



## Emerging Nanotechnology Approaches for HIV/AIDS treatment and prevention

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### Abstract

Currently, neither a vaccine nor a treatment exist for HIV/AIDS. Combination antiretrovirals have greatly improved treatment, but they must be used for the remainder of one's life, have harmful side effects, and are ineffective in patients whose viruses develop resistance to them. The trans disciplinary science of nanotechnology is transforming medicine in the twenty-first century. It could make substantial advancements in HIV/AIDS treatment and prevention. We discuss the shortcomings of the disease's current treatment in this assessment and draw attention to the tremendous potential of nanotechnology to provide more effective anti retro viral medication, gene therapy, and immunotherapy for HIV/AIDS treatment and prevention, microbicides, and vaccine.

The particle can enter the body mostly through inhalation, direct injection, and oral intake. It has proven to have the potential to enhance viral agent treatment and prevention. Numerous NPs tested in vitro for self-therapeutic activity against the virus.

**Key words:** Nanotechnology, HIV, Vaccine, Nanomedicine, Antibodies

### Introduction

Currently, there is no effective medication available to treat the HIV infection, which affects approximately 37 million people worldwide. There are two main types of the virus: HIV-1 and HIV-2. The study focuses on HIV-1 therapy possibilities since it is more prevalent, damaging, and preferentially infects CD4+ T cells, helping cells. HIV-1 can infect macrophages, dendritic cells, and other types of cells. High-dose antiretroviral therapy (HAART) is an effective HIV-1 treatment strategy, but it does not provide patients with a functional or sterilising cure because the mechanisms of infection for microglia and astrocytes have not yet been fully identified and understood. Additionally, a number of adverse comorbidities are brought on by HAART (highly active anti retroviral

therapy). As highly active antiretroviral treatment (HAART) focuses on the HIV-1 enters a state of latency during its replication cycle to avoid being targeted. HIV was first identified as the disease's a etiology in 1983, after which AIDS's beginning had been detected in 1981. Today, HIV/AIDS is the most prevalent infectious disease in the world that kills adults. By 2006, more than 65 million people had acquired the HIV virus globally, and 25 million had died from AIDS. By the end of 2007, the virus had infected about 33 million people, and it was responsible for 2 million fatalities annually. Particularly on developing nations in Sub-Saharan Africa, this has had a tremendous detrimental social and economic impact on the entire world.

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### Nanotechnology for HIV/AIDS treatment

Similar advantages might be provided by nanotechnology-based platform that distribute antiviral drugs throughout the body. Controlled-release delivery systems can extend their half-lives, keeping them in the bloodstream for longer periods of time at therapeutic concentrations. This might significantly improve adherence to medicine. Nanoscale delivery techniques enhance and control the distribution of hydrophobic and hydrophilic drugs into and throughout diverse tissues due to their small size. This specific feature seems to be the most promising component of nanoscale delivery systems for the therapeutic treatment and prevention of HIV.

In a recent study, dogs and mice were given nanosuspensions (200 nm) of the drug dipivefrine (TMC278) stabilized by polyethylene-polypropylene glycol (poloxamer 338) and PEGylated tocopheryl succinate ester (TPGS 1000). polymeric systems-based study [35]. A single dose of the medicine given in nanosuspensions generated sustained release over 3 months in dogs and 3 weeks in mice, compared to a half-life of 38 hours for free medication. These results demonstrate the potential for nanoscale medicine delivery to increase adherence and decrease dosing frequency.

### Types of Nanoparticles and Nano pharmaceuticals:

Liposomes, Micelles, Nanospheres, Nano capsules, Organic Nanoparticles, Polymeric Nanoparticles, Dendrimers

Solid Lipid Nanoparticles, second

1. Silver nanoparticles (SNPs) and gold nanoparticles (GNPs) are examples of inorganic nanoparticles.

2. Organic nanoparticles are the type of nanoparticle that have been the subject of the most research and are the most commonly approved for use in the delivery of medications and for therapeutic purposes in human systems. The most common varieties of organic nanoparticles include nanoparticles made of polymers - Sizes of polymeric nanoparticles, which are solid colloids, range from 10 to 1000 nm. Higher concentrations at the target areas are the result of smaller size, which enhances capillary entrance

and cell absorption. In order to serve as therapeutic providers, NPs made from biodegradable and biocompatible polymers have received extensive research. those employed in pharmacology and medicine The WHO and FDA have approved polyglycolides, poly(PGA), polylactides (PLA), and Lactide-co-glycolide polymer. Because of its outstanding potential for biocompatibility and biodegradation, poly(D, L-lactide-co-glycoside, or PLGA) (PLG)- based nanoparticles are used extensively. The effectiveness and security of the drugs they contain can frequently be improved by them. It falls into the category of nanospheres or nano capsules.

Nanocapsules include Nanocapsules as spherical hollow spheres with polymer coatings within, and they have a size range of 50 to 300 nm, a high loading capacity, and a low density.

These nanospheres: They have an equal distribution of the medication throughout a matrix system with a size range of 100 to 200 nm. There have been numerous investigations on the therapeutic potential of nanospheres for viruses other than HIV/AIDS.

The first nanoparticle (NP) platform for the delivery of genes and drugs was liposomes. Liposomes are. They are sphere-like vehicles with a diameter of 20–30 nm. It is made up of an aqueous structure at the centre of a bilayer phospholipid structure. The interior aqueous cavity or bilayer phospholipid can be supplemented with hydrophilic or lipophilic drugs, respectively. Because of their wide range of compositional variations, ability to hold and protect a variety of

varieties of biomolecules, as well as biocompatible and biodegradable characteristics. Liposomal formulations are extensively researched in vaccination due to their potential as immunological adjuvants. About twelve of our liposome-based drugs are registered clinically.

Micelles:-

The diameter of micelles varies from 10 to 100 nm. They consist of an inside water-phobic core and an outside water-loving polymer. They are made of polymeric micelles, which are interesting because vehicles with high therapeutic potential for drug delivery. The encapsulation of

pharmaceuticals in polymeric micelles is an innovative application of nanotechnologies that can improve the water solubility and stability of unstable medications. The use of micelles in therapy has many advantages, including their decreased dissociation rate, which lengthens the time that medications are retained and accumulate at the target site.

Dendrimers include Dendrimers are symmetrical macromolecules where interaction takes place. They have a structure of hyper-branches that emerge from a central stick through connectors and units of branches. The target domain management is under the purview of the terminal groups. These are spherical and have three separate domains, organizations operating. For groups you want to target molecularly, for detecting, imaging, and other purposes, the outside face could be altered to generate chemical functional groupings, website attachments for a therapeutic agent.

1. Solid Lipid Nanoparticles (SLNs): These are a different type of pharmaceutical delivery mechanism from the general colloidal nanoparticles mentioned above. The usage of SLNs also reaps the benefits of conventional nanocarriers while avoiding their drawbacks. For instance, a significant barrier that reduces the usage of drug delivery is mass production of polymeric

nanoparticles, whereas financial help can be given for the synthesis of SLNs and other materials.

2. Nanoparticles that are organic: Inorganic nanoparticles are far smaller in size than organic nanoparticles. The loading efficiency has enhanced with its size ranges of 1-100 nm. There are two major ways to create inorganic nanoparticles: "top-down" techniques that use physical and/or chemical processes to shrink the inorganic nanoparticles to their typical nanosized size, and "bottom-up" techniques that gradually build the nanoparticle. The reaction conditions, in particular, can vary the shape and size of the nanoparticles, while the choice of reducing agent can alter other characteristics of the particles, such as their loading capacity and aggregation and release profiles.

GNPs, or gold nanoparticles: - GNPs are being extensively investigated as nanoparticle carriers

due to their superior conductivity, flexibility in surface modification, biocompatibility, and straightforward production methods. They also have unique photophysical properties, physical and chemical features, and the flexibility of functionalization via thiol linkages.

SNPs, or silver nanoparticles: - Because of silver's inherent inhibitory and antibacterial qualities as well as its increased conductivity, SNPs are significant inorganic nanoparticles with effectiveness due to their chemical stability and catalytic characteristics. efficiency, too. The main mechanism of action of SNPs is the release of silver ions, which increases the activity of antimicrobials and leads to denaturation of nucleic acids and distortion of cell membranes.

#### **Nanotechnology for HIV/AIDS treatment**

Similar advantages might be provided by a nanotechnology-based platform that distributes antiviral drugs throughout the body. Controlled-release delivery systems can extend their half-lives, keeping them in the bloodstream for longer periods of time at therapeutic concentrations. This might significantly improve adherence to medicine. Nanoscale delivery techniques enhance and control the distribution of hydrophobic and hydrophilic drugs into and throughout diverse tissues due to their small size. This specific feature seems to be the most promising component of nanoscale delivery systems for the therapeutic treatment and prevention of HIV.

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#### **Nanotechnology for HIV/AIDS treatment**

#### **Nanotechnology for anti retro viral drug delivery**

Nanotechnology platforms for drug distribution are revolutionizing a number of facets of sickness therapy. Cancer patients have so far benefited the most from this revolution because there have been significant improvements in recent decades. There are numerous FDA-approved or in-progress clinical nanoscale technologies for treating systemic cancer. This remarkable accomplishment is a result of the distinctive qualities that nanotechnology gives drug delivery systems. Nanotechnology has made it

feasible to deliver pharmaceuticals that aren't very water-soluble more effectively, administer medications only to certain cells or tissues, and distribute macromolecules inside cells.

Similar advantages might be provided by nanotechnology-based platforms that distribute antiviral drugs throughout the body. Controlled-release delivery methods can extend their half-lives, which

maintain them in the bloodstream for extended periods of time at therapeutic dosages. This might significantly improve adherence to medicine. Nanoscale delivery techniques enhance and control the distribution of hydrophobic and hydrophilic drugs into and throughout diverse tissues due to their small size.

This specific feature seems to be the most promising component of nanoscale delivery systems for the therapeutic treatment and prevention of HIV. To ensure that antiretroviral drugs reach latent reservoirs, they could be given specifically to CD4+ T cells, macrophages, the brain, and other organ systems. By controlling the release profiles of the delivery systems, drugs might also

be administered to the intended targets for a longer duration and at higher effective doses. To achieve these objectives, many nanoscale drug delivery methods similar to those in Figure 1 might be looked at. Amiji and Nowacek *et al.* have thoroughly assessed the use of nanotechnology systems for the delivery of antiretroviral drugs. This section only highlights a small number of the most recent and notable applications of nanotechnology in drug delivery.

#### **Nanomaterials as medical tools**

Although nanomaterials are used as delivery systems, it has been shown that they also possess therapeutic qualities on their own. Studies suggest that developing drugs based on the structure of the HIV capsid could stop viral replication. The result is

In computational and experimental study, compounds have been identified that may hinder the HIV capsid's elaboration. Several factors have been found to prevent in vitro viral replication. It is believed that the effects

of nanomaterials on viral assembly are caused by structural interference.

### Gene therapy for HIV/AIDS

In addition to efforts to find new HIV/AIDS treatment alternatives, existing antiretroviral medications are being enhanced. A gene is inserted into a cell as part of the potential alternative

method known as gene therapy to stop viral infection or viral replication. Other nucleic acid-based compounds, such as DNA, siRNA, RNA decoys, ribozymes, and aptamers, as well as protein-based compounds, such as fusion inhibitors and zinc-finger nucleases, can be used to stop viral proliferation.

In the early stages of gene therapy for HIV/AIDS, viral vectors were the main delivery method used; certain clinical trials are currently underway. Benitec Ltd. and City of Hope are collaborating on one of these studies to examine the viability and safety of a gene therapy strategy based on a single lentiviral vector that leverages stem cells for delivery and combines three different inhibitory genes. UCLA researchers recently showed that cell-derived gene transfer is both safe and biologically beneficial in HIV-infected persons in a Phase II clinical trial of gene therapy. These programmes encourage and support the growing interest in gene therapy as a potential treatment for HIV/AIDS. However, lessons learned over the past two decades suggest that the use of viral vectors for gene delivery may bring fundamental problems such as toxicity, immunogenicity, insertion mutagenesis, and limitations with scale-up techniques. These problems have sparked research into nonviral vectors for gene delivery, a field where nanotechnology platforms appear especially promising.

#### Mechanism for siRNA-based gene therapy of HIV/AIDS

These siRNA degrade mRNA in at least two different ways: (A) by preventing the development of receptors or coreceptors, which limits entry and fusion; and (B) by obstructing the translation and transcription of viral genes, which obstructs the production of proteins and genomic RNA. (The viral entrance

and replication stages listed below are the targets of the antiretroviral drugs.)

Similar to other gene therapy techniques, the challenge of delivering siRNA to specific cells and tissues has significantly impeded the use of RNAi. New nanotechnology platforms that provide nonviral replacements for effective and secure delivery are addressing this issue. Self-assembling, cyclodextrin polymer-based nanoparticles for the first nontargeted administration of siRNA in human phase I clinical studies just got going.

Nonviral siRNA delivery for the treatment of HIV infection is progressing, albeit being in its early stages. A fusion protein with an aptamer transduction domain and a double-stranded RNA-binding domain was used to encapsulate and deliver siRNA to T cells *in vivo*. When siRNA targeting CD4 and CD8 were delivered, the RNAi responses that resulted had no adverse effects related to cytotoxicity or immunological activation. Similar to this, it has been demonstrated that siRNA administration using a protamine-antibody fusion protein can stop HIV replication in primary T cells.

It has been shown that single-walled nanotubes can deliver siRNA specific to CXCR4 and CD4 to human T cells and peripheral blood mononuclear cells. CXCR4 receptors were shut down on T cells. CXCR4 receptors on peripheral blood mononuclear cells were knocked down by up to 60%, CD4 expression was decreased by up to 90%, and vice versa. In a different work, amino-terminated carbosilane dendrimers with internal carbon-silicon connections were used to transport siRNA to HIV-infected cells.

#### Immunotherapy for HIV/AIDS

The various therapy approaches listed above either specifically target HIV at the level of the host cell or the virus itself in order to effectively cure HIV/AIDS. An alternative method that alters the immune system's reaction to HIV is immunotherapy. CD8+ cytotoxic T-cell responses to acute HIV infection appear to be quite normal, despite the fact that B cell production of neutralizing antibodies is either delayed or nonexistent. Viral mutation causes

CD8+ T lymphocytes to lose their capacity for cytotoxicity over time. The primary effect of HIV infection is, however, the reduction in CD4+ T cells. When these "helper" T cells are lost, significant immunosuppression results, which is visible in people with chronic HIV infection. These "helper" T cells play a number of supportive roles for other immune populations, characterized by the presence of aberrant macrophages, natural killer cells, and B-cells. In recent years, increased focus has been placed on the therapeutic use of immune responses to restore the immune system's regular operation as an effective HIV/AIDS treatment. There is mounting evidence that the immune system may be able to regulate HIV in some individuals. Techniques that restore or enable the restoration of immunological function may therefore be among the finest means of effective treatment.

Immunotherapy is the use of immunomodulatory medications to modify the immune system's response to a disease. By immunizing people with various immunologic formulations, it functions similarly to vaccinations but treats HIV-infected patients rather than protecting the healthy (preventive vaccines will be covered in a forthcoming article). The foundation of the various HIV/AIDS immunotherapy techniques may be the delivery of cytokines (such as IL-2, IL-7, and IL-15) or antigens. APCs are required for the development of both cellular immunity and, to a significant extent, humoral immunity. APCs process and present antigen to CD4+ and CD8+ T cells. Dendritic cells (DCs), the model of a professional APC, start and direct the development of cellular and humoral (antibody) immunity. Then, protein/peptide antigens or DNA immunogens could be delivered by viral vectors to endogenous or ex vivo-produced DCs, resulting in the generation of endogenous proteins.

#### Nanotechnology for HIV/AIDS prevention

This search for a risk-free and efficient HIV/AIDS vaccine has been challenging in the nearly three decades since the

disease was identified. Many debates over vaccine development have been ignited by recent high-profile clinical trial failures, with some saying that there should be a greater emphasis on fundamental research and less on clinical trials.

The key challenges in developing a preventive HIV/AIDS vaccine have been the extensive viral strain and sequence variety, viral evasion of humoral and cellular immune responses, as well as a lack of methods to produce widely reactive neutralizing antibodies and cytotoxic T cells. To display protein antigens to CD4+ T lymphocytes (extracellular antigen in MHC class II), protein antigens must enter

APCs (like DCs), where peptides are digested and loaded into MHC class II to induce T cell responses (intracellular antigen in MHC class I) and CD8+ T cells. It is challenging to distribute exogenous antigens (like nanoparticles) to APCs because they require special "cross-presentation" in order to be presented by MHC class I and activate CD8+ cytotoxic T cells. The need for cytosolic delivery of antigens and cross-presentation is another barrier to the development of an intracellular HIV antigen vaccine, while this may be a benefit of nano delivery. It is difficult to

elicit just one cellular or humoral reaction; rather, it is difficult to elicit both. In response to intact antigens that are displayed on the surface of viruses or nanoparticles, hematopoietic responses (neutralizing antibodies produced by B cells) are produced. However, CD4+ T cells frequently need to "assist" these humoral reactions.

#### Implication of nano particles in HIV/AIDS therapy

Patients were had to take up to 40 drugs per day when this disease was first being treated. It now only calls for a

few medications per day because of advancements and developments developed in the last several decades of treatment. It has been demonstrated that an enhanced way for making therapy effective and long-lasting is the synthesis of nanoparticles with polymers that can transport ART therapies to the systems and brain cells. In essence, ART drugs are divided into groups based on

the stages of the viral agent's life-sustaining replication cycle. A combination treatment plan known as HAART is utilised to actively halt the transmission of HIV while preventing drug resistance. Antiretroviral drug administration has greatly benefited from nanotechnology, and in expanding conformity rates. Lymphatic tissues are frequently HIV-loving and infection sites.

According to research, ART drug-loaded nanoparticles specifically targeted in vitro macrophages and monocytes. Nanoparticle technology has been used as a well-known example of a breakthrough in the targeted and long-term delivery of medications. Three ART drugs (efavirenz, ritonavir, and lopinavir) were encapsulated as nanoparticles by the researchers utilizing PLGA. The nanoparticle approach provided a consistent release of drug for 4 weeks and beyond, while free medications were gone in 48 hours. HIV infection and residence in the CNS, another location (HAND), result in severe neurocognitive impairment that is associated with HIV. Additionally, nanoparticles are known to be able to phagocytose their way beyond the BBB. Studies show that anti-HIV medications are successfully administered. The most effective way to stop infections is and the ones for which immunizations are the greatest treatments since they focus more on prevention than healing. A lot of work has gone into developing vaccines that block the viral agent effectively and efficiently. New methods are emerging that can be used to advance nanotechnology, such as genetic treatment and immunotherapy. Some nanoparticles themselves possess therapeutic properties.

### Conclusion

A problem for global public health continues to be HIV/AIDS.

Through this review, it is clear that the use of nanoparticles in HIV prevention and treatment has gained more traction recently. However, there are still barriers that need to be removed in order for NPs to reach their intended target sites, particularly in macrophages and brain tissues where antiretroviral drug penetration is less than ideal, leading to a slow and ongoing intracellular replication of the viral

agent. Different NPs are utilised to deliver ART medications both within and outside of cells, and some NPs, including fullerenes, inorganic nanoparticles, and dendrimers, have demonstrated anti-HIV efficacy outside of cells.

With a number of cutting-edge strategies, nanotechnology has the potential to influence HIV/AIDS prevention and therapy. Using nanotechnology platforms for antiretroviral drug delivery may enhance treatment choices. The effectiveness of the treatment may rise as a result of better patient adherence to medication regimens brought on by controlled and prolonged drug release. Targeted nanoparticles have been utilised to attack macrophages, a significant HIV viral reservoir, using ligands such as mannose, galactose, tuftsin, and fMLF peptides. Targeted co-delivery of two or more antiviral medications in nanoparticle technology may significantly enhance treatment of viral reservoirs in the future. Our team, together with other researchers, has created nanoparticles that may co-deliver hydrophobic and hydrophilic pharmaceuticals or genes, offering adaptability for the co-delivery of antiviral medications. Nanomaterials have demonstrated their capacity to prevent viral multiplication on their own, in addition to delivering antiviral medications. Dendrimers, gold nanoparticles, fullerenes, and inorganic nanoparticles like silver have antiviral properties or enhance the antiviral properties of other compounds.

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