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Review Article

A Review on Applications of Nanotechnology for Enhancing Antiviral Drug Delivery

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ABSTRACT

The crucial significance of nanomaterials-based nanostructures has ushered in a new era of nanomedicine. Nanoparticles have evolved into the primary catalyst for the modification of numerous traditional materials' properties due to their smaller size and larger surface area, which causes them to be more reactive to other molecules. Nanoparticles have better biocompatibility and biodegradability, as well as the ability to modify surfaces. Nanomedicine has opened up a new therapeutic route for combating viral infections and improving treatment outcomes. Antiviral release kinetics could be altered, increasing bioavailability, improving efficacy, limiting adverse drug side effects, and lowering treatment costs with nanoparticulate-based devices. They may also allow antiviral medications to be delivered to specific target locations and viral reservoirs in the body. These appearances are most common in viral infections, where more treatment doses are required; pharmaceuticals are expensive, and therapeutic success is dependent on a patient's compliance with the administration protocol. This review discusses the current state of nanoparticulate delivery systems in antiviral therapy, as well as its definition and description, as well as certain unique characteristics. The report concludes with a review of the various hurdles that must be overcome before nanotechnology may be used to develop safe and effective antiviral compositions for clinical use.

INTRODUCTION

Viruses are important pathogenic agents that cause a variety of diseases in humans, animals, and plants. Antiviral drugs are medications that fight viral infections. Many viral infections have no effective antiviral medicines. On the other hand, there are numerous influenza medications, a couple of herpes virus drugs, and a few novel antiviral drugs for HIV and hepatitis C infections [1].

To achieve a favourable therapeutic index, antiviral medications should ideally target only the virus's exact and required activities. Antiviral medications have a number of negative effects, some of which are life threatening. Furthermore, cross-interactions with other medications from the same or different classes, such as antihistamines, antiarrhythmics, and antipsychotics, can reduce or increase the plasma concentration of the drug of interest, resulting in decreased efficacy or the induction of adverse effects, respectively [2].

There has been a dramatic increase in study and technology development at the atomic, molecular, and macromolecular sizes in recent years, allowing for the controlled manipulation and learning of structural ranges from 1 to 100 nm. Nanoparticles are a type of colloidal drug delivery system that behaves like a complete unit in terms of characteristics and transport mechanism. These are employed as a medication carrier system to improve cellular absorption and bodily circulation. Nanoparticles became the foremost reason for the transform in different properties of many conventional materials by good quality of their greater surface area per weight than microparticles which makes them to be added active drug carriers. Numerous group of nanoparticulate system which encompass polymeric nanoparticles, polymeric micelles,

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solid nanoparticles, lipid based nanoparticles, for example, solid lipid nanoparticles (SLN), nanostructured lipid carriers (NLC), and lipid drug conjugate (LDC), liposomes, inorganic nanoparticles, dendrimers, magnetic nanoparticles, nanocrystals, and nanotubes [3, 4].

In 2009, the global market for antiviral drugs collected total sales of around USD 28 billion. Sales of antivirals enlarged by approximately 20% from 2004 to 2006, and a continuing growth trend have been probable until 2011. Furthermore, due to unmet needs, rising populations, improved diagnostics, novel drugs, and new therapeutics, the market is expected to grow even more in the future. However, developing a safe and effective antiviral drug is a difficult task, and the list of viral diseases for which antiviral therapies are available is still relatively short [5].

Antiviral medication research is hampered by a number of variables. Because viruses are obligate intracellular parasites that rely on the host cell's biosynthetic machinery for replication, antiviral medications can only target a small number of virus-specific metabolic processes without harming the host. These are primarily viral proteins, which are required for viral replication and pathogenicity and are sufficiently distinct from any host protein to allow for selectivity. Furthermore, because the bulk of these functions are unique to each virus, it's difficult to build broad-spectrum antivirals that work against a variety of viruses that cause comparable symptoms. Antivirals developed against certain viruses (such as HSV) address the acute infection but not the dormant infection. As a result more frequent or chronic disorders are there which require longer-term therapy. These and other issues are at the heart of a major debate in antiviral research and development [6, 7].

The creation of novel medication formulations is the next major challenge for antiviral therapies. This entails using technical ways to change the physicochemical and biological properties of antiviral compounds during the manufacture of their dosage forms [8].

Current Antiviral Therapies

Antiviral medicines that have been approved so far involve tiny molecular weight medications or proteins to boost the innate immune response (interferon). Furthermore, an antisense oligonucleotide (fomivirsen) has been approved for the treatment of retinitis caused by HCMV strains (Human cytomegalovirus strains) that are resistant to traditional medicines. The antiviral drugs on the market and in clinical use are listed in Table 1**.**

Table1: Approved Antivirals drugs for herpes, vari cells & zoster virus

Drug Name	Route of Administration
Approved for HBV	
adefovir dipivoxil	Oral
entecavir	Oral
interferon alfa-2b	Subcutaneous
lamivudine	Oral
pegylated interferon alfa-2b	Subcutaneous
telbivudine	Oral
tenofovir disoproxil fumarate	Oral
Approved for HCV	
ribavirin	Oral
pegylated interferon alfa-2b	Subcutaneous
Approved for HCV and VZV	
acyclovir	I.V, Oral, Topical
brivudine	Oral
Famciclovir	Oral
idoxuridine	I.V
penciclovir	Topical
Trifluridine	Eye drop
valaciclovir	Oral
Approved for HCMV	
Ganciclovir	I.V,Oral
cidofovir	I.V
valganciclovir	Oral

HCMV-Human Cytomegalovirus, HBV- *herpes simplex virus* , VZV- varicella- zoster virus

Many antiviral medications have issues that reduce their effectiveness, such as insufficient solubility, a short half-life, or sluggish, reduced, or highly variable absorption. As a result, higher doses and more frequent administration are required, which might significantly impact patient compliance and result in severe side effects [9].

When given orally, several antivirals, such as the antiretrovirals acyclovir and ganciclovir, have low bioavailability. The efficacy of an antiviral depends on its bioavailability (that is, adequate absorption by the gastrointestinal tract, which is determined by solubility and permeability). Good

solubility and permeability are important indicators of optimal oral bioavailability and are required for antiviral medicines. Using the Biopharmaceutics Classification System, all orally administered medications were classified into four classes (I, II, III, and IV) based on their solubility and permeability values, which decreased with increasing solubility and permeability (BCS) [10].

Because of its slow and poor absorption in the gastrointestinal tract (BCS class III), acyclovir, which is used to treat HSV and VZV infections in a variety of dosage forms, has a low oral bioavailability (15–20%), necessitating high doses (up to 1,200 mg/day). Acyclovir is not absorbed at all in about 80% of the time [11].

Another issue with antiviral medicines is that long-term use of these drugs might cause moderate drug toxicity, which can cause significant complications in the patient. Furthermore, prolonged antiviral therapy increases the risk of drug-resistant virus strains emerging [12].

It is conceivable that traditional dose formulations will be changed to improve the therapeutic activity of antivirals now on the market. Many pharmaceutical companies have developed and are currently investigating fundamentally modified formulations of drug dosage forms, such as depot-like injectables, modified release tablets, and improved topical delivery systems, for use in the administration of antiviral drugs currently on the market. Novel formulations of traditional dosage forms that can change the residence time and reduce the dose provided [13].

Nanotechnologies to Improve Antiviral Drug Delivery

Nanotechnology is a strategy to creating materials or structures in the 1–100nm size range with a designed look. Nanotechnology is concerned with the creation and application of materials and mechanisms at the intracellular and molecular scales. The procedure and the amount of material used are usually in that order of <100 nm [14].

Nanotechnology is a hot topic in research and development around the world, and nanotechnologies are already found in hundreds of items, including sunscreens, cosmetics, fabrics, and sports equipment. Drug delivery, biosensors, and other medicinal applications are all being upgraded by nanotechnology. Additionally, nanotechnologies are being developed for use in environmental applications, such as pollution cleanup [15].

When compared to bigger particles of the same composition, nanotechnology uses particles and surfaces with very high surface area to volume ratios that are usually different in bioactivity, solubility, and antibacterial properties. Nanoparticulate systems (including nanoparticles, nanocapsules, vesicles, dendrimers, micelles, and inorganic nanomaterials) have been used to deliver small molecular weight medications, but they can also be used to deliver macromolecules and biological treatments like oligonucleotides [16].

These nanocarriers could assist regulate solubility and dissolution rates (improvement in BCS score), raise drug bioavailability, protect sensitive pharmaceuticals from degradation, reduce side effects, and improve tissue drug tolerance, among other things. Furthermore, this form of nanotechnological route allows for passive or active targeting of certain biological locations [17].

Nanocarriers can focus pharmaceuticals to specific tissues or organs, such as the liver or the brain, due to their unique properties, such as size and lipophilicity. Modifying nanocarrier surfaces allows them to reach specific areas and deliver drugs to precise cellular targets [18].

The creation of integrated multifunctional nanosystems for diagnostic and therapy is another rapidly growing area of research. These new devices, known as theranostics, are designed solely for the detection and treatment of cancer in real time. To achieve simultaneous and targeted imaging and treatment, the nanosystem must have the ability to biomark cancer cells. These integrated medical nanosystems may prove useful for molecular diagnosis, treatment, and management of viral infections at the cellular level in the future [19].

Targeted Delivery of Antiviral Agents

Paul Ehrlich, who proposed the magic bullet notion in 1906, was the first to propose the targeted drug theory. Targeted drug delivery by functionalized nanocarriers has become one of the most striking and promising areas of

nanomedicine research a century after this perception [20].

Direct injection to a specified place, passive targeting, and active targeting, are three different ways of drug targeting. Because of the presence of leaky vasculature, passive targeting combined with nanocarrier size allows nanoparticles to penetrate tumour tissues [21].

This result, known as the "enhanced permeability and retention (EPR) effect," results in nanoparticle accumulation within tumours, as seen in Fig. 1.

Active targeting can be performed using a variety of techniques that all include surface changes, most notably via a ligand-receptor-like mechanism. Monoclonal antibodies produced against specific cells or tissues are the principal method. Other compounds that can be utilised as homing devices include sugars, polymers, proteins, vitamins, lectins, and aptamers, as shown in Fig. 2 [22].

The use of surface-modified nanocarriers to target drugs enables for delivery at the organ or even cell level. It was recently shown that attaching TAT peptides or cell penetrating peptides to the nanoparticle surface can influence intracellular distribution and enhance endosomal escape. This is especially critical for medications that function within the cytoplasm or must reach the nucleus [23].

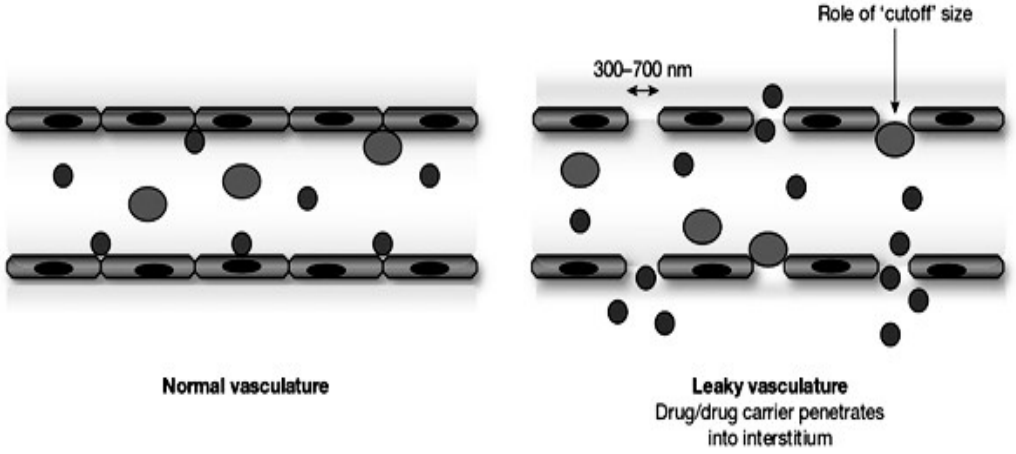

Figure 1: Enhanced permeability and retention (EPR) effect in passive drug targeting

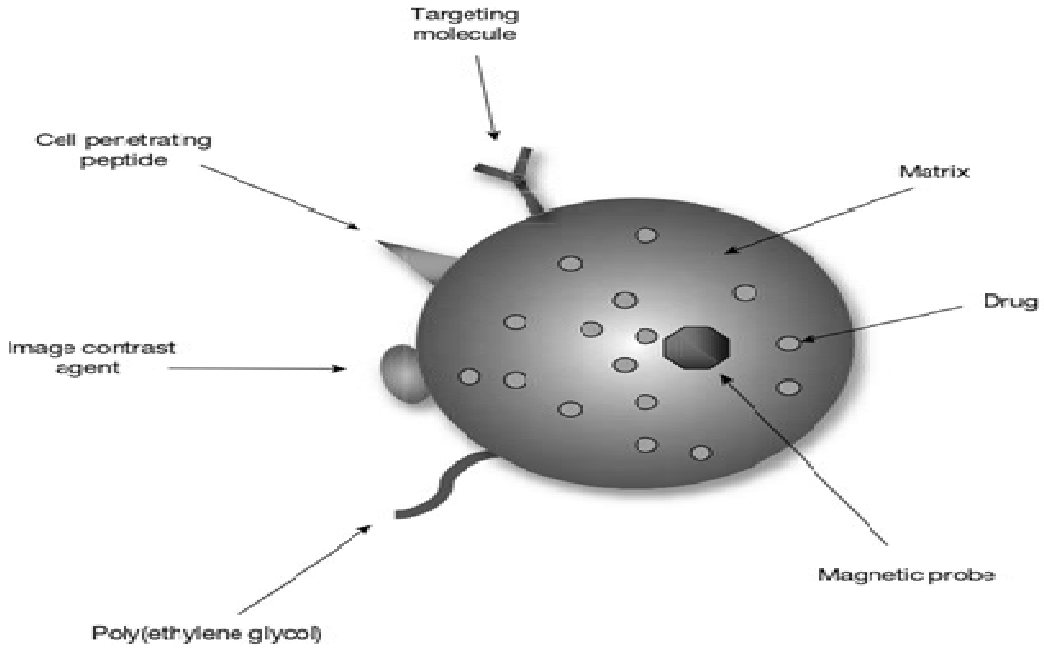

Figure 2: Functional nanoparticles with homing device

Nanoparticles

Nanoparticles are solid colloidal particles with a diameter of less than one micron that can be formed using polymers, lipids, proteins, or other substances like inorganic materials. As with microspheres, they can have a matrix-like or capsule-like structure, resulting in nanoparticles and nanocapsules, respectively. The active chemicals can either dissolve or be enclosed within nanoparticles. Because of their small size, they can be given intravenously. Because the presence of hydrophilic moieties on the surface of liposomes, such as PEG chains, can limit opsonization of nanoparticles in the blood, Secret nanoparticles are what they're called [24].

Drug carriers made of protein nanoparticles have also been developed. Coacevation and chemical cross-linking with glutaraldehyde primed albumin nanoparticles for ganciclovir administration. Nanoparticles between 200–400 nm with a distinct drug incorporation and release profile were achieved, controlled by the step in which glutaraldehyde was added in the research technique [25].

Conclusions and Future Perspectives

Nanoparticulate-based solutions, in example, could improve antiviral efficacy, reduce drug side effects, and lower treatment costs. These symptoms are most common in viral infections, where higher treatment doses are sought, pharmaceuticals are expensive, and therapeutic success is dependent on patient adherence to the administration regimen. This last point is critical in viral therapies, where intricate or long-term regimens are common. Nanotechnology has the ability to lower intake frequency and treatment time, potentially making the treatment more cost-effective.

Nanoparticle drug delivery systems are expected to play an important role in the treatment of a variety of life-threatening diseases because they provide safe, effective, and consistent therapeutic effects, while nanoparticles show promise in nasal, pulmonary, and other areas.

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