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Bilayer Tablet of Antiviral Drugs

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Abstract: *Bilayer tablets are prepared with one layer of drug for immediate release while second layer designed to release drug, later, either as second dose or in an extended release manner. HIV/AIDS has always been one of the most thoroughly global of diseases.*
Antiretroviral therapy can inhibit HIV replication in patients and prevent progression to AIDS. However, it is not curative. Here we provide an overview of what antiretroviral drugs do and how the virus persists during therapy in rare reservoirs, such as latently infected CD4+ T cells. We also outline several innovative methods that are currently under development to eradicate HIV from infected individuals. These strategies include gene therapy approaches intended to create an HIV-resistant immune system, and activation/elimination approaches directed towards flushing out latent virus. This latter approach could involve the use of novel chemically synthesized analogs of natural activating agents

Keywords: Bilayer tablet, HIV, AIDS, CD4 cells (T cells), Antiretroviral drugs, Nucleoside Reverse Transcriptase Inhibitors (NRTIs), Lamivudine (3TC), hepatitis B virus (HBV), Non- Nucleoside Reverse Transcriptase Inhibitors (NNRTIs).

I. INTRODUCTION

The human immunodeficiency virus (HIV) is the virus that causes HIV infection. Ifuntreated, HIV may cause acquired immunodeficiency syndrome (AIDS), the most advanced stage of HIV infection.
HIV (Human Immunodeficiency Virus) is a virus that attacks the body's immune system, specifically the CD4 cells (T cells), which are crucial for fighting infections. Over time, ifuntreated, HIV can destroy so many of these cells that the body becomes unable to defend itself against infections and diseases. This can lead to the development of acquired immunodeficiency syndrome (AIDS), the most severe phase of HIV infection.[1]
AIDS (Acquired Immunodeficiency Syndrome) is the final and most severe stage of HIV (Human Immunodeficiency Virus) infection. It occurs when HIV has significantly damaged the immune system, reducing the body's ability to fight off infections and certain cancers. This leads to a greater susceptibility to opportunistic infections and illnesses that would not typically affect people with a healthy immune system. AIDS is diagnosed when a person's CD4 cell count, a key component of the immune system, drops below a critical level or when they develop specific serious infections or cancers. While AIDS is life-threatening without treatment, advancements in antiretroviral therapy (ART) can prevent the progression from HIV to AIDS, allowing individuals with HIV to live long, healthy lives

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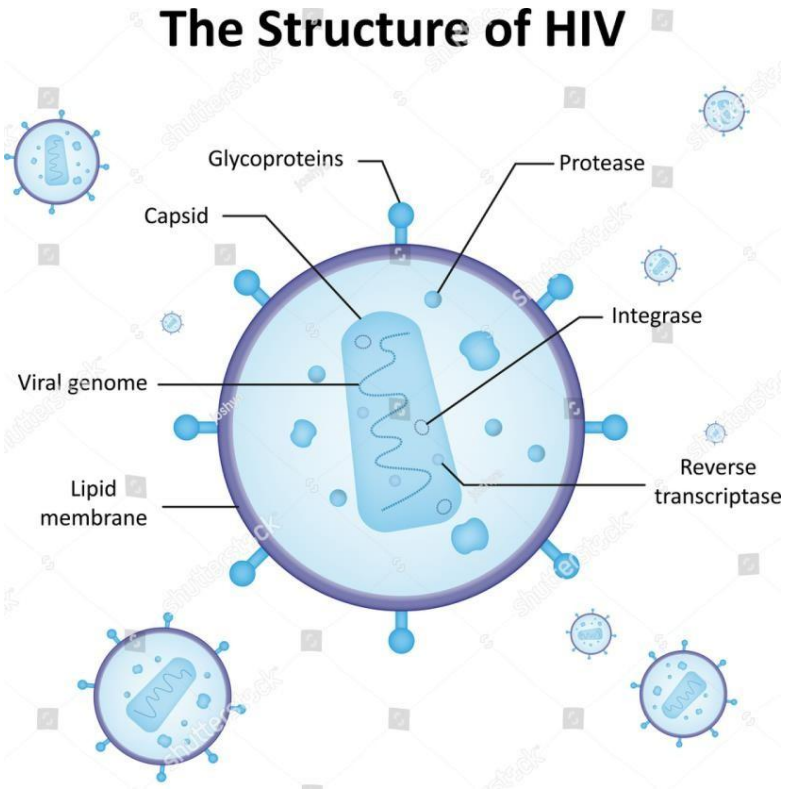

Fig.1

Drugs:

Drugs used to treat HIV are known as Antiretroviral Medications, and the combination of these drugs is called Antiretroviral Therapy (ART)**.** ART does not cure HIV, but it helps control the virus, prevent the progression to AIDS, and reduce the risk of transmission. There are several classes of antiretroviral drugs, each targeting different stages of the HIVlifecycle.

Classes of antiretroviral drugs:

Nucleoside Reverse Transcriptase Inhibitors (NRTIs)
Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs)
Protease Inhibitors (PIs)
Integrase Strand Transfer Inhibitors (INSTIs**)**
Entry Inhibitors

- CCR5 Antagonists:
- Fusion Inhibitors:

Pharmacokinetic Enhancers (Boosters) [2]

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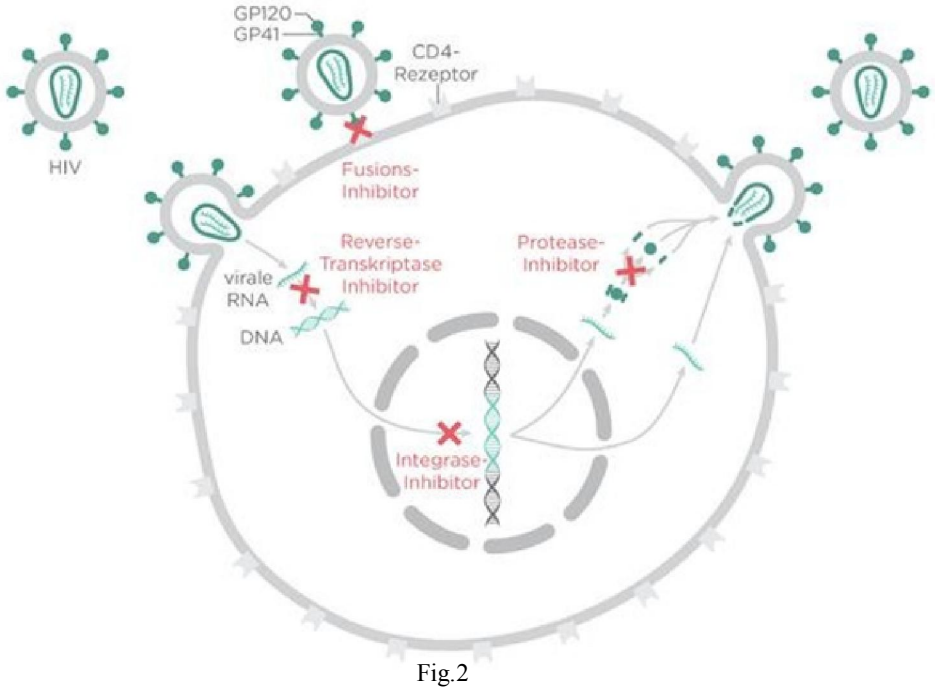

Fig.2

Class	Common Drugs
1. Nucleoside Reverse Transcriptase Inhibitors (NRTIs)	Tenofovir disoproxil fumarate (TDF) Emtricitabine (FTC) Abacavir (ABC) Lamivudine (3TC)
2. Non-Nucleoside Reverse Transcriptase Inhibitors(NNRTIs)	Efavirenz (EFV) Rilpivirine (RPV) Doravirine (DOR) Nevirapine (NVP)
3. Protease Inhibitors (PIs)	Darunavir (DRV) Atazanavir (ATV) Lopinavir (LPV) Ritonavir (RTV) (booster)
4. Integrase Strand Transfer Inhibitors (INSTIs)	Dolutegravir (DTG) Bictegravir (BIC) Raltegravir (RAL) Elvitegravir (EVG)
5. Entry Inhibitors	**CCR5 Antagonists**: - Maraviroc(MVC) **Fusion Inhibitors**: - Enfuvirtide (T20)
6. Pharmacokinetic Enhancers (Boosters)	Ritonavir (RTV) Cobicistat (COBI)

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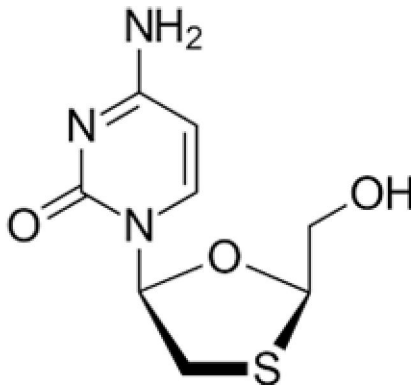
Drug Profile of Antiretroviral Drug:

1. Nucleoside Reverse Transcriptase Inhibitors (NRTIs):

Lamivudine (3TC):



Molecular Formula: C8H11N3O3S
Molecular Weight: 229.26 g/mol

Mechanism of Action:

Lamivudine (3TC) works by inhibiting the reverse transcriptase enzyme that HIV uses to convert its RNA into DNA. It is a cytidine analog, meaning it mimics the natural nucleotide cytidine. When 3TC is incorporated into the viral DNA chain during replication, it causes chain termination, thus preventing the virus from reproducing. [3]

Uses

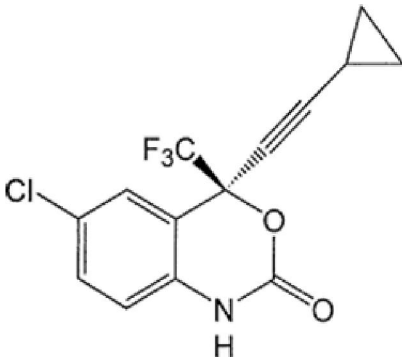
Antiviral treatment for human immunodeficiency virus type-1 (HIV-1) and as a monotherapy for hepatitis B virus (HBV).

Adverse Drug Reaction:

Headache, Fatigue,Nausea,Diarrhea [4]

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

Efavirenz (EFV):



Molecular formula: C14H9ClF3NO2
Molecular weight: 315.675 g/mol

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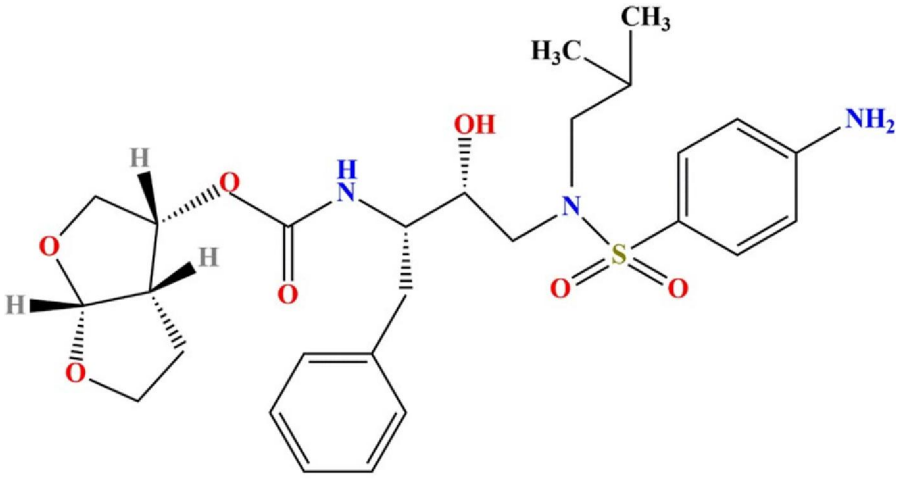
Mechanism of Action:
Efavirenz works by binding directly to the HIV reverse transcriptase enzyme. This binding induces a conformational change in the enzyme, inhibiting its function and preventing the conversion of viral RNA into DNA. Unlike NRTIs, efavirenz does not mimic nucleotides but directly inhibits the enzyme through non-competitive inhibition.[5]

Uses:
Efavirenz (EFV) is used primarily in the treatment of HIV-1 infection

Adverse Drug Reaction:
As a drug class, NNRTIs are commonly associated with central nervous system (CNS) effects. These effects include impaired concentration, vivid or abnormaldreams, insomnia, suicidal ideation, nausea, and vomiting.[10] Patients who experience these adverse effects are more likely to be non-adherent and discontinue their antiretroviral therapy, leading to anti-virologic therapeuticfailure.[6]

3. Protease Inhibitors (PIs)
Darunavir (DRV):



Darunavir (DRV)

Molecular formula: C27H37N3O7S
Molecular weight: 547.67 g·mol−1

Mechanism of Action:
Darunavir works by inhibiting the HIV protease enzyme, which is essential forthe virus to process its polyproteins into functional viral proteins. By blocking this enzyme, darunavir prevents the virus from maturing and becoming infectious, thereby reducing the viral load in the body.[7]

Uses:
Darunavir (DRV) is primarily used in the treatment of HIV-1 infection

Adverse Drug Reaction:
Most side effects reported during therapy with darunavir/ritonavir were mild inseverity. The most common side effects were diarrhea, nausea, vomiting, headache, rash, and abdominal pain.[8]

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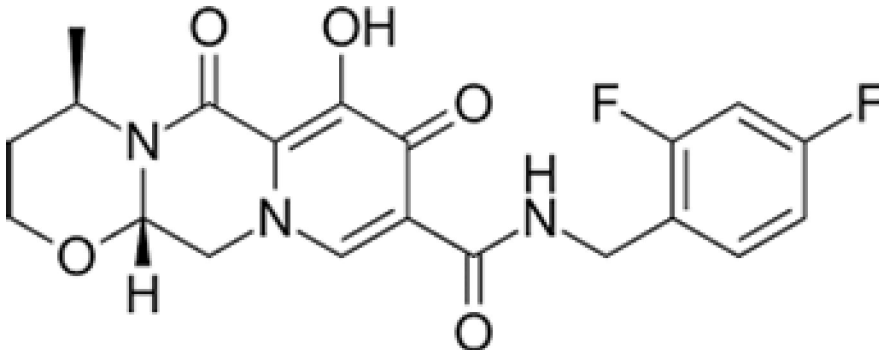
4. Integrase Strand Transfer Inhibitors (INSTIs)

Dolutegravir (DTG):



Molecular formula: C20H19F2N3O5
Molecular weight: 419.38 g/mol

Mechanism of Action:

Dolutegravir is an HIV-1 antiviral agent. It inhibits HIV integrase by binding to the active site and blocking the strand transfer step of retroviral DNA integrationin the host cell. The strand transfer step is essential in the HIV replication cycle and results in the inhibition of viral activity.[9]

Uses:

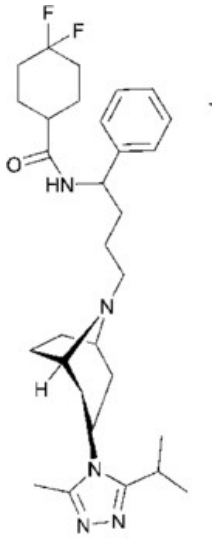
Dolutegravir (DTG) is primarily used for the treatment of HIV-1 infection

Adverse Drug Reaction:

Hepatotoxicity (elevated liver enzymes)Depression and suicidal ideation
Weight gain (especially in combination with tenofovir alafenamide.

5. Entry Inhibitors:

CCR5 Antagonists: - Maraviroc (MVC)



Maraviroc (MVC)

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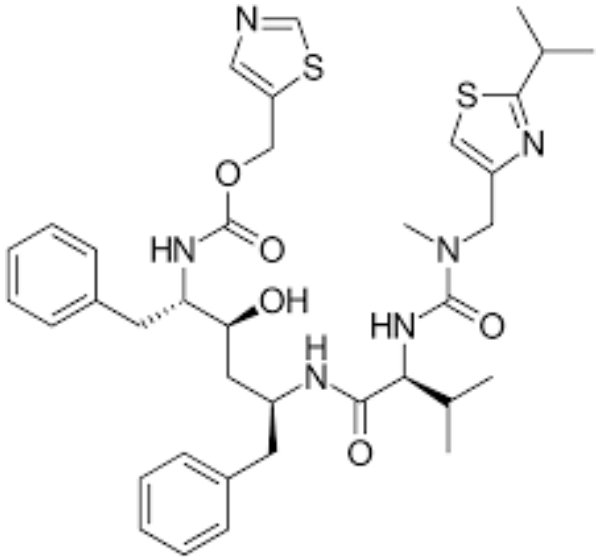
Molecular formula: C29H41F2N5O
Molecular weight: 513.7 g/mol

Mechanism of Action:
Maraviroc works by blocking the CCR5 receptor on the surface of immune cells,such as T-cells. The CCR5 receptor is one of the main co-receptors that HIV uses to enter these cells. By preventing the virus from binding to CCR5, maraviroc stops the virus from entering and infecting the cells. This makes it an entry inhibitor [10]

Uses:
Maraviroc (MVC) has several specific uses in the treatment of HIV-1 infection.

Adverse Drug Reaction:
Cough, Fever,Rash ,Upper respiratory tract infections, Dizziness, Muscle andjoint pain ,Stomach pain. [11]

6. Pharmacokinetic Enhancers (Boosters)
Ritonavir (RTV):



Molecular formula: $C_{37}H_{48}N_6O_5S_2$
Molecular weight: 720.95 $g \cdot mol^{-1}$

Mechanism of Action:
Ritonavir is used at low doses as a booster to enhance the efficacy of other protease inhibitors. It does this by inhibiting the CYP3A4 enzyme, which metabolizes many protease inhibitors. This results in higher plasma levels of the co-administered drug, allowing for less frequent dosing or smaller doses of the primary antiretroviral. [12]

Uses:
Ritonavir (RTV) is primarily used in the treatment of HIV-1 infection, but its role is distinct from many other antiretroviral drugs.

Adverse Drug Reaction: Pancreatitis
Lipodystrophy (fat redistribution)

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Hyperlipidemia (increased cholesterol and triglycerides) Increased risk of cardiovascular events (due to dyslipidemia) Hyperglycemia (can worsen or cause diabetes) [13]

II. CONCLUSION

The bilayer tablets Dolutegravir and lamivudine are used to treatment of HIV.

Dolutegravir is an integrase strand transfer inhibitor (INSTI) that blocks the integration of viral DNA into the host genome, while lamivudine is a nucleoside reverse transcriptase inhibitor (NRTI) that interferes with viral replication.New classes in these drugs enhance the probability of individually framed treatment pattern that will bring about improvement in adherence with betterment of the health outcome.

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