e-ISSN: 2320-4230, p-ISSN: 2961-6085

Journal of Drug Discovery and Therapeutics

Available Online at www.jddt.in

CODEN: - JDDTBP (Source: - American Chemical Society)

Volume 12, Issue 06; 2024, 153-156

Review on Anti-HIV Drugs

Shubhangi Eknath Sawant[1], Vivek Subhash Tarate[2], Jagadishchandra Pati[3]

[1]Research Scholars, Department of Pharmacy, Sabarmati University, Ahmedabad, Gujrat

[2]Supervisor & Professor, Department of Pharmacy, Sabarmati University, Ahmedabad, Gujrat

[3]Co-Supervisor & Professor, Department of Pharmacy, Sabarmati University, Ahmedabad, Gujrat

Received: 19-10-2024 / Revised: 18-11-2024 / Accepted: 17-12-2024

Corresponding author: Shubhangi Eknath Sawant

Conflict of interest: No conflict of interest.

Abstract:

Human Immunodeficiency Virus (HIV) infection remains a major global health challenge. Antiretroviral therapy (ART) has significantly improved the survival and quality of life of people living with HIV by suppressing viral replication and preventing disease progression. Among the most widely used antiretroviral agents are **Efavirenz**, a non-nucleoside reverse transcriptase inhibitor (NNRTI), and **Tenofovir**, a nucleotide reverse transcriptase inhibitor (NRTI). These drugs are frequently used in combination with other antiretroviral agents as first-line therapy. This review discusses their pharmacology, mechanism of action, pharmacokinetics, clinical uses, adverse effects, drug interactions, and recent advances.

Keywords: HIV, Antiretroviral therapy, Efavirenz, Tenofovir, Reverse transcriptase inhibitors, AIDS.

Introduction

Human Immunodeficiency Virus (HIV) attacks the immune system, particularly **$CD4^+$ T lymphocytes**, leading to progressive immune deficiency and, if untreated, **Acquired Immunodeficiency Syndrome (AIDS)**. According to the World Health Organization (WHO), millions of people worldwide are living with HIV. Although there is no cure, combination antiretroviral therapy (ART) effectively suppresses viral replication, restores immune function, and reduces HIV transmission.

Efavirenz and Tenofovir have played a key role in first-line ART regimens because of their potent antiviral activity and convenient once-daily dosing.

Classification

Drug	Class
Efavirenz	Non-Nucleoside Reverse Transcriptase Inhibitor (NNRTI)
Tenofovir Disoproxil Fumarate (TDF) / Tenofovir Alafenamide (TAF)	Nucleotide Reverse Transcriptase Inhibitor (NtRTI/NRTI)

Efavirenz

Chemical Class

Benzoxazinone derivative

Mechanism of Action

Efavirenz binds directly to HIV-1 reverse transcriptase at a site distinct from the active site, producing a conformational

change that inhibits viral DNA synthesis. Unlike nucleoside analogues, it does not require intracellular phosphorylation for activity.

Pharmacokinetics

- Oral bioavailability: Good; absorption increases with high-fat meals.
- Protein binding: Approximately 99%.
- Metabolism: Hepatic (primarily CYP2B6 and CYP3A4).
- Half-life: 40–55 hours.
- Excretion: Mainly as metabolites in urine and feces.

Clinical Uses

- First-line treatment of HIV-1 infection (in combination with other antiretroviral drugs).
- Prevention of disease progression.
- Reduction of viral load and improvement of immune function.

Adverse Effects

1. Dizziness
2. Insomnia
3. Vivid dreams
4. Headache
5. Rash
6. Hepatotoxicity
7. Depression and anxiety
8. Rare neuropsychiatric reactions

Drug Interactions

Efavirenz induces CYP450 enzymes and may reduce the effectiveness of:

- Oral contraceptives
- Antifungal agents
- Certain anticonvulsants
- Some antitubercular drugs

Tenofovir

Available Forms

- Tenofovir Disoproxil Fumarate (TDF)
- Tenofovir Alafenamide (TAF)

Mechanism of Action

Tenofovir is converted intracellularly to its active metabolite, tenofovir diphosphate, which competes with natural nucleotides for incorporation into viral DNA. This causes DNA chain termination and inhibits HIV reverse transcriptase.

Pharmacokinetics

- Good oral absorption.
- Minimal metabolism.
- Eliminated primarily unchanged by the kidneys.
- Once-daily dosing.

Clinical Uses

- HIV-1 infection.
- Chronic hepatitis B infection.
- HIV pre-exposure prophylaxis (PrEP) when combined with other agents.

Adverse Effects

TDF:

- Renal toxicity
- Fanconi syndrome (rare)
- Decreased bone mineral density
- Nausea
- Diarrhea

TAF:

- Lower risk of kidney toxicity.
- Less effect on bone mineral density.

Drug Interactions

- Nephrotoxic drugs (e.g., aminoglycosides, NSAIDs) may increase the risk of renal toxicity.
- Caution with other renally eliminated drugs.

Combination Therapy

Efavirenz and Tenofovir are commonly combined with **Emtricitabine** or **Lamivudine** as part of combination ART.

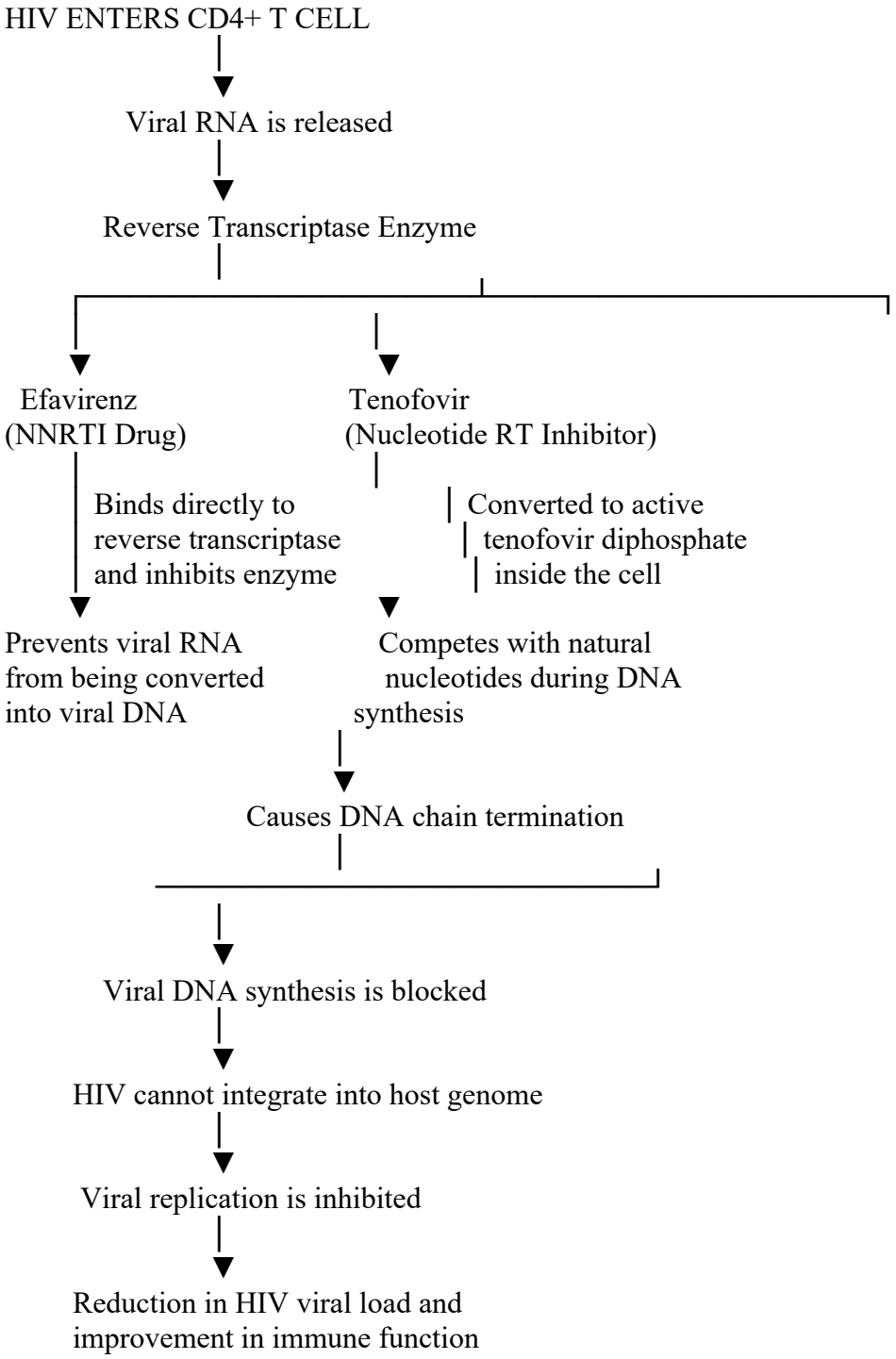
Advantages

- Potent viral suppression.
- Once-daily dosing.
- Reduced risk of drug resistance when used in combination.
- Improved patient adherence.
- Long-term clinical experience.

Comparison Between Efavirenz and Tenofovir

Parameter	Efavirenz	Tenofovir
Drug class	NNRTI	Nucleotide RT inhibitor
Target	Reverse transcriptase (allosteric inhibition)	Reverse transcriptase (chain termination)
Activation required	No	Yes (intracellular phosphorylation)
Major adverse effects	Neuropsychiatric effects, rash	Kidney toxicity, bone loss (mainly TDF)
Metabolism	Liver	Minimal metabolism
Elimination	Hepatic	Renal

Flow diagram illustrating the anti-HIV mechanism of **Efavirenz** and **Tenofovir**.



Recent Advances

- **Tenofovir Alafenamide (TAF)** has largely replaced TDF in many treatment regimens due to improved renal and bone safety.
- Current HIV treatment guidelines increasingly favor **integrase strand transfer inhibitor (INSTI)-based regimens** (e.g., dolutegravir) over efavirenz because they have a higher barrier to resistance and fewer central nervous system adverse effects.
- Long-acting injectable antiretroviral therapies are expanding treatment options and may improve adherence in selected patients.

Advantages

- Effective suppression of HIV replication.
- Reduction in HIV-related morbidity and mortality.
- Once-daily dosing enhances adherence.
- Effective in combination therapy.
- Widely available globally.

Limitations

- Lifelong treatment is required.
- Potential adverse effects.
- Risk of drug resistance with poor adherence.
- Drug interactions.
- Cost may limit access in some settings.

Conclusion

Efavirenz and Tenofovir have been important components of antiretroviral therapy for HIV infection. Efavirenz inhibits reverse transcriptase through non-competitive binding, while Tenofovir acts as a nucleotide analogue that terminates viral DNA synthesis. Together, they have contributed substantially to reducing HIV-related morbidity and mortality. Although newer regimens based on integrase inhibitors are now preferred in many guidelines, Efavirenz and Tenofovir remain clinically important in many settings because of their proven efficacy, availability, and role in combination therapy.

References

1. Brunton LL, Hilal-Dandan R, Knollmann BC. Goodman & Gilman's The Pharmacological Basis of Therapeutics. 14th ed. McGraw-Hill; 2022.
2. Katzung BG. Basic and Clinical Pharmacology. 16th ed. McGraw-Hill; 2024.
3. World Health Organization. Consolidated Guidelines on HIV Prevention, Testing, Treatment, Service Delivery and Monitoring. Latest update.
4. U.S. Department of Health and Human Services. Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV. Latest edition.
5. Rang HP, Ritter JM, Flower RJ, Henderson G. Rang & Dale's Pharmacology. 10th ed. Elsevier; 2024.
6. National Institutes of Health (NIH). HIV Clinical Guidelines.