RECENT PERSPECTIVES IN THE TREATMENT OF HIV AND MODERN MEDICINES IN CONCERN WITH NOVEL DRUG DELIVERY SYSTEM

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Abstract: Human Immunodeficiency Virus (HIV) infection remains one of the most significant infectious diseases worldwide. Although combination antiretroviral therapy (ART) has transformed HIV into a manageable chronic condition, limitations such as drug resistance, toxicity, poor adherence, and viral latency still prevent complete eradication. Recent advances in HIV treatment focus not only on discovering new drugs but also on improving drug delivery strategies. Novel drug delivery systems (NDDS), including nanoparticles, long-acting injectables, implants, and gene-based delivery platforms, are emerging as crucial tools for improving therapeutic efficacy and patient compliance. This review discusses modern HIV therapeutics, newly emerging drug classes, and the role of advanced delivery technologies in shaping future HIV management.
Keywords: HIV, antiretroviral therapy, nanotechnology, long-acting delivery, targeted delivery, NDDS

1.Introduction- Human Immunodeficiency Virus (HIV) infection continues to be a major global health concern, affecting millions of individuals worldwide. The virus progressively destroys CD4+ T-lymphocytes, leading to immune suppression and ultimately Acquired Immunodeficiency Syndrome (AIDS). According to the World Health Organization, despite significant improvements in prevention and treatment, HIV remains a chronic lifelong condition requiring continuous medical management. The introduction of combination antiretroviral therapy (ART) has dramatically reduced HIV-related mortality and transformed the disease into a manageable condition. However, conventional therapy still faces several limitations, including poor patient adherence, long-term toxicity, drug resistance, and inadequate penetration of drugs into viral reservoirs such as the brain and lymphatic tissues.

To address these challenges, recent research is shifting toward modern medicines supported by Novel Drug Delivery Systems (NDDS). Advanced delivery approaches such as nanoparticles, long-acting injectable formulations, implants, and targeted carriers are being explored to improve drug bioavailability, prolong therapeutic action, enhance tissue targeting, and reduce dosing frequency. These innovations are expected to play a crucial role in improving treatment outcomes and may contribute to future strategies aimed at long-term viral suppression or functional cure.

Causes- HIV infection is caused by the Human Immunodeficiency Virus, a retrovirus that primarily targets immune cells, especially CD4+ T-lymphocytes. The virus belongs to the *Lentivirus* group and spreads through exposure to infected body fluids. Main routes of transmission:

- Unprotected sexual contact with an infected person
- Transfusion of contaminated blood or blood products
- Sharing infected needles or syringes
- Transmission from mother to child during pregnancy, delivery, or breastfeeding
- Occupational exposure in healthcare settings (needle-stick injury)

HIV does not spread through casual contact, food, water, or air.

Symptoms- Clinical manifestations vary depending on the stage of infection.

1. Acute HIV Infection (Primary Stage)

Common symptoms-Fever, Sore throat, Fatigue, Swollen lymph nodes, Skin rash, Headache and muscle pain.

This stage often resembles flu or viral fever and may be misdiagnosed.

2. Chronic HIV Infection (Latent Stage)

During this phase, the virus continues replicating slowly while the immune system gradually weakens.

Symptoms may include- Persistent lymph node enlargement, Mild fever, Weight loss, Recurrent infections, Night sweats
Some patients may remain asymptomatic for several years.
3. AIDS Stage (Advanced Disease)
When CD4 count falls below critical levels, severe opportunistic infections develop.
Common manifestations- Severe weight loss (wasting syndrome) ,Chronic diarrhea, Tuberculosis and fungal infections, Pneumonia, Neurological disorders, Certain cancers such as Kaposi's sarcoma
At this stage, immune failure becomes life-threatening.

Pathophysiology- HIV pathophysiology involves progressive destruction of the immune system.
1. Viral Entry into the Body
The virus enters through mucosal surfaces or bloodstream and targets immune cells expressing CD4 receptors, mainly: CD4+ T lymphocytes, Macrophages, Dendritic cells
HIV binds to the CD4 receptor and co-receptors (CCR5 or CXCR4), allowing fusion with the host cell membrane.
2. Viral Replication Cycle
The HIV life cycle includes several steps:

1. Attachment and fusion – Virus binds CD4 receptors
2. Reverse transcription – Viral RNA converts into DNA
3. Integration – Viral DNA inserts into host genome
4. Transcription and translation – New viral proteins form
5. Assembly and budding – New virions released
6. Maturation – Protease enzyme produces infectious virus

This continuous replication gradually damages immune cells.
3. Immune System Destruction
HIV causes:

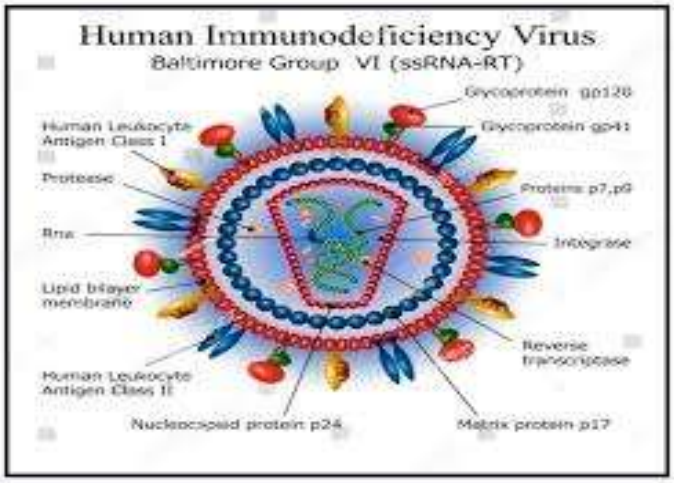
- Direct killing of infected CD4 cells
- Immune-mediated destruction of infected cells
- Chronic immune activation leading to exhaustion
- Damage to lymphoid tissues where immune cells develop

Over time, CD4 count declines and the body becomes vulnerable to opportunistic infections.
4. Formation of Viral Reservoirs
A key challenge in HIV treatment is the formation of latent reservoirs in:

- Lymph nodes
- Brain microglial cells
- Macrophages
- Gut-associated lymphoid tissue

In these sites, the virus remains hidden from drugs and immune responses, making complete eradication extremely difficult. This is why lifelong therapy is required.
5. Progression to AIDS
Without treatment, progressive immune damage leads to:

- Severe CD4 depletion
- Opportunistic infections
- Malignancies
- Multi-organ complications



2.Conventional Treatment of HIV-

The conventional treatment of HIV primarily involves combination antiretroviral therapy (ART), which suppresses viral replication, restores immune function, and prevents progression to AIDS. Current treatment guidelines recommended by global health authorities such as the World Health Organization emphasize early initiation of ART for all diagnosed individuals.

ART uses a combination of drugs from different classes to block various stages of the HIV life cycle and reduce the development of resistance.

Major Classes of Antiretroviral Drugs

1. Nucleoside/Nucleotide Reverse Transcriptase Inhibitors (NRTIs) **:** These drugs inhibit reverse transcriptase enzyme and prevent conversion of viral RNA into DNA Examples: Tenofovir, Zidovudine, Lamivudine.

2. Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs)**:** They bind directly to reverse transcriptase and block viral replication.Examples: Efavirenz, Nevirapine.

3. Protease Inhibitors (PIs) **:** These drugs prevent maturation of newly formed virus particles, making them non-infectious.Examples: Ritonavir, Lopinavir, Darunavir.

4. Integrase Strand Transfer Inhibitors (INSTIs**) :** They block integration of viral DNA into the host genome and are now first-line drugs in many regimens. Examples: Dolutegravir, Raltegravir.

5. Entry and Fusion Inhibitors **:** These drugs prevent the virus from entering host cells by blocking receptor binding or membrane fusion.Examples: Enfuvirtide, Maraviroc.

3.Limitations of Conventional Therapy –

Although combination antiretroviral therapy (ART) has significantly improved survival and quality of life in HIV patients, several limitations reduce its long-term effectiveness.

One major limitation is the requirement for lifelong daily medication, which often leads to poor patient adherence and increases the risk of treatment failure. Conventional drugs may also cause systemic toxicity and adverse effects, including metabolic disorders, liver damage, and gastrointestinal complications, which further reduce compliance.

Another important issue is the development of drug resistance due to viral mutations, especially when adherence is inconsistent. Conventional oral formulations also show limited drug penetration into viral reservoirs such as the brain, lymph nodes, and macrophages, allowing the virus to persist in the body.

In addition, many antiretroviral drugs suffer from poor bioavailability, short half-life, and lack of sustained drug release, requiring frequent dosing. High treatment cost and long-term toxicity monitoring also place a burden on healthcare systems.

These limitations highlight the need for improved delivery approaches such as Novel Drug Delivery Systems to enhance targeting, reduce toxicity, and improve patient compliance.

4.Novel Drug Delivery System (NDDS)-

Novel Drug Delivery Systems (NDDS) represent advanced approaches designed to deliver antiretroviral drugs in a controlled, targeted, and sustained manner to improve therapeutic effectiveness in HIV treatment. Conventional oral formulations often show poor bioavailability, systemic toxicity, and limited penetration into viral reservoirs. NDDS helps overcome these limitations by enhancing drug stability, improving tissue targeting, and providing prolonged drug release.

In HIV therapy, NDDS such as nanoparticles, liposomes, polymeric carriers, nanostructured lipid systems, hydrogels, and long-acting injectable formulations are being explored to improve pharmacokinetic performance and reduce dosing frequency. These systems increase drug concentration at infected tissues, enhance intracellular uptake by immune cells, and improve delivery to difficult-to-reach sites such as the brain and lymphatic tissues.

NDDS also supports the development of long-acting therapies that maintain therapeutic drug levels for weeks or months, thereby improving patient adherence and reducing resistance risk. In addition, advanced carriers such as ligand-targeted nanoparticles and lipid-based gene delivery platforms are being investigated for selective targeting of viral reservoirs.
Thus, NDDS plays a crucial role in modern HIV management by improving drug bioavailability, reducing toxicity, enhancing targeting efficiency, and enabling sustained antiviral activity.

5.Types of Novel Drug Delivery Systems (NDDS) in HIV-
Various Novel Drug Delivery Systems have been developed to improve the effectiveness of antiretroviral therapy by enhancing drug targeting, bioavailability, and sustained release.
1. Nanoparticles : Nanoparticles are nanosized carrier systems that improve drug stability, enhance intracellular uptake, and allow targeted delivery to infected immune cells. They also provide controlled drug release and improved penetration into viral reservoirs.
2. Liposomes : Liposomes are lipid-based vesicles capable of carrying both hydrophilic and lipophilic drugs. They protect drugs from degradation, improve bioavailability, and enhance delivery to macrophages and lymphatic tissues.
3. Polymeric Micelles : Polymeric micelles are formed from amphiphilic polymers and are useful for delivering poorly water-soluble antiretroviral drugs. They improve solubility, stability, and sustained drug release.
4. Dendrimers : Dendrimers are highly branched polymeric carriers that provide precise drug targeting, high drug loading capacity, and controlled release. Some dendrimers also show intrinsic antiviral activity.
5. Hydrogels : Hydrogels are three-dimensional polymer networks that can release drugs slowly over time. They are useful for sustained and localized delivery of antiretroviral agents.
6. Nanostructured Lipid Carriers (NLC) and Solid Lipid Nanoparticles (SLN) : These lipid-based systems improve drug stability, enhance bioavailability, and allow controlled drug release. They are especially useful for lipophilic HIV drugs.
7. Long-Acting Injectable Systems : These include nanosuspensions, depot injections, and implantable formulations that maintain drug levels for weeks or months, reducing dosing frequency and improving adherence.

6.Modern Medicines used with Novel Drug Delivery Systems (NDDS)- Modern antiretroviral drugs used in combination with Novel Drug Delivery Systems (NDDS) have significantly improved HIV treatment by enhancing drug targeting, reducing toxicity, and providing sustained antiviral activity. NDDS allows these medicines to be delivered in a controlled and site-specific manner, improving therapeutic effectiveness and patient adherence.
1. Tenofovir : Tenofovir is a widely used nucleotide reverse transcriptase inhibitor. Nanoformulations such as lipid nanoparticles and polymeric carriers improve its tissue penetration, prolong drug release, and reduce dosing frequency.
2. Efavirenz : Efavirenz is a non-nucleoside reverse transcriptase inhibitor with poor aqueous solubility. Delivery through nanoparticles and lipid-based carriers enhances solubility, bioavailability, and reduces central nervous system side effects.
3. Dolutegravir : Dolutegravir, an integrase inhibitor, is now a first-line drug in many treatment regimens. Long-acting nano-depot systems and injectable formulations help maintain therapeutic levels for extended periods and improve viral suppression.
4. Darunavir : Darunavir is a protease inhibitor used in resistant HIV infections. NDDS such as polymeric nanoparticles and liposomes enhance its solubility, stability, and intracellular targeting.
5. Cabotegravir : Cabotegravir is an integrase inhibitor used in long-acting injectable therapy. When delivered through nanosuspension-based depot systems, it maintains drug levels for months and significantly improves patient adherence.
6. Oligonucleotide-Based Therapies : Modern gene-targeted approaches such as siRNA and antisense therapies are being explored for HIV treatment. Lipid nanoparticles and polymeric carriers improve their stability, cellular uptake, and gene-silencing efficiency.
Overall, the combination of modern antiretroviral medicines with NDDS enhances drug bioavailability, improves targeting of viral reservoirs, reduces systemic toxicity, and supports the development of long-acting HIV therapies.

7.Recent Advances in HIV Treatment using Novel Drug Delivery Systems- Recent years have seen major progress in HIV therapy through the integration of Novel Drug Delivery Systems (NDDS) aimed at improving adherence, targeting viral reservoirs, and achieving long-term viral suppression.
One of the most important advances is the development of long-acting injectable antiretroviral formulations. These systems allow drug release over weeks or months, reducing the need for daily oral therapy. Clinical evidence shows that long-acting injectables maintain viral suppression in nearly all treated patients and are especially beneficial for individuals with adherence difficulties.
Another major innovation is the use of nanotechnology-based delivery systems, such as polymeric nanoparticles, liposomes, and lipid-based carriers. These carriers enhance drug stability, improve intracellular uptake, and enable targeted delivery to HIV reservoirs such as lymph nodes and macrophages, which are difficult to reach with conventional therapy.

Recent research also highlights capsid-targeting long-acting drugs delivered through advanced formulations. For example, newer injectable antivirals that act early in the viral life cycle can be administered only a few times per year, offering extremely high preventive and therapeutic efficacy.

In addition, RNA-based and gene-delivery approaches using NDDS platforms are being explored to address latent HIV infection. These systems attempt to either reactivate hidden virus ("shock and kill") or permanently silence it ("block and lock"), which could move therapy closer to a functional cure.

Overall, modern NDDS strategies in HIV treatment focus on:

- Long-acting injectable formulations
- Nanoparticle-mediated targeted delivery
- Depot-based sustained drug release
- RNA/gene delivery systems targeting viral latency

These advances are shifting HIV therapy from daily lifelong medication toward long-duration, targeted, and potentially curative approaches.

8.Advantages of Novel Drug Delivery Systems (NDDS)-

Novel Drug Delivery Systems (NDDS) offer several advantages over conventional antiretroviral therapy by improving drug delivery efficiency, safety, and patient compliance.

NDDS enables targeted drug delivery to infected tissues such as macrophages, lymph nodes, and the brain, which helps increase drug concentration at viral reservoir sites while minimizing exposure to healthy tissues. These systems also provide controlled and sustained drug release, allowing maintenance of therapeutic drug levels for extended periods and reducing the need for frequent dosing.

Another key benefit is improved bioavailability, especially for poorly soluble antiretroviral drugs. NDDS protects drugs from degradation, enhances absorption, and improves intracellular uptake. By reducing systemic drug exposure, NDDS also helps minimize toxicity and adverse effects, thereby improving patient tolerance.

In addition, long-acting NDDS formulations significantly improve treatment adherence, which is crucial for preventing resistance development and maintaining viral suppression. Overall, NDDS enhances therapeutic efficacy, reduces dosing burden, improves drug stability, and supports the development of more effective long-acting HIV therapies.

9.Future Perspectives-

Future strategies in HIV treatment are expected to focus on integrating modern medicines with advanced Novel Drug Delivery Systems (NDDS) to achieve safer, long-acting, and more targeted therapy. One major direction is the development of ultra-long-acting injectable formulations and implantable delivery systems that can maintain therapeutic drug levels for several months or even a year, thereby reducing dosing frequency and improving patient adherence.

Research is also progressing toward targeted delivery systems capable of transporting drugs specifically to viral reservoirs such as the brain, lymph nodes, and macrophages. Ligand-mediated nanoparticles, antibody-linked carriers, and receptor-specific delivery platforms are being explored to enhance selectivity and therapeutic effectiveness.

Another important future direction involves gene- and RNA-based therapies, including siRNA delivery, CRISPR-based gene editing, and therapeutic vaccines, which aim to suppress or eliminate latent HIV infection. Advances in nanotechnology and lipid-based carriers are expected to play a crucial role in safely delivering these therapies into target cells.

In addition, the growth of personalized medicine and AI-assisted drug design may allow treatment to be tailored according to individual viral characteristics and patient response. Overall, the combination of modern antiretroviral drugs with innovative delivery technologies is expected to improve long-term viral control and move closer to the goal of a functional cure for HIV.

Conclusion-

HIV remains a major chronic infectious disease requiring lifelong treatment despite significant progress in antiretroviral therapy. Although conventional ART effectively suppresses viral replication, its limitations such as toxicity, resistance, and poor adherence highlight the need for improved therapeutic strategies. Novel Drug Delivery Systems offer promising solutions by enhancing drug targeting, improving bioavailability, enabling sustained release, and reducing dosing frequency. The integration of modern antiretroviral medicines with NDDS is transforming HIV management toward long-acting, targeted, and more patient-friendly therapies. Continued research in nanotechnology, gene delivery, and precision medicine is expected to further improve treatment outcomes and may ultimately contribute to long-term viral control or functional cure.

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