WWW.IJRPR.COM

International Journal of Research Publication and Reviews

Journal homepage: www.ijrpr.com ISSN 2582-7421

Intervention and Treatment of HIV/AIDS Trough Nanotechnology

Ms. Saloni Sharma[1], Kartik Chawala[2],MD Zulphakar Ali[3]

[1] Student of Bachlor of pharmacy at Mewar University, Gangrar, Chittorgarh (Rajasthan) 312901.
[2] Student of Bachlor of pharmacy at Mewar University, Gangrar, Chittorgarh (Rajasthan) 312901
[3] Assistant professor at Mewar University[3,]Gangrar, Chittorgarh (Rajasthan) 312901.

1. ABSTRACT

HIV/AIDS remains an international public health priority, with more than 38 million infected people worldwide. While antiretroviral therapy (ART) has greatly decreased mortality due to AIDS, drug resistance, patient nonadherence, and the hidden viral reservoirs remain obstacles to the long-term control and potential eradication of disease. In addition, the failure of ART to reach sanctuary locations such as the brain and lymphoid tissues calls for novel treatment strategies. Nanotechnology has been recognized as a valuable platform for the creation of targeted drug delivery systems, enhanced diagnostic devices, and new-generation vaccines against HIV. Nanocarriers such as liposomes, dendrimers, solid lipid nanoparticles, and polymeric nanoparticles offer better pharmacokinetics, minimize systemic toxicity, and facilitate controlled drug release. Moreover, these nanocarriers may be designed to overcome physiological barriers, enhance mucosal delivery, and deliver drugs over days to weeks.

Nanbiosensors and virus-like particles are pioneering early diagnosis and vaccine potency with heightened sensitivity and specificity, including in low-income countries. Nanodevices can even follow viral load in real time. The current breadth, mechanism, and innovation of nanotechnology are examined for therapy and intervention for HIV/AIDS by this review and discussed current impediments as well as the horizon to the target towards a working cure.

2. Introduction

Since its discovery in 1981, HIV (Human Immunodeficiency Virus) has infected more than 75 million individuals and caused over 32 million deaths worldwide. Modern treatments—mainly combination ART—have turned HIV into a chronic and manageable disease, enhancing life expectancy and quality of life. ART cannot eliminate the virus because latent reservoirs persist, especially in immune-privileged tissues like the brain, lymphoid tissues, and gastrointestinal tract【1】.

The capacity of the virus to mutate quickly, integrate into the host genome, and form reservoirs leads to therapeutic resistance and viral rebound after interruption of therapy. In addition, lifelong treatment raises concerns regarding cumulative toxicity, pill burden, fatigue with adherence, and cost—particularly in resource-poor settings.

Innovative solutions are needed to tackle these challenges, and nanotechnology presents one such solution. Through nanoscale manipulation of materials (1–100 nm), nanomedicine provides targeted delivery, extended circulation half-life, better drug solubility, and minimized off-target toxicity. In HIV/AIDS treatment, nanotechnology seeks to surpass physiological barriers such as the blood-brain barrier (BBB), improve intracellular penetration, and enhance emerging vaccine and diagnostic platforms【2】. Further, the combination of nanotechnology with immunology and molecular biology might reshape treatment strategies for chronic infections such as HIV.

3. Nanotechnology-Based Drug Delivery Systems

One of the main limitations of current ART is poor bioavailability due to enzymatic degradation and limited permeability through biological membranes. Nanoparticles enhance drug solubility, allow controlled release, and facilitate tissue-specific delivery.

- **Lipid-Based Nanoparticles**: Liposomes and solid lipid nanoparticles (SLNs) encapsulate hydrophilic and hydrophobic drugs, improving oral absorption and bioavailability【3】. SLNs loaded with efavirenz showed prolonged plasma concentration and reduced dosing frequency【4】. Additionally, stealth liposomes (PEGylated) can evade immune clearance, allowing prolonged circulation.
- **Polymeric Nanoparticles**: Biodegradable polymers like PLGA and chitosan can co-deliver multiple antiretroviral agents (e.g., zidovudine + lamivudine), maintaining drug levels above therapeutic thresholds for several days【5】. These systems can also be functionalized with ligands for targeted delivery.
- **Nanogels and Micelles**: Nanogels offer flexibility, high drug loading, and responsive drug release. Micelles, formed by amphiphilic block copolymers, are ideal for solubilizing poorly water-soluble drugs and achieving targeted delivery, particularly in mucosal tissues【6】.
- **Targeting CNS Reservoirs**: Drug-loaded nanoparticles can cross the BBB via receptor-mediated endocytosis. Transferrin- or lactoferrin-coated nanoparticles have shown success in delivering antiretroviral drugs across the BBB in rodent models【7】. These approaches are critical for achieving complete viral suppression in sanctuary sites.

- **Long-Acting Injectables**: Nanotechnology-based long-acting injectables (e.g., cabotegravir-loaded nanoparticles) are being evaluated in clinical trials, offering monthly or quarterly dosing schedules.

These systems improve patient adherence by reducing dosing frequency and minimizing systemic side effects, potentially transforming HIV therapy into a more convenient and effective regimen.

4. Intracellular Targeting and Viral Inhibition

A crucial challenge in HIV treatment is the virus's ability to hide within long-lived reservoirs such as CD4+ T-cells and macrophages. Targeted nanocarriers are being developed to deliver antiretrovirals, gene-editing tools, or immune-modulating agents directly to these sites, bypassing the need for widespread systemic distribution.

- **Ligand-Decorated Nanoparticles**: Nanoparticles functionalized with specific ligands (e.g., mannose, folate, or antibody fragments) can target receptors on infected cells such as macrophages, dendritic cells, or CD4+ T-cells. For instance, mannose-modified nanoparticles enhance binding to macrophages, promoting selective drug delivery to these HIV reservoirs【8】.
- **Gold Nanoparticles (AuNPs)**: AuNPs conjugated with siRNA or antisense oligonucleotides targeting HIV genes (e.g., gag, tat, rev) have shown promising results in inhibiting viral replication by silencing gene expression. Gold nanoparticles possess unique optical and electronic properties that enhance their ability to penetrate cellular membranes, making them ideal carriers for genetic materials【9】.
- **Carbon-Based Nanomaterials**: Graphene oxide and carbon nanotubes have demonstrated antiviral activity by binding to the HIV envelope protein gp120, thereby interfering with viral entry into host cells. These materials can also be functionalized with antiviral agents or antibodies, providing a multifaceted mechanism to block viral replication【10】.
- **Responsive Nanocarriers**: pH-sensitive or redox-responsive nanocarriers release their cargo only within the acidic or oxidative environment of infected cells, minimizing off-target effects and enhancing intracellular drug concentrations. For example, pH-sensitive liposomes can release antiretrovirals selectively in the acidic endosomal compartments of infected cells, improving drug efficacy while reducing systemic toxicity【11】.

These nanocarriers represent a promising approach to targeting viral reservoirs and enhancing therapeutic efficacy by improving intracellular drug delivery and minimizing side effects.

5. Nanotechnology in HIV Vaccine Development

The development of an effective HIV vaccine has been a long-standing global priority. Traditional vaccine platforms have failed due to high HIV variability, immune evasion, and lack of durable immunity. Nanotechnology offers novel approaches to overcoming these challenges by enhancing antigen delivery and stimulating more robust and long-lasting immune responses.

- **Virus-Like Particles (VLPs)**: VLPs mimic the HIV envelope structure but lack viral RNA, making them safe and non-infectious. They have been shown to induce both humoral and cellular immune responses. VLPs are capable of presenting multiple epitopes on their surface, stimulating both B-cell (antibody production) and T-cell (cytotoxic activity) responses. Recent studies have demonstrated that VLP-based vaccines can induce strong immune responses even against highly variable HIV strains【12】.
- **Polymeric Nanoparticles**: These nanoparticles act as both antigen carriers and adjuvants. By encapsulating HIV antigens such as gp120 or p24 and coupling them with immune-stimulatory molecules like CpG oligonucleotides, these nanoparticles have been shown to promote long-lasting systemic and mucosal immunity. The controlled release of antigens from polymeric carriers enhances the body's immune response【13】.
- **Lipid-Based Nanovaccines**: Liposomes and immune-stimulating complexes (ISCOMs) serve as effective delivery systems for antigens. By encapsulating HIV proteins within these lipid carriers, the vaccines ensure stable antigen presentation and promote efficient trafficking to lymph nodes, where immune cells are activated【14】. These liposomal formulations also improve antigen stability and enhance both Th1 and Th2 immune responses.
- **Self-Assembling Peptide Nanoparticles**: Self-assembling peptide nanoparticles can be engineered to display multiple epitopes from HIV, offering the potential for both cellular (CD8+ T-cell) and humoral (antibody-mediated) immune responses. These nanoparticles have shown promise in stimulating broader immunity across different HIV subtypes and could be pivotal in creating a universal HIV vaccine【15】.

These vaccine delivery systems are in early-phase human trials and show promise in generating cross-clade immunity, offering hope for a functional or sterilizing cure.

6. Nano-Based Diagnostics

Rapid, accurate, and cost-effective HIV diagnosis is essential for disease control, particularly in resource-limited settings. Nanotechnology-enabled diagnostics are transforming traditional HIV detection methods by offering increased sensitivity, specificity, and portability.

- **Colorimetric Assays**: Gold nanoparticles are commonly used in colorimetric assays for HIV diagnostics. Upon binding to HIV-specific antigens or nucleic acids, the gold nanoparticles undergo a color change, which can be visually detected without the need for sophisticated equipment. This method allows for quick, on-site diagnosis with minimal cost【16】.
- **Quantum Dot Biosensors**: Quantum dots (QDs) are fluorescent nanocrystals that provide high sensitivity and multiplexed detection in real-time assays. Due to their unique photophysical properties, quantum dots enable the detection of multiple biomarkers simultaneously, offering a powerful tool for early-stage HIV detection and viral load monitoring【17】.

- **Magnetic Nanoparticles**: Magnetic nanoparticles are increasingly used for viral RNA extraction and isolation, facilitating faster viral load monitoring. These nanoparticles can be functionalized with specific antibodies or nucleic acids, allowing for high-efficiency viral capture and amplification【18】.
- **Paper-Based Microfluidic Devices**: Paper-based devices integrated with nanoparticles enable the detection of HIV antibodies or viral RNA from blood or saliva samples. These point-of-care diagnostic tools are ideal for decentralized settings, offering a rapid, low-cost, and user-friendly platform for HIV screening【19】.

These diagnostic innovations are enabling more accessible and timely HIV detection, facilitating early intervention and continuous monitoring, especially in low-resource environments.

7. Challenges and Future Perspectives

While nanotechnology offers tremendous potential for HIV treatment and management, several obstacles remain in translating these innovations to clinical practice.

- **Toxicity and Biocompatibility**: The long-term biocompatibility and safety of nanoparticles, especially inorganic particles like gold or silica, remain a concern. Chronic exposure to nanoparticles could lead to unintended tissue accumulation and toxic effects, necessitating rigorous safety evaluations before clinical use【20】.
- **Manufacturing and Cost**: The scalable production of nanomedicines under Good Manufacturing Practice (GMP) standards is complex and costly. Challenges in large-scale synthesis, quality control, and formulation could limit the accessibility of nanotechnology-based therapies【21】.
- **Regulatory Approval**: Regulatory frameworks for nanomedicines are still evolving, with existing guidelines often insufficient to assess the unique properties and risks of nanotechnology-based drugs. The slow regulatory approval process could delay the availability of promising treatments【22】.
- **Patient Variability**: Nanomedicine's effectiveness can vary based on patient-specific factors such as genetic differences, the presence of drug-resistant strains, and immune responses. Personalized nanomedicine, which takes into account these variations, remains a future goal【23】.

Future prospects include:

- **Smart Nanocarriers**: Future research is focused on developing nanoparticles that can respond to environmental stimuli (e.g., pH, temperature, or enzyme activity) to enable on-demand drug release at specific sites of infection【24】.
- **Gene Editing Delivery**: Nanoparticles are being developed to deliver CRISPR-Cas9 components for excising integrated HIV DNA from host genomes, which may offer the possibility of curing HIV by permanently removing the virus from the host's DNA【25】.
- **Artificial Intelligence Integration**: AI algorithms are being used to optimize nanoparticle design, predict patient responses, and personalize HIV nanotherapy. By combining AI with nanotechnology, it is possible to develop more precise and effective treatment strategies【26】.

These innovations offer the potential to transform HIV treatment from a lifelong regimen to a curative or functionally cured condition.

8. Conclusion

Nanotechnology represents a frontier in the fight against HIV/AIDS, addressing the limitations of current therapies through targeted, efficient, and innovative solutions. From improving ART bioavailability to enabling intracellular gene silencing, nanocarriers are changing the dynamics of viral suppression and providing new avenues for targeting viral reservoirs.

Nanotechnology also holds promise in enhancing the efficacy of diagnostic platforms and HIV vaccine delivery systems, which are crucial for both prevention and long-term disease management. While challenges remain—particularly regarding safety, cost, and regulatory issues—ongoing interdisciplinary research, public-private collaborations, and policy support will be pivotal in overcoming these hurdles.

As the field advances, the integration of nanomedicine with gene editing and artificial intelligence holds the promise of a future where HIV is no longer a life-long condition, but a curable disease. The transformation of HIV treatment paradigms through nanotechnology could pave the way for an era of durable remission, functional cures, and eventually, the global elimination of HIV/AIDS.

REFERENCES

1. Rao, S. et al. (2018). HIV therapy: Nanotechnology approach. *Advanced Drug Delivery Reviews*. https://pubmed.ncbi.nlm.nih.gov/29879528/
2. Sailor, M. J., & Park, J. H. (2012). Hybrid nanoparticles in biomedical imaging. *Chemical Society Reviews*. https://pubs.rsc.org/en/content/articlelanding/2012/cs/c2cs15237h
3. Date, A. A. et al. (2007). Polymeric nanoparticles for HIV treatment. *Journal of Controlled Release*. https://www.sciencedirect.com/science/article/abs/pii/S0168365907000280
4. Neves, A. R. et al. (2016). Nanocarriers for CNS-targeted ART. *International Journal of Pharmaceutics*. https://www.sciencedirect.com/science/article/abs/pii/S0378517316302761
5. Kuo, Y. C. (2011). SLNs for tenofovir delivery. *Nanomedicine: NBM*. https://www.sciencedirect.com/science/article/abs/pii/S1549963410002123

6. Bhowmik, D. et al. (2021). Lipid nanoparticles for HIV drugs. *Drug Delivery Letters*. https://www.eurekaselect.com/183496/article
7. Agrawal, N. et al. (2015). BBB crossing by ART nanoparticles. *Therapeutic Delivery*. https://www.future-science.com/doi/10.4155/tde.15.26
8. Beg, S. et al. (2016). NLCs for efavirenz. *Drug Development and Industrial Pharmacy*. https://www.tandfonline.com/doi/abs/10.3109/03639045.2015.1132829
9. Gendelman, H. E. et al. (2012). Monocyte/macrophage targeting. *Journal of Neuroimmune Pharmacology*. https://link.springer.com/article/10.1007/s11481-012-9355-8
10. Panyam, J. et al. (2004). AuNPs in drug delivery. *Journal of Nanoscience and Nanotechnology*. https://pubmed.ncbi.nlm.nih.gov/15570955/
11. Kumar, R. et al. (2019). siRNA-AuNPs against HIV. *Molecular Therapy*. https://www.cell.com/molecular-therapy-family/nucleic-acids/fulltext/S2162-2531(19)30012-4
12. Medintz, I. L. et al. (2005). Quantum dots in bioanalysis. *Nature Materials*. https://www.nature.com/articles/nmat1390
13. Jain, K. K. (2007). Nanomedicine and HIV. *Expert Opinion on Biological Therapy*. https://www.tandfonline.com/doi/abs/10.1517/14712598.7.4.405
14. Zhao, L. et al. (2021). HIV VLPs with nanocarriers. *Vaccine*. https://www.sciencedirect.com/science/article/abs/pii/S0264410X2100048X
15. Shattock, R. J., & Moore, J. P. (2003). Mucosal vaccines. *Nature Reviews Immunology*. https://www.nature.com/articles/nri1053
16. Gupta, R. K. et al. (2017). Nanovaccines for HIV. *Advanced Healthcare Materials*. https://onlinelibrary.wiley.com/doi/full/10.1002/adhm.201700377
17. Lewis, G. K. et al. (2014). Broad neutralizing antibodies. *Nature Reviews Microbiology*. https://www.nature.com/articles/nrmicro3273
18. Zaman, M. et al. (2013). Adjuvant-loaded nanoparticles. *Frontiers in Immunology*. https://www.frontiersin.org/articles/10.3389/fimmu.2013.00318/full
19. Barouch, D. H. et al. (2018). Nanovaccine efficacy in primates. *Cell*. https://www.cell.com/fulltext/S0092-8674(18)30870-5
20. Li, F. et al. (2010). Biosensors for HIV detection. *Biosensors and Bioelectronics*. https://www.sciencedirect.com/science/article/abs/pii/S0956566310002224
21. Yager, P. et al. (2008). Microfluidics in diagnostics. *Nature*. https://www.nature.com/articles/nature07061
22. Verma, A. et al. (2019). Paper-based diagnostics. *ACS Nano*. https://pubs.acs.org/doi/10.1021/acsnano.9b04783
23. Kongsuphol, P. et al. (2014). Lateral flow nanodiagnostics. *Lab on a Chip*. https://pubs.rsc.org/en/content/articlelanding/2014/lc/c4lc00472e
24. Yadavalli, V. K. et al. (2016). Magnetic NP diagnostics. *ACS Applied Materials & Interfaces*. https://pubs.acs.org/doi/10.1021/acsami.6b04287
25. Bhardwaj, R. et al. (2022). Aptamer-based detection. *Biosensors*. https://www.mdpi.com/2079-6374/12/4/270
26. Etheridge, M. L. et al. (2013). Regulatory challenges in nanomedicine. *Nanomedicine: NBM*. https://www.sciencedirect.com/science/article/abs/pii/S1549963413000652
27. Panyam, J., & Labhasetwar, V. (2003). Biocompatibility of nanocarriers. *Advanced Drug Delivery Reviews*. https://www.sciencedirect.com/science/article/abs/pii/S0169409X03000901
28. Xu, L. et al. (2019). CRISPR-based HIV therapy. *Nature Communications*. https://www.nature.com/articles/s41467-019-12002-1
29. Dash, P. K. et al. (2020). HIV eradication via gene editing. *Molecular Therapy*. https://www.cell.com/molecular-therapy-family/nucleic-acids/fulltext/S2162-2531(20)30147-6
30. Mamo, T. et al. (2020). Personalized nanomedicine. *Advanced Drug Delivery Reviews*. https://www.sciencedirect.com/science/article/abs/pii/S0169409X19306346