A Review On Vaccines On COVID-19 And Their Formulations

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Abstract - The coronavirus disease (COVID-19) pandemic, caused by the SARS-CoV-2 virus, has posed a major global health crisis, creating an urgent demand for effective preventive measures. Among all interventions, vaccination has proven to be the most powerful strategy for controlling viral transmission and reducing disease severity. This review highlights the development and advancement of various COVID-19 vaccines, emphasizing their mechanisms of action, formulation techniques, and immunological principles. It also explores the use of different platforms such as mRNA-based, vector-based, inactivated, and protein subunit vaccines, each offering distinct benefits and limitations. Furthermore, the article examines challenges related to vaccine distribution, storage, efficacy against emerging variants, and long-term immunity. In addition, novel formulation approaches and delivery systems are discussed as potential solutions to enhance vaccine stability, safety, and immune protection. Overall, this review provides valuable insights into the scientific progress, formulation strategies, and future perspectives of COVID-19 vaccine development.

Keywords: COVID-19, SARS-CoV-2, mRNA Vaccines, Viral Vector Vaccines, Formulations, Immunology, Vaccine Delivery Systems.

1. Introduction

Coronavirus disease 2019 (COVID-19) emerged in December 2019 in Wuhan, China, after clusters of pneumonia of unknown origin were linked to a novel coronavirus, later named SARS-CoV-2. Classified under the β-coronavirus genus, it is related to the viruses that caused SARS in 2002 and MERS in 2012. However, SARS-CoV-2 exhibited far greater transmissibility, a wide spectrum of clinical symptoms, and the ability to spread through asymptomatic carriers, allowing the infection to rapidly escalate into a global crisis. By March 11, 2020, the World Health Organization officially declared COVID-19 a pandemic as cases surged across continents and healthcare systems struggled with rising hospitalizations and fatalities.

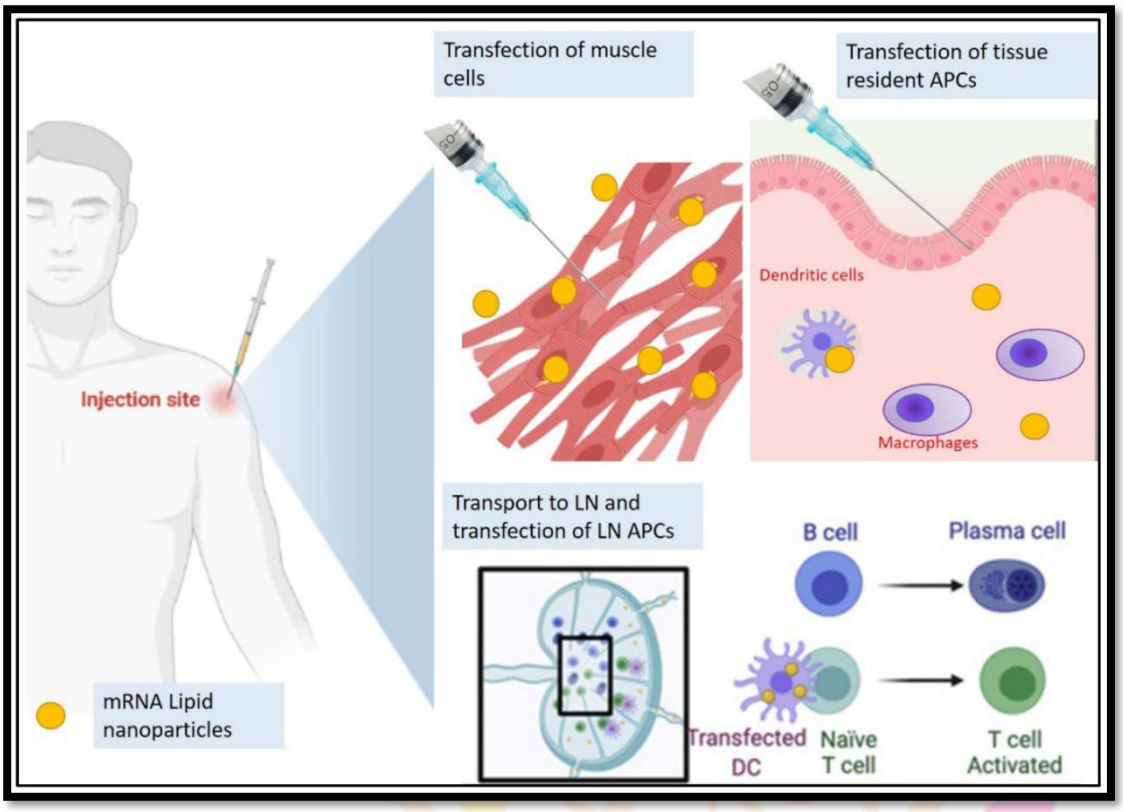

Figure 1: mRNA lipid nanoparticles' (mRNA-LNPs) site of intramuscular administration and modes of action of the mRNA-LNPs.

The pandemic triggered severe disruptions worldwide, affecting economies, education, mental health, and international travel. With no effective antiviral treatments available early in the outbreak, countries relied heavily on preventive strategies such as mask-wearing, social distancing, movement restrictions, and lockdowns. These interventions helped reduce transmission but provided only temporary relief, highlighting the urgent need for a long-term protective solution.

This urgency sparked an unprecedented global mobilization of scientific research, funding, and collaboration. Advances in genomic sequencing and existing knowledge from SARS and MERS research enabled rapid design of vaccines targeting the viral spike (S) protein. Within months, multiple vaccine platforms were developed—including mRNA vaccines, viral vector vaccines, inactivated virus vaccines, and protein subunit vaccines. These innovations marked a major milestone in vaccinology and played a crucial role in controlling the spread and severity of COVID-19 worldwide..

2. Mechanism of Action of COVID-19 Vaccines

COVID-19 vaccines work by training the immune system to recognize and fight SARS-CoV-2 without causing illness. Most vaccines focus on the spike (S) protein, the viral component that allows the virus to enter human cells.

2.1 Antigen Delivery

Vaccines introduce either the spike protein itself or genetic instructions to produce it. This familiarizes the immune system with the key viral antigen.

2.2 Immune Recognition

Antigen-presenting cells (APCs) take up the vaccine components and display spike protein fragments on their surface. This alerts the immune system and triggers both antibody and T-cell responses.

2.3. T-Helper Cell Activation

$CD4^+$ T cells recognize the presented antigen and release cytokines that coordinate the immune response, boosting both antibody production and cellular immunity.

2.4. Antibody Production

B cells, with T-cell support, differentiate into plasma cells that produce neutralizing antibodies. These antibodies block the spike protein, preventing viral entry. Memory B cells remain for long-term protection.

2.5. Cytotoxic T-Cell Response

$CD8^+$ T cells become activated and destroy infected cells, limiting viral replication and disease severity.

2.6. Platform-Specific Mechanisms

- **mRNA vaccines**: deliver mRNA that instructs cells to make the spike protein.
- **Viral vector vaccines**: use engineered adenoviruses to deliver spike-encoding DNA.
- **Inactivated vaccines**: contain killed viral particles that cannot replicate but still stimulate immunity.
- **Protein subunit vaccines**: supply purified spike protein fragments with adjuvants.

2.7. Immune Memory

Vaccination generates long-lasting memory B and T cells that provide fast, strong protection upon re-exposure..

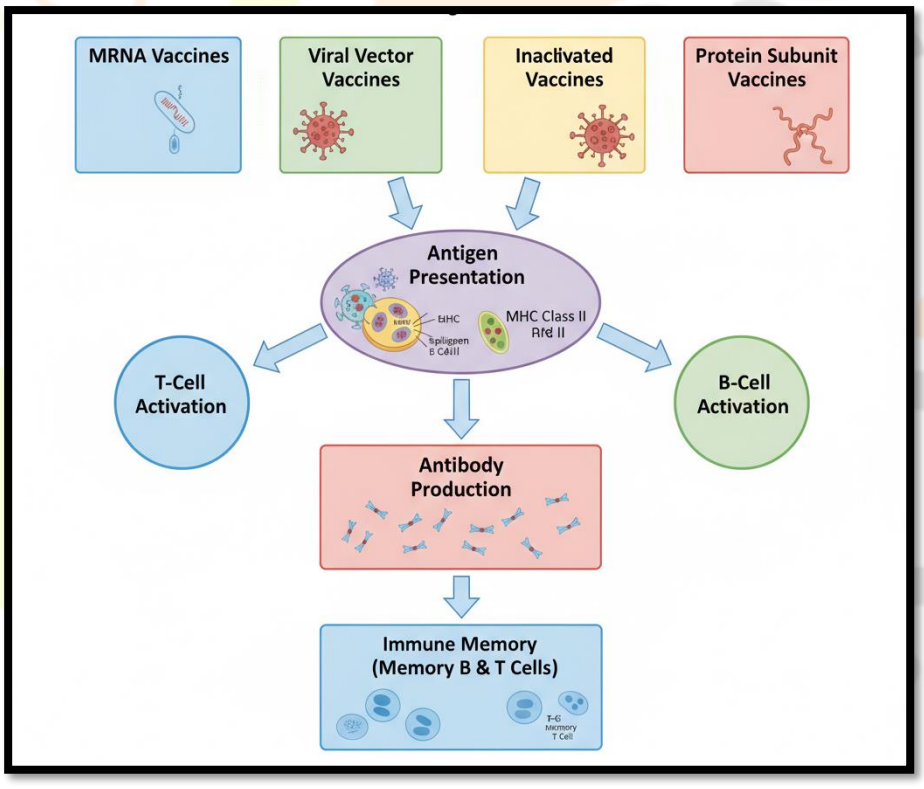

Figure 2: Mechanism of Action of COVID-19 Vaccines

3. Types of COVID-19 Vaccines

COVID-19 vaccines were developed using several advanced platforms, each designed to stimulate protective immunity against SARS-CoV-2 in different ways. The major vaccine types include mRNA vaccines, viral vector vaccines, inactivated virus vaccines, and protein subunit vaccines

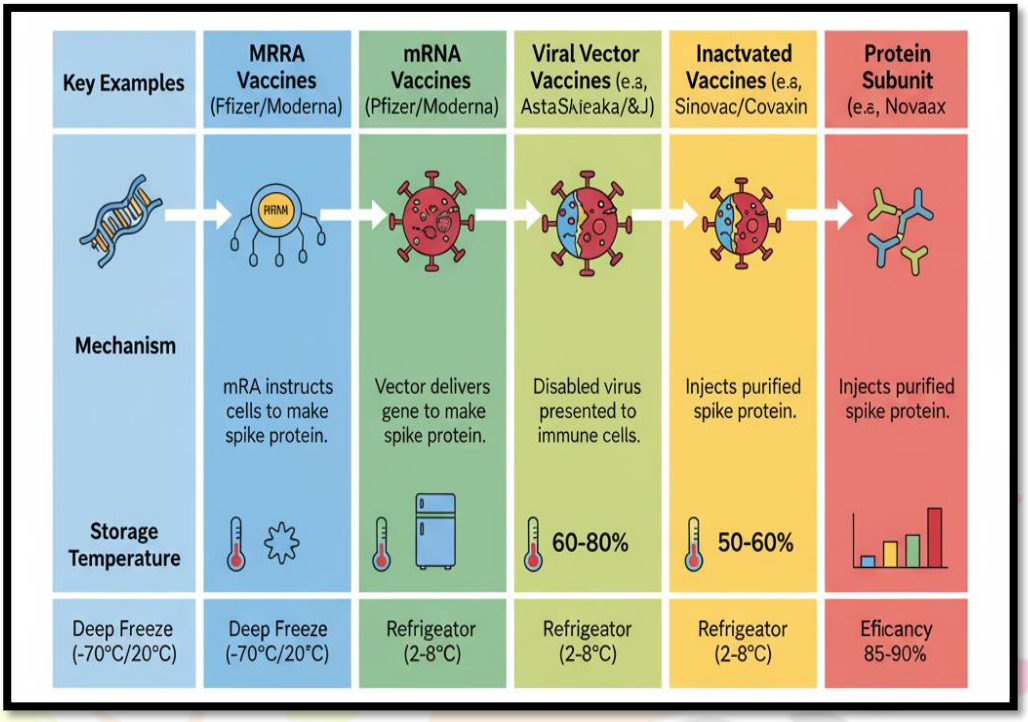

Figure 3: Classification and Development Platforms of COVID-19 Vaccines

3.1 mRNA Vaccines

Examples: Pfizer-Biotech (BNT162b2), Moderna (mRNA-1273)
These vaccines contain synthetic mRNA packed in lipid nanoparticles that instruct host cells to produce the viral spike protein. This triggers strong antibody and T-cell responses. They show over 90% efficacy and can be updated quickly for new variants. However, they require ultra-cold storage and may cause mild side effects such as fever and fatigue.

3.2 Viral Vector Vaccines

Examples: Oxford-AstraZeneca (ChAdOx1 nCoV-19), Johnson & Johnson (Ad26.COV2.S)
These use harmless, non-replicating adenoviruses to deliver DNA encoding the spike protein. Once inside cells, the DNA leads to spike protein production and activates both humoral and cellular immunity. They are easier to store (2–8°C) but may be less effective in people with pre-existing adenovirus immunity. Rare cases of blood clotting have been reported.

3.3 Inactivated Virus Vaccines

Examples: Covaxin, CoronaVac
these vaccines contain whole SARS-CoV-2 particles that are chemically or physically inactivated. They cannot replicate but still trigger antibody and T-cell responses. They are safe, stable at normal refrigerator temperatures, and offer broad immune protection. However, they often require booster doses and usually show slightly lower efficacy than mRNA or vector vaccines.

3.4 Protein Subunit Vaccines

Example: Novavax (NVX-CoV2373)
these vaccines deliver purified spike protein fragments combined with an adjuvant to enhance immune activity. They provide strong antibody responses, have an excellent safety profile, and are easy to store. Their drawbacks include complex manufacturing and the need for multiple doses to maintain protection.

4. Vaccine Formulations and Delivery Systems

Vaccine formulation is essential for maintaining stability, ensuring efficient delivery, and promoting strong immune responses. Each COVID-19 vaccine platform uses specialized components to protect the active ingredient and enhance immunogenicity.

4.1 Importance of Vaccine Formulation

A vaccine formulation includes the antigen (or genetic material), stabilizers, adjuvants, preservatives, and delivery systems. Proper formulation:

- Protects the active ingredient from degradation
- Enhances immune recognition
- Improves delivery to target cells
- Ensures adequate shelf life and global distribution Overall, formulation strongly influences vaccine safety, potency, and scalability.

4.2 mRNA Vaccine Formulations

mRNA vaccines (Pfizer-Biotech, Moderna) rely on lipid nanoparticles (LNPs) containing:

- **Ionizable lipids** for mRNA encapsulation and cell entry
- **Cholesterol** for structural stability
- **Phospholipids** to form the lipid bilayer
- **PEG** to prevent aggregation

4.3 Viral Vector Vaccine Formulations

Vaccines like AstraZeneca and Johnson & Johnson use non-replicating adenoviruses suspended in buffered solutions with stabilizers. These ingredients preserve viral integrity and allow storage at 2–8°C. Cryoprotectants help maintain stability during freezing and transport

4.4 Inactivated & Protein Subunit Vaccine Formulations

- **Inactivated vaccines** (Covaxin, Sinopharm):
  - Contain chemically or heat-inactivated SARS-CoV-2
  - Use aluminum-based adjuvants to enhance immune activation
  - Include stabilizers to prevent particle aggregation
- **Protein subunit vaccines (Novavax):**
  - Deliver purified spike protein with Matrix-M adjuvant
  - Generate strong antibody and T-cell responses
  - Available in liquid or freeze-dried forms for improved stability

4.5 Novel and Next-Generation Delivery Approaches

Emerging technologies aim to improve convenience and strengthen mucosal immunity:

- **Microneedle patches** enable painless, cold-chain-free self-administration.
- **Nasal sprays** target respiratory mucosa to boost local IgA defences.
- **Oral vaccines** use capsules or liquids for easy delivery to gut-associated immunity.
- **Nanoparticle and DNA vaccines** offer enhanced stability and adaptability to future variants.

4.6 Role of Adjuvants and Stabilizers

- **Adjuvants** (aluminum salts, sapiens, CpG, MF59) strengthen immune activation and memory formation.
- **Stabilizers** (sucrose, trehalose, polysorbate 80) protect vaccine components during storage, ensuring safety and extended shelf life.

Table 1 : Formulation Components of Different COVID-19 Vaccines

Vaccine	Delivery System	Adjuvants	Stabilizers / Preservatives	Storage Requirements (°C)
Pfizer-Biotech (BNT162b2)	Lipid nanoparticles (LNPs) encapsulating mRNA	None (immune stimulation via mRNA itself)	Polyethylene glycol (PEG), cholesterol, phospholipids, salts, sucrose	–70
Moderna (mRNA-1273)	Lipid nanoparticles containing nucleoside-modified mRNA	None	PEG, cholesterol, DSPC (phospholipid), tromethamine, sucrose	–20
Oxford-AstraZeneca (ChAdOx1 nCoV-19)	Non-replicating chimpanzee adenoviral vector	None (vector induces immune response)	Magnesium chloride, ethanol, polysorbate 80, sucrose	2–8
Johnson & Johnson (Ad26.COV2.S)	Human adenovirus serotype 26 vector	None	Citric acid monohydrate, polysorbate 80, sodium chloride	2–8
Covaxin (BBV152)	Inactivated whole SARS-CoV-2 virus	Aluminum hydroxide gel	2-phenoxyethanol, phosphate buffer, sodium chloride	2–8
Sinopharm (BBIBP-CorV)	Chemically inactivated SARS-CoV-2	Aluminum hydroxide	Disodium hydrogen phosphate, sodium dihydrogen phosphate, sodium chloride	2–8
Novavax (NVX-CoV2373)	Recombinant spike protein nanoparticles	Matrix-M (saponin-based adjuvant)	Polysorbate 80, sodium chloride, phosphate buffer	2–8

5. Global Vaccine Development and Distribution

The global response to COVID-19 vaccine development was one of the fastest and most coordinated public health efforts ever undertaken. Within months of identifying SARS-CoV-2, researchers and governments worldwide collaborated to design, test, and manufacture vaccines to curb transmission and mitigate the pandemic's health and economic impact.

5.1 Global Research and Development Efforts

- By 2021, more than 200 vaccine candidates were undergoing preclinical or clinical testing, reflecting strong international scientific cooperation.
- Modern platforms such as mRNA, viral vectors, inactivated virus, and protein subunits dramatically shortened development timelines.
- WHO, regulatory agencies, and research bodies streamlined clinical trials and safety monitoring to accelerate approvals.
- Companies like Pfizer-Biotech, Moderna, AstraZeneca, Johnson & Johnson, Sinovac, and Bharat Biotech led large-scale manufacturing, supported by academic and biotech partnerships.
- Global data sharing enabled rapid detection of variants and timely updates to vaccine formulations.

5.2 International Cooperation and COVAX

- The COVAX initiative (led by Gavi, CEPI, and WHO) aimed to ensure fair vaccine access for low- and middle-income countries.
- Through pooled purchasing and global partnerships, COVAX supplied billions of doses, reducing—though not eliminating—inequities.
- Barriers such as limited production capacity, export restrictions, and cold-chain demands affected distribution efficiency.

5.3 Key Challenges in Global Vaccine Deployment

1. Vaccine Hesitancy
Misinformation, cultural beliefs, and political influence fueled scepticism, slowing vaccination rates. Effective communication and community outreach remain essential.

2. Emerging Variants
Variants like Delta and Omicron reduced the effectiveness of earlier vaccines, requiring booster doses and updated formulations.

3. Inequitable Distribution
High-income countries acquired large supplies early, while many low-income regions faced delayed access and infrastructure limitations. Initiatives like COVAX and AVAT attempted to reduce disparities.

4. Manufacturing and Supply Chain Issues
Shortages of raw materials, intellectual property limits, and production bottlenecks hindered global supply. Technology transfer and regional manufacturing hubs helped improve long-term resilience.

5.4 Global Vaccination Campaigns and Impact

- Countries launched large-scale vaccination programs prioritizing healthcare workers, the elderly, and high-risk groups.
- Strategies varied globally, from centralized government-run systems to community-based outreach.
- By late 2022, billions of doses had been administered, leading to significant reductions in severe disease, hospitalizations, and deaths.
- Booster campaigns were introduced to maintain protection, especially during variant-driven surges.

Table 2: Global Vaccine Production and Distribution Statistics

Region	Major Vaccines Used	Total Doses Distributed (Million)	% Population Vaccinated (at least one dose)	Key Challenges
North America	Pfizer-Biotech, Moderna, Johnson & Johnson	1,200+	~80%	Vaccine hesitancy in rural areas; booster fatigue
Europe	Pfizer-Biotech, Moderna, AstraZeneca	1,800+	~75%	Supply-chain disruptions; variant-specific boosters
Asia	Covaxin, Sinovac, Sinopharm, AstraZeneca, Pfizer	6,000+	~70%	Population density; cold chain logistics; access inequality
Africa	Johnson & Johnson, AstraZeneca, Sinopharm	900+	~35%	Limited manufacturing; funding constraints; misinformation
South America	Pfizer-Biotech, Sinovac, AstraZeneca, Sputnik V	1,100+	~65%	Distribution disparities; inconsistent supply
Oceania	Pfizer-Biotech, Moderna, AstraZeneca	200+	~85%	Import dependency; logistical delays for remote areas

6. Role of Pharmacists in COVID-19 Pandemic

Pharmacists have played an indispensable role in combating the COVID-19 pandemic by serving as accessible healthcare professionals, ensuring the continuity of care, and contributing to public health efforts at multiple levels. Their responsibilities extended far beyond traditional dispensing duties, encompassing patient education, medication management, vaccine distribution, and participation in clinical research.

1. Public Health Education and Awareness:

Pharmacists were among the first points of contact for the public, providing accurate information about COVID-19 symptoms, preventive measures, and the importance of vaccination. They helped counter misinformation and promoted adherence to safety protocols such as mask-wearing, social distancing, and hygiene practices.

2. **Medication Management and Supply Chain Maintenance:**

Pharmacists ensured the uninterrupted supply of essential medicines, oxygen, and other medical supplies during lockdowns and supply chain disruptions. They managed drug inventories, prevented stockpiling, and provided guidance on appropriate medication use, especially for patients with chronic illnesses.

3. **Vaccine Storage, Distribution, and Administration:**

During mass immunization campaigns, pharmacists played a critical role in the **storage, handling, and administration of COVID-19 vaccines**. Their expertise in cold-chain management ensured vaccine stability and many pharmacists were directly involved in administering vaccines and monitoring post-vaccination adverse reactions.

4. **Telepharmacy and Patient Counselling:**

With restrictions on physical consultations, pharmacists adopted **telepharmacy services**, offering remote counselling to patients. They provided virtual medication reviews, dosage adjustments, and advice on managing side effects, ensuring continuity of pharmaceutical care during lockdowns.

5. **Pharmacovigilance and Clinical Support:**

Pharmacists actively contributed to **Pharmacovigilance programs** by reporting adverse drug reactions (ADRs) and vaccine-related side effects. In hospitals, clinical pharmacists collaborated with physicians to optimize COVID-19 treatment regimens, adjust dosages based on patient conditions, and prevent drug interactions.

6. **Research and Development Support:**

Many pharmacists participated in **clinical trials and research studies** related to antiviral drugs, vaccine formulations, and supportive therapies. Their knowledge of pharmacokinetics and formulation science supported the rapid evaluation and development of safe and effective treatments.

7. **Community Support and Mental Health Guidance:**

Pharmacists also served as sources of psychological support, offering reassurance and counselling to anxious patients and caregivers. Their community engagement helped maintain trust in healthcare systems during times of uncertainty.

7. Future Prospects

1. The future development of COVID-19 vaccines is focused on enhancing their **breadth, durability, and accessibility** to ensure sustained global protection against SARS-CoV-2 and its emerging variants. One of the most promising directions is the creation of **universal or pan-coronavirus vaccines** designed to target the **conserved regions of the viral genome**—those less likely to mutate. Such vaccines could provide **broad-spectrum protection** not only against existing SARS-CoV-2 variants but also against potential future coronaviruses with pandemic potential.
2. Improving the **thermo stability of mRNA vaccines** is another major research goal. Current mRNA formulations require ultra-cold storage, which limits their widespread distribution in low-resource settings. Advances in lipid nanoparticle technology, novel stabilizing agents, and freeze-drying (lyophilization) techniques are being explored to enable **room-temperature stability**, making global distribution more feasible and cost-effective.

3. Furthermore, the development of **pan-variant protection strategies**—including multivalent vaccines and adaptive formulations that can rapidly incorporate new variant sequences—is essential to maintain efficacy against evolving strains.
4. To achieve **long-term immunity**, ongoing measures such as **periodic booster doses**, **genomic surveillance**, and the use of **next-generation delivery systems** (such as intranasal, oral, or microneedle-based vaccines) will play a critical role. These approaches aim to strengthen both systemic and mucosal immunity, reduce transmission, and improve patient compliance.
5. Overall, the future of COVID-19 vaccination lies in **innovative vaccine design, improved stability, and global accessibility**, ensuring sustained protection and preparedness against future viral threats.

8. Conclusion

The rapid development of COVID-19 vaccines represents one of the most remarkable achievements in modern medical science. Through the combined use of mRNA, viral vector, inactivated, and protein subunit technologies, scientists successfully developed safe and effective vaccines in record time, significantly reducing global morbidity and mortality associated with SARS-CoV-2. These vaccines have not only curbed infection rates but have also demonstrated the power of global collaboration, innovation, and advanced biotechnology in combating pandemics. However, challenges such as unequal vaccine distribution, the emergence of new variants, and issues of vaccine hesitancy continue to hinder complete global control. Future research must focus on developing next-generation vaccines with broader variant coverage, enhanced stability, and more accessible delivery systems. The integration of novel approaches—such as intranasal and oral vaccines, thermostable formulations, and universal coronavirus vaccines—holds great promise for long-term pandemic preparedness. In conclusion, sustained global cooperation, continuous innovation, and equitable distribution will be essential to ensure comprehensive protection and a resilient future against evolving viral threats.

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