicity, and potential efficacy before human trials (Lipsitch & Eyal, 2017). Only promising candidates proceed to human trials.

Phase I Clinical Trial: A small group of healthy volunteers (typically 20–100) receives the vaccine to assess its safety, dosage, and initial immune response (Krammer, 2020). The focus is on identifying any immediate adverse effects.

Phase II Clinical Trial: This phase expands to several hundred participants and evaluates the immune response, optimal dose, and potential side effects (WHO, 2020). It includes a more diverse population, often incorporating at-risk groups.

Phase III Clinical Trial: Large-scale trials (thousands to tens of thousands of participants) assess the vaccine's efficacy in preventing disease and monitor for rare side effects (Poland *et al.,* 2018). This phase provides the critical data needed for regulatory approval.

Post-Market Surveillance (Phase IV): After regulatory approval, ongoing monitoring and real-world data collection help detect rare adverse reactions, long-term efficacy, and potential updates needed for variants (Lurie *et al.,* 2020).

Stringent guidelines follows genetic and mRNA-based vaccines, requiring extensive safety evaluations. During the COVID-19 pandemic, Emergency Use Authorizations (EUAs) helped accelerate vaccine approval, but long-term monitoring remains essential (Voysey *et al.,* 2021).

5. Public trust and scientific misinformation

Public skepticism towards biotechnology-based vaccines, especially genetic vaccines (mRNA, viral vectors), is a significant challenge (Larson *et al.*, 2016). These challenges range from concerns about long-term safety despite rigorous testing, misinformation about DNA alteration by mRNA vaccines, to ethical debates over genetic modification and biotechnology applications.

6. Ethical Concerns in Genetic Vaccine Development

Use of genetic modification technologies raises ethical questions about unintended consequences. Some vaccine production methods involve human or animal-derived cells, leading to religious or ethical concerns. Patents and intellectual property rights may also limit vaccine accessibility, particularly in developing nations. For example, debates over patent waivers for COVID-19 vaccines highlighted the conflict between innovation protections versus global health equity (WHO, 2021).

7. Risk of vaccine escape Variants

As viruses mutate, there is a risk of vaccine escape variants that reduce vaccine effectiveness (Voysey *et al*., 2021). For example: The Delta and Omicron variants of SARS-CoV-2 showed partial resistance to first-generation COVID-19 vaccines. Influenza vaccines require annual updates due to frequent viral mutations.

Future Trends and Innovations in Vaccine Biotechnology

As biotechnology continues to advance, several innovations are shaping the future of vaccine development (Cohen, 2022). Emerging technologies, novel delivery methods and next-generation platforms are expected to improve vaccine efficacy, accessibility and scalability. Scientists are exploring universal vaccines that provide long-term protection against multiple virus strains by targeting conserved antigenic regions, particularly for influenza and coronaviruses (Erbelding *et al*., 2018).

mRNA Vaccine Advancements: The success of mRNA vaccines during the COVID-19 pandemic has paved the way for expanded applications in

infectious diseases and personalized medicine (Kowalzik *et al*., 2021). Additionally, personalized mRNA vaccines are being developed to tailor immunization based on an individual's genetic profile, potentially improving vaccine responses in immunocompromised patients (Chakraborty *et al*., 2021). Self-amplifying RNA (saRNA) vaccines, an advanced form of mRNA vaccines, can generate stronger immune responses with lower doses, making vaccine production more efficient (Pardi *et al.,* 2018).

Alternative vaccine delivery systems, such as micro needle patches and inhalable vaccines, are also in development to eliminate the need for cold chain storage and improve ease of administration in remote areas (Rouphael *et al.*, 2017). Furthermore, plant-based and edible vaccines are being researched as cost-effective solutions for global immunization efforts, reducing manufacturing dependencies and improving vaccine accessibility (Ward *et al.*, 2021).

The future advancements include:

i. **Thermostable mRNA Vaccines:** Researchers are working on heat-resistant mRNA formulations that can be stored at room temperature, eliminating the need for ultra-cold storage. This advancement will enhance vaccine distribution in low-resource settings.
ii. **Cancer Vaccines**: Personalized mRNA cancer vaccines are being developed to stimulate the immune system against tumors. Examples include mRNA-based immunotherapies targeting melanoma and lung cancer (Kowalzik *et al*., 2021).
iii. **Universal vaccines that are mRNA based**: Research is underway to create universal flu vaccines using mRNA technology, providing long-lasting protection against all influenza strains (Pardi *et al.*, 2018). The promise of mRNA-based universal vaccines lies in their ability to generate broad and durable immune responses by targeting conserved antigens across diverse viral and bacterial families (Muodiaju and Madu, 2025)

CRISPR and Gene-Edited Vaccines: CRISPR (Clustered Regularly Interspaced Short Palindromic Repeats) technology is being explored for vaccine development. Genome editing can be used to create safer and more effective live-attenuated vaccines. CRISPR-based vaccines may provide long-term immunity by modifying immune cells to enhance pathogen recognition. For example, researchers are investigating CRISPR-modified viral vectors to develop vaccines against HIV and persistent viral infections (Barrangou and Doudna, 2016).

Nanotechnology in vaccine delivery: Nanoparticles are being used to enhance vaccine stability and immune response. Nanotechnology-based vaccines are being explored for HIV, tuberculosis, and cancer immunotherapy (Zhao *et al*., 2014 and Zhang *et al*., 2022).

Below are the following examples:

i. Lipid nanoparticles (LNPs): This improves mRNA delivery and enhance antigen expression.
ii. Virus-like nanoparticles (VLPs): Mimic natural infections, improving immune response without using live viruses.
Iii. Polymeric nanoparticles: Allow slow and sustained antigen release for longer-lasting immunity.

Artificial Intelligence (AI) in vaccine design: AI and machine learning are revolutionizing vaccine development by accelerating the design process through enabling robust in silico prediction and optimization of antigen selection for stronger immune responses, and protein folding kinetics, drastically reducing the experimental burden and time required to identify high-efficacy vaccine candidates. For example, AI was used in the rapid design of COVID-19 vaccines by analyzing SARS-CoV-2 spike protein structures (Chinazzi, *et al.,* 2020)**.** One method for accomplishing this is the leveraging of computational methods to discover new candidate drugs and vaccines *in silico*. In the last decade, machine learning-based models, trained on specific biomolecules, have offered inexpensive and rapid implementation methods for the discovery of effective viral therapies (Arash *et al.*, 2020).

DNA Vaccines and Next-Generation Platforms

DNA vaccines offer several advantages, such as ease of production, stability, and long-term immunity. Recent breakthroughs include the ZyCoV-D COVID-19 vaccine, the first approved DNA vaccine, developed in India. Also, DNA vaccines for Zika virus are in advanced clinical

trials (BBC News, 2021; NIAID, 2016). Future DNA vaccines faced with the issues of efficient delivery may be enhanced with electroporation technology, which improves DNA uptake into human cells (Morrow *et al.*, 2020).

Plant-based and edible vaccines

Plant biotechnology is being used to develop vaccines grown in genetically modified plants, such as: Tobacco plants engineered to produce viral antigens (e.g., Medicago's COVID-19 vaccine), also, edible vaccines in crops like tomatoes and bananas, offering oral immunization without needles (The Scientist, 2022; Nature Medicine, 2002). These innovations could reduce vaccine production costs and improve accessibility in low-income regions.

Universal and pan-viral vaccines

Researchers aim to develop one-shot vaccines capable of protecting against multiple viruses. Vaccines designed to provoke broadly neutralizing antibodies (bNAbs) are being explored by targeting conserved epitopes for universal flu, HIV, and coronavirus vaccines. The NIH is developing a universal coronavirus vaccine targeting conserved viral regions, which could protect against all SARS-like viruses (Cohen, 2022).

AI-Generated and synthetic biology vaccines

Synthetic biology is enabling the creation of fully synthetic vaccines, eliminating the need for traditional cell culture. AI-generated antigens can be designed for optimal immune response. Synthetic mRNA vaccines could be rapidly adapted to emerging pathogens. For example, synthetic biology was used in the development of Novavax's recombinant protein-based COVID-19 vaccine (Vogel *et al.*, 2021).

Vaccine patches and needle-free delivery

Future vaccines may not require injections, as researchers develop alternative delivery methods like microneedle patches that allow pain-free vaccination and self-administration; Nasal and inhalable vaccines could provide mucosal immunity against respiratory infections; Oral vaccines for cholera, polio, and norovirus are in development. For instance, microneedle patches for flu vaccines are in clinical trials, showing comparable efficacy to traditional injections (Rouphael *et al.*, 2017).

Conclusion

Biotechnology has significantly advanced vaccine development, enabling faster, safer, and more effective immunization strategies through innovations such as recombinant DNA, mRNA, CRISPR, and nanotechnology. These advancements have revolutionized disease prevention by improving vaccine precision, scalability, and adaptability to emerging pathogens. However, challenges such as high production costs, cold chain requirements, regulatory complexities, and vaccine hesitancy must be addressed to maximize the impact of biotechnological vaccines. Future innovations, including AI-assisted vaccine design, universal vaccines, and needle-free delivery systems, promise to enhance accessibility and effectiveness. By continuing to invest in research, fostering global collaboration, and ensuring equitable distribution, biotechnology will remain a cornerstone in combating infectious diseases and improving public health worldwide.

In order to improve biotechnology based vaccines in terms of accessibility and effectiveness, it is recommended to invest in genetic engineering, mRNA technology, nanotechnology and thermostable platforms.

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Conflict of interest

The authors declare that the paper review was written without any conflict of interest among the authors

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