REVIEW PAPER

mRNA Vaccine Technology: Advancements, Challenges, and Future Applications in Global Health.

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ABSTRACT

Vaccination is a cornerstone of public health, playing a pivotal role in preventing infectious diseases and reducing global morbidity and mortality. Traditional vaccine development methods often face challenges in responding rapidly to emerging outbreaks, highlighting the need for innovative approaches. mRNA (messenger RNA) vaccine technology has revolutionized the field with its adaptability, scalability, and rapid development timelines. The COVID-19 pandemic caused by SARS-CoV-2 deep-rooted the unprecedented success of mRNA vaccines in mitigating severe outcomes, reducing hospitalizations, and controlling the outbreak globally. In this review, the advancements in mRNA vaccine technology are highlighted, focusing on its unique mechanism of action, where synthetic mRNA directs cells to produce antigens, triggering targeted immune responses. The challenges and opportunities associated with deploying mRNA vaccines during outbreaks, including manufacturing scalability, distribution logistics, and public acceptance, are discussed. Furthermore, the potential applications of mRNA platforms in addressing a wide range of diseases, from infectious pathogens to non-communicable conditions such as cancer, are explored. With continued progress in mRNA pharmacology and immunology, this technology is poised to become a cornerstone for next-generation vaccines, enhancing global pandemic preparedness and enabling rapid, effective responses to future health crises.

Keywords: mRNA vaccine; vaccine development; infectious diseases; global health; pandemic..

How to cite this article: Karthika R, Gnanendra T S, Ashok Kumar L, Malarvizhi A, Prabhakaran S G. mRNA Vaccine Technology: Advancements, Challenges, and Future Applications in Global Health. Int J Drug Deliv Technol. 2026;16(37s): 867-875. DOI: 10.25258/ijddt.16.37s.112

Source of support: Nil.

Conflict of interest: The author declares no conflict of interest, and this work represents independent academic research conducted in a personal capacity, not associated with any employer or commercial entity.

INTRODUCTION

Vaccines are biological preparations that helps the body's immune system recognize and fight harmful pathogens [1]. Traditionally, they contain attenuate or inactivated forms of diseases causing microbes, which stimulate the immune system to produce antibodies. [2] These antibodies not only protect the individual from the targeted disease but also allow the immune system to "remember" how to combat future infections. Thus, vaccines play a crucial role in preventing serious illnesses and saving millions of lives worldwide [3].

Vaccination has been a keystone of global health, significantly reducing the burden of infectious diseases. Between the mid - 1960's and 2015, viral vaccines are estimated to have saved nearly 10 million lives by preventing childhood infections such as measles, mumps, rubella, chickenpox, and hepatitis. According to world health organization (WHO), vaccination prevents 2-3 million deaths annually. Historic achievements include the eradication of smallpox over 40 years ago and rinderpest in 2011, while polio is nearing eradication. Overall, global vaccination efforts have reduced mortality by 90-100% compared to the 20th century. [4]

Wide range of vaccine platforms - including inactivated, subunit, recombinant, polysaccharide, conjugate, toxoid, and viral vector vaccines- have contributed to this success. [5] However, traditional vaccine platforms often face challenges in rapidly responding to emerging outbreaks, highlights the need for innovative approaches. One such ground-breaking approach is mRNA vaccine technology (messenger RNA), which demonstrated immense potential during the COVID-19 pandemic [6, 7].

This platform has revolutionized vaccine development with its speed, safety, and flexibility, while also opening doors for treating complex diseases like cancer and genetic disorders [8, 9]

The Noble prize in physiology or medicine was awarded to katalin kariko and Drew wesissmen for their discoveries related to modified nucleotides, which enable the development of effiective mRNA vaccines, their contribution markerd a major turning point on morden vaccine science https://www.who.int/srilanka/news/detail/15-12-2023-

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**Author for Correspondence: sgpprabhakaran@gmail.com* katalin-karik--and-drew-weissman-were-jointly-awarded-the-nobel-prize-in-physiology-or-medicine-2023#:~:text [10]

Its adaptability and precision make it a strong candidate for combating emerging infectious diseases and advancing fields like gene therapy. mRNA, or messenger RNA, is a single-stranded molecule synthesized during the transcription process of DNA.An enzyme called RNA polymerase reads the genetic information from DNA and produces an mRNA strand. This mRNA then exits the nucleus and enters the cytoplasm, where ribosomes decode the sequence and use it as a template to produce specific proteins.In mRNA vaccine technology, synthetic mRNA is injected into the body and enters the cytoplasm directly – by passing the natural export step. This allows for immediate translation into a target protein [11]

For example, in the case of COVID-19 vaccines, the mRNA encodes the spike protein found on the surface of the SARS-COV-2 virus. After administration, cells take up the mRNA and begin producing the spike protein. The immune system recognizes it as foreign and mounts a defences response, preparing the body to fight future infections.one of the key benefits of mRNA is that it is short lived. After the protein is produced, the mRNA is broken down and eliminated from the body without altering the host DNA.This ensures the process is temporary, with no long- term changes to the individuals genetic makeup (Medlineplus,n.d)[12]

Despite the remarkable success of the mRNA vaccines, challenges remain in terms of molecule stability, delivery systems, larger-scale production, and equitable global access.However,with ongoing advancements in formulation, cold-chain storage, and distribution,mRNA vaccines are poised to become a corner stone of morden healthcare- offering rapid,adaptable,and personalized solutions to some of the world's most urgent medical needs. Looking ahead, mRNA technology not only holds promise for the prevention of infectious diseases bit also has the potential to transform therapeutic strategies for cancer, autoimmune diseases, and rare genetic disorders.AS the world embrances precision medicine, mRNA vaccines stand as a powerful and innovative platform capable of reshaping global health and paving the way for a healthier, more resilient next-generation society.

HISTORICAL MILESTONES OF mRNA VACCINE

The discovery of mRNA vaccines involved the contributions of several scientists over the years. While it's difficult to attribute the discovery to a single person, some important milestones of mRNA vaccine technology can be traced back to the foundational discovery of the central dogma of life by scientist Francis crick during 1958. Followed by the identification of the RNA role in protein synthesis by crick and Brenner in 1960[13].

The first successful transfection of synthetic mRNA into cells using liposomal Nano particles was reported in 1989, and by 1990 unprotected mRNA was shown to produce specific proteins in living tissues[14].In 1993, liposome -encapsulated mRNA encoding viral antigen was successfully stimulate immune response in mice, and shortly thereafter, self-amplifying mRNA was developed to enhance immune activation[15].In the early 2000 s, progress accelerated with the initiation of the first human clinical trial of an mRNA- based cancer vaccine in 2001[16], and the discovery of modified nucleosides in 2005 , which improved mRNA stability and reduced immunogenicity[17].The establishment of companies like BIONTECH in 2008 and MODERNA in 2010[18] [19], coupled with strategic funding from DARPAS ADEPT program[20] [21], further accelerated advancements in the flied. By 2013,the first human clinical trials for an mRNA vaccine targeting an infectious agent, rabies,was conducted and subsequent trails explored applications for the rapid development and success of mRNA vaccines[22] [23] during the COVID-19 pandemic, highlighting their adaptability and transformative potential in Morden medicine. On December 11, 2020, the U.S. Food and Drug Administration (FAD) issued an emergency use authorization for the Pfizer-Biotech COVID-19 mRNA vaccine, followed by a similar approval for Moderns COVID-19 [24].

MOLECULAR BASIS OF mRNA VCCAINES

mRNA vaccines provide genetic instruction that enable host cells to synthesize specific disease related proteins. These proteins once produced, triggered, targeted immune response. The mRNA sequence can be engineered to improve translation efficiency, allowing precise and effective expression of antigenic protein [25].unlike DNA based vaccines pose a significantly lower risk of genomic integration because they do not require nuclear entry and lack CPG islands –DNA motifs that could trigger unwanted immune responses [25, 26].

The use of in vitro transcription allows rapid, standardized ,and scalable vaccine production, making them suitable for outbreak response and global immunization [https://cepi.net/project-explore-speed-mrna-vaccine-production-deployable-local-outbreaks#:~:text=The%20ambition%20is%20that%20taking%20a%20seamless,a%20novel%20outbreak%20or%20a%20pandemic%20threat][27].

In vitro transcription simplifies the production of mRNA vaccines, saving both time and cost. In vivo expression of mRNA also minimizes contamination risks from proteins or viruses. Since mRNA is translated directly in the cytoplasm without needing to enter the nucleus, it enables faster and more efficient protein expression than DNA-based vaccines [28].

After administration, into host cells, the mRNA is translated into immunogenic proteins, which are presented on MHC class I and II molecules, thereby inducing both humoral and cell-mediated immunity. Specifically, mRNA vaccines trigger CD8+ cytotoxic T-cell responses, which recognize antigens via MHC class I molecules and destroy infected cells. They also stimulate CD4+ T-cells, which activate B-cells and other immune cells to produce neutralizing antibodies. This well-regulated immune response helps prevent excessive inflammation and tissue damage. Ultimately, the activation of both the innate and adaptive immunity results in a robust and effective defense against the target disease. [29, 30]

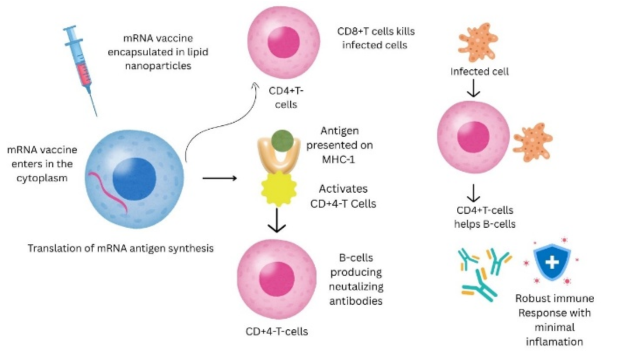

Figure 1: Molecular Mechanism of mRNA Vaccine: mRNA vaccines work by delivering mRNA inside lipid nanoparticles into the cells. The cells use this mRNA to make the antigen, which then activates both T cells and B cells to build immunity.

DESIGN AND CONSTRUCTIONS OF mRNA BASSED VACCINES

mRNA – Based vaccines are generally classified into two categories: conventional (non – replicating) and self-replicating (self-amplifying). Non-replicating mRNA constructs are smaller, simpler, and do not contains extra proteins that might trigger unintended immune responses [30]. These vaccines encode the immunogen of interest and typically include untranslated regions (UTRs) at the 5' and 3' ends, a 5' cap structure, and a 3' poly (A) tail. The 5' cap, a modified guanine nucleotide (7-methylgunosine, or m7G) attached to the mRNA'S 5' end, it blocks recognition by RNA sensors, preventing unwanted immune response. This cap also enhancing translation efficiency by facilitating ribosomes binding, supporting codon optimization, and suppressing Toll-like receptor recognition to reduce innate immune responses. The poly (A) tail, a long sequence of adenine nucleotides - added to the 3' end protects the mRNA from exonuclease degradation. Removal of impurities such as small oligo ribonucleotides and double-stranded RNA, is crucial to promoting protein synthesis. [31]

Two the untranslated regions (UTRs), although not coding for proteins, play an essential role in regulating gene expression by controlling the timing and level of protein production [32].

In contrast, self-Replicating mRNA vaccines are designed to replicate themselves within the host cells. They include sequences for viral replicase proteins such RNA-dependent RNA polymerase (RDRP), which enable the mRNA to replicate .This can significantly boost protein expression over time. However, excessive replication may sometimes suppress the expression of the desired immunogen [33]. The main advantage of self-Replicating mRNA is its ability to sustain high levels of protein production for longer and durations [34]. Furthermore, multiple gene sequences can be incorporated into a single replicon, enabling the vaccine to express multiple proteins with distinct functions, such as simultaneously inducing immunogenic and immune modulatory responses.

Self-replicating mRNA vaccines produces double-stranded RNA intermediates during replication that are recognized by cellular RNA sensors, such as including RIG-I (Retinoic Acid-Inducible Gene1) and MDA5 Melanoma Differentiation-Associated protein 5). These sensors detect the mRNA as foreign RNA, activating signalling pathways that lead to production of type I interferons (IFNα/β) and pro-inflammatory cytokines. This activation promotes a robust immune response, including the activation of dendritic cells, T-cells, and B-cells. [35]

Research indicates that self-replicating mRNA vaccines have intrinsic adjuvant properties, potentially inducing strong immune responses at lower doses. However, the role type I interferon (IFNα/β)are remains controversial- while they may enhance immune activation, excessive IFN-α/β responses can also suppress protective immunity.Thus,careful design is needed to balance immune stimulation without overstimulation [36].

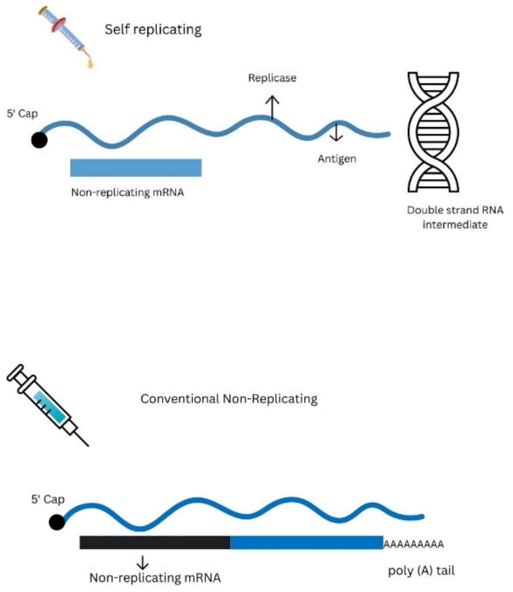

Figure 2: There are two types of mRNA vaccines, Conventional mRNA only makes the antigen, while self-replicating mRNA also carries instruction to copy itself, leading to stronger and longer lasting protein production

While non-replicating mRNA vaccines elicit good immune responses, their short half-life can limit prolonged protein expression. On the other hand, self-replicating mRNA provides extended antigen expression but poses challenges due to its larger size and reduce stability .A promising future alternative is circular RNA (circRNA) vaccines, which involves circularizing exogenous RNA to form a covalently closed loop. Circular RNAs are naturally occurring single – stranded molecules generated via back-splicing from liner RNA precursors. They offer improved stability and longer expression duration, making them ideal for durable protein and immunogen production. Current circRNA vaccine production includes linear RNA synthesis, RNA circularization, and encapsulation using delivery systems like lipid nanoparticles. Although still in preclinical stages, circRNA vaccines are gaining attention for their potential in treating emerging infectious diseases and tumors, and are being explored by both pharmaceutical industries and research institutions [37].

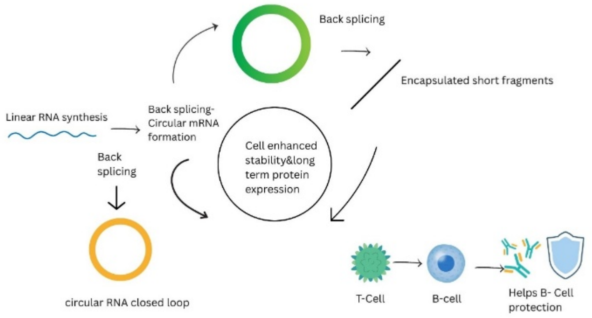

Figure 3: Circular mRNA Vaccine are made by joining the ends of linear RNA to form loop. This circular RNA is packed in lipid nanoparticles, stays stable for longer, and produces the antigen over an extended period to trigger immunity

DELIVERY SYSTEMS

The delivery of mRNA vaccines into cells present several challenges, primarily because mRNA is a highly unstable molecule that is rapidly degraded by extracellular ribonucleases (RNases) - enzymes found in body fluids that break down RNA through hydrolysis. To overcome this, researchers have explored various materials such as, lipids, lipid-like compounds, polymers, and protein derivatives to protect mRNA and facilitate its effective delivery [38].

Among these, Lipid nanoparticles (LNPs) are considered one of the most effective delivery vehicles. LNPs are composed of ionizable lipids, which are positively charged at low PH and neutral at physiological PH, enhancing their biocompatibility. [39] These nanoparticles deliver mRNA via endocytosis, a natural cellular process where the membrane engulfs particles. Once inside, LNPs are enclosed in endosomes. In the acidic environment of the endosome, the ionizable lipids become charged, destabilize the endosomal membrane, and release the mRNA into the cytoplasm. [40] [41]

Several cationic lipids, ionisable lipids, and other lipid formulations have been developed for mRNA – based vaccines. Frist, in vitro transcribed (IVT) mRNA is highly susceptible to rapid degradation by nucleases in biological environments, reducing its stability and efficacy. Second, in vitro transcribed mRNA (IVT) can trigger innate immune responses similar to those caused by pathogenic RNA, potentially leading to unwanted inflammation.

A promising solution to these challenges is the use of pseudouridine (ψ), a modified form of uridine. Pseudouridine naturally occurs in many cells and is more chemically stable than regular uridine. Incorporating pseudouridine into mRNA vaccines enhances stability increases resistance to RNase degradation, and reduces the risk of excessive immune activation [42].

The recent advancement in mRNA vaccine technology the research focused on alternative routes of administration and improving stability for broader applications, one such approach involves an inhalable mRNA delivery system by using Nano technology ,specifically hyper branched poly (Beta-amino esters).This method has demonstrated high protein expression in mice (example: luciferase protein expression in mice). It offers an effective strategy for combating respiratory infections by delivering mRNA directly to the lungs and triggering mucosal immune response. Another innovation includes the oral mRNA vaccine developed by BIoNTech and matinas Biopharma, which uses a lipid Nano crystal platform. This system encapsulates mRNA molecules through the interaction of calcium and anionic phospholipids, the oral route is Non-invasive, patient-friendly, and potentially fast to deploy [42] [43]

APPLICATIIONS IN MEDICINE

The mRNA vaccines have been used in numerous medical fields, including infectious diseases, cancer, genetic disorders, and regenerative medicines. mRNA has shown notable efficacy and safety against COVID – 19 and is being developed pathogens, including influenza, zika, rabies, HIV, and tuberculosis. These vaccines are designed to deliver mRNA into cells, instructing them to produce specific antigens that trigger the immune system to provide protection. They can targets multiple antigens or strains, making them effective against variants and co – infections.

mRNA vaccines for cancer therapy represents a next-generation treatment. mRNA can deliver tumour antigens, immune modulator, or gene editing components to trigger the antitumor immune responses or correct genetic defects in cancer patients [44]. Tumour cells express unique tumour antigens that trigger immune responses, making them valuable targets for mRNA-based therapies. Immune modulators like cytokines or checkpoint inhibitors, can enhance or regulate the immune responses. Gene-editing tools such as CRISPR-cas 9, TALEN, and Zinc – finger nucleases can alter the genome of targeted cells. Delivering mRNA encoding these molecules to tumour or immune cells can activate the immune responses or modify cancer-linked genes. [43] [45]

mRNA vaccines also have potential in treating genetic disorders by replacing faulty or missing proteins. For example, in haemophilia (a bleeding disorder) mutation affect clotting factor- encoding genes, cystic fibrosis results from mutations in the CFTR gene, and muscular dystrophy is due to mutations in the dystrophin gene. Delivering mRNA encoding these critical proteins to affected cells or tissues, can restored normal function and alleviate symptoms. [https://www.chop.edu/parents-pack/parents-pack-newsletter/feature-article-are-mrna-vaccines-type-gene-therapy][46]

mRNA based regenerative medicine has proven a significant role in repairing damaged cells and tissues. Various approaches including tissue engineering and cell based assays, have been developed to restore normal function. Proteins are essential molecules that regulate key cellular processes such as growth, differentiation proliferation, metabolism and apoptosis, while traditional protein deliver faces challenges due to low in vivo stability and limited activity mRNA technology offers a safer and more effective alternative by enabling therapeutic protein production directly at the repair site. [47]

GLOBAL AND REGIONAL UTILIZATION OF mRNA VACCINES

The global vaccine market, as highlighted in the world health organization's global vaccine market report (2023), remains heavily dominated by a small number of manufactures in 2022, just ten companies accounted for more than 85% of the global market value and nearly 75% of the vaccine doses produced worldwide https://www.who.int/publications/m/item/global-vaccine-market-report-2024[48] among them, Pfizer led the market, contributing around 36% of the total value, followed by modern with 15% - primarily due to their large-scale supply of mRNA –based COVID-19 vaccines. Other major players included Merck/MSD (9%). Glaxo smith Kline (8%), Sanofi (6) %, BIoNTech (3%) Johnsen& Johnsen (2%) and Asterazenceca (2%), each contributing to various segments of global immunization efforts.

When considering the world vaccine usage, population level data from Europe revealed that Pfizer BIoNTech accounted for over 40% of COVD-19 vaccine does administered, while moderna made up around 15%. This reflects both their production dominance and widespread acceptance due to early regulatory approvals and strong government procurement in high-income countries. https://ourworldindata.org/grapher/covid-vaccine-doses-by-manufacturer [49]

In terms of production volume, India's serum India (SII) emerged as one of the leading contributors, accounting, accounting for 24% of total global vaccine does, particularly those used in lower- and middle- income countries. While chain's CNBG contributed 3% by market value, other Indian manufactures like Bharat Biotech and Biological E also play a meaningful roles, especially in traditional vaccine segments. However, India footprint in the mRNA vaccine value in high – income countries, while nations like India took the lead in volume – based production of non-COVID vaccines, recognizing this imbalance, WHO calls for greater investment in regional manufacturing and more equitable vaccine distribution to improve global preparedness for future health emergencies. [50]

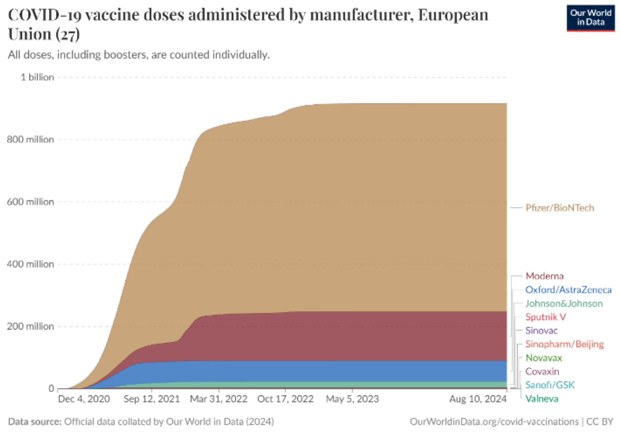

Figure 4 : COVID-19 vaccine doses administered by manufacturer In the European union (2022-2024) Pfizer/BIoNTech accounted for the majority of doses administered, followed by moderna, oxford/Astrezeneca,and Johnson& Johnson(Source: our world in data 2024)

Global vaccine market shared by manufacturer (2022)

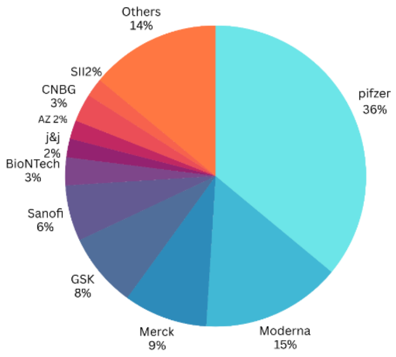

Figure 5: market share of leading vaccine manufacturer in 2022. Pfizer and moderna together accounted for over 50% of global vaccine market value, largely driven by the production of mRNA – based vaccines. Other players included Merck, Sanofi, BIoNTech, and Johnson&Johnsn. (Source WHO Global Market report, 2023)

CURRENT CHALLENGES

The preservation, storage and transportation are the essential aspect of mRNA therapeutics are critical components of the logistics chain and significantly contribute to the high cost of the final product. Unlike traditional vaccines based on inactivated microorganisms, which can be stored under refrigeration conditions (2◦-8◦ c) for six months [https://www.immunize.org/wp-content/uploads/guide/pdfs/vacc-adults-step3.pdf][54], current mRNA vaccines required ultra – low temperature storage, This poses substantial challenges for distribution especially in developing countries with limited cold chain infrastructure[51].

Maintaining physical, chemical, microbiological, and biological stability of vaccines during storage is essential.mRNA molecules are inherently unstable and highly sensitive to environmental conditions. Instability arises from both physical and chemical factors .physical instability includes loss of secondary and tertiary structure, aggregation, and precipitation, which can impair translation .chemically, mRNA is highly susceptible to hydrolysis and oxidation, leading to degradation. To mitigate these issues, research has focused on improving formulation and freezing conditions. LPN systems help minimize the chemical degradation, and cryoprotectants like sucrose are added to stabilize the mRNA –LNP formulation during freezing. For instance, both spikevax and comirnaty (COVID-19 vaccines) include 10% sucrose to protect LNP integrity. Initially, spikevax required storage at (-15◦ C to – 20◦ C), while comirnaty required (- 60◦ C to - 80◦ C), However, formulation advancements such as replacing phosphate-buffer saline (PBS) with tris as a buffering in comirnaty, have improved stability, allowing short- term storage at - 15◦ C to -25◦ C.

Lyophilisation (freeze-drying) is another promising approach for stabilizing mRNA vaccines at refrigeration temperature by removing water through sublimation. However, freezing and dehydration during lyophilisation can damage LNP structures, a notable example is GEMCOVAC-19, a lyophilized, lipoplex-based COVID-19 vaccine approved in India. It uses DOTAB and squalene, stabilized with sucrose, and reportedly remains stable for up to 21 months at room temperature, though detailed stability data is limited [52].

FUTURE DIRECTIONS IN mRNA VACCINE DESIGN: TYPES OF NEXT –GENERATION mRNA

The successful development of COVID-19 mRNA vaccines has paved the way for next generation mRNA technologies with enhanced expression and improved molecular stability, these advancements have also led to more efficient delivery systems in preclinical studies, accelerating clinical translation and expanding the potential application of mRNA vaccines in global healthcare.

Self-amplifying (SaRNA) is engineered a include a replicon derived from alphaviruses, allowing the encoded protein to be amplified within cells. This technology significantly reduces the required dosage effective doses range from 1 to 10 µg compared to 30 to 100 µg for conventional mRNAs used in SARS-COV-2 vaccines. The additional replicon gene in saRNA enhances immunogenicity but limits the inclusion of nucleotide modifications due to structural constraints. Despite this, several SaRNA candidates are currently in clinical trials. Preclinical studies on SARs- COV-2 saRNA vaccines have shown high levels of neutralizing antibody induction [53].

Trans-Amplifying RNA (taRNA)

Trans-amplifying RNA (taRNA) represents a promising next generation mRNA vaccine platform designed to improve efficiency, safety, and scalability. Unlike self-amplifying RNA (saRNA) vaccines, where both the replicase and antigen are encoded on a single long RNA molecule, taRNA separates the system into two components: one RNA encoding the replicase, and a second shorter "trans replicon" RNA encoding the antigen of interest. This bipartite design offers several advantages and was first explored by researchers using alphavirus based platforms (Beissert etal, 2020) [54] Like saRNA, taRNA leverages intracellular replication to amplify antigen expression, enabling strong immune responses with lower RNA doses. However, by decoupling the replicase from the antigen, taRNA overcomes many challenges faced by saRNA-such as the complexity, instability, and delivery issues associated with long RNA strands. This modular design also improves manufacturing flexibility and enhances safety by limiting non-target effects. (Beissert, T.etal, 2024) [55]

Recent preclinical studies have demonstrated that taRNA-based vaccines can generate strong immune responses using doses up to 40 times lower than conventional mRNA vaccines. This efficiency could significantly reduce production coast and enhance accessibility in low and middle-income countries (Kuchipudi etal, 2025) [56] this findings highlight taRNA potential as a scalable, affordable solution in future global immunization strategies.

A FUTURE PRESPECTIVE IN mRNA VACCINE DELIVERY

Recent advancement in mRNA delivery system aim to improve efficiency, reduce toxicity, and expand therapeutic applications. Lipid nanoparticle (LNPs) remains one of the most significant systems for mRNA delivery. However, future innovations are now exploring non-LNP alternatives For instance , retrovirus like PEG10 proteins, are gaining attention due to their minimal immune stimulation and toxicity[53].companies like entospharma have developed a fusogenic proteolipid vehicles, which combine properties of both proteins and lipids. This systems use low toxicity lipids along with fusion-associated small transmembrane proteins (FAST) to directly delivery mRNA into the cytoplasm. Additionally, redox – responsive peptides are being used to enable cytosolic delivery and redox- activated release of mRNA [57] [58].

Innovations in LNP formulations, such as incorporating heterocyclic unsaturated and alkyne lipids have been shown to enhanced efficacy. Structural modifications using thiol or bisphosphate groups further enable tissue- specific targeting, such as to mucus membranes or bone [59, 60].ionizable dendrimers are also emerging as simplified alternatives to the traditional four- component LNP systems, maintaining high delivery -component LNP system while maintaining high delivery efficiency. Exosomes, small vesicles derived from biological membranes, are being considered a breakthrough in mRNA delivery due to their natural origin, low immunogenicity, and ability to deliver mRNA effectively. clinical trials using engineered exosomes, especially in cancer therapies, have shown stronger immune responses compared to LNPs.Other biological membranes, such as bacterial outer membrane vesicles , are also being explored for similar purpose.[61] Current research also focuses on improving organ – and cell- type selectivity of mRNA delivery. Using nanotechnology, organ –selective nanoparticles are being designed to specifically target tissues such as the lungs, liver, or spleen, thereby improving the precision and effectiveness of treatment [60].Furthermore, non-traditional administration routes are under development, such as intra-vesicular, oral robotic pills, and inhalation – based delivery methods. These approaches aim to target difficult-to-reach body sites like the bladder, gastrointestinal tract, or lungs [62].

CONCLUSION

mRNA vaccine set a historic moment during COVID - 19 pandemic, the global response to COVID-19 emphasized the importance of collaboration and equity in health care, and also it proves the necessity of vaccination to ensure global health security. The major impact of the mRNA vaccine is manufacture and speed of development and strong immune responses, flexibility. The construction and design of both non-replicating and self-replicating types which brings a challenges from safety, delivery, and immune activation.Eventhough it has so many questions remains, research is improving how these vaccines are designed and delivered. mRNA vaccine technology holds the promise of next generation vaccines, Research shows that its potential not only infectious diseases-with growing applications in cancer, autoimmune disorders, and more, looking ahead, this discovery has the power to reshape global health care and move forward to a future of personalized and precise medicine

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