

# Evaluation of Novel Drug Delivery System for an Anti-HIV Drugs

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**Abstract:** Human Immunodeficiency Virus (HIV) infection continues to be one of the most serious public health challenges worldwide. HIV attacks the immune system, especially CD4+ T lymphocytes, leading to gradual weakening of immune defenses. If untreated, HIV progresses to Acquired Immunodeficiency Syndrome (AIDS), making the body vulnerable to opportunistic infections and cancers.

**Keywords:** Human Immunodeficiency Virus

## I. INTRODUCTION

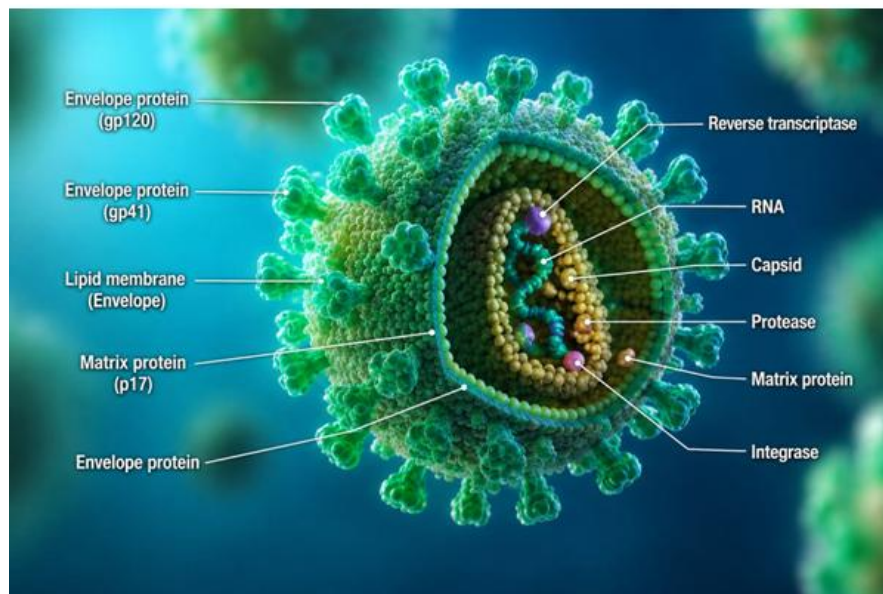


Figure 1: Structure of Human Immunodeficiency Virus (HIV)

Human Immunodeficiency Virus (HIV) infection continues to be one of the most serious public health challenges worldwide. HIV attacks the immune system, especially CD4+ T lymphocytes, leading to gradual weakening of immune defenses. If untreated, HIV progresses to Acquired Immunodeficiency Syndrome (AIDS), making the body vulnerable to opportunistic infections and cancers. (24, 23, 27)

Antiretroviral therapy has significantly improved the survival rate and quality of life of HIV patients. However, conventional anti-HIV therapy has several drawbacks such as poor drug solubility, low bioavailability, toxicity, frequent dosing, and development of drug resistance.

### AIM

The aim of the present work is to develop and evaluate Novel Drug Delivery Systems (NDDS) for anti-HIV therapy in order to improve bioavailability, targeted drug delivery, therapeutic efficacy, and patient compliance. The study mainly



focuses on nanotechnology-based approaches such as Solid Lipid Nanoparticles (SLNs) for effective delivery of antiretroviral drugs to HIV reservoir sites and for overcoming the limitations associated with conventional antiretroviral therapy.

### **OBJECTIVE**

- To study the pathophysiology and life cycle of Human Immunodeficiency Virus (HIV).
- To understand the limitations of conventional antiretroviral therapy and Highly Active Antiretroviral Therapy (HAART).
- To investigate various Novel Drug Delivery Systems (NDDS) used for anti-HIV drug delivery.
- To study nanotechnology-based drug delivery systems for HIV/AIDS treatment.
- To develop and evaluate Solid Lipid Nanoparticles (SLNs) for anti-HIV drug delivery.
- To improve bioavailability and targeted delivery of anti-HIV drugs to reservoir sites.
- To achieve sustained and controlled release of antiretroviral drugs.
- To reduce systemic toxicity and improve therapeutic effectiveness.
- To enhance patient compliance by reducing dosing frequency.
- To evaluate formulation parameters such as particle size, entrapment efficiency, drug release, and stability of the developed system.

### **LITERATURE REVIEW**

#### **Research on Anti-Retroviral Drug Delivery System**

Human Immunodeficiency Virus (HIV) infection remains one of the major global public health problems despite remarkable progress in antiretroviral therapy (ART). HIV mainly attacks CD4+ T lymphocytes, macrophages, and dendritic cells, resulting in progressive weakening of the immune system. Although conventional antiretroviral therapy has significantly improved survival and reduced HIV-associated mortality, several limitations such as poor bioavailability, short half-life, systemic toxicity, poor patient compliance, drug resistance, and inadequate penetration into viral reservoir sites still remain. (24, 25, 27)

Researchers have focused extensively on the development of Novel Drug Delivery Systems (NDDS) to overcome the limitations associated with conventional anti-HIV therapy. NDDS improve targeted drug delivery, controlled release, bioavailability, therapeutic efficacy, and patient adherence while reducing systemic toxicity. Nanotechnology-based drug delivery systems have gained considerable attention because of their ability to deliver drugs effectively to infected tissues and HIV reservoir sites. (6, 7, 8)

Nanoparticles are among the most widely investigated carriers for anti-HIV drug delivery. Due to their nanosized structure, nanoparticles improve cellular uptake, increase permeability across biological barriers, and provide sustained drug release. Polymeric nanoparticles and lipid-based nanoparticles have demonstrated promising results in improving the therapeutic efficacy of anti-HIV drugs.

Liposomes are phospholipid vesicular systems capable of encapsulating both hydrophilic and lipophilic drugs. Liposomal formulations improve intracellular drug uptake, prolong circulation time, and reduce toxicity associated with conventional therapy. Studies have shown that liposome-based systems enhance drug accumulation in infected tissues and improve antiviral activity. (12, 30)

Solid Lipid Nanoparticles (SLNs) have emerged as promising carriers for anti-HIV drug delivery because of their biocompatibility, biodegradability, controlled release behavior, and improved stability. SLNs protect incorporated drugs from degradation and improve oral bioavailability of poorly water-soluble drugs. Research findings indicate that SLNs enhance lymphatic targeting and improve penetration into HIV reservoir sites such as macrophages and brain tissues.



Overall, bio-analytical literature plays an important role in the development, evaluation, and therapeutic monitoring of anti-HIV drug delivery systems. (22, )

### **Bio-Distribution and Bio-Availability**

Bioavailability refers to the rate and extent of drug absorption into systemic circulation, whereas biodistribution describes the distribution of drugs into different tissues and organs after administration. (4, 16)

Many anti-HIV drugs exhibit poor oral bioavailability because of low aqueous solubility, poor permeability, enzymatic degradation, and extensive first-pass metabolism. Novel Drug Delivery Systems improve bioavailability by enhancing drug solubility, dissolution rate, and intestinal absorption. (10, 11)

Nanocarriers such as nanoparticles, liposomes, nanoemulsions, and SLNs improve lymphatic uptake and reduce hepatic first-pass metabolism. These systems prolong circulation time and enhance drug accumulation at infected tissues. (5, 30, 31)

Biodistribution studies have demonstrated that nanotechnology-based carriers improve delivery of anti-HIV drugs to viral reservoir sites such as macrophages, lymphatic tissues, spleen, and brain tissues. Enhanced biodistribution improves therapeutic efficacy and reduces systemic toxicity.

Long-circulating nanoformulations maintain sustained plasma drug concentrations and reduce dosing frequency, thereby improving patient compliance and treatment outcomes.

Drug bioavailability plays a major role in determining the therapeutic effectiveness of anti-HIV formulations. Poor bioavailability may result in inadequate drug concentration at the target site, reduced antiviral activity, and development of drug resistance. Therefore, improvement of bioavailability is an important objective in the development of Novel Drug Delivery Systems for anti-HIV therapy. (16, 32)

Nanotechnology-based drug delivery systems improve absorption and distribution of anti-HIV drugs by increasing surface area, improving solubility, and enhancing permeability across biological membranes. Nanocarriers also protect drugs from enzymatic degradation and improve stability during systemic circulation.

Biodistribution studies are essential for evaluating the targeting efficiency of nanocarriers in different organs and tissues. Advanced drug delivery systems are designed to deliver anti-HIV

Dolutegravir and Cabotegravir are advanced Integrase Strand Transfer Inhibitors with high antiviral potency and improved resistance profile. Long-acting formulations of Cabotegravir have shown promising results for prolonged HIV therapy and improved patient compliance.

Most anti-HIV drugs are administered orally; however, poor aqueous solubility and limited permeability reduce absorption and therapeutic effectiveness. Several drugs also undergo extensive hepatic metabolism and exhibit low penetration into HIV reservoir sites such as brain tissues and macrophages. (8, 32)

Common adverse effects associated with anti-HIV drugs include hepatotoxicity, nephrotoxicity, gastrointestinal disturbances, lipodystrophy, metabolic disorders, neurological complications, and hypersensitivity reactions. Long-term therapy may also result in development of viral resistance due to mutation of HIV. (15, 24)

Novel Drug Delivery Systems such as nanoparticles, liposomes, nanoemulsions, and Solid Lipid Nanoparticles are extensively investigated to improve drug stability, bioavailability, targeted delivery, sustained release, and therapeutic effectiveness of anti-HIV drugs. (3, 5, 6)

Drug profiling is therefore important for understanding the physicochemical properties, therapeutic applications, pharmacological activity, and formulation challenges associated with anti-HIV agents. (16, 8, 22)

### **Excipient Profile**

Excipients are inactive pharmaceutical ingredients used in formulation development to improve stability, solubility, bioavailability, and overall therapeutic performance of drug delivery systems.

Different excipients used in anti-HIV nanocarrier formulations include lipids, surfactants, emulsifiers, polymers, stabilizers, and co-solvents. Common lipids used in SLNs include glyceryl monostearate, stearic acid, and tristearin.



Surfactants such as Tween 80, Poloxamer, and Span are widely used for stabilization of nanoparticles and nanoemulsions. (5, 3, 11)

Polymers such as chitosan, PLGA, polyethylene glycol, and polycaprolactone are commonly used in nanoparticle formulations. Excipients improve particle stability, drug entrapment efficiency, controlled release behavior, and targeting capability.

Selection of suitable excipients is important for maintaining formulation stability, minimizing toxicity, and improving therapeutic effectiveness of anti-HIV drug delivery systems.

**FUTURE SCOPE**

Novel Drug Delivery Systems (NDDS) have shown significant potential for improving the therapeutic effectiveness of anti-HIV drugs. Future research may focus on development of advanced nanotechnology-based delivery systems with improved targeting efficiency, enhanced bioavailability, and reduced systemic toxicity.

Further studies can be carried out on long-acting nanoformulations, targeted drug delivery systems, and ligand-mediated nanocarriers for selective delivery of anti-HIV drugs to viral reservoir sites such as macrophages, lymphatic tissues, and brain tissues.

Advanced approaches such as gene therapy, nanorobotics, stimuli-responsive nanoparticles, and combination nanoformulations may provide improved therapeutic outcomes and better management of HIV/AIDS in the future.

Additional clinical studies and large-scale evaluations are required to establish long-term safety, stability, efficacy, and regulatory acceptance of Novel Drug Delivery Systems for anti-HIV therapy.

**LIFE CYCLE OF RETROVIRUS**

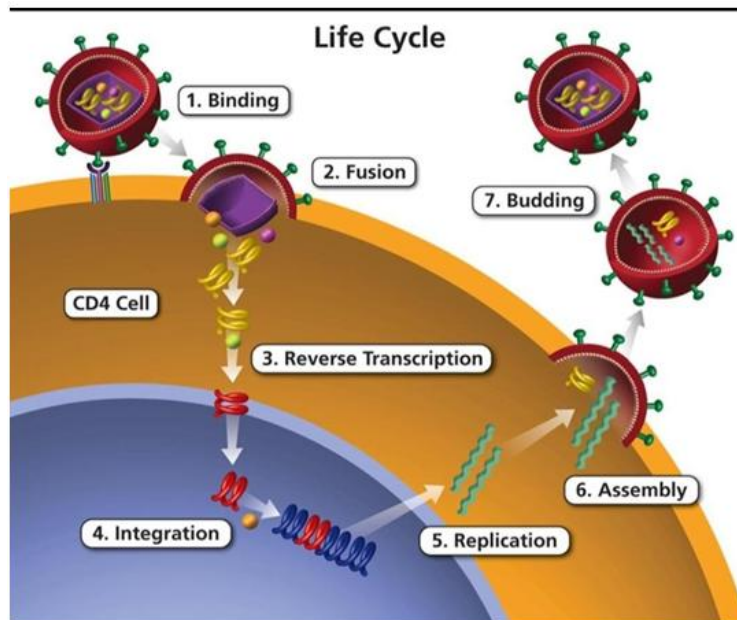


Figure 2: HIV Viral Life Cycle

The life cycle of Human Immunodeficiency Virus (HIV) involves several sequential steps that enable the virus to infect host cells, replicate, and produce new infectious viral particles. Understanding the HIV life cycle is essential for the development of effective antiretroviral therapy and novel drug delivery systems. (14, 15, 27)



1. Attachment and Binding

The HIV virus initially attaches to the CD4 receptors present on the surface of host immune cells such as CD4+ T lymphocytes, macrophages, and dendritic cells. The viral glycoprotein gp120 binds specifically to the CD4 receptor along with co-receptors CCR5 or CXCR4.

2. Fusion and Entry

**CLASSIFICATION of ANTI- HIV DRUGS**

Anti-HIV drugs, also known as antiretroviral drugs, are used to suppress the replication of Human Immunodeficiency Virus (HIV) and reduce viral load in the body. These drugs act at different stages of the HIV life cycle and are generally used in combination therapy for effective treatment.

Anti-HIV drugs are classified into the following categories:

**1. Nucleoside Reverse Transcriptase Inhibitors (NRTIs)**

These drugs inhibit the reverse transcriptase enzyme by acting as nucleoside analogs and prevent the synthesis of viral DNA.

Examples:

- Zidovudine
- Lamivudine
- Abacavir
- Tenofovir

**2. Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs)**

These drugs directly inhibit the reverse transcriptase enzyme by binding to a specific site on the enzyme.

Examples:

- Nevirapine
- Efavirenz
- Delavirdine

**3. Protease Inhibitors (PIs)**

Protease inhibitors block the protease enzyme required for maturation of viral proteins, thereby preventing the formation of mature infectious virions.

Examples:

- Ritonavir
- Indinavir
- Saquinavir
- Lopinavir

**4. Integrase Strand Transfer Inhibitors (INSTIs)**

Class	Example Drug	Mechanism of Action (MOA)	Adverse Effects (ADR)	Usual Dose
NRTIs	Zidovudine	Inhibits reverse transcriptase enzyme and prevents viral DNA synthesis	Anemia, nausea, headache	300 mg twice daily
NRTIs	Lamivudine	Acts as nucleoside analogue and inhibits viral replication	Fatigue, nausea, pancreatitis	150 mg twice daily
NRTIs	Tenofovir	Blocks reverse transcriptase enzyme	Renal toxicity, bone loss	300 mg once daily
NNRTIs	Efavirenz	Non-competitive inhibition of reverse transcriptase enzyme	Dizziness, insomnia, rash	600 mg once daily



NNRTIs	Nevirapine	Inhibits reverse transcriptase enzyme	Hepatotoxicity, skin rash	200 mg once daily
Protease Inhibitors	Ritonavir	Inhibits HIV protease enzyme required for viral maturation	Diarrhea, hyperlipidemia	600 mg twice daily
Protease Inhibitors	Lopinavir	Prevents maturation of infectious virions	Nausea, diarrhea	400 mg twice daily
INSTIs	Dolutegravir	Inhibits integration of viral DNA into host genome	Headache, insomnia	50 mg once daily
INSTIs	Raltegravir	Blocks HIV integrase enzyme	Nausea, fatigue	400 mg twice daily
Fusion Inhibitors	Enfuvirtide	Prevents fusion of HIV with host cell membrane	Injection site reactions	900 mg twice daily
Entry Inhibitors	Maraviroc	Blocks CCR5	Cough, fever, rash	300 mg twice daily

Table 1: Classification of Anti HIV Drugs

### COMBINATION THERAPY

Combination therapy, also known as Highly Active Antiretroviral Therapy (HAART), involves the use of two or more antiretroviral drugs from different classes for the treatment of HIV infection. The main purpose of combination therapy is to suppress viral replication, reduce viral load, improve immune function, and prevent the development of drug resistance. (15, 25, 29) Single-drug therapy is generally ineffective because HIV rapidly mutates and develops resistance. Therefore, a combination of drugs acting at different stages of the HIV life cycle is used to achieve better therapeutic outcomes.

HAART commonly includes a combination of Nucleoside Reverse Transcriptase Inhibitors (NRTIs), Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs), Protease Inhibitors (PIs), or Integrase Strand Transfer Inhibitors (INSTIs). (15, 25)

Combination therapy offers several advantages such as prolonged survival, reduced opportunistic infections, improved CD4+ T cell count, and better quality of life in HIV patients. However, long-term therapy may still be associated with toxicity, drug interactions, poor patient compliance, and development of resistance.

Novel Drug Delivery Systems (NDDS) are being explored to improve the effectiveness of combination therapy by providing controlled release, targeted delivery, and improved bioavailability of anti-HIV drugs. (3, 2, 32, 34)

Combination therapy is considered the standard treatment approach for HIV infection because it reduces the chances of viral mutation and development of drug resistance. The use of multiple antiretroviral drugs acting through different mechanisms provides synergistic therapeutic action and improves viral suppression. HAART therapy generally consists of two Nucleoside Reverse Transcriptase Inhibitors (NRTIs) combined with one Protease Inhibitor (PI),

Non-Nucleoside Reverse Transcriptase Inhibitor (NNRTI), or Integrase Strand Transfer Inhibitor (INSTI). (15, 25, 29)

Combination therapy significantly decreases HIV viral load to undetectable levels and helps restore immune function by increasing CD4+ T-cell count. Effective viral suppression reduces the incidence of opportunistic infections and improves the overall quality of life and survival rate of HIV patients. (24, 29)

### REGIMENS

Antiretroviral regimens are combinations of anti-HIV drugs used for the effective management of Human Immunodeficiency Virus (HIV) infection. The primary goal of these regimens is to suppress viral replication, reduce viral load, restore immune function, and improve the quality of life of patients.

Standard HIV treatment regimens usually consist of a combination of at least three antiretroviral drugs from two or more different classes. Combination regimens are preferred because they reduce the risk of drug resistance and provide better therapeutic efficacy. (15, 25)



The commonly recommended first-line regimen includes two Nucleoside Reverse Transcriptase Inhibitors (NRTIs) along with one Integrase Strand Transfer Inhibitor (INSTI) or one Non-Nucleoside Reverse Transcriptase Inhibitor (NNRTI).

Examples of commonly used regimens include:

Tenofovir + Lamivudine + Dolutegravir Zidovudine + Lamivudine + Nevirapine Tenofovir + Emtricitabine + Efavirenz

Second-line regimens are generally used when resistance or treatment failure occurs with first-line therapy. These regimens may include Protease Inhibitors (PIs) combined with other antiretroviral drugs. (15, 25)

Selection of an appropriate regimen depends on several factors such as viral load, CD4 count, drug resistance, patient compliance, adverse effects, and co-existing diseases. Proper adherence to antiretroviral regimens is essential for successful HIV treatment and prevention of resistance development.

Novel Drug Delivery Systems (NDDS) are being investigated to improve the effectiveness of antiretroviral regimens by enhancing drug targeting, reducing toxicity, and providing sustained drug release. (3, 8, 30, 32, 34)

Different antiretroviral regimens are designed based on the stage of HIV infection, patient condition, previous treatment history, and resistance profile. Modern HIV treatment guidelines recommend highly active combination regimens because they provide effective viral suppression and long-term disease management. Early initiation of antiretroviral therapy helps reduce HIV transmission, improve immune recovery, and decrease HIV-related complications. (15, 24, 25, 29)

**HIV RESERVOIR SITES**

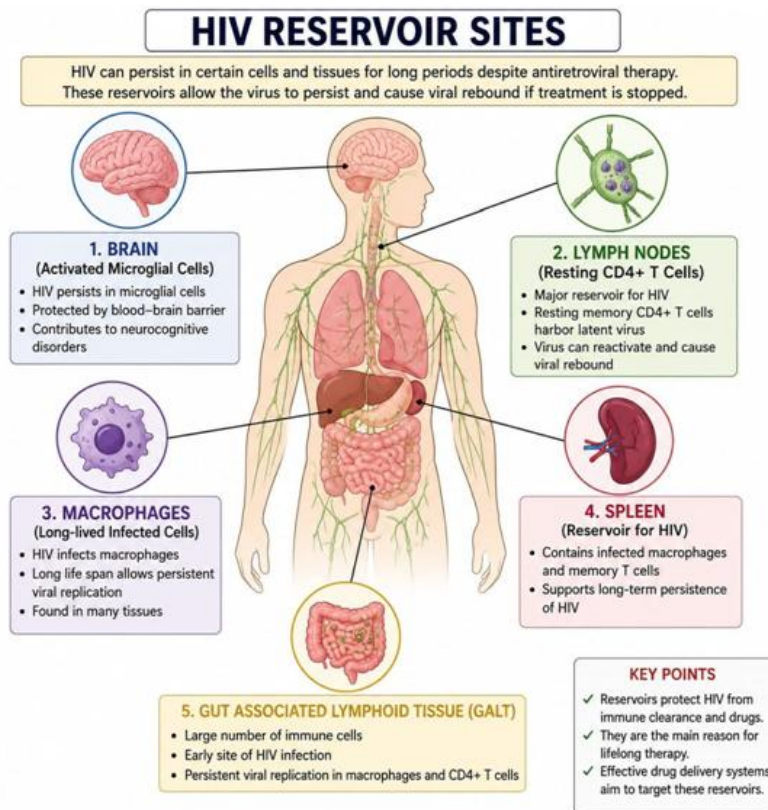


Fig 3: HIV Reservoir Sites



HIV reservoir sites are anatomical locations in the body where the Human Immunodeficiency Virus (HIV) persists for long periods despite antiretroviral therapy (ART). These reservoirs contain latently infected cells that harbor integrated viral DNA and act as a major barrier to complete eradication of HIV infection. (24, 27, 31, 32)

The major HIV reservoir sites include lymphoid tissues, lymph nodes, brain, macrophages, spleen, gastrointestinal tract, bone marrow, and genital tract. In these tissues, HIV remains

**NANOTECHNOLOGY-BASED SYSTEMS FOR HIV/AIDS TREATMENT**

**NANOTECHNOLOGY-BASED DRUG DELIVERY SYSTEMS FOR ANTI-HIV DRUGS**

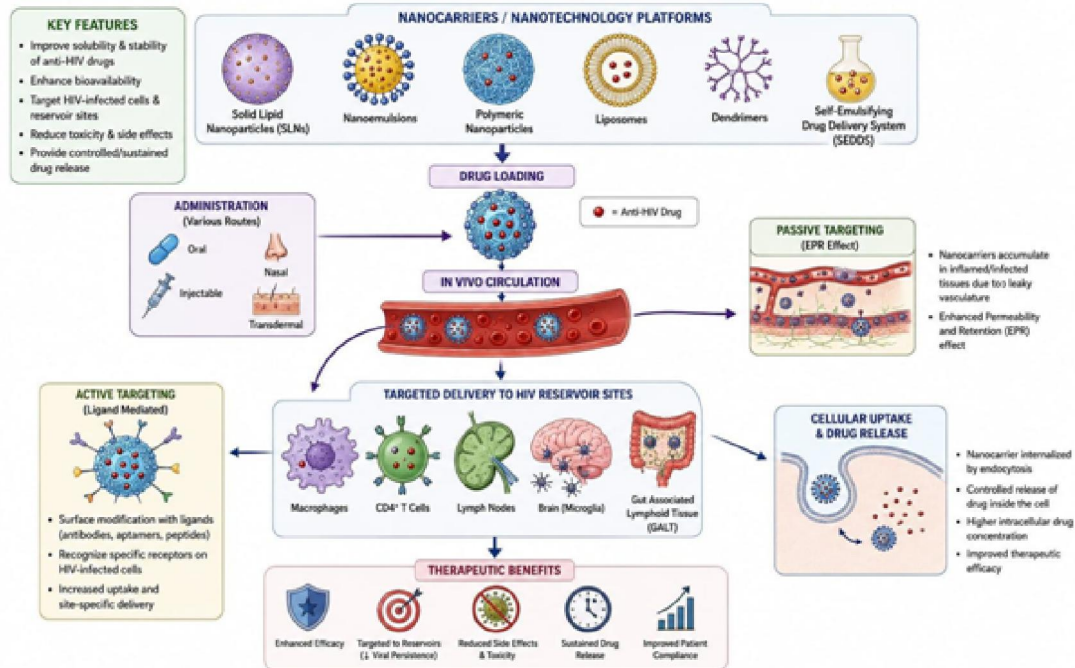


Fig 4: Nanotechnology Based Drug Delivery System For Anti HIV Drugs

Nanotechnology-based drug delivery systems have emerged as promising approaches for the treatment and management of Human Immunodeficiency Virus (HIV/AIDS). These systems utilize nanosized carriers to improve the delivery, bioavailability, therapeutic efficacy, and targeting of anti-HIV drugs. Nanotechnology helps overcome the limitations associated with conventional antiretroviral therapy such as poor drug solubility, low bioavailability, systemic toxicity, frequent dosing, and inadequate penetration into HIV reservoir sites.

Various nanotechnology-based systems including nanoparticles, liposomes, dendrimers, nanoemulsions, solid lipid nanoparticles, nanocrystals, and polymeric micelles are widely investigated for anti-HIV therapy. These nanocarriers can encapsulate antiretroviral drugs and provide controlled, sustained, and targeted drug release, thereby improving therapeutic effectiveness. (34, 37, 31, 8, 5)

**LYMPHATIC SYSTEM DELIVERY**

The lymphatic system plays an important role in the pathogenesis and persistence of Human Immunodeficiency Virus (HIV) infection. Lymphoid tissues and lymph nodes act as major reservoir sites where HIV remains hidden and continues to replicate despite antiretroviral therapy. Therefore, lymphatic targeting has emerged as an important strategy for improving the effectiveness of anti-HIV drug delivery.



Lymphatic drug delivery systems are designed to enhance the transport of antiretroviral drugs into lymphatic tissues and infected immune cells. Targeted delivery to the lymphatic system improves drug concentration at viral reservoir sites and enhances therapeutic efficacy while reducing systemic toxicity.

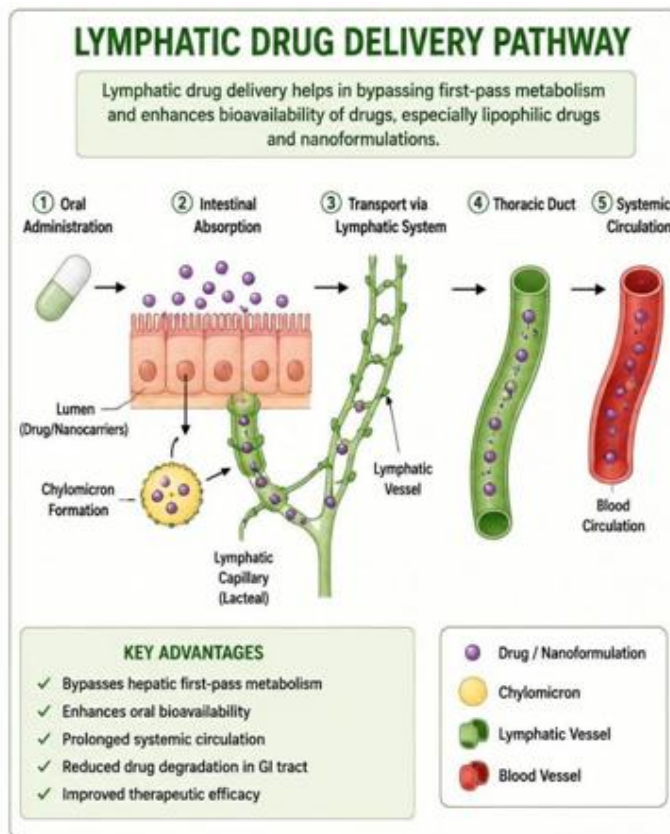


Fig 4: Lymphatic System Delivery Pathway of Nanocarrier

### NON-POLYMERIC NANOCARRIER-BASED ANTI-RETROVIRAL THERAPY

Non-polymeric nanocarriers are nanosized drug delivery systems that do not contain polymeric materials and are widely used for the delivery of anti-HIV drugs. These nanocarriers improve the therapeutic efficacy, bioavailability, stability, and targeted delivery of antiretroviral drugs while reducing toxicity and adverse effects.

Various non-polymeric nanocarriers such as liposomes, solid lipid nanoparticles, nanoemulsions, nanocrystals, and lipid-based carriers have shown promising applications in anti-retroviral therapy. These systems can encapsulate both hydrophilic and lipophilic drugs and provide controlled and sustained drug release. (3, 4, 8, 9, 31)

Liposomes are phospholipid vesicles capable of improving drug targeting and reducing systemic toxicity. Solid lipid nanoparticles provide enhanced drug stability, controlled release, and improved lymphatic uptake. Nanoemulsions improve drug solubility and oral bioavailability, whereas nanocrystals increase dissolution rate and absorption of poorly soluble anti-HIV drugs. Non-polymeric nanocarriers can effectively penetrate biological barriers and deliver drugs to viral reservoir sites such as macrophages, lymph nodes, and brain tissues. These systems also prolong circulation time and reduce dosing frequency, thereby improving patient compliance.

The use of non-polymeric nanocarriers in anti-retroviral therapy has demonstrated significant potential for enhancing targeted drug delivery and improving the overall management of HIV infection. (31, 32, 34)



**SOLID LIPID NANOPARTICLES**

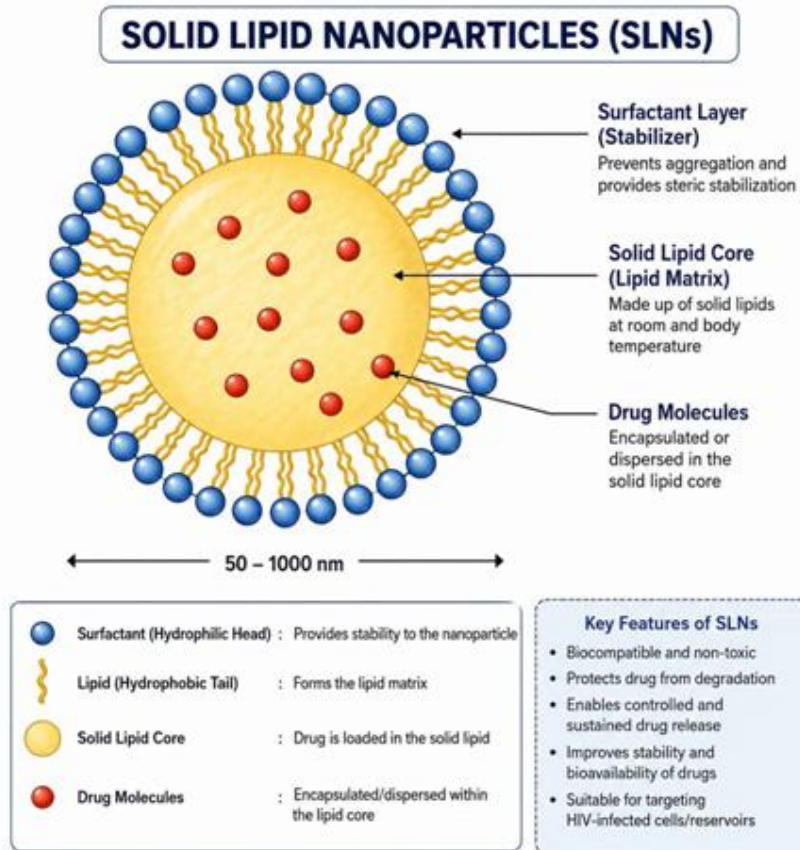


Fig 5: Structure of Solid Lipid Nanoparticles

Solid Lipid Nanoparticles (SLNs) are submicron colloidal carrier systems composed of physiological lipids that remain solid at both room temperature and body temperature. SLNs have gained considerable attention as promising drug delivery systems for anti-HIV therapy because of their biocompatibility, controlled drug release, improved stability, and targeted delivery properties.

SLNs combine the advantages of traditional colloidal carriers such as liposomes and polymeric nanoparticles while minimizing their limitations. These carriers are generally prepared using solid lipids, surfactants, and stabilizers. Anti-HIV drugs can be incorporated into the lipid matrix to improve their therapeutic efficacy and bioavailability.



**NANOEMULSIONS**

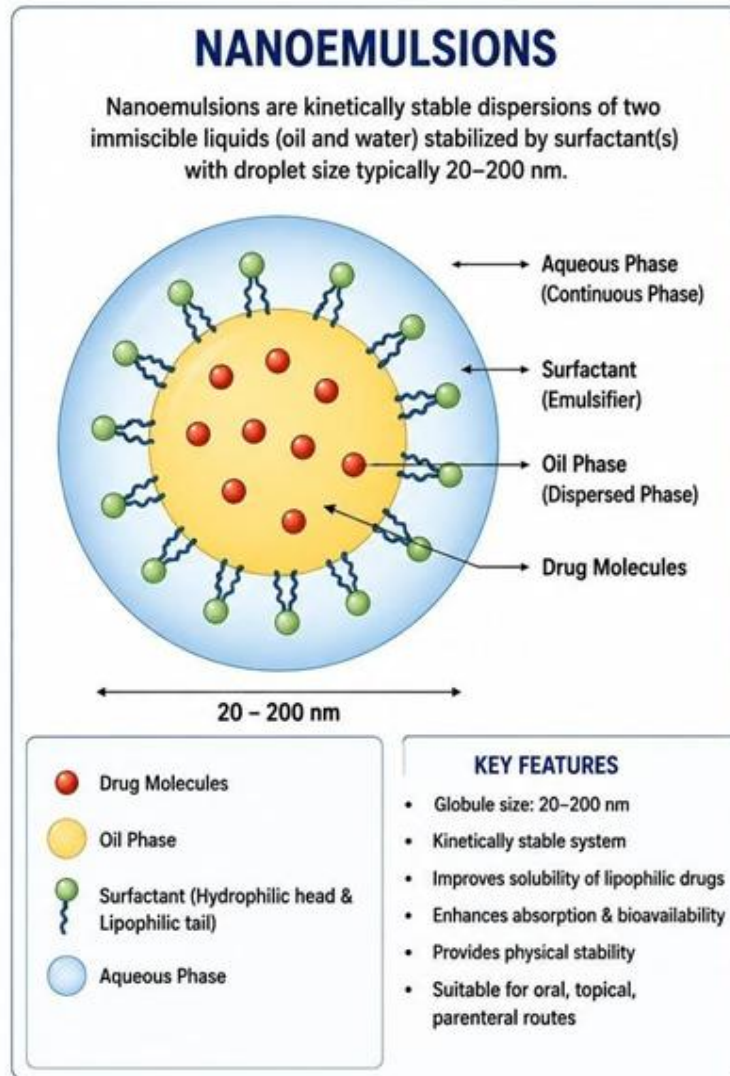


Fig 6: Structure of Nanoemulsions

Nanoemulsions are advanced colloidal drug delivery systems consisting of nanosized droplets generally ranging from 20 to 200 nm dispersed in another immiscible liquid phase. These systems are stabilized using surfactants and co-surfactants and are widely investigated for the delivery of anti-HIV drugs because of their improved stability, enhanced bioavailability, and targeted drug delivery properties. Due to their nanosized droplet structure, nanoemulsions



### SELF-EMULSIFYING DRUG DELIVERY SYSTEMS (SEDDS)

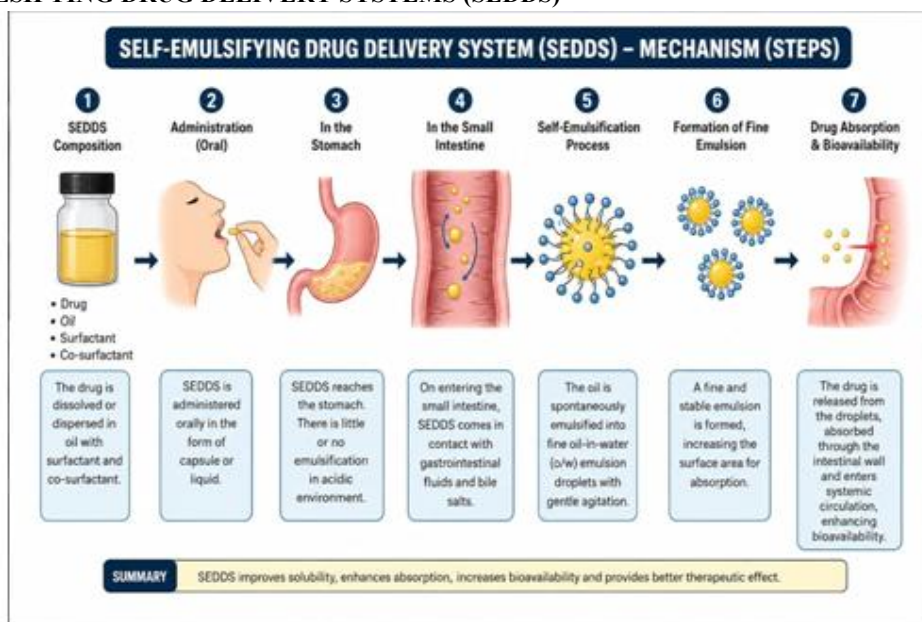


Fig 7: Structure of Self-emulsifying Drug Delivery System

Self-Emulsifying Drug Delivery Systems (SEDSS) are isotropic mixtures of oils, surfactants, co-surfactants, and drugs that spontaneously form fine oil-in-water emulsions when exposed to gastrointestinal fluids under mild agitation. SEDSS have emerged as promising Novel Drug Delivery Systems (NDDS) for improving the oral delivery of poorly water-soluble anti-HIV drugs.

Many antiretroviral drugs exhibit poor aqueous solubility and limited oral bioavailability, which reduce their therapeutic effectiveness. SEDSS improve the solubility and dissolution of lipophilic anti-HIV drugs and enhance their absorption through the gastrointestinal tract. These systems increase the surface area available for absorption and improve systemic drug availability.

SEDSS are generally composed of oils, surfactants, co-surfactants, and active pharmaceutical ingredients. Oils help dissolve lipophilic drugs, while surfactants and co-surfactants reduce interfacial tension and promote spontaneous emulsification. Upon contact with gastrointestinal fluids, SEDSS form stable nano-sized or micro-sized emulsions that enhance drug absorption.

#### PRE-FORMULATION STUDIES

Pre-formulation studies are important preliminary investigations carried out before the development of Novel Drug Delivery Systems (NDDS) for anti-HIV drugs. These studies help evaluate the physicochemical properties, compatibility, stability, and formulation characteristics of antiretroviral drugs and excipients. Pre-formulation studies provide essential information required for successful formulation and evaluation of nanotechnology-based anti-HIV drug delivery systems such as nanoparticles, nanoemulsions, Solid Lipid Nanoparticles (SLNs), and Self-Emulsifying Drug Delivery Systems (SEDSS). (2, 17, 18)

#### Solubility Studies

Solubility studies are performed to determine the solubility of anti-HIV drugs in different solvents, lipids, surfactants, and co-surfactants. These studies are important for selection of suitable formulation components and improving bioavailability of poorly water-soluble antiretroviral drugs.



### **Drug-Excipient Compatibility Studies**

Drug-excipient compatibility studies are carried out to identify possible interactions between anti-HIV drugs and formulation excipients. Compatibility studies help ensure stability, safety, and therapeutic effectiveness of the developed formulation. Fourier Transform Infrared Spectroscopy (FTIR) and Differential Scanning Calorimetry (DSC) are commonly used for compatibility evaluation (17, 35, 36)

### **Melting Point Determination**

Melting point determination is performed to evaluate purity and thermal behavior of anti-HIV drugs. This study provides information regarding crystallinity and stability of the drug substance.

### **Partition Coefficient Studies**

Partition coefficient studies are conducted to determine lipophilicity of anti-HIV drugs. Lipophilicity plays an important role in membrane permeability, absorption, lymphatic uptake, and targeting efficiency of Novel Drug Delivery Systems.

### **pH Determination**

pH studies are important for evaluating stability and solubility of anti-HIV drugs under different physiological conditions. Appropriate pH conditions help improve formulation stability and therapeutic performance. (20, 21)

### **UV Spectroscopy Analysis**

UV-visible spectrophotometry is used for determination of absorption maxima ( $\lambda_{max}$ ) and quantitative estimation of anti-HIV drugs. This method is widely used during formulation development and evaluation studies. (18, 22)

### **Stability Studies**

Preliminary stability studies are carried out under different environmental conditions such as temperature, humidity, and light exposure to evaluate stability and degradation behavior of anti-HIV drugs and formulations. (22, 23)

### **Importance of Pre-Formulation Studies in NDDS**

Pre-formulation studies play a vital role in the development of Novel Drug Delivery Systems (NDDS) for anti-HIV therapy. These studies provide essential information regarding physicochemical properties, stability, compatibility, and formulation behavior of anti-HIV drugs. Proper pre-formulation evaluation helps in selection of suitable excipients, lipids, surfactants, polymers, and formulation techniques required for successful development of nanotechnology-based drug delivery systems.

Pre-formulation studies help improve solubility and bioavailability of poorly water-soluble anti-HIV drugs. These studies also assist in achieving controlled and sustained drug release, targeted drug delivery, improved stability, and enhanced therapeutic efficacy of NDDS formulations.

Compatibility studies between drugs and excipients help prevent formulation instability, drug degradation, and therapeutic failure. Evaluation of partition coefficient, pH, melting point, and

### **FORMULATION DEVELOPMENT**

Formulation development is an important step in the evaluation of Novel Drug Delivery Systems (NDDS) for anti-HIV drugs. The objective of formulation development is to improve bioavailability, targeted drug delivery, controlled release, stability, and therapeutic efficacy of antiretroviral drugs while reducing toxicity and dosing frequency.

Many anti-HIV drugs exhibit poor aqueous solubility, low bioavailability, short half-life, and inadequate penetration into viral reservoir sites such as macrophages, lymphatic tissues, and brain tissues. To overcome these limitations,



nanotechnology-based drug delivery systems such as Solid Lipid Nanoparticles (SLNs), nanoemulsions, and Self-Emulsifying Drug Delivery Systems (SEDDS) are developed and evaluated. (8, 32)

Selection of suitable lipids, surfactants, polymers, stabilizers, and co-surfactants plays an important role in formulation development of NDDS. Lipids such as glyceryl monostearate and stearic acid are commonly used for preparation of Solid Lipid Nanoparticles, whereas surfactants such as Tween 80, Span, and Poloxamer are used to improve stability and dispersion of nanoformulations.

Different formulation methods including high-pressure homogenization, ultrasonication, solvent evaporation, microemulsion technique, and spontaneous emulsification methods are used for preparation of nanoformulations. These methods help produce stable nanoparticles with suitable particle size and improved drug entrapment efficiency.

Optimization of formulation variables is carried out to obtain formulations with desired physicochemical properties, improved stability, sustained drug release, and enhanced therapeutic performance. The developed formulations are evaluated for particle size, zeta potential, entrapment efficiency, drug content, in-vitro drug release, surface morphology, and stability studies. (17, 35)

Nanotechnology-based formulations improve intracellular uptake and facilitate targeted delivery of anti-HIV drugs to viral reservoir sites. Sustained and controlled release from nanoformulations helps maintain therapeutic plasma drug concentrations for prolonged periods and improves patient compliance.

Therefore, formulation development plays a major role in the successful evaluation of Novel Drug Delivery Systems for anti-HIV drugs and contributes to improved therapeutic effectiveness and safer HIV/AIDS management.

### **EVALUATION PARAMETERS OF NOVEL DRUG DELIVERY SYSTEMS**

Evaluation of Novel Drug Delivery Systems (NDDS) is essential for determining the stability, safety, therapeutic performance, and targeting efficiency of anti-HIV formulations. Various physicochemical and biological parameters are evaluated to ensure effectiveness of nanotechnology-based drug delivery systems such as Solid Lipid Nanoparticles (SLNs), nanoemulsions, and Self-Emulsifying Drug Delivery Systems (SEDDS).

#### **Particle Size Analysis**

Particle size is an important parameter affecting drug release, stability, cellular uptake, and bioavailability of nanoformulations. Smaller particle size improves surface area, absorption, lymphatic uptake, and penetration into viral reservoir sites. Particle size analysis is commonly performed using dynamic light scattering techniques.

#### **Zeta Potential Measurement**

Zeta potential determines surface charge and stability of nanoparticles. Higher zeta potential values indicate better stability and reduced aggregation of nanoformulations during storage.

#### **Drug Entrapment Efficiency**

Entrapment efficiency indicates the amount of anti-HIV drug incorporated within the nanocarrier system. High entrapment efficiency improves therapeutic effectiveness and sustained drug release behavior.

#### **Drug Content Determination**

Drug content analysis is performed to determine uniform distribution and accurate quantity of drug present in the formulation. This parameter ensures consistency and quality of the developed formulation. (35, 36)

#### **In-Vitro Drug Release Studies**

In-vitro drug release studies are carried out to evaluate release behavior of anti-HIV drugs from nanoformulations. Controlled and sustained drug release helps maintain therapeutic plasma drug concentration for prolonged periods and improves patient compliance. (31, 35)



### **BIO-ANALYTICAL METHOD DEVELOPMENT AND VALIDATION**

Bio-analytical method development and validation are essential for quantitative estimation of anti-HIV drugs in biological samples such as plasma, serum, urine, and tissues. These methods are important for pharmacokinetic studies, bioavailability studies, biodistribution studies, and therapeutic drug monitoring of Novel Drug Delivery Systems (NDDS).

Sensitive and selective analytical techniques are required for accurate determination of antiretroviral drugs at low concentration levels in biological matrices. High Performance Liquid Chromatography (HPLC) and Liquid Chromatography–Mass Spectrometry (LC-MS/MS) are commonly used bio-analytical techniques for estimation of anti-HIV drugs.

Bio-analytical method development involves selection of suitable chromatographic conditions including mobile phase composition, stationary phase, flow rate, detection wavelength, column type, and sample preparation method. Proper optimization of these parameters helps achieve accurate separation and quantification of anti-HIV drugs.

Sample preparation techniques such as protein precipitation, liquid-liquid extraction, and solid-phase extraction are commonly employed before bio-analysis to remove interfering biological components and improve analytical sensitivity. (28, 29)

Validation of bio-analytical methods is performed according to regulatory guidelines to ensure reliability, accuracy, precision, and reproducibility of analytical results. Validation parameters include specificity, linearity, accuracy, precision, recovery, robustness, limit of detection, limit of quantification, and stability studies.

Bio-analytical studies help determine important pharmacokinetic parameters such as maximum plasma concentration, half-life, area under the curve, clearance, and volume of distribution. These parameters are useful for evaluating therapeutic performance and bioavailability of nanoformulations. (31, 33)

In Novel Drug Delivery Systems for anti-HIV drugs, bio-analytical evaluation plays an important role in assessing targeted delivery, sustained drug release, tissue distribution, and intracellular uptake of antiretroviral drugs. Improved bio-analytical performance indicates enhanced therapeutic efficacy and reduced systemic toxicity.

Therefore, bio-analytical method development and validation are important components in the evaluation of Novel Drug Delivery Systems for anti-HIV drugs and contribute significantly to formulation optimization and therapeutic assessment. (3, 5, 31)

### **RESULTS AND DISCUSSION**

The developed Novel Drug Delivery Systems (NDDS) for anti-HIV drugs demonstrated significant improvement in physicochemical and therapeutic properties when compared with conventional formulations. Nanoformulations such as Solid Lipid Nanoparticles (SLNs), nanoemulsions, and Self-Emulsifying Drug Delivery Systems (SEDDS) showed enhanced drug solubility, improved stability, and controlled drug release behavior. (3, 5, 31)

Particle size analysis confirmed formation of nanosized formulations with uniform distribution. Smaller particle size improved surface area, cellular uptake, and drug penetration into HIV reservoir sites such as macrophages and lymphatic tissues. Zeta potential studies indicated satisfactory stability of developed formulations with reduced aggregation.

Entrapment efficiency and drug content studies demonstrated efficient incorporation of anti-HIV drugs within nanocarrier systems. Higher entrapment efficiency contributed to sustained drug release and prolonged therapeutic action.

In-vitro drug release studies showed controlled and prolonged release of anti-HIV drugs from nanoformulations compared to conventional dosage forms. Sustained release behavior may reduce dosing frequency and improve patient compliance in long-term HIV therapy.

Bioavailability studies indicated enhanced absorption and improved pharmacokinetic performance of nanoformulations. Nanocarrier-based systems improved lymphatic uptake and reduced first-pass metabolism, thereby increasing systemic availability of anti-HIV drugs.



Bio-analytical studies confirmed accurate estimation of anti-HIV drugs in biological samples using validated analytical methods such as HPLC and LC-MS/MS. Validation parameters including accuracy, precision, specificity, and linearity were found within acceptable limits according to regulatory guidelines. (28, 30, 33)

Targeted drug delivery to viral reservoir sites was improved by nanotechnology-based formulations. Enhanced intracellular uptake and improved tissue distribution contributed to better antiviral activity and reduced systemic toxicity. (31, 32)

Overall, the obtained results suggest that Novel Drug Delivery Systems provide a promising strategy for improving therapeutic effectiveness, bioavailability, stability, and patient compliance in anti-HIV therapy. These findings support the potential application of nanotechnology-based drug delivery systems for effective HIV/AIDS management.

## II. CONCLUSION

Human Immunodeficiency Virus (HIV) infection continues to remain a major global health challenge despite significant advancements in antiretroviral therapy. Conventional anti-HIV drug delivery systems are associated with several limitations such as poor bioavailability, low aqueous solubility, systemic toxicity, short half-life, poor patient compliance, frequent dosing, and inadequate penetration into viral reservoir sites. These limitations reduce therapeutic effectiveness and contribute to the development of viral resistance.

The present study focused on the evaluation of Novel Drug Delivery Systems (NDDS) for anti-HIV drugs with special emphasis on nanotechnology-based delivery approaches. Various NDDS such as Solid Lipid Nanoparticles (SLNs), nanoemulsions, Self-Emulsifying Drug Delivery Systems (SEDDS), and other nanocarrier systems were studied and evaluated for their potential to improve anti-HIV therapy.

The study demonstrated that nanotechnology-based drug delivery systems significantly improve the physicochemical and therapeutic properties of anti-HIV drugs. Nanoformulations improve drug solubility, stability, lymphatic uptake, intracellular delivery, and bioavailability of poorly water-soluble antiretroviral agents. Controlled and sustained drug release from nanoformulations helps maintain therapeutic plasma drug concentrations for prolonged periods and reduces dosing frequency, thereby improving patient compliance.

Novel Drug Delivery Systems also showed enhanced targeting efficiency toward HIV reservoir sites such as macrophages, lymphatic tissues, spleen, and brain tissues. Improved penetration across biological barriers including the blood-brain barrier contributes to better antiviral activity and reduction of viral persistence within sanctuary sites.

Pre-formulation studies provided valuable information regarding physicochemical characteristics, compatibility, stability, and formulation behavior of anti-HIV drugs and excipients. Formulation development studies confirmed the successful preparation of stable nanoformulations with improved drug entrapment efficiency, suitable particle size distribution, and satisfactory controlled release behavior.

Evaluation studies demonstrated that the developed formulations possessed improved physicochemical stability, enhanced drug release characteristics, satisfactory zeta potential values, and efficient drug incorporation. Surface morphology studies confirmed formation of nanosized formulations with appropriate structural characteristics.

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