Available online on 15.09.2026 at http://jddtonline.info

Journal of Drug Delivery and Therapeutics

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Review Article

Nanotechnology-Enabled Therapeutics for Global Viral Diseases: From COVID-19 to Emerging Viral Infections

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Article Info:

Article History:

Received 20 June 2026
Reviewed 29 July 2026
Accepted 24 Aug 2026
Published 15 Sep 2026

Cite this article as:

Kumar A, Parihar AG, Nanotechnology-Enabled Therapeutics for Global Viral Diseases: From COVID-19 to Emerging Viral Infections, Journal of Drug Delivery and Therapeutics. 2026; 16(9):357-371 *DOI:* https://doi.org/10.22270/jddt.v16i9.8013

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Abstract

The threat of viral disease remains one of the biggest concerns regarding global public health, as is evident from the recent global pandemic caused by the coronavirus and the repeated outbreaks of new pathogens like influenza virus, Ebola virus, Zika virus, Nipah virus, monkey pox virus, and coronaviruses that are pathogenic. Traditional approaches to antiviral therapy may pose certain limitations, like poor bioavailability, systemic toxicity, mutation rate of the virus, multiple drug resistance, and the inability of drugs to target tissues specifically. The development of nanotechnology has been a breakthrough solution in overcoming the limitations posed by traditional methods. This review aims at assessing the latest advancements in the field of nanotechnology in terms of developing therapeutic interventions in viral diseases, especially COVID-19 and other emerging viral infections. These approaches improve drug stability, bioavailability, controlled drug delivery, and immunogenicity, all while minimizing toxicity in the body. Despite the fact that there are several promising applications for nanomedicines in both pre-clinical and clinical studies, issues pertaining to biosafety, scalability, and regulation prevent their full clinical implementation. Nanotechnology-based treatments constitute a paradigm shift within antiviral medicine with respect to their integration of targeted drug delivery, immune manipulation, and precision medicine. It is important that further interdisciplinary efforts, regulation, and clinical trials contribute to the development of such nanotechnologies to combat viral pandemics in the present and in the future.

Keywords: Nanotechnology; Viral infections; COVID-19; Antiviral drug delivery; Nanovaccines.

1. INTRODUCTION

Viral diseases continue to be one of the leading public health threats to global health due to the morbidity, mortality, and socio-economic consequences that come along with them. The fast emergence and re-emergence of viral pathogens in recent years have underscored the need for innovation in treatment and prevention approaches. In the case of the COVID-19 pandemic, the speed at which the virus spread worldwide has emphasized how unprepared we were when it comes to the current methods of antiviral treatment. Not only SARS-CoV-2 but other viruses including the influenza viruses, HIV, HBV, HCV, dengue, Zika, Ebola, Nipah, RSV, and monkeypox viruses continue to be a threat to regional and global health. The increasing globalization, climate change, urbanization, international travels, ecological changes, and human-animal interactions have further accelerated the emergence of viral infections from animals. Despite remarkable advances in virology, immunology, and pharmaceutical sciences, conventional antiviral therapies continue to face multiple challenges. These limitations underscore the necessity for innovative therapeutic platforms capable of improving drug delivery, enhancing antiviral efficacy, and enabling rapid responses to newly emerging viral pathogens[1-2].

One of the most successful methods that have been discovered is nanotechnology. It works by modifying substances at the nanolevel (usually between 1-100 nm). This allows for a fine regulation of the physicochemical properties of substances, including such as size, surface charge, structure, capacity of loading with the drug, and its release. Nanovehicles allow increasing the solubility and stability of antiviral drugs, protecting sensitive compounds from any premature destruction, targeting them to the infected area and drug delivery over time. The unprecedented success of lipid nanoparticle (LNP)-based mRNA vaccines during the COVID-19 pandemic firmly established nanotechnology as a cornerstone of modern antiviral medicine and accelerated research into advanced nanotherapeutic platforms for future viral outbreaks[3].

1.1 Global Burden of Viral Diseases

Viral infections continue to account for millions of illnesses and deaths annually, affecting individuals

across all age groups and geographic regions. Respiratory viruses such as influenza viruses, SARS-CoV-2, and RSV remain major causes of hospitalization and mortality, particularly among elderly individuals, young children, pregnant women, and immunocompromised patients. Chronic viral infections, including HIV, HBV, and HCV, continue to impose a substantial long-term healthcare burden through progressive liver disease, acquired immunodeficiency syndrome (AIDS), hepatocellular carcinoma, and other chronic complications. Vector-borne viruses such as dengue, chikungunya, Zika, and yellow fever have expanded their geographical distribution owing to climate change and increased vector proliferation, threatening billions of people worldwide. Emerging and re-emerging zoonotic viruses have become increasingly frequent over the past two decades. Furthermore, increasing international travel and global trade facilitate the rapid dissemination of infectious agents, emphasizing the need for universally adaptable therapeutic platforms capable of responding to diverse viral threats[4].

1.2 Challenges in Conventional Antiviral Therapies

Although several antiviral drugs have significantly improved patient outcomes, conventional antiviral therapies possess inherent limitations that restrict their overall clinical effectiveness. Many antiviral agents suffer from poor aqueous solubility, rapid systemic clearance, low oral bioavailability, and inadequate penetration into infected tissues, necessitating frequent administration and higher therapeutic doses. These pharmacokinetic limitations often increase the risk of systemic toxicity and reduce patient compliance. Another major challenge is the extraordinary genetic variability of viruses. RNA viruses possess high mutation rates that facilitate the rapid emergence of antiviral resistance, diminishing therapeutic efficacy and necessitating continual development of new antiviral agents. Viral latency, intracellular persistence, immune evasion mechanisms, and bioanatomical barriers further complicate treatment strategies. In addition, many conventional antivirals exhibit limited specificity, increasing the likelihood of adverse effects due to interactions with host cellular pathways.

The development of broad-spectrum antiviral drugs remains difficult because different viral families exhibit distinct replication mechanisms and molecular targets. Furthermore, antiviral drug discovery is often time-consuming and expensive, limiting rapid responses during newly emerging outbreaks. These challenges highlight the necessity for innovative drug delivery systems capable of enhancing therapeutic concentrations at sites of infection while minimizing systemic exposure and toxicity[5-6].

1.3 Emergence of Nanotechnology in Antiviral Medicine

Nanotechnology has transformed antiviral medicine by providing highly versatile platforms for targeted drug delivery, vaccine development, molecular diagnostics, and antiviral immunotherapy. Owing to their nanoscale dimensions and tunable surface characteristics, nanoparticles can efficiently encapsulate small-molecule drugs, nucleic acids, proteins, peptides, and immunomodulatory agents while protecting them from enzymatic degradation and premature elimination. Surface functionalization with targeting ligands enables selective accumulation within infected tissues or immune cells, thereby improving therapeutic efficacy and reducing off-target toxicity. A broad range of nanocarriers-including lipid nanoparticles, liposomes, polymeric nanoparticles, dendrimers, metallic nanoparticles, mesoporous silica nanoparticles, nanogels, extracellular vesicles, and virus-like nanoparticles-have demonstrated significant antiviral potential against both acute and chronic viral infections. These systems support controlled drug release, enhanced cellular uptake, prolonged circulation, and combination therapies that simultaneously target multiple stages of the viral life cycle. Beyond drug delivery, nanotechnology has played a transformative role in vaccine science[6]. Lipid nanoparticle-mediated delivery of messenger RNA enabled the rapid development, high efficacy, and global deployment of COVID-19 vaccines, demonstrating the clinical feasibility of nanomedicine on an unprecedented scale. Nanotechnology also facilitates RNA interference (RNAi), CRISPR-based antiviral gene editing, immunomodulation, and multifunctional theranostic platforms integrating diagnosis and therapy within a single nanosystem.

Although significant progress has been made, there are several issues that must be addressed before the technology becomes clinically feasible. The long-term safety of the nanoparticles, their biodistribution, immunocompatibility, manufacturing, quality control, regulations, and cost-effectiveness all need to be further studied. However, advances in materials science, biotechnology, artificial intelligence-enabled nanoparticle engineering, and precision medicine will help facilitate this process. Collectively, these developments position nanotechnology as a powerful and adaptable platform capable of addressing current viral diseases while strengthening global preparedness for future emerging infectious threats[6-7].

2. PATHOGENESIS OF VIRAL INFECTIONS AND THERAPEUTIC TARGETS

It is essential to understand the process of pathogenesis involved in viral infections to formulate effective antiviral therapies. Viral infections are the result of an interaction between the modes of replication of virus, response of the host cells to the virus, and tissue pathology. Once a virus enters the body, it uses the cellular machinery for replication and spread while avoiding the attacks of innate and adaptive immunity. Several factors influence the severity of viral infections, which include the virulence of virus, viral inoculum, tissue tropism, genetic predisposition of the host, immunity of the host, and the presence of co-morbidities. There are several stages of infection that are common among all viruses. These stages represent important therapeutic targets for antiviral intervention.

Furthermore, dysregulated immune responses, particularly excessive inflammatory cytokine production, contribute significantly to disease progression and organ damage, highlighting additional opportunities for immunomodulatory therapies[8].

2.1 Viral Structure and Life Cycle

Viruses are obligate intracellular pathogens composed of genetic material enclosed within a protective protein capsid, with many clinically important viruses also possessing a lipid envelope derived from host cell membranes. Their genomes consist of either DNA or RNA, which may be single-stranded or double-stranded and organized in linear, circular, or segmented forms. Structural proteins facilitate host-cell recognition and entry, while non-structural proteins regulate genome replication, transcription, immune evasion, and viral assembly. The viral life cycle begins with attachment to specific receptors expressed on susceptible host cells. Viral surface proteins recognize host receptors with high specificity, determining tissue tropism and host range. Following receptor binding, viruses enter cells through membrane fusion, receptor-mediated endocytosis, macropinocytosis, or direct penetration. After internalization, viral particles undergo uncoating, releasing the viral genome into the cytoplasm or nucleus depending on the virus. Genome replication and transcription subsequently occur using either host enzymes or virus-encoded polymerases. DNA viruses generally replicate within the nucleus, whereas most RNA viruses replicate in the cytoplasm.

Each stage of the viral life cycle represents a potential therapeutic target. Entry inhibitors prevent receptor binding or membrane fusion, polymerase inhibitors suppress viral genome replication, protease inhibitors interfere with viral protein maturation, while neuraminidase or budding inhibitors block viral release. Understanding these molecular events forms the foundation for the rational design of targeted antiviral therapeutics and nanotechnology-based drug delivery systems[9-10].

2.2 Host–Virus Interactions

The process of infection is based on complicated interactions between the viral proteins and cellular pathways of the host organism. After the penetration into the host cells, viruses utilize many biological processes in order to replicate themselves, while at the same time interfering with the processes of defense against the viruses. Viruses control the transcription, metabolism, membrane trafficking, and protein synthesis in order to maximize their reproduction. Innate immunity constitutes the primary line of defense against viruses. Pattern recognition receptors (PRRs), such as Toll-like receptors (TLRs), RIG-I-like receptors (RLRs), and NOD-like receptors (NLRs), recognize viral nucleic acids and initiate signaling through NF-κB, IRF3, and IRF7. These pathways stimulate production of type I and type III interferons (IFNs), pro-inflammatory cytokines, and chemokines that establish an antiviral state and recruit immune cells to infected tissues. However, viruses have evolved sophisticated immune-evasion mechanisms.

Many viruses inhibit interferon signaling, suppress antigen presentation, prevent apoptosis of infected cells, interfere with autophagy, and alter cytokine production (Fig. 1). Some viruses establish latent infections or persist within immune-privileged sites, allowing long-term survival despite host immune surveillance. Others undergo frequent antigenic variation through mutation or genetic reassortment, enabling escape from neutralizing antibodies and reducing vaccine effectiveness[11]

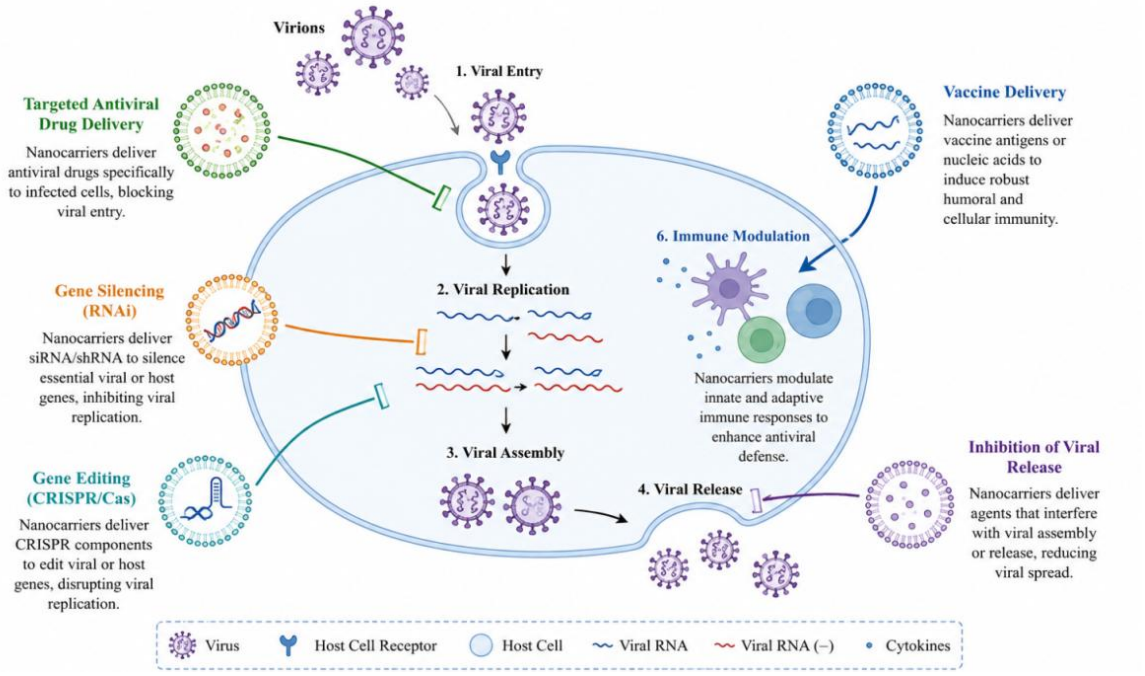

Figure 1. Mechanisms of nanotechnology-enabled therapeutics against viral infections. Schematic illustration of viral entry, replication, assembly, and release, highlighting the role of nanocarriers in targeted antiviral drug delivery, inhibition of viral replication, immune modulation, gene silencing, and vaccine delivery.

Adaptive immunity further contributes to viral clearance through virus-specific $CD8^+$ cytotoxic T lymphocytes, $CD4^+$ helper T cells, and neutralizing antibodies produced by B lymphocytes. Nevertheless, prolonged antigen exposure may lead to T-cell exhaustion, impaired immune function, and persistent viral infection. The balance between effective antiviral immunity and excessive inflammation ultimately determines clinical outcomes and disease severity.

2.3 Immune Response and Cytokine Storm

The immune response plays a dual role during viral infections by limiting viral replication while simultaneously contributing to tissue injury when dysregulated. Early antiviral defense involves activation of interferons, macrophages, dendritic cells, natural killer (NK) cells, and complement proteins that collectively suppress viral spread and promote adaptive immune activation. Under physiological conditions, inflammatory cytokines facilitate viral clearance by recruiting leukocytes to infected tissues and coordinating antiviral immune responses. However, severe viral infections may trigger uncontrolled cytokine production, commonly referred to as a cytokine storm. This hyperinflammatory syndrome is characterized by excessive release of cytokines and chemokines, including interleukin-6 (IL-6), interleukin-1β (IL-1β), tumor necrosis factor-alpha (TNF-α), interferon-gamma (IFN-γ), granulocyte-macrophage colony-stimulating factor (GM-CSF), CXCL10, and CCL2. Cytokine storms contribute to increased vascular permeability, endothelial dysfunction, coagulation abnormalities, oxidative stress, immune cell infiltration, and widespread tissue damage. In respiratory viral infections such as COVID-19 and severe influenza, excessive pulmonary inflammation may progress to diffuse alveolar damage, acute respiratory distress syndrome (ARDS), respiratory failure, and multiorgan dysfunction. Similar hyperinflammatory responses have also been reported in infections caused by Ebola virus, dengue virus, Nipah virus, and other highly pathogenic viruses[12-13].

2.4 Molecular Targets for Antiviral Therapy

Identification of critical molecular targets has transformed antiviral drug development. Therapeutic strategies are designed either to inhibit essential viral proteins or to modulate host cellular pathways required for viral replication. Because viruses depend extensively on host biological machinery, both virus-directed and host-directed therapeutic approaches have gained considerable attention.

Host-derived therapeutic targets include:

- ACE2 and TMPRSS2 involved in coronavirus entry.
- Endosomal acidification pathways required for viral uncoating.
- Host lipid metabolism supporting viral replication.
- PI3K/Akt/mTOR signaling pathways.
- JAK/STAT signaling.
- NF-κB-mediated inflammatory pathways.
- Autophagy-related proteins.
- Interferon signaling cascades.
- Cytokines such as IL-6, IL-1β, and TNF-α[14-15].

Targeting host pathways offers advantages because host genes mutate less frequently than viral genomes, thereby reducing the likelihood of resistance. However, host-directed therapies require careful optimization to minimize toxicity and preserve normal physiological functions. Nanotechnology enhances these molecular-targeting strategies by facilitating intracellular delivery of small molecules, monoclonal antibodies, peptides, messenger RNA (mRNA), small interfering RNA (siRNA), CRISPR-Cas systems, and gene-editing components. Surface-modified nanoparticles further enable receptor-specific targeting and controlled release, significantly improving therapeutic precision[16].

2.5 Challenges in Treating Emerging Viral Diseases

The treatment of newly emerging viral pathogens poses several difficulties due to their unpredictable epidemiology, fast spread, lack of knowledge about their biology, and lack of drugs. In particular, new viruses often arise due to spillovers, whereby viruses infecting animals gain the capability to infect people. The growing number of global travelers, cities, changes in the climate, ecological disturbances, and contacts between wildlife and people have intensified the occurrence of these types of outbreaks. The first challenge is associated with the fast mutation of many RNA viruses, leading to the constant appearance of new strains with new transmissibility, virulence, and sensitivity to antivirals. Often, viral mutations make vaccines less effective and increase the resistance to drugs. Another significant difficulty is connected with a very long development of new antiviral drugs. During rapidly evolving outbreaks, these timelines are often incompatible with urgent public health needs. Furthermore, broad-spectrum antivirals effective against multiple viral families remain scarce because viruses utilize diverse replication mechanisms and host interactions.

Emerging viral infections also exhibit considerable clinical heterogeneity, ranging from asymptomatic infection to fulminant multiorgan failure. Differences in host genetics, age, immune competence, and comorbid conditions further complicate therapeutic decision-making. Limited healthcare infrastructure in resource-constrained regions, inequitable access to medicines, manufacturing bottlenecks, and regulatory challenges additionally hinder effective outbreak control. Nanotechnology provides several potential solutions to these challenges. Nanocarriers can accelerate reformulation of existing antiviral agents, improve targeted drug delivery, enable combination therapies, facilitate rapid vaccine development, and support nucleic acid-based therapeutics adaptable to newly emerging viral variants. Advances in biomimetic nanoparticles, multifunctional nanoplatforms, artificial intelligence-assisted nanomedicine design, and personalized antiviral therapeutics are expected to play

increasingly important roles in future pandemic preparedness[17-18].

3. NANOTECHNOLOGY-BASED THERAPEUTIC PLATFORMS

Nanotechnology has emerged as a transformative approach in modern antiviral therapy, offering innovative solutions to overcome the limitations of conventional drug delivery systems. The nanoscale dimension (1–100 nm) enables unique physicochemical properties such as high surface-area-to-volume ratio, tunable surface chemistry, enhanced permeability, and controlled drug release. These features allow nanocarriers to improve the solubility, stability, bioavailability, and targeted delivery of antiviral agents. In the context of viral diseases, nanotechnology not only enhances pharmacokinetics and pharmacodynamics but also enables site-specific delivery to infected tissues, intracellular compartments, and immune cells, thereby improving therapeutic efficacy while minimizing systemic toxicity.

Nanomedicine-based platforms are particularly valuable in antiviral therapy due to the intracellular nature of viral replication. Since viruses exploit host cellular machinery, effective treatment requires drug delivery systems capable of penetrating biological barriers, entering infected cells, and releasing therapeutic payloads in a controlled manner. Additionally, nanotechnology facilitates the co-delivery of multiple therapeutic agents, including antiviral drugs, immunomodulators, nucleic acids, and vaccine antigens, enabling synergistic therapeutic strategies. These advantages have positioned nanotechnology as a cornerstone in next-generation antiviral drug development and pandemic preparedness[19].

3.1 Fundamentals of Nanomedicine for Viral Diseases

Nanomedicine refers to the application of nanotechnology in the diagnosis, prevention, and treatment of diseases at the molecular and cellular levels. In viral infections, nanomedicine aims to interfere with viral entry, replication, assembly, and release while simultaneously modulating host immune responses. The fundamental principle underlying nanomedicine is the ability to engineer nanoscale carriers that can interact with biological systems in a highly controlled and predictable manner. One of the key advantages of nanomedicine in antiviral therapy is improved drug solubility and stability. Many antiviral compounds suffer from poor aqueous solubility, rapid degradation, or limited bioavailability. Encapsulation within nanocarriers protects these drugs from enzymatic degradation and premature clearance, thereby enhancing their therapeutic half-life. Furthermore, nanocarriers can be functionalized with ligands such as antibodies, peptides, or aptamers to achieve active targeting of virus-infected cells or specific tissues such as the lungs, liver, or lymphatic system. Nanomedicine also plays a critical role in vaccine development. Nanoparticles can serve as antigen delivery systems and immune adjuvants, enhancing antigen presentation and stimulating robust humoral and cellular immune responses. Lipid nanoparticles, for example, have been instrumental in the success of mRNA vaccines against SARS-CoV-2, demonstrating the clinical relevance of nanotechnology in infectious disease control.

3.2 Classification of Nanocarriers

Nanocarriers are broadly classified based on their composition, structure, and functional properties. Each type offers distinct advantages in antiviral drug delivery, depending on the therapeutic requirements and biological environment[20].

Liposomes

Liposomes are spherical vesicles composed of one or more phospholipid bilayers enclosing an aqueous core. Their amphiphilic structure allows encapsulation of both hydrophilic and hydrophobic drugs. Liposomes are biocompatible, biodegradable, and capable of reducing drug toxicity while enhancing circulation time. In antiviral therapy, liposomes have been used to deliver nucleic acids, antiviral drugs, and vaccine antigens. Surface modification with polyethylene glycol (PEG) or targeting ligands further improves their stability and specificity.

Polymeric Nanoparticles

Polymeric nanoparticles are solid colloidal systems made from natural or synthetic polymers such as PLGA, chitosan, alginate, and polyethyleneimine. These nanoparticles offer controlled and sustained drug release, high structural stability, and tunable degradation rates. They are widely used for encapsulating antiviral drugs and gene therapy agents. Their surface can be engineered for targeted delivery to infected cells or immune tissues.

Solid Lipid Nanoparticles (SLNs)

SLNs are composed of solid lipids stabilized by surfactants. They combine the advantages of liposomes and polymeric nanoparticles while offering improved physical stability and controlled drug release. SLNs are particularly useful for delivering lipophilic antiviral drugs and protecting them from degradation. Their lipid-based structure enhances biocompatibility and reduces toxicity.

Nanostructured Lipid Carriers (NLCs)

NLCs are second-generation lipid nanoparticles composed of a mixture of solid and liquid lipids. This hybrid structure creates imperfections in the lipid matrix, allowing higher drug loading capacity and improved release profiles compared to SLNs. NLCs are effective in enhancing the bioavailability of poorly soluble antiviral agents and improving intracellular delivery.

Dendrimers

Dendrimers are highly branched, tree-like macromolecules with well-defined size, shape, and surface functionality. Their multivalent surface allows attachment of multiple drug molecules or targeting

ligands. Dendrimers exhibit strong antiviral activity by inhibiting viral entry and replication, in addition to serving as drug carriers. Their ability to interact with viral particles makes them promising candidates for broad-spectrum antiviral applications.

Micelles

Polymeric micelles are self-assembled nanostructures formed by amphiphilic block copolymers in aqueous environments. They possess a hydrophobic core for drug encapsulation and a hydrophilic shell for stability. Micelles are particularly useful for delivering hydrophobic antiviral drugs and improving their solubility and circulation time.

Metallic Nanoparticles

Metallic nanoparticles such as gold, silver, zinc oxide, and selenium nanoparticles exhibit unique optical, electronic, and antimicrobial properties. In antiviral applications, they can inhibit viral attachment, entry, and replication through direct interaction with viral proteins or genetic material. Additionally, they can serve as diagnostic tools and drug delivery platforms[21-23].

Table 2. Recent preclinical, clinical, and approved nanotechnology-based therapeutics and vaccines for COVID-19 and other emerging viral infections, highlighting nanoplatform, therapeutic payload, target virus, development status, and key outcomes

Nanoplatform	Therapeutic Payload / Vaccine	Target Virus	Development Status	Key Outcomes	Ref.
Lipid Nanoparticles (LNPs)	mRNA-1273 (Spike protein mRNA)	SARS-CoV-2 (COVID-19)	Approved	High protective efficacy, strong neutralizing antibody and T-cell responses, reduced hospitalization and mortality.	[24]
Lipid Nanoparticles (LNPs)	BNT162b2 (Spike protein mRNA)	SARS-CoV-2	Approved	Rapid immune activation, >90% efficacy against original strains, scalable manufacturing, favorable safety profile.	
Lipid Nanoparticles	Self-amplifying mRNA vaccines	SARS-CoV-2	Clinical/Phase II–III	Enhanced antigen expression with lower mRNA dose, prolonged immune response.	
Liposomes	Remdesivir liposomal formulation	SARS-CoV-2	Preclinical	Improved pulmonary drug delivery, sustained release, enhanced intracellular antiviral activity, reduced systemic toxicity.	[25]
Polymeric Nanoparticles (PLGA)	Favipiravir-loaded nanoparticles	SARS-CoV-2	Preclinical	Controlled drug release, improved bioavailability, prolonged circulation, enhanced antiviral efficacy.	
Nanostructured Lipid Carriers (NLCs)	Molnupiravir-loaded NLCs	SARS-CoV-2	Preclinical	Sustained drug release, improved oral bioavailability, enhanced therapeutic efficacy.	
Liposomes	Recombinant glycoprotein vaccine	Marburg virus	Preclinical	Enhanced antigen delivery, robust humoral and cellular immune responses.	[26]
Virus-Like Nanoparticles	Recombinant VLP vaccine	Lassa virus	Preclinical	Induced protective immune responses and long-term immunological memory.	[26]

Mesoporous Silica Nanoparticles (MSNs)

MSNs are characterized by highly ordered porous structures with large surface areas and tunable pore sizes. These features allow high drug loading capacity and controlled release kinetics. MSNs can be functionalized with targeting ligands and stimuli-responsive coatings, making them versatile platforms for antiviral drug delivery and gene therapy.

Extracellular Vesicles and Biomimetic Nanocarriers

Extracellular vesicles (EVs), including exosomes, are naturally occurring nanoscale particles involved in intercellular communication. Their biocompatibility, low immunogenicity, and inherent targeting ability make them attractive drug delivery systems. Biomimetic nanocarriers, which mimic natural cell membranes, further enhance immune evasion and targeting efficiency. These systems are increasingly explored for

delivering antiviral drugs, RNA therapeutics, and vaccines.

3.3 Physicochemical Properties Influencing Antiviral Performance

The therapeutic efficacy of nanocarriers is strongly influenced by their physicochemical properties, including size, shape, surface charge, hydrophobicity, and stability. Particle size determines biodistribution, cellular uptake, and tissue penetration. Nanoparticles in the range of 10–200 nm are generally optimal for systemic circulation and cellular internalization. Surface charge plays a critical role in interactions with biological membranes. Positively charged nanoparticles exhibit enhanced cellular uptake due to electrostatic interactions with negatively charged cell membranes, although they may also induce higher cytotoxicity. Neutral or slightly negative nanoparticles tend to have improved biocompatibility and longer circulation times. Shape also influences biological behavior, with spherical nanoparticles generally showing efficient uptake, while rod-shaped or filamentous particles may exhibit prolonged circulation. Surface hydrophobicity affects protein adsorption, immune recognition, and clearance by the mononuclear phagocyte system.

Colloidal stability is essential for maintaining nanoparticle integrity in physiological environments. Aggregation can reduce therapeutic efficacy and increase toxicity. Therefore, surface modification strategies such as PEGylation are commonly employed to enhance stability and reduce immune recognition[28-29].

3.4 Cellular Uptake and Intracellular Drug Delivery

Efficient cellular uptake is essential for antiviral nanocarriers, as most viral replication processes occur intracellularly. Nanoparticles enter cells primarily through endocytic pathways, including clathrin-mediated endocytosis, caveolae-mediated endocytosis, macropinocytosis, and phagocytosis. The uptake mechanism depends on particle size, shape, surface chemistry, and cell type. Once internalized, nanoparticles are typically trafficked to endosomes and lysosomes. To ensure therapeutic efficacy, nanocarriers must escape endosomal compartments and release their payload into the cytoplasm or nucleus. Various strategies, such as pH-sensitive materials, proton sponge effect, and membrane-disruptive peptides, are employed to facilitate endosomal escape.

Intracellular drug delivery enables direct interaction with viral replication machinery, including polymerases, proteases, and nucleic acids. Nanocarriers can also deliver siRNA, mRNA, and CRISPR-Cas systems to silence viral genes or edit host factors required for viral replication. This level of precision significantly enhances antiviral efficacy while reducing off-target effects.

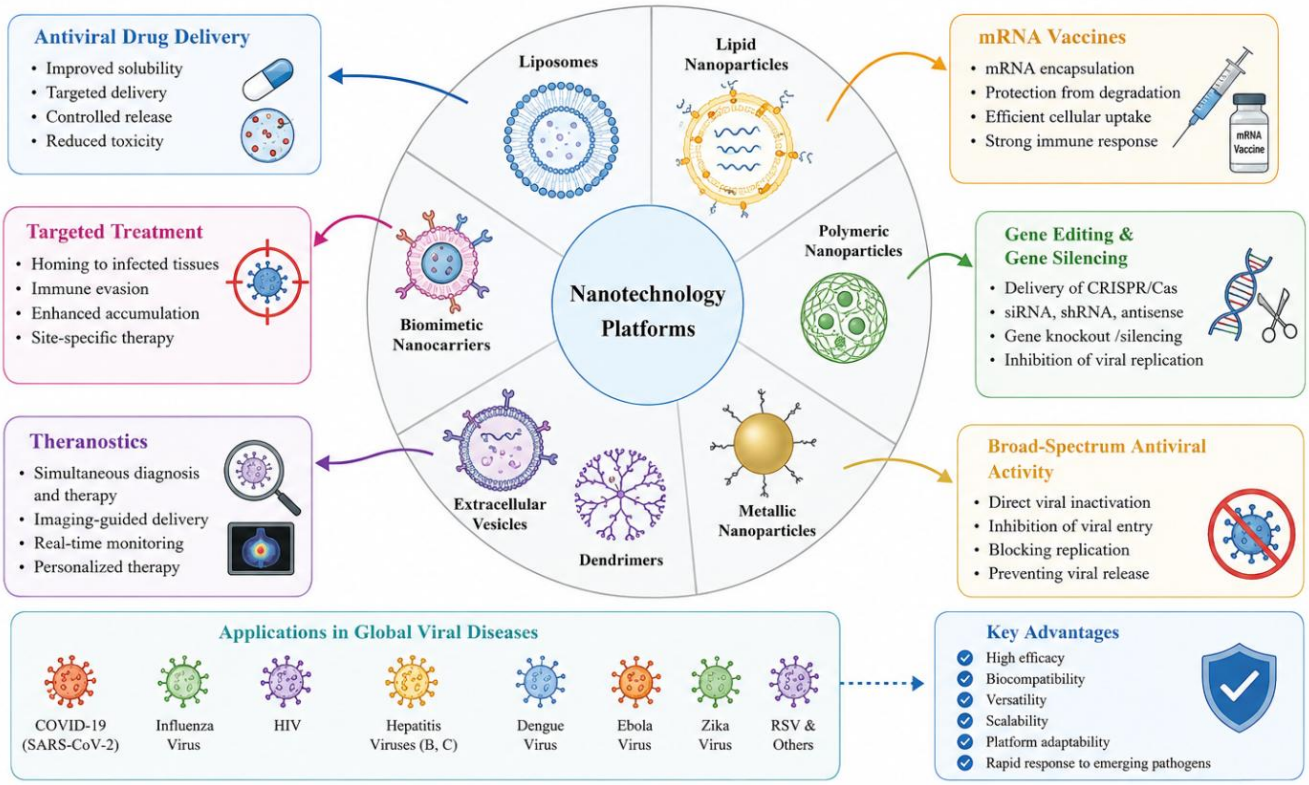

Figure 2. Nanotechnology platforms for the prevention, diagnosis, and treatment of global viral diseases. Overview of liposomes, lipid nanoparticles, polymeric nanoparticles, metallic nanoparticles, dendrimers, extracellular vesicles, and biomimetic nanocarriers for antiviral drug delivery, mRNA vaccines, gene editing, theranostics, and targeted treatment of COVID-19 and emerging viral infections.

3.5 Targeted and Stimuli-Responsive Nanocarriers

Targeted nanocarriers are designed to selectively deliver therapeutic agents to infected cells or tissues, thereby improving efficacy and minimizing systemic toxicity. Targeting strategies include passive targeting, based on enhanced permeability and retention (EPR) effect, and active targeting, which involves ligand-receptor interactions. Ligands such as antibodies, peptides, aptamers, and small molecules can be conjugated to nanoparticle surfaces to recognize viral receptors or infected cell markers.

These intelligent systems enable on-demand drug delivery, improving therapeutic precision and reducing adverse effects. For example, pH-sensitive nanoparticles can release antiviral drugs specifically within acidic endosomes of infected cells, while enzyme-responsive systems can be activated by viral or host proteases. Overall, targeted and stimuli-responsive nanocarriers represent a major advancement in antiviral therapy, offering highly efficient, controlled, and site-specific drug delivery systems capable of addressing the complex challenges of viral diseases[30].

4. THERAPEUTIC APPLICATIONS OF NANOTECHNOLOGY AGAINST VIRAL DISEASES

Nanotechnology has brought about tremendous change in antiviral therapy through targeted treatment methods, which have overcome the constraints associated with traditional antiviral medicines. The treatment of viral infections is very difficult because the viruses replicate intracellularly, mutate fast, escape immune recognition, and develop drug resistance. Nanotechnology solves these problems through increased drug solubility, improved bioavailability, targeting of the medicine to the infected tissues, and multiple medicine delivery. Furthermore, nanotechnology is an essential component in vaccine, gene therapy, and RNA-based therapies.

4.1 Nanotechnology in COVID-19 Management

The COVID-19 pandemic caused by SARS-CoV-2 highlighted the urgent need for rapid, effective, and adaptable therapeutic platforms. Nanotechnology played a central role in both prevention and treatment strategies. One of the most significant contributions of nanomedicine was the development of mRNA vaccines, where lipid nanoparticles (LNPs) were used to protect fragile mRNA molecules from degradation and facilitate their delivery into host cells. These LNP-based vaccines enabled efficient antigen expression and robust immune activation, marking a milestone in vaccine technology. Beyond vaccines, nanocarriers have been extensively explored for antiviral drug delivery in COVID-19 management. Nanoparticles such as liposomes, polymeric nanoparticles, and solid lipid nanoparticles have been used to deliver antiviral agents like remdesivir, favipiravir, and ivermectin with improved pharmacokinetics and reduced systemic toxicity. Targeted nanodelivery systems have also been designed to concentrate drugs in lung tissues, the primary site of SARS-CoV-2 infection. In addition, nanotechnology has been applied in diagnostic platforms for rapid detection of viral RNA and antigens. Gold nanoparticles, quantum dots, and biosensor-based nanodevices have enabled highly sensitive and rapid point-of-care testing. Furthermore, nanomaterials with intrinsic antiviral properties, such as silver and zinc oxide nanoparticles, have demonstrated the ability to inhibit viral entry and replication by interacting with viral surface proteins.

Immunomodulatory nanotherapies have also been investigated to manage cytokine storms associated with severe COVID-19. Nanoparticles delivering corticosteroids, IL-6 inhibitors, and antioxidant agents have shown potential in reducing hyperinflammation and preventing acute respiratory distress syndrome (ARDS). Collectively, nanotechnology has significantly contributed to the global response against COVID-19 by integrating therapeutic, diagnostic, and preventive strategies.

4.2 Nanotherapeutics for Influenza Virus

Influenza viruses remain a major global health concern due to their high mutation rates and seasonal outbreaks. Conventional antiviral drugs such as oseltamivir and zanamivir face limitations including resistance development and suboptimal bioavailability. Nanotechnology offers promising solutions to enhance influenza treatment and prevention. Nanocarriers such as liposomes, polymeric nanoparticles, and dendrimers have been used to improve the delivery of neuraminidase inhibitors and polymerase inhibitors. These systems enhance drug stability, prolong circulation time, and enable targeted delivery to respiratory epithelial cells, where influenza virus primarily replicates. Inhalable nanoparticle formulations have been developed to directly deliver antiviral agents to the lungs, increasing local drug concentration while minimizing systemic exposure.Nanoparticles also play a significant role in influenza vaccine development. Virus-like nanoparticles and lipid-based nanovaccines enhance antigen presentation and stimulate strong humoral and cellular immune responses. Additionally, nanoparticle-based adjuvants improve vaccine efficacy by enhancing dendritic cell activation and cytokine production.

Metallic nanoparticles such as silver and gold nanoparticles have demonstrated direct antiviral activity against influenza viruses by binding to viral hemagglutinin proteins, thereby preventing viral attachment and entry into host cells. These multifunctional nanoplatforms provide both therapeutic and prophylactic benefits against influenza infections[31-32].

4.3 Nanotechnology Against HIV Infection

Human immunodeficiency virus (HIV) remains a chronic viral infection requiring lifelong antiretroviral therapy (ART). Despite significant advances in ART, challenges such as poor drug adherence, systemic toxicity, drug resistance, and viral latency persist. Nanotechnology offers innovative strategies to overcome these limitations. Nanocarrier-based drug delivery systems, including liposomes, polymeric nanoparticles, and solid lipid nanoparticles, have been developed to improve the

pharmacokinetics of antiretroviral drugs such as zidovudine, efavirenz, and ritonavir. These systems enable sustained drug release, reduced dosing frequency, and improved patient compliance. Targeted nanodelivery systems are particularly important in HIV therapy due to the virus's ability to establish reservoirs in lymphoid tissues, macrophages, and the central nervous system. Nanoparticles functionalized with ligands targeting CD4 receptors or macrophage-specific markers enhance drug accumulation in viral reservoirs, improving therapeutic outcomes. Gene therapy approaches using nanocarriers have also gained attention. siRNA-loaded nanoparticles can silence viral genes, while CRISPR-Cas systems delivered via nanocarriers offer potential for genome editing of integrated proviral DNA. Additionally, Nanovaccines are being explored to induce broadly neutralizing antibodies against diverse HIV strains.

Long-acting injectable nanomedicines represent a major advancement in HIV treatment, enabling sustained drug release over weeks or months, thereby reducing dosing frequency and improving adherence. These innovations collectively contribute to improved management and potential functional cure strategies for HIV infection[33].

4.4 Nanomedicine for Hepatitis B and Hepatitis C

Hepatitis B virus (HBV) and hepatitis C virus (HCV) are major causes of chronic liver disease, cirrhosis, and hepatocellular carcinoma. Conventional antiviral therapies face challenges such as incomplete viral clearance, drug resistance, and hepatotoxicity. Nanotechnology provides advanced solutions for targeted liver delivery and improved therapeutic efficacy. Liver-targeted nanoparticles, including liposomes, polymeric nanoparticles, and lipid-based nanocarriers, have been developed to deliver antiviral drugs such as tenofovir, entecavir, and sofosbuvir directly to hepatocytes. Surface modification with galactose or other liver-targeting ligands enhances uptake via asialoglycoprotein receptors, improving drug accumulation in hepatic tissues. RNA interference (RNAi)-based nanotherapeutics have shown significant promise in HBV treatment. siRNA-loaded nanoparticles can suppress viral gene expression, reduce viral replication, and decrease antigen production. Similarly, antisense oligonucleotides delivered via nanocarriers are being explored for long-term viral suppression.

For HCV, nanotechnology has improved the delivery of direct-acting antivirals (DAAs), enhancing their stability and reducing systemic side effects. Nanoparticle-based vaccine platforms are also under development to induce protective immunity against HBV and HCV. In addition, nanodiagnostic tools enable early detection of viral infections and monitoring of treatment response through highly sensitive biosensors and imaging agents. These integrated therapeutic and diagnostic (theranostic) approaches are transforming the management of chronic hepatitis infections[33-34].

4.5 Nanotechnology for Dengue, Zika, and Chikungunya

Arthropod-borne viral infections such as dengue, Zika, and chikungunya pose significant global health challenges, particularly in tropical and subtropical regions. The absence of specific antiviral drugs for many of these infections highlights the need for innovative therapeutic strategies. Nanotechnology has been explored for both antiviral therapy and vaccine development against these viruses. Nanoparticles can deliver antiviral agents such as ribavirin, interferons, and nucleic acid-based therapeutics to infected cells, enhancing their efficacy. Lipid nanoparticles and polymeric systems have been used to improve drug stability and targeted delivery. In dengue virus infection, nanocarriers delivering siRNA or antisense oligonucleotides can inhibit viral replication by targeting essential viral genes. Metallic nanoparticles with intrinsic antiviral properties have demonstrated the ability to inhibit viral entry and replication in these arboviral infections. Additionally, nanodiagnostic platforms enable rapid and sensitive detection of viral infections, facilitating early intervention and outbreak control[35].

4.6 Nanotechnology Against Ebola and Other Emerging Viral Infections

Ebola virus and other emerging viral pathogens such as Nipah virus, Marburg virus, and Lassa virus represent severe public health threats due to their high mortality rates and limited treatment options. Nanotechnology offers promising strategies for rapid therapeutic development and deployment during outbreaks. Nanoparticle-based drug delivery systems have been used to enhance the stability and efficacy of antiviral agents and monoclonal antibodies targeting viral glycoproteins. Lipid nanoparticles and polymeric systems enable targeted delivery of therapeutics to infected tissues, improving survival outcomes in preclinical models.

RNA-based nanotherapeutics, including siRNA and mRNA platforms, have shown potential in rapidly responding to emerging viral outbreaks. These systems can be quickly designed and modified to target specific viral genomes, making them highly adaptable for pandemic response. Nanovaccines have also been developed for Ebola virus, demonstrating strong immunogenicity and protective efficacy in experimental studies. Additionally, nanodiagnostic tools enable rapid field detection of viral infections, which is critical for outbreak containment in resource-limited settings. The multifunctional nature of nanotechnology allows integration of therapy, diagnosis, and prevention, making it a powerful tool for managing emerging viral diseases with high epidemic potential[36-37].

5. RECENT ADVANCES IN NANOTECHNOLOGY FOR GLOBAL VIRAL DISEASES

The rapid evolution of nanotechnology has transformed the landscape of antiviral therapeutics by enabling highly targeted, programmable, and multifunctional treatment strategies. Lessons learned during the COVID-

19 pandemic accelerated the development of innovative nanoplatforms capable of delivering nucleic acids, antiviral drugs, immunomodulators, and diagnostic agents with unprecedented precision. Beyond SARS-CoV-2, these technologies are increasingly being adapted for influenza, HIV, hepatitis viruses, respiratory syncytial virus (RSV), dengue, Zika, Ebola, monkeypox (mpox), chikungunya, and other emerging viral pathogens. Recent advances integrate nanotechnology with gene editing, biomimetic engineering, artificial intelligence (AI), and precision medicine, paving the way for next-generation antiviral interventions. This section highlights the latest breakthroughs that are shaping the future of nanotechnology-enabled therapeutics against global viral diseases.

5.1 Lipid Nanoparticles for mRNA Therapeutics and Vaccines

The success of lipid nanoparticle (LNP)-based messenger RNA (mRNA) vaccines against SARS-CoV-2 represents one of the most significant achievements in modern nanomedicine. LNPs protect fragile mRNA molecules from enzymatic degradation, facilitate cellular uptake through endocytosis, promote endosomal escape, and enable efficient intracellular translation into antigenic proteins that stimulate robust immune responses[38].

Modern LNP formulations typically consist of four major components: ionizable lipids, phospholipids, cholesterol, and polyethylene glycol (PEG)-conjugated lipids. Ionizable lipids remain neutral in physiological conditions, minimizing systemic toxicity, but become positively charged within acidic endosomes, promoting membrane disruption and cytoplasmic release of mRNA. Cholesterol stabilizes nanoparticle structure, phospholipids improve membrane fusion, while PEG lipids enhance circulation time and reduce aggregation. The remarkable efficacy of the Pfizer-BioNTech (BNT162b2) and Moderna (mRNA-1273) vaccines demonstrated that LNP-mediated delivery can induce potent humoral and cellular immune responses within weeks. These vaccines also established scalable manufacturing platforms that have accelerated the development of mRNA therapeutics beyond COVID-19.

LNP technology is now being investigated for vaccines against influenza, HIV, RSV, cytomegalovirus (CMV), Zika virus, dengue virus, and Ebola virus. Researchers are also exploring multivalent mRNA vaccines capable of simultaneously targeting multiple viral pathogens or rapidly emerging variants. Furthermore, inhalable LNP formulations designed for pulmonary delivery are under investigation for respiratory viruses, aiming to generate stronger mucosal immunity at the primary site of infection. Despite these advances, challenges remain, including cold-chain storage requirements, PEG-associated hypersensitivity reactions, inflammatory responses induced by ionizable lipids, and limited organ-specific targeting. Continuous optimization of lipid chemistry and formulation strategies is expected to further enhance safety, stability, and clinical efficacy.

5.2 CRISPR-Enabled Nanotherapeutics

Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR)-based genome editing has emerged as a revolutionary antiviral strategy capable of directly targeting viral genomes or modifying host factors essential for viral replication. Nanotechnology plays a pivotal role in translating CRISPR therapeutics into clinical applications by enabling safe, efficient, and non-viral delivery of CRISPR components. Different CRISPR systems exhibit distinct antiviral applications. CRISPR-Cas9 primarily edits DNA viruses such as hepatitis B virus (HBV), herpes simplex virus (HSV), human papillomavirus (HPV), and Epstein–Barr virus (EBV), whereas CRISPR-Cas13 specifically targets RNA viruses including SARS-CoV-2, influenza virus, respiratory syncytial virus, and dengue virus.

Nanocarriers including lipid nanoparticles, polymeric nanoparticles, gold nanoparticles, silica nanoparticles, exosomes, and biomimetic vesicles have been engineered to deliver Cas proteins, guide RNAs (gRNAs), messenger RNA encoding Cas enzymes, or ribonucleoprotein complexes. These systems improve intracellular delivery while avoiding insertional mutagenesis associated with viral vectors. During the COVID-19 pandemic, CRISPR-Cas13 systems demonstrated the ability to selectively degrade SARS-CoV-2 RNA within infected cells. Similar strategies have shown promising antiviral activity against influenza A virus and respiratory syncytial virus in preclinical studies. For chronic viral infections such as HBV, CRISPR-mediated disruption of covalently closed circular DNA (cccDNA) represents a promising strategy toward functional cure.

Recent developments include multiplex CRISPR systems capable of simultaneously targeting multiple conserved viral genes to minimize viral escape mutations. Researchers are also combining CRISPR therapy with nanoparticle-mediated immune modulation to achieve synergistic antiviral effects. However, clinical translation requires overcoming several challenges, including off-target genome editing, immune responses against Cas proteins, transient gene-editing efficiency, manufacturing complexity, and regulatory concerns. Advances in biodegradable nanoparticles, programmable delivery systems, and transient CRISPR expression are expected to improve therapeutic safety and precision[39-40].

5.3 Biomimetic and Cell Membrane-Coated Nanoparticles

Biomimetic nanoparticles represent a new generation of antiviral nanocarriers that imitate the structural and functional characteristics of natural cells. By coating synthetic nanoparticles with biological membranes derived from erythrocytes, leukocytes, macrophages, platelets, stem cells, or extracellular vesicles, these systems inherit immune-evasive and targeting capabilities that substantially improve therapeutic performance. Cell membrane-coated nanoparticles possess surface proteins, receptors, and adhesion molecules identical to those of their source cells. These

biological features reduce recognition by the mononuclear phagocyte system, prolong circulation time, and facilitate accumulation at sites of viral infection or inflammation.

Macrophage membrane-coated nanoparticles are particularly promising because macrophages naturally migrate toward inflamed tissues where viral replication occurs. Such nanoparticles can deliver antiviral drugs directly into infected organs while simultaneously neutralizing excessive inflammatory cytokines. Similarly, platelet membrane-coated nanoparticles exhibit affinity toward inflamed vascular endothelium and may reduce virus-induced thrombosis. Red blood cell membrane-coated nanoparticles demonstrate prolonged systemic circulation and reduced immunogenicity, making them suitable for sustained antiviral drug delivery. Extracellular vesicles and exosomes have also gained considerable attention because they naturally transport proteins, RNAs, and signaling molecules between cells. Engineered exosomes have shown promising potential for delivering siRNA, microRNA, antiviral proteins, and CRISPR components to infected tissues.

5.4 Multifunctional Theranostic Nanoplatforms

Theranostic nanotechnology integrates therapeutic and diagnostic functions within a single nanosystem, enabling simultaneous disease detection, targeted treatment, and real-time monitoring of therapeutic responses. Such multifunctional platforms are particularly valuable for viral infections because disease progression often changes rapidly and requires timely therapeutic intervention. Theranostic nanoparticles typically combine antiviral drugs or nucleic acids with imaging agents such as fluorescent dyes, magnetic nanoparticles, quantum dots, radionuclides, or contrast agents. These multifunctional systems allow clinicians to visualize nanoparticle biodistribution, quantify viral burden, monitor drug release, and evaluate treatment efficacy using imaging modalities including magnetic resonance imaging (MRI), computed tomography (CT), positron emission tomography (PET), fluorescence imaging, and photoacoustic imaging[41-42].

5.5 Artificial Intelligence in Nanomedicine Design

Machine learning (ML), deep learning, artificial neural networks, and reinforcement learning algorithms are increasingly employed to predict nanoparticle size, surface charge, drug loading efficiency, encapsulation stability, biodistribution, toxicity, cellular uptake, and antiviral efficacy. AI models also facilitate virtual screening of lipid formulations, polymers, ligands, and targeting molecules before laboratory synthesis, substantially reducing development time and cost. During the COVID-19 pandemic, AI-assisted computational platforms accelerated vaccine antigen selection, epitope prediction, antiviral drug repurposing, and optimization of lipid nanoparticle compositions. Digital modeling further enabled rapid evaluation of nanoparticle–virus interactions and prediction of immune responses against newly emerging viral variants[43-44].

5.6 Clinical Translation and Ongoing Clinical Trials

The COVID-19 pandemic dramatically accelerated the clinical translation of nanotechnology, demonstrating that nanoparticle-based therapeutics can be developed, manufactured, and deployed globally within unprecedented timeframes. The regulatory approval of lipid nanoparticle-based mRNA vaccines established a new paradigm for nanomedicine and validated decades of translational research. Currently, numerous nanoparticle-based antiviral therapeutics are undergoing clinical evaluation for COVID-19, influenza, RSV, HIV, hepatitis B, hepatitis C, cytomegalovirus, Ebola, and other emerging viral infections. Clinical investigations include lipid nanoparticles delivering mRNA vaccines, siRNA therapeutics, self-amplifying RNA vaccines, nanoparticle-adjuvanted vaccines, polymeric nanoparticle drug delivery systems, and inhalable nanoformulations targeting respiratory viruses.

Several nanomedicine platforms are also being explored for long-acting antiviral drug delivery, sustained-release injectable formulations, intranasal vaccines, mucosal immunization, and combination therapies integrating antiviral drugs with immunomodulatory agents. Personalized nanotherapeutics designed according to viral genomic mutations and host immune profiles are emerging as promising precision medicine approaches[45].

6. CURRENT CHALLENGES, LIMITATIONS, AND FUTURE PERSPECTIVES

Though nanotechnology has transformed antiviral therapies by providing targeted drug delivery, enhanced vaccine efficiency, drug release control, and multivalent therapy systems, there are a number of scientific, technological, regulatory, and economic hurdles that prevent the extensive use of nanotechnology in the medical practice. The impressive success of nanotechnology during the time of COVID-19 outbreak highlighted the immense capabilities of nanotechnology; but taking experimental nanotherapeutics from the laboratory to safe, efficient, economical, and globally accessible antiviral treatments is far from being easy.

6.1 Biological and Therapeutic Challenges

Biological complexity remains one of the greatest obstacles to successful antiviral nanotherapy. Viral pathogens possess remarkable adaptability and continuously evolve mechanisms that reduce therapeutic efficacy, while host biological barriers further restrict efficient nanoparticle delivery. Understanding these biological limitations is essential for developing more effective and clinically translatable nanomedicines[46-47].

6.1.1 Viral Mutation and Immune Escape

Rapid viral mutation represents one of the most significant challenges in antiviral drug development. RNA viruses, including SARS-CoV-2, influenza virus, HIV, dengue virus, Zika virus, and respiratory syncytial virus, exhibit high mutation rates because of error-prone viral polymerases. Continuous genetic evolution enables

viruses to evade host immune responses, reduce vaccine effectiveness, and develop resistance to antiviral drugs.

Nanotechnology offers adaptable therapeutic platforms capable of rapidly incorporating updated antigens, nucleic acids, or antiviral agents. Lipid nanoparticle-based mRNA vaccines demonstrated exceptional flexibility during the COVID-19 pandemic, allowing relatively rapid redesign against newly emerging viral variants. Similarly, nanoparticle-mediated siRNA, CRISPR-Cas systems, and antisense oligonucleotides can be reprogrammed to target conserved viral genomic regions. Nevertheless, frequent viral evolution continues to challenge the long-term efficacy of nanotherapeutics, highlighting the need for broad-spectrum antiviral platforms targeting highly conserved viral proteins and essential host pathways[48].

6.1.2 Intracellular Delivery Barriers

Most viruses replicate within host cells, requiring antiviral therapeutics to efficiently cross multiple biological barriers before reaching intracellular targets. Following systemic administration, nanoparticles encounter plasma proteins, immune cells, vascular endothelium, extracellular matrices, cellular membranes, and intracellular endosomal compartments. After cellular uptake through endocytosis, many nanoparticles become trapped within endosomes and are subsequently degraded in lysosomes before releasing their therapeutic payloads. This phenomenon substantially reduces the intracellular bioavailability of antiviral drugs, nucleic acids, and gene-editing components.

6.1.3 Target Specificity

Selective targeting of infected cells while sparing healthy tissues remains a major challenge in antiviral nanomedicine. Although nanoparticles can accumulate preferentially in inflamed tissues through passive mechanisms, many viral infections are widely disseminated throughout the body, limiting opportunities for passive targeting alone. Active targeting strategies employ ligands such as antibodies, peptides, aptamers, sugars, and receptor-specific molecules that recognize viral receptors or infected cells.

6.1.4 Long-Term Safety and Toxicity

Although many nanomaterials demonstrate favorable short-term safety profiles, comprehensive understanding of their long-term biological effects remains limited. Chronic exposure may lead to nanoparticle accumulation in organs such as the liver, spleen, kidneys, lungs, brain, and lymph nodes. Potential toxicological concerns include oxidative stress, inflammatory responses, mitochondrial dysfunction, DNA damage, complement activation, immunogenicity, fibrosis, and unintended interactions with healthy tissues. Certain inorganic nanoparticles may exhibit prolonged tissue retention because of limited biodegradability. Development of biodegradable, metabolizable, and environmentally sustainable nanomaterials represents an important priority for future antiviral therapeutics[49-50].

6.2 Manufacturing, Regulatory, and Clinical Challenges

Despite encouraging laboratory and clinical results, large-scale commercialization of antiviral nanomedicines remains constrained by manufacturing complexity, quality control, regulatory uncertainty, and economic considerations. Addressing these challenges is essential for widespread clinical adoption.

6.2.1 Large-Scale Manufacturing

Most antiviral nanoparticles are initially optimized under laboratory conditions using small-scale synthesis methods that are difficult to reproduce at industrial scale. Manufacturing processes involving lipid mixing, nanoprecipitation, emulsification, microfluidics, or self-assembly require precise control of formulation parameters to ensure consistent nanoparticle characteristics. Industrial production must comply with Good Manufacturing Practice (GMP) standards while maintaining particle size, encapsulation efficiency, sterility, purity, and therapeutic performance. Continuous manufacturing technologies, automated production systems, and advanced microfluidic platforms offer promising solutions for scalable production.

6.2.2 Batch-to-Batch Reproducibility

Maintaining consistent nanoparticle quality across manufacturing batches is critical for regulatory approval and clinical reliability. Small variations in raw materials, synthesis conditions, mixing rates, purification methods, or storage conditions may significantly affect nanoparticle size distribution, drug loading, surface chemistry, and biological activity. Robust quality control systems incorporating real-time monitoring, process analytical technologies (PAT), quality-by-design (QbD), standardized characterization protocols, and automated manufacturing are essential to ensure reproducibility and product consistency.

6.2.3 Stability and Storage

Many nanoparticle formulations are sensitive to temperature fluctuations, moisture, oxidation, and mechanical stress during storage and transportation. Lipid nanoparticle-based mRNA vaccines highlighted significant cold-chain challenges during the COVID-19 pandemic, particularly in low-resource settings. Approaches such as lyophilization (freeze-drying), spray drying, cryoprotectants, improved lipid compositions, and thermostable formulations are being investigated to enhance long-term stability. Development of room-temperature-stable nanomedicines would substantially improve global vaccine distribution and antiviral preparedness[51-52].

6.2.4 Regulatory Approval

The regulatory evaluation of nanomedicines remains more complex than that of conventional pharmaceuticals because nanoparticle behavior depends on multiple interrelated physicochemical and

biological properties. Regulatory agencies require comprehensive characterization of particle morphology, surface chemistry, pharmacokinetics, biodistribution, immunogenicity, toxicity, manufacturing consistency, and environmental impact. Currently, internationally harmonized regulatory guidelines specific to antiviral nanomedicines remain limited. Establishing standardized evaluation protocols, validated analytical methods, and globally accepted regulatory frameworks will facilitate faster clinical translation while ensuring patient safety.

6.3.1 Broad-Spectrum Antiviral Nanotherapeutics

Rather than targeting individual viruses, future nanomedicines are increasingly being designed to inhibit conserved viral structures or common host pathways essential for viral replication. Broad-spectrum antiviral nanotherapeutics would provide immediate therapeutic options against newly emerging pathogens before virus-specific drugs become available. Multifunctional nanoparticles capable of simultaneously delivering antiviral drugs, immune modulators, RNA therapeutics, and gene-editing systems may significantly reduce the likelihood of antiviral resistance and improve treatment outcomes during future outbreaks[53].

6.3.2 AI-Assisted Nanocarrier Optimization

Artificial intelligence, machine learning, and computational modeling are expected to become central components of antiviral nanomedicine development. AI can rapidly predict optimal nanoparticle composition, particle size, surface charge, encapsulation efficiency, biodistribution, pharmacokinetics, toxicity, and therapeutic efficacy using large biological datasets. Integration of AI with robotic synthesis, digital twins, high-throughput screening, molecular simulations, and automated manufacturing will substantially accelerate formulation development while reducing research costs and experimental failures[54-55].

6.3.3 Pandemic Preparedness Through Nanotechnology

One of the biggest takeaways from the COVID-19 pandemic is that there is a necessity for a versatile therapeutic platform that can quickly react to emerging pathogens. Nanotechnology provides an unparalleled level of adaptability through modular vaccines, programmable RNA delivery, manufacturing capabilities, and theranostic nanoparticles. Preparation for future pandemics should involve the creation of internationally coordinated nanomedicine manufacturing facilities, regulatory pathways, stockpiling of adaptable nanoparticle platforms, and international information sharing. Collectively, these advances position nanotechnology as a cornerstone of global preparedness against both current viral diseases and future pandemics, supporting more resilient, equitable, and responsive healthcare systems worldwide[55].

CONCLUSION

Nanotechnology has become one of the most revolutionary strategies in the treatment of viral diseases all over the world, since it provides some unique solutions which have solved many problems of traditional methods of antiviral drugs and vaccines. Nanotechnology has been proved to be highly successful during the pandemic of COVID-19, when it accelerated vaccine production, improved effectiveness of treatments and enhanced global reaction on newly appearing viral diseases. However, nanotechnology has already made some progress in the treatment of other types of viruses, such as influenza virus, human immunodeficiency virus, hepatitis viruses, respiratory syncytial virus, dengue, Zika, Ebola, mpox, chikungunya, and many others. Through increasing drug solubility, preventing biological substances degradation, controlling drug release and ensuring intracellular delivery, nanocarriers have improved the therapeutic efficiency of antiviral agents and decreased systemic toxicity. This review emphasizes the significant advancements that have been made within the field of nanotechnology therapy delivery platforms, which include lipid nanoparticles, polymeric nanoparticles, dendrimers, inorganic nanoparticles, liposomes, micelles, exosomes, biomimetic nanoparticles, virus-like particles, and nanocarrier hybrids. Such systems have shown promising results in terms of the delivery of antiviral drugs, siRNA, mRNA, CRISPR tools for gene editing, immunomodulators, and vaccine antigens with high precision.

LIST OF ABBREVIATIONS

ACE2: Angiotensin-Converting Enzyme 2; **ADE:** Antibody-Dependent Enhancement; **AI:** Artificial Intelligence; **AIDS:** Acquired Immunodeficiency Syndrome; **AgNPs:** Silver Nanoparticles; **ARDS:** Acute Respiratory Distress Syndrome; **ART:** Antiretroviral Therapy; **AuNPs:** Gold Nanoparticles; **CCL2:** C-C Motif Chemokine Ligand 2; **CD4:** Cluster of Differentiation 4; **CD8:** Cluster of Differentiation 8; **cccDNA:** Covalently Closed Circular DNA; **CMV:** Cytomegalovirus; **COVID-19:** Coronavirus Disease 2019; **CRISPR:** Clustered Regularly Interspaced Short Palindromic Repeats; **CRISPR-Cas:** CRISPR-associated system; **CT:** Computed Tomography; **CXCL10:** C-X-C Motif Chemokine Ligand 10; **DAAs:** Direct-Acting Antivirals; **DNA:** Deoxyribonucleic Acid; **EBV:** Epstein–Barr Virus; **EPR:** Enhanced Permeability and Retention; **EVs:** Extracellular Vesicles; **GM-CSF:** Granulocyte-Macrophage Colony-Stimulating Factor; **GMP:** Good Manufacturing Practice; **gRNAs:** Guide RNAs; **HBV:** Hepatitis B Virus; **HCV:** Hepatitis C Virus; **HIV:** Human Immunodeficiency Virus; **HPV:** Human Papillomavirus; **HSV:** Herpes Simplex Virus; **IFNs:** Interferons; **IFN-γ:** Interferon-Gamma; **IL-1β:** Interleukin-1 Beta; **IL-6:** Interleukin-6; **IRF3:** Interferon Regulatory Factor 3; **IRF7:** Interferon Regulatory Factor 7; **JAK:** Janus Kinase; **LNPs:** Lipid Nanoparticles; **mRNA:** Messenger RNA; **MPS:** Mononuclear Phagocyte System; **MSNs:** Mesoporous Silica Nanoparticles; **MRI:** Magnetic Resonance Imaging; **NK:** Natural Killer; **NLCs:**

Nanostructured Lipid Carriers; **NLRs:** NOD-Like Receptors.

CONSENT FOR PUBLICATION

Not applicable.

HUMAN AND ANIMAL ETHICAL RIGHT

Not applicable.

CONFLICT OF INTEREST

The authors declare no conflict of interest, and no funding was required to conduct these review data.

ACKNOWLEDGMENTS

The corresponding authors would like to thank, all involved members and faculty staff for their collaboration.

AVAILABILITY OF DATA AND MATERIALS

The data supporting this study's findings will be available in the cited references.

FUNDING

The research received no external funding.

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