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RECENT ADVANCES IN ANTIVIRAL DRUG DELIVERY SYSTEMS (NANOTECHNOLOGY-BASED): A COMPREHENSIVE REVIEW

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ABSTRACT

Viral infections remain a major global health challenge due to rapid mutation rates, drug resistance, and limited therapeutic efficacy. Nanotechnology-based drug delivery systems have emerged as promising strategies to enhance antiviral therapy. This review provides a comprehensive overview of recent advances in nanocarriers including liposomes, solid lipid nanoparticles (SLNs), polymeric nanoparticles, dendrimers, and nanoemulsions. These systems improve drug bioavailability, enable targeted delivery, and reduce toxicity. Recent innovations such as ligand-targeted nanoparticles, biomimetic systems, and nanovaccines are also discussed. Despite significant progress, challenges related to toxicity, scalability, and regulatory approval persist. Future perspectives highlight the role of personalized nanomedicine and clinical translation.

KEYWORDS: Antiviral, Nanotechnology, Drug delivery, Nanoparticles, SLN, SNEDDS, Targeted therapy etc.

INTRODUCTION:

Viral infections such as influenza, HIV, hepatitis, and coronaviruses continue to pose significant health threats worldwide. Conventional antiviral therapies often suffer from poor bioavailability, systemic toxicity, and drug resistance. Nanotechnology-based drug delivery systems offer innovative solutions to these limitations by enabling targeted and controlled drug delivery.

Nanocarriers provide enhanced permeability, improved pharmacokinetics, and site-specific drug delivery, thereby increasing therapeutic efficacy and minimizing adverse effects. [1-5] Nanotechnology has revolutionized the field of drug delivery by offering innovative solutions to overcome the limitations of conventional antiviral therapies. Viral infections such as HIV, influenza, hepatitis, and COVID-19 require efficient therapeutic strategies. [5-6]

Figure 1: Recent advances in antiviral drug delivery systems based on nano technology.

Limitations of Conventional Antiviral Therapy: Conventional antiviral therapy is often associated with several inherent limitations that significantly reduce its therapeutic effectiveness. One of the primary challenges is the poor solubility of many antiviral drugs, particularly those belonging to the Biopharmaceutics Classification System (BCS) Class II and IV, which leads to inadequate dissolution and absorption. This directly contributes to low bioavailability, resulting in sub-therapeutic drug concentrations at the target site. Additionally, many antiviral agents require frequent dosing due to their short half-life and rapid metabolism, which can reduce patient compliance and increase the risk of missed doses. [7-9]

Another critical concern is the development of drug resistance, especially in rapidly mutating viruses such as HIV and influenza. Continuous exposure to antiviral agents can lead to genetic mutations in viral strains, rendering the drugs less effective or even ineffective over time. Furthermore, conventional antiviral therapies are often associated with systemic toxicity, as non-specific distribution of drugs can affect healthy tissues and cause adverse effects such as hepatotoxicity, nephrotoxicity, and gastrointestinal disturbances. Collectively, these limitations highlight the urgent need for advanced drug delivery systems that can enhance solubility, improve bioavailability, enable controlled release, and provide targeted delivery, thereby improving the overall efficacy and safety of antiviral therapy. [10-11]

Nanotechnology-Based Drug Delivery Systems: Nanotechnology-based drug delivery systems have emerged as highly promising platforms for improving the therapeutic efficacy of antiviral agents. These systems are designed to overcome the limitations of conventional therapies by enhancing solubility, stability, bioavailability, and targeted delivery. Various nanocarriers have been extensively explored for antiviral applications, each offering unique advantages.

Liposomes: Liposomes are spherical vesicles composed of phospholipid bilayers capable of encapsulating both hydrophilic and lipophilic drugs. Due to their structural similarity to biological membranes, liposomes exhibit excellent biocompatibility and can effectively deliver antiviral agents to specific sites. They enhance drug stability, reduce degradation, and enable targeted delivery, thereby minimizing systemic side effects. Additionally, liposomes provide controlled and sustained drug release, improving therapeutic outcomes.

Solid Lipid Nanoparticles (SLNs): Solid lipid nanoparticles (SLNs) are submicron-sized carriers composed of physiologically compatible solid lipids. These systems have gained significant attention in antiviral drug delivery due to their ability to enhance drug stability and protect labile drugs from degradation. SLNs offer controlled drug release and improved bioavailability, making them particularly suitable for poorly soluble antiviral drugs. Their excellent tolerability and scalability further support their application in pharmaceutical formulations. [12-15]

Polymeric Nanoparticles: Polymeric nanoparticles are formulated using biodegradable polymers such as poly(lactic-co-glycolic acid) (PLGA). These carriers provide sustained and controlled drug release, which helps maintain therapeutic drug levels for extended periods. Furthermore, polymeric nanoparticles can be engineered for target-specific delivery by surface modification, thereby enhancing drug accumulation at the site of infection. This targeted approach improves the therapeutic index while reducing off-target toxicity.

Nano emulsions and SNEDDS: Nano emulsions and self-nanoemulsifying drug delivery systems (SNEDDS) are isotropic mixtures of oils, surfactants, and co-solvents that spontaneously form fine oil-in-water emulsions upon dilution. These systems significantly enhance the solubility and dissolution rate of poorly water-soluble antiviral drugs. As a result, they improve oral bioavailability and facilitate efficient drug absorption. SNEDDS are particularly advantageous for oral delivery of lipophilic antiviral agents. [16-18]

Dendrimers: Dendrimers are highly branched, tree-like macromolecules with well-defined structures and numerous surface functional groups. These features allow high drug loading and precise control over drug release. Dendrimers can be functionalized with targeting ligands to enhance site-specific delivery. Moreover, certain dendrimers possess intrinsic antiviral activity by interfering with viral attachment and replication processes.

Metallic Nanoparticles: Metallic nanoparticles, particularly silver and gold nanoparticles, have demonstrated intrinsic antiviral properties. These nanoparticles can inhibit viral entry, replication, and assembly by interacting with viral proteins and genetic material. Their unique physicochemical properties make them attractive candidates for antiviral applications, although concerns regarding toxicity and biocompatibility must be carefully addressed. [19-25]

Recent Advances in Antiviral Nanotechnology: Recent advancements in nanotechnology have significantly improved antiviral drug delivery strategies. Targeted nanocarriers utilizing ligand-based approaches enable precise delivery to infected cells, enhancing therapeutic efficacy. Biomimetic nanoparticles, which mimic natural biological systems such as cell membranes, have shown improved immune evasion and targeting capabilities.

Nano vaccines represent another major breakthrough, where nanotechnology is employed to enhance antigen delivery and immune response, as seen in modern mRNA vaccine platforms. Additionally, stimuli-responsive nanocarriers have been developed to release drugs in response to specific triggers such as pH, enzymes, or temperature, ensuring site-specific action.

Overall, these advancements have led to improved targeting, reduced toxicity, and enhanced therapeutic outcomes, positioning nanotechnology as a transformative approach in antiviral therapy. [26-35]

Mechanisms of Nanocarrier-Based Antiviral Delivery: Nanocarriers enhance antiviral therapy through multiple mechanisms. They facilitate targeted drug delivery to infected cells, thereby increasing drug concentration at the site of action while minimizing systemic exposure. Enhanced cellular uptake is achieved through endocytosis and membrane fusion mechanisms. Additionally, nanocarriers enable controlled and sustained drug release, maintaining effective drug levels over prolonged periods. Prolonged circulation time further improves therapeutic efficiency. Importantly, nanoparticle characteristics such as particle size, surface charge, and functionalization play a crucial role in determining their antiviral performance.

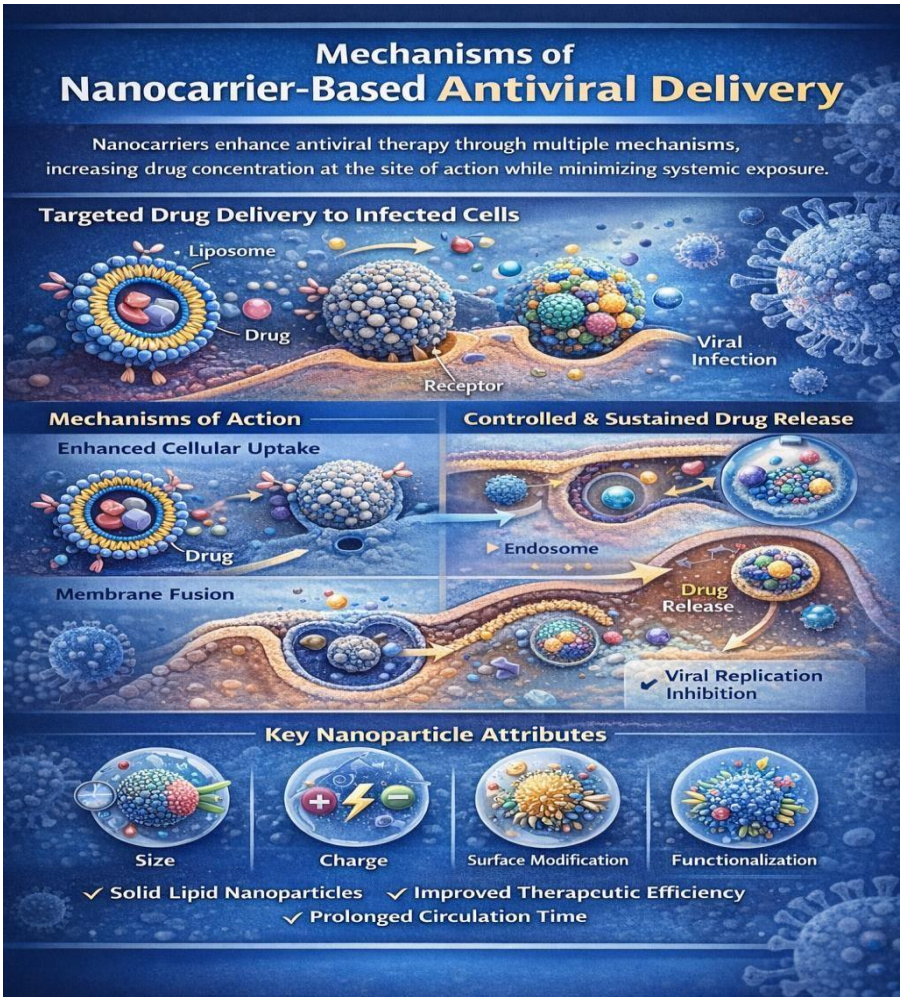

Figure 2: Mechanisms of action Nanocarrier-Based Antiviral Delivery.

Applications in Viral Diseases: Nanotechnology-based drug delivery systems have demonstrated significant potential in the treatment and management of various viral infections by improving drug efficacy, targeting, and safety profiles.

1) **Human Immunodeficiency Virus (HIV):** Nanocarriers such as liposomes, polymeric nanoparticles, and dendrimers have been extensively studied for HIV therapy. These systems enable targeted delivery of antiretroviral drugs to infected cells, particularly macrophages and lymphocytes, which act as viral reservoirs. Nanoparticles also provide sustained drug release, reducing dosing frequency and improving patient compliance. Additionally, dendrimers have shown the ability to inhibit viral entry by blocking interactions between the virus and host cells.

2) **Hepatitis (HBV and HCV):** In hepatitis B and C infections, nanotechnology enhances the delivery of antiviral agents such as interferons and nucleoside analogues. Nanocarriers improve drug stability and facilitate liver-targeted

delivery, thereby increasing therapeutic concentration at the site of infection while minimizing systemic side effects. Lipid-based nanoparticles have shown promising results in enhancing the bioavailability of poorly soluble antiviral drugs used in hepatitis treatment.

3) Influenza: Nanoparticles have been used to improve the delivery of antiviral drugs like oseltamivir and zanamivir. They enhance drug solubility, stability, and absorption, leading to improved therapeutic outcomes. Furthermore, nanotechnology plays a critical role in the development of influenza vaccines by enhancing antigen delivery and immune response through nano vaccine platforms.

4) **COVID-19 (SARS-CoV-2):** Nanotechnology has been pivotal in combating COVID-19, particularly through the development of mRNA vaccines using lipid nanoparticles. These nanocarriers protect the genetic material and facilitate its delivery into host cells, leading to effective immune responses. Additionally, nanoparticles have been explored for targeted delivery of antiviral drugs and diagnostic applications, improving both treatment and detection of the virus. [35-40]

CHALLENGES AND LIMITATIONS:

Despite the significant advancements in nanotechnology-based antiviral drug delivery systems, several challenges and limitations hinder their widespread clinical application. One of the major concerns is nanotoxicity, as certain nanoparticles may induce cytotoxicity, immunogenicity, or long-term accumulation in biological systems. Additionally, large-scale production of nanocarriers with consistent quality and reproducibility remains a critical challenge, particularly for industrial manufacturing. Regulatory hurdles also pose significant barriers, as the lack of standardized guidelines for evaluation and approval of nanomedicines complicates their translation from laboratory to clinical use. Furthermore, stability issues, including aggregation and degradation of nanoparticles during storage, can affect their efficacy and shelf life.

Future Perspectives: Looking ahead, future research should emphasize the development of personalized nanomedicine, where therapies are tailored based on individual patient characteristics and disease profiles. The design of smart delivery systems, capable of responding to specific biological stimuli such as pH, enzymes, or temperature, holds great promise for achieving precise and controlled drug release. Moreover, efforts should focus on enhancing clinical translation through improved scalability, safety profiling, and regulatory compliance.

CONCLUSION: nanotechnology-based antiviral drug delivery systems represent a transformative and innovative approach in modern therapeutics, offering improved efficacy, safety, and targeted treatment of viral infections.

Conflicts of Interest: None.

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