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HIV LIFE CYCLE AND ANTIRETROVIRAL TREATMENT DRUGS

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ABSTRACT

Viruses are thought-out as intracellular parasites that are authentically dependent on living host cells for duplication. The foremost targets of human immune virus are class of differentiation 4+ helper T cells, that are coordinating with regulators of the humoral and cellular immune responses. Retroviruses are a family of viruses that give within its envelope a single-strand of ribonucleic acid, not a double strand of deoxyribonucleic acid. Antiretroviral medicines can decrease the capability of virus from duplication, and they also decrease the injury caused by virus over time to the person's immune system and other essential organs. Recently the recommendation for human immune virus/ acquired immune deficiency syndrome patient is dual nucleoside reverse transcriptase inhibitors + lone protease inhibitors (zidovudine + lamivudine + lopinavir/ritonavir) or dual nucleoside reverse transcriptase inhibitors + non-nucleoside reverse transcriptase inhibitors (zidovudine + lamivudine + nevirapine).

KEY WORDS : Antiretroviral Treatment, Apothegmatic, Human Immune Virus Life Cycle, Drugs

INTRODUCTION

In worldwide human immunodeficiency virus is considered as pandemic, and it is the cause of AIDS [1]. A retrovirus is capable to introduce its genetic substance (HIV RNA) into the host's genetic substance (host DNA). These cells then duplicate and HIV is duplicated in the procedure [2].

Definitions Of Foremost Terms

Host cell: A host is a place where a microbes lives in animal or plant. Cluster of differentian-4/T-cell serves as host cell for human immunodeficiency targets [3]. The **Cluster of differentiation-4 cell** is partition of an aggregation of cells and materials that constitute the immune system. It is accountable for invigorating other immune cells to react to infection [4]. **DNA (Deoxyribonucleic Acid):** Renders the genetic directions for the advancement and work of microorganism. DNA permits for the transmission of genetic information from one generation to the next [5]. **Ribonucleic Acid:** There are several types of RNA. RNA plays significant functions in protein secretions and other cell activities [6]. A **virion** is the perfect, infective figure of a virus exterior a host cell, with a core of RNA or DNA and a capsid (a protein shell) [7]. **CD4 receptor:** A protein available on the exterior of infection- fighting white blood cells. CD4 receptors permit HIV to bind to and penetrate cells [8]. **Co-receptor:** Besides to binding a CD4 receptor, HIV must also bind either a CCR5 or CXCR4 co-receptor protein to get into a cell [9]. **T-lymphocyte:** A type of white blood cell that ascertains and fights foreign engaging of the body [10].

HIV life cycle:

The HIV life cycle delineates the prudent and alters the virus undertakes from its first keep in touch with a target cell to the generation of fresh infectious viral particles that can induce the next round of duplication. The combination of reverse transcription of viral RNA into DNA and integration of the rearmost into the host cell genome is a conciliate character of the retroviral duplication cycle [11]. HIV-1 belongs to the Lentivirus genus (lentis = sluggish) of the retroviridae family. The viral envelope is recollected of a lipid membrane, which is derived from the host cell and bears cellular proteins, of viral Env protein. Env resides of the extrinsic gp120 that intermediates viral devotedness and the transmembrane gp41 that is hypercritical for viral synthesis. Gp41 is consociated with the viral p17 matrix protein and includes a shaped like cone capsid that involves of the viral Gag protein, p24 [12]. HIV, like other viruses, dearth's the cellular machinery to duplicate itself. It integrates its DNA into the DNA of the host cell; then, when the host cell attempts to create fresh proteins, it unintentionally creates fresh HIV as well [13]. The steps in the HIV life cycle are briefly delineated beneath: **(1) Viral attachment:** CD4 is the initial receptor, and the chemokine receptors CCR5 and CXCR4 are the main co-receptors of HIVentry [14]. HIV must connect to the CD4 cell receptors in a specific way in order for the message to the CD4 cell for entry to occur [15]. **(2) Fusion:** Fusion is either straightway or following unspecific binding of HIV to its target cell, the infection procedure is induced by the interaction of the extrinsic viral gp120 with the cellular CD4 receptor [16]. The virus then mixes with the host cell [17]. **(3) Reverse transcriptions:** After fusion, the single stranded viral RNAs are transcribed into linear double-stranded DNAs by a procedure called reverse transcription. It is called "reverse" transcription because it reverses the arrangement of episodes that take place during the regular transcription procedure, i.e., production of messenger RNA from nuclear DNA followed by export into the cytoplasm and protein secretions or it transforms the single-stranded HIV RNA to double-stranded HIV DNA [18]**. (4) Integration:** The freshly formed HIV DNA penetrates the host cell's nucleus, where an HIV enzyme called integrase "conceals" the HIV DNA within the host cell's own DNA. The integrated HIV DNA is called provirus. The provirus perhaps stays inactive for several years, generating few or no fresh copies of HIV [19]. **(5) Transcription:** After integration, HIV uses the CD4 cell like a production workshop to make "bundles" for creating fresh HIV. The nucleus allows long chains of HIV RNA and proteins that enclose information to create fresh HIV. The mRNA is used as a pivotal to create lengthy chains of HIV proteins [20]. **(6) Assembly:** An HIV enzyme called protease cuts the extended chains of HIV proteins into lesser individual proteins. Protease is a type of enzyme that interrupts down proteins into slighter proteins or lesser protein units, such as peptides or amino acids [21]. **(7) Budding:** The freshly assembled virus propels out ("nascent") from the host cell. During budding, the fresh virus steals segment of the cell's exterior envelope. These HIV glycoproteins are compulsory for the virus to bind CD4 and co- receptors. The fresh copies of HIV can currently depart on to infect other cells [22]. **(8) Maturation:** The HIV particles are secreted in a premature and noninfectious figure that is morphologically described by a thick layer of radially organized Gag and Gag-Pol precursors is called Maturation [23].

Antiretroviral Treatment:

Medications which prevent each of the steps in the duplication of HIV are, thereupon, called ARVs medications. These medications are virustatic [24].

However multiple medications are used for treatment of human immunodeficiency virus infection, no medication able to cure

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human immunodeficiency virus /acquired immunodeficiency syndrome. Antiretroviral medicines decrease the capability of virus from duplication, and decrease the injury caused by virus over time to the person's immune system and other essential organs [25].

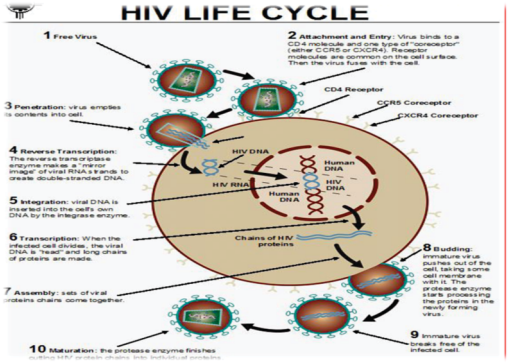

Figure 1 schematic illustration of HIV life cycle

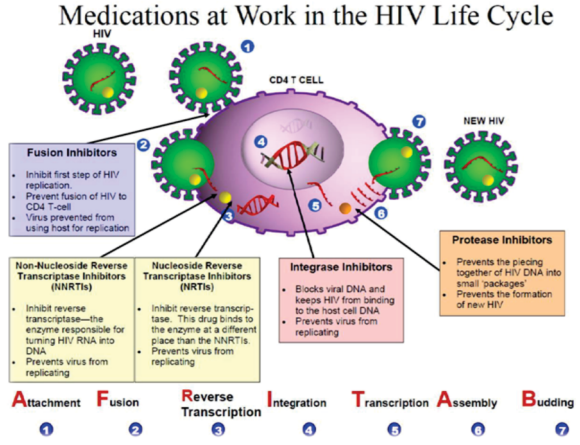

Figure 2 schematic illustration of medications work site in the HIV life cycle

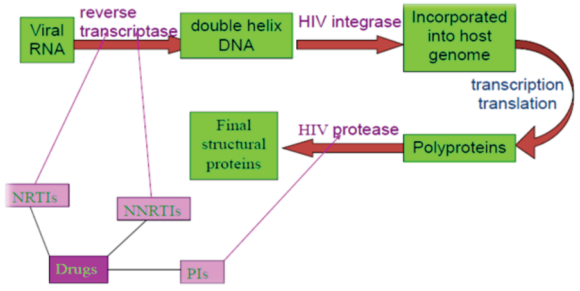

Figure 3 schematic illustrations of ART medications binding site

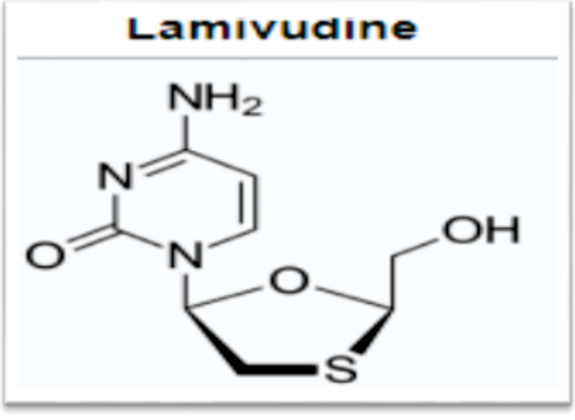

Figure 4 Chemical structure of lamivudine

Treatment Objectives:

The intentions of antiretroviral treatment involve the greatest and strong inhibition of HIV duplication, reinstatement and conservation of immune role, advancement in marvelous of wholeness. Decrease in HIV-related morbidity and mortality [26]. There are six categories of HIV medicines. HIV medicines are categorized coinciding to how they against HIV.

1. Nucleoside reverse transcriptase inhibitors (Nukes):

These groups of drugs inhibit the HIV enzyme which used to transforming single-stranded HIV RNA into double-stranded HIV DNA called reverse transcriptase. Reverse transcriptase enzyme is inhibited by NRTIs. Life cycle of virus is not succeeding if HIV RNA is not transformed into HIV DNA. Indispensably duplication is ceased by intervention of these medicines [27].

Lamivudine: Cytosine analog

Preponderance of 3TC is excreted unchanged in urine, and the dose should be decrease in patients with renal impairment or less body weight.

Drug interactions:

If 3TC given with TMP-SMX; 3TC absorption accelerates because TMP suppress renal elimination of lamivudine.

Emtricitabine: Fluorinated analog of lamivudine

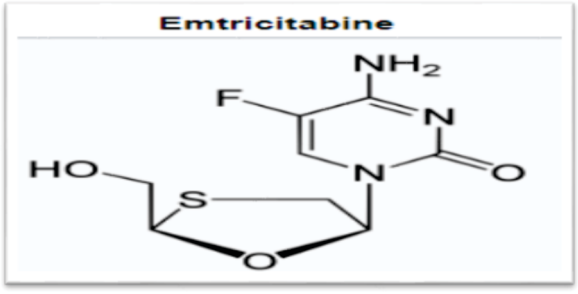

Figure 5 Chemical structure of emtricitabine

Emtricitabine eliminated by both glomerular filtration and active tubular secretion.

Drug Interactions:

No drug-drug interactions of notation have been demonstrated to date; but 3TC and FTC is not recommended due to their identical mechanism of action and resistance profiles.

Zalcitabine: Cytosine analog

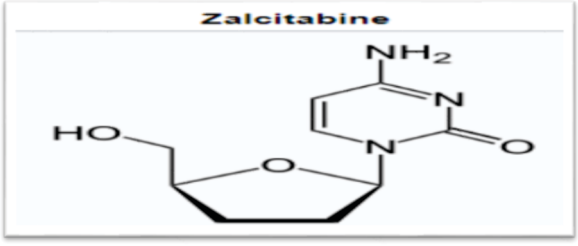

Figure 6 Chemical structure of zalcitabine

Has antiviral activity against AZT sensitive and resistance strains.

Drug Interactions:

Concomitant administration of zalcitabine with D4T, DDI and INH cause or accelerates the risk of peripheral neuropathy toxicity. 3TC importantly inhibits the intracellular phosphorylation of DDC to the active figure, and accordingly the medicines should not be administered coincidentally [28].

Stavudine: Thymine analog

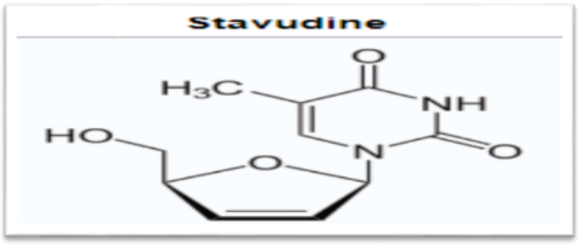

Figure 7 Chemical structure of stavudine

Stavudine excreted by active tubular secretion and glomerular filtration. Recently d4T phased out from the market because of its well-recognized metabolic toxicities.

Drug Interactions:
DDI and D4T should not be used simultaneously owing to great risk of toxicity. Coincident usage with AZT is not recommended, as it can inhibit the intracellular phosphorylation of D4T [29].

Zidovudine: Thymine analog

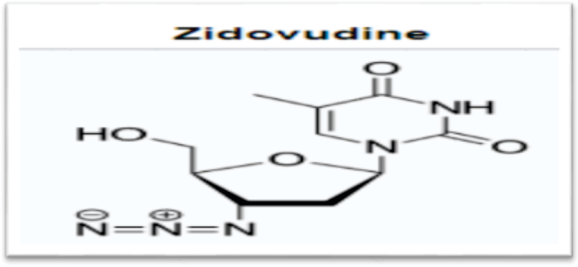

Figure 8 Chemical structure of zidovudine

ZDV thus prevents the infection of fresh cells by HIV but has no effects on the virus directed DNA that has already incorporated into the host chromosome. It is effective against retrovirus only. It decreases the rate of clinical development and extends survival in HIV infected patients.

Therapeutic use: Treatment of adults and children with HIV infection, PMCT & PEP

Drug Interactions:
d4T plus AZT (antagonistic). Paracetamol increased AZT toxicity. Accelerateded serum levels of ZDV perhaps happen with coincident administration of probenecid, phenytoin, methadone, fluconazole, atovaquone, valproic acid, and lamivudine, either through prevention of first-pass metabolism or through lowered clearance. If zidovudine and phenytoin administrated concurrently; AZT decreases the serum levels. Concomitant administration of AZT with myelosuppressive medications such as ganciclovir, ribavirin, and cytotoxic agents causes the risk of hematologic toxicity [30].

Didanosine: Inosine analog

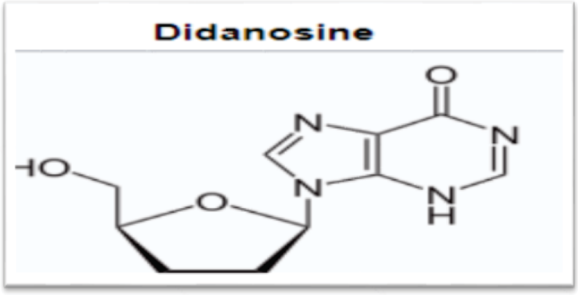

Figure 9 Chemical structure of didanosine

Food creases absorption, dosing on an empty stomach is necessitateded. The medicine is eliminated by glomerular filtration and tubular secretion.

Drug Interactions:
DDI has the ability to decreased plasma concentrations of antibiotics such as fluoroquinolones, ketoconazole, itraconazole, and tetracyclines due to its chelation or buffering agent interactions if administrated concurrently, so antibiotics administrated at least two hours before or after DDI. TDF and ganciclovir has the ability to accelerate serum levels of DDI if administered concurrently and also DDI accelerating the risk of toxicity with them. If DDI, DDC and D4T are administered concomitantly they increase the risk of lactic acidosis toxicity. In concurrent administration of DDI with allopurinol; the risk peripheral neuropathy is accelerated. If alcohol and DDI given together the lactic acidosis from DDI toxicity is accelerated [31].

Tenofovir: Only nucleotide analog

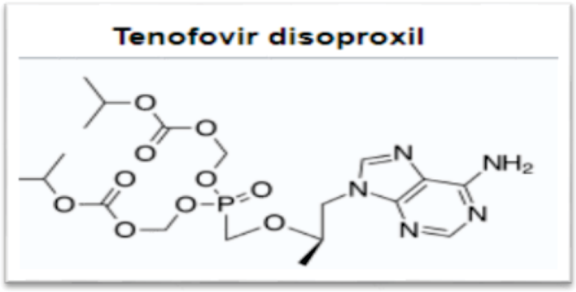

Figure 10 Chemical structure of tenofovir

Has activity against Hepatitis B

TDF may be received with or without food. A high-fat meal increases the bioavailability of tenofovir.

Drug interactions:
TDF increases DDI accumulations and can sequence in adverse effects such as pancreatitis and neuropathy. TDF also interacts with HIV-1 protease inhibitors such as atazanavir, by reducing atazanavir concentrations while accelerating TDF concentrations.

Abacavir: Guanine analog

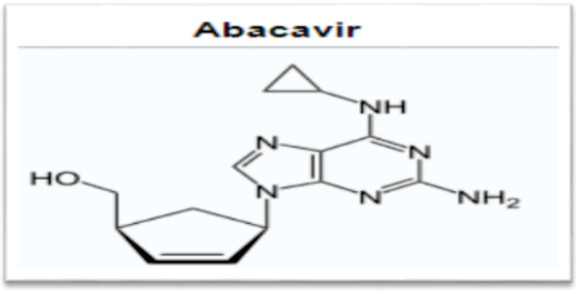

Figure 11 Chemical structure of abacavir

The elimination $t1/_2$ is one point five hrs, and the intracellular $t1/_2$ ranges from twelve to twenty six hrs. CSF serums are comparatively 1/3 those of plasma serums.

Drug Interactions:
PIs such as tipranavir or ritonavir perhaps decrease the serum concentration of ABC through initiation of glucuronidation. ABC is metabolized by both alcohol dehydrogenase and glucuronidation. Ethanol perhaps sequence in increased levels of ABC through the inhibition of alcohol dehydrogenase. Methadone perhaps decreases the therapeutic outcomes of ABC. ABC perhaps decreases

the serum concentration of Methadone [32].

Note: **Tenofovir, Emtricitabine** and **Lamivudine** also treat **Hepatitis B [48]**

2. Non-nucleoside reverse transcriptase inhibitors (Non-nukes):
Function by bind to the enzyme RT, interfering with the enzyme's capability to transform HIV RNA into HIV DNA & inhibit HIV RNA from creating HIV DNA [33].

Nevirapine:
The medicine is greatly lipid soluble and reaches CSF serums that are forty five percent of those in plasma levels. Serum $t1/_2$ is twenty five to thirty hrs.

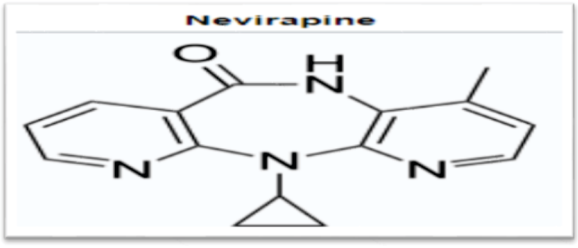

Figure 12 Chemical structure of nevirapine

Nevirapine extendedly metabolized by the CYP3A isoform to hydroxylated metabolites and then excreted, firstly in the urine.

Drug Interactions:
Concurrent administration of NVP with the inducer of CYP3A metabolism; NVP resulting in reduced levels of amprenavir, indinavir, lopinavir, saquinavir, efavirenz, clarithromycin, ketoconazole, PIs, OCs and methadone. Medicines that induce the CYP3A system, such as tipranavir, rifampin, rifabutin, and St. John's wort, can lower levels of NVP, although those that prevent CYP3A activity, such as fluconazole, ketoconazole, and clarithromycin, can elevate NVP levels [34].

Efavirenz:
EFV is universally metabolized by CYP3A4 and CYP2B6. EFV is an inducer and an inhibitor of CYP3A4, thus initiating its own metabolism and interacting with the metabolism of multiple other medicines.

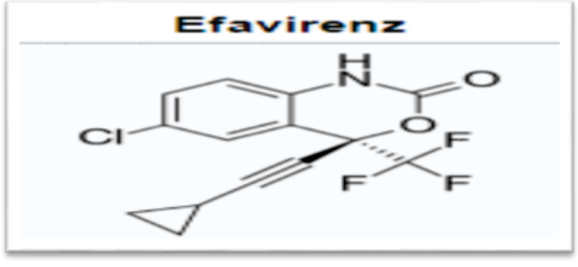

Figure 13 Chemical structure of efavirenz

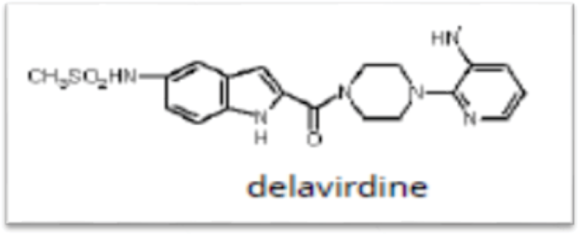

Figure 14 Chemical structure of delavirdine

EFV is the preferred NNRTI for individuals with, HIV and TB (pharmacological compatibility with TB drugs). HIV and HBV co-infection (least risk of hepatotoxicity) and can be used among pregnant women, involving those in the 1st trimester.

Delavirdine*:
Delavirdine are used for management of HIV-1 infection as a part of combination treatment.

Drug interactions:
Hormonal contraceptives, antibacterial such as rifampicin, rifabutin, clarithromycin, enzyme inducers, St. Johns wort if administered with efavirenz they decrease the level of EFV. If NVP administered with metabolized and suppresses CYP3A4 medicines; NVP accelerates the plasma conc. of several PIs such as amprenavir, indinavir, lopinavir, ritonavir, saquinavir and NVP decreases the levels of methadone if administered concomitantly [35].

Etravirine * (ETV)-New drug

3. Protease Inhibitors:
Inhibit the protease enzyme from cutting lengthy chains of proteins into smaller "bundles" that are used figure fresh HIV. Protease enzyme used to convert polyproteins to final structural proteins; PIs intervene with this enzyme and interrupt its conversion. The enzyme protease used for formation of mature virus by cascading polyproteins to individual proteins, but if this enzyme not work properly new virus can't assemble [36].

Prototype: saquinavir

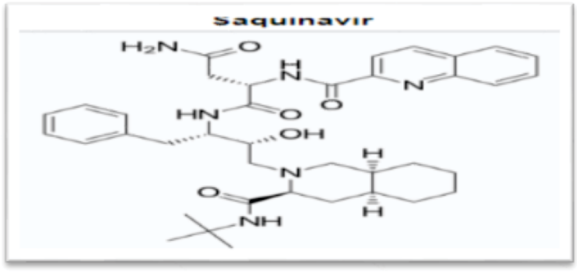

Figure 15 Chemical structure of saquinavir

Others PIs medication such as indinavir, nelfinavir, ritonavir, atazanavir, fosamprenavir, amprenavir, lopinavir, darunavir used in combination with other ARV therapy.

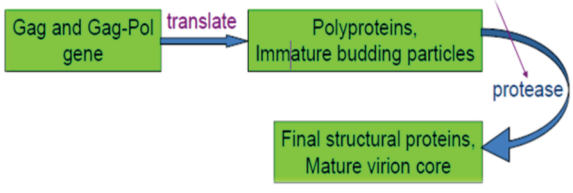

Figure 16 Schematic illustration of protease inhibitors site of action

Drug Interactions:
If medication metabolized with CYP3A4 administered with PIs: PIs increased their plasma concentrations. Concomitant administration of PIs and the following drugs cause life threating toxicities with respective to their order including toxicities; example cisapride (arrhythmias'), ergot alkaloids (vasospasm), Statins (rhabdomyolysis), midazolam (resp. depression). Enzyme inducers medications may be lower plasma levels of PIs [37].

4. Integrase Inhibitors:
These drugs function by weakening the integrase enzyme; the enzyme serves integrate HIV DNA within the host cell's own DNA; but integrase inhibitors inhibit HIV DNA from binding to the CD4 host cell's DNA [38].

Drug Interactions:

If concurrently given raltegravir with rifampicin; rifampicin reduces its serum levels. If integrase inhibitor medication concomitantly administered with antacids as magnesium trisilicate, aluminium hydroxide, magnesium hydroxide etc and iron such as ferrous sulfate, ferrous gluconate, ferrous fumarate, etc the dose of integrase inhibitors should be separated by two hours of their administration [39].

Dolutegravir

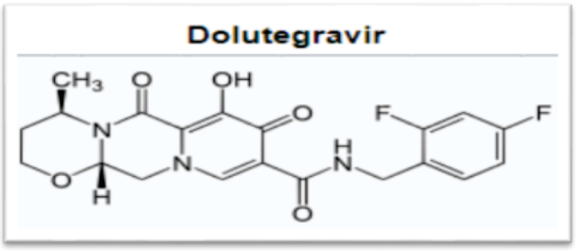

Figure 17 Chemical structure of dolutegravir

5. Entry Inhibitors:

Prevent HIV's penetration into the CD4 host cell. **Maraviroc** is the most ubiquitously used. Entry inhibitor is called a CCR5 antagonist because it inhibits HIV from binding to the CCR5 receptors on the surface of the CD4 cell. Other least ubiquitously used medicine in this class is **enfuvertide**. Enfuvertide is a fusion inhibitor and inhibits HIV from entering the CD4 cell to break off its contents for duplication/ suppresses entry into cell, and binds to gp41 subunit of viral envelope gp. Inhibits formational alters necessitated for fusion of viral & cellular membranes. Entry inhibitors function at the attachment and fusion stages of the viral life cycle [40].

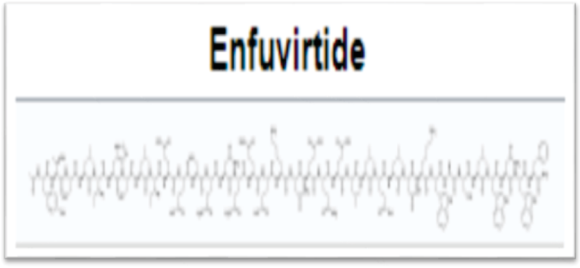

Figure 18 Chemical structure of enfuvertide

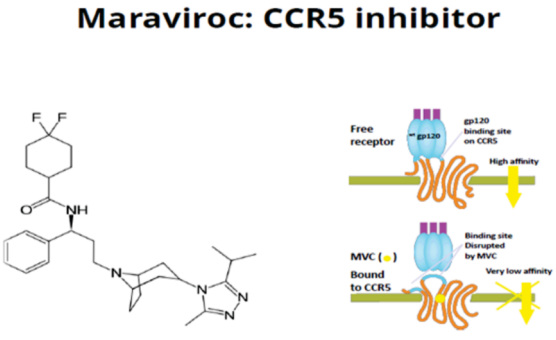

Figure 19 Schematic illustration of CCR-5 inhibitors site of action

6. Boosters (pharmacokinetic enhancers):

Boosters are medicines that are received with other medicine are used to accelerate the activity other medicine. They function by assisting other medicine remains in the body extended at greater concentrations without accelerating toxicity. These medications boost the effects of accompanying HIV medications, but they don't interfere with the HIV life cycle [41].

Ritonavir

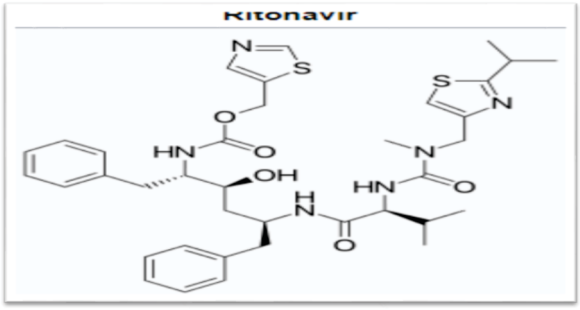

Figure 20 Chemical structure of ritonavir

Common Side Effects Of Antiretroviral Medications

ADRs associated with the usage of ARVs can hastily reverse the benefits of ART sequencing in worse health consequences and accelerated mortality.

NRTIs

Abacavir:

Potential risk of heart disease, increase in cholesterol, hypersensitivity syndrome (fever, myalgia, malaise, nausea, vomiting, anorexia)

Didanosine:

Peripheral neuropathy, pancreatitis, hyperuricemia, lactic acidosis, fat mislay in arms, legs or face, nausea

Emtricitabine:

Rash and skin darkening of palms or soles/hyperpigmentation of palms and soles

Lamivudine: Skin rash/secure medicine

Stavudine:

Peripheral neuropathy, lactic acidosis, fat mislay in arms, legs, or face, lipoatrophy/metabolic syndrome, diarrhea, dyslipidemia

Tenofovir Disiproxil Fumarate:

Kidney disease (renal toxicity) and bone damage, increase in cholesterol, weight gain, asthenia, flatulence, abdominal discomfort

Zidovudine:

Anemia, lactic acidosis, severe GI intolerance, neutropenia, hyperpigmentation of skin and nails, myopathy

Non-nucleoside reverses transcriptase inhibitor, Protease inhibitors, Integrase inhibitors, Entry Inhibitors

NNRTIs

Efavirenz:

Abnormal dreams, severe CNS toxicity (anxiety, depression, insomnia, dizziness), rare skin rash, liver damage (elevations in liver function tests, hyperlipidemia, suicidal ideation, implicit teratogenecity

Nevirapine:

Severe or life threatening skin rash (SJS), liver damage (hepatitis), depression, difficulty sleeping,

Pis (Lopinavir/ritonavir (Kaletra):

Atazanavir, saquinavir, indinavir, etc: Hyperglycemia, hyperlipidemia (increase in bad cholesterol), lipodystrophy, liver damage, skin rash, taste alters, bleeding, GI disturbance, kidney stones, hyperbilirubenemia, alopecia

INSTIs (Dolutegravir):

Weight gains, insomnia, skin rash, suicidal ideation, depression, and

increase in serum creatinine.

EIs (fusion inhibitors (Enfuvirtide, CCR5 antagonist (maraviroc, etc) Erythema, nodules, rash, hepatotoxicity

When to launch ART:

In individuals who infected first with human immuno deficiency virus ART is not launched; however certain confirmation implies that launching medications before a individual is symptomatic can extend life, there are multiple stumbling blocks to such early management. Antiretroviral medications are very expensive and also the virus can increase resistance to with these medicines, in similar way to which bacteria are resistant to antibiotics activity [42]. ART medications are extremely difficult to receive because they cause multiple adverse drug reactions. Individuals who are free from illness may not will to receive ART treatment. When individuals start to take ART medication they should have to take the medicine daily without missing the dose. Patient motivation is significant to guarantee that medicine programs are followed authentically [43].

Table1. When To Launch ART In Adults, Adolescents, Pregnant And Breast Feeding Mother And Children

Population	Recommendation
Adults and adolescents (≥10 years)	Initiate ART if CD4 cell count ≤500 cells/mm³ • As a priority, initiate ART in all individuals with severe/advanced HIV disease (WHO clinical stage 3 or 4) or CD4 count ≤350 cells/mm³
	Initiate ART regardless of WHO clinical stage and CD4 cell count • Active TB disease • HBV coinfection with severe chronic liver disease • Pregnant and breastfeeding women with HIV • HIV-positive individual in a serodiscordant partnership (to reduce HIV transmission risk)
Children ≥5 years old	Initiate ART if CD4 cell count ≤500 cells/mm³ • As a priority, initiate ART in all children with severe/advanced HIV disease (WHO clinical stage 3 or 4) or CD4 count ≤350 cells/mm³
	Initiate ART regardless of CD4 cell count • WHO clinical stage 3 or 4 • Active TB disease
Children 1–5 years old*	Initiate ART in all regardless of WHO clinical stage and CD4 cell count • As a priority, initiate ART in all HIV-infected children 1–2 years old or with severe/advanced HIV disease (WHO clinical stage 3 or 4) or with CD4 count ≤750 cells/mm³ or <25%, whichever is lower
Infants <1 year old*	Initiate ART in all infants regardless of WHO clinical stage and CD4 cell count

*Initiate ART in all HIV infected children below 18 months of age with plausible clinical diagnostic criteria of HIV infection.

What ART regimen to launch with the combinations:

Multi-drug regimens are serving for the management of HIV infection is referred as HAART ("Highly active anti-retroviral drugs"). To obtain strong inhibition of viral duplication combine dual NRTIs with either an NNRTI or a protease inhibitor. Combination of ritonavir with other PI results in boosting consequence by elevating plasma concentration of these medicines thereby; lowering their doses frequency and pill load. Dual NRTIs universally figure the cornerstone of most combinations. Recently the recommendation for HIV / AIDS patient is dual NRTIs + alone PIs (ZDV+3TC+LPV/r) or dual NRTIs + NNRTIs (ZDV+3TC+NEV). ART with single or dual drug regimen is not recommended except for the inhibition of mother to child transmission and PEP of human immuno deficiency virus [44-46].

1st-line ART:

Tenofovir + Lamivudine (or Emtricitabine) + Efavirenz as a FDC is a least routinely associated with severe side effects and also has a better virological and management response when compared with other once-or twice-daily regimens. If Tenofovir + Lamivudine (or Emtricitabine) + Efavirenz is not given for their contraindication or not avail, one of the following alternatives is given: Zidovudine + Lamivudine + Efavirenz**;** Zidovudine + Lamivudine + Nevirapine**;** Tenofovir + Lamivudine (or Emtricitabine) + Nevirapine**.** 1st-line ART for adults should enclose of dual NRTIs plus a NNRTIs or an integrase inhibitors. Tenofovir + Lamivudine (or Emtricitabine) + Efavirenz as a FDC is given as the preferred choice to induce ART. Tenofovir + Lamivudine (or Emtricitabine) + dolutegravir or Tenofovir + Lamivudine (or Emtricitabine) + Efavirenz 400 mg/day perhaps used as alternative options to induce ART. As of December 1, 2007, U.S. Guidelines recommend that most ART-naïve patients initiate either an NNRTI-based regimen (alone NNRTI + dual NRTIs) or a PI-based regimen (alone PI + dual NRTIs). Occasionally a triple-NRTI regimen (AZT + lamivudine [3TC] + abacavir [ABC]) perhaps have usefulness [47,48].

Table2. First-line ART Regimens For Adults, Pregnant Or Breastfeeding Women, Adolescents And Children

First-line ART	Preferred first-line regimens	Alternative first-line regimens a, b
Adults	TDF + 3TC (or FTC) + EFV	AZT + 3TC + EFV (or NVP)
		TDF + 3TC (or FTC) + DTG c
		TDF + 3TC (or FTC) + EFV400 c, e
		TDF + 3TC (or FTC) + NVP
Pregnant or breast feeding women	TDF + 3TC (or FTC) + EFV	AZT + 3TC + EFV (or NVP)
		TDF + 3TC (or FTC) + NVP
Adolescents	TDF + 3TC (or FTC) + EFV	AZT + 3TC + EFV (or NVP)
		TDF (or ABC) + 3TC (or FTC) + DTG c, d
		TDF (or ABC) + 3TC (or FTC) + EFV400 c, d, e
		TDF (or ABC) + 3TC (or FTC) + NVP
Children 3 years to less than 10 years	ABC + 3TC + EFV	ABC + 3TC + NVP
		AZT + 3TC + EFV (or NVP)
		TDF + 3TC (or FTC) + EFV (or NVP)
Children less than 3 years	ABC (or AZT) + 3TC + LPV/r	ABC (or AZT) + 3TC + NVP

Post Exposure management including Prophylaxis

Low-risk Exposure:

Vulnerability to little volume of blood or blood contaminated fluids from asymptomatic HIV positive patients, following damage with a sober needle, asymptomatic origin patient [49]

High-risk Exposure:

Vulnerability to a great volume of blood or potentially infectious fluids, liable to blood or potentially infectious fluids from a patient with clinical AIDS or acute HIV infection, affliction with a concavity needle, needle used in origin patient artery or vein, apparent blood on device, deep and extended affliction [50].

Timing Of Initiation Of Prophylaxis:

To be effective, PEP should begin as soon as possible (within one to two hrs). The maximum holding pattern for induction of treatment which would prevent infection is not understood in humans. In most advanced countries, PEP is begun within two to four hrs. Don't thought-out PEP beyond seventy two hrs post vulnerability. Prophylaxis is to be given for twenty eight days [51-53].

Table3. Recommended ARV Medicine Regimens For PEP

ARV drug regimen	Dose	Frequency	Duration
AZT + 3TC	AZT 300 mg, 3TC 150 mg	12 hourly	28 days
AZT + 3TC + EFV (/LPV/r (alternative)	AZT 300 mg, 3TC 150 mg EFV 600 mg (daily), LPV/r 400/100 mg	12 hourly	28 days

Recommendations For Hiv Prophylaxis After Sexual Assault:

PEP is not recommended if casualty presents greater than seventy two hrs after exposure, following condom leak or tear [54]. Recommended regimen is Zidovudine + Lamivudine + Efavirenz or Zidovudine + Lamivudine + lopinavir/ ritonavir for twenty eight days [108]. Substitute Kaletra alternately for EFV.

CONCLUSION

CD4+ helper T cells are the preeminent targets of HIV which act as a clue to regulators of the humoral and cellular immune responses. The protein available on the exterior of host receptor used for fight infections against white blood cell is called CD4 receptor. CD4 receptors permit HIV to bind to and penetrate cells. Medications which prevent each of the steps in the duplication of HIV are, thereupon, called ARVs. The intentions of antiretroviral treatment are used for greatest and strong inhibition of HIV duplication, reinstatement and conservation of immune work, advancement in marvelous of wholeness and also decrease in HIV-related morbidity and mortality. Multi-drug regimens are serving for the management of HIV infection is referred as HAART ("Highly active anti-retroviral drugs"). Tenofovir + Lamivudine (or Emtricitabine) + Efavirenz as a FDC is a least routinely associated with severe side effects and also has a better virological and management response when compared with other once-or twice-daily regimens. PEP is not recommended if casualty presents greater than seventy two hrs after vulnerability, following condom leak or tear.

Abbreviations

ABC: Abacavir; ADRs: Adverse Drug Reactions; ART: Antiretroviral Treatment Failure; ARV: Antiretroviral; CCR-5: Chemokine-5 receptor inhibitors; CSF: Cerebrospinal fluid; CD4: Cluster of Differentiation 4; CNS: Central Nervous System; CYP450: Cytochrome P450; DDC: Zalcitabine; DDI: Didanosine; D4T: Stavudine; DTG: Dolutegravir; EFV: Efavirenz; EIs: Entry Inhibitors; FTC: Emtricitabine; HIV/AIDS: Human Immune Virus/ Acquired Immune Deficiency Syndrome; INH: Isoniazid; INSTI: Integrase inhibitor; NRTIs: Nucleoside Reverse Transcriptase Inhibitor; NNRTIs: Non-Nucleoside Reverse Transcriptase Inhibitor; NVP: Nevirapine; OI: Opportunistic Infections; PEP: Post Exposure Prophylaxis; PIs: Protease Inhibitors, RT: Reverse Translation; RV: Reverse Transcriptase; SJS: Stevens Johnson Syndrome; TDF: Tenofovir Disiproxil Fumarate; TMP-SMX: Trimethoprim-Sulfamethoxazole; 3TC: Lamivudine; ZDV/AZT: Zidovudine.

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