



REVIEW OF ANTIRETROVIRAL MEDICATIONS, INCLUDING CLASSIFICATION, MODE OF ACTION, AND TREATMENT WITH SIDE EFFECTS

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Abstract: A person is said to have AIDS when their immune system is too weak to fight off infection, and they develop certain defining symptoms and illnesses. AIDS is not a virus but a set of symptoms caused by the HIV virus. AIDS alters the immune system, making people much more vulnerable to infections and diseases. The development of effective drug delivery approaches for the treatment of AIDS and HIV infection is a global challenge. HIV is a lifelong condition and currently there is no cure, although many scientists are working to find one. However, with medical care, including treatment called antiretroviral therapy, it's possible to manage HIV and live with the virus for many years. Treatment of HIV started as monotherapy initially, and then multiple drugs in regimens were given where patients had to consume 11-16 tablets per day. Now the mainstay of the treatment is a single fixed dose combination of Tenofovir, Lamivudine and Efavirenz per day or Zidovudine, Lamivudine and Nevirapine twice daily. Toxicity, resistance and adherence still remain a crucial issue. We need long acting depot preparations which would be efficacious for prevention, treatment and have fewer side effects. AIDS and HIV infection have reached pandemic levels in many parts of the world. Due to the complexities of virus infection cycle and the targets for delivery of antiretroviral drugs, more efficient drug delivery systems are needed

Index Terms - Medications, classification, adverse effects, Mechanism of action

I. INTRODUCTION

According to global report of UNAIDS 2010 on average 33 million people in the world are living with HIV¹⁻². Sub Saharan Africa shares the biggest burden of HIV in the world with 22.5 million people living with HIV. Second highest number of HIV is in our part of the world- South and South East Asia where the estimated number of people living with HIV is 4.1 million. Even with the available efforts, it is becoming difficult to tackle HIV in the high burden countries of Asia and Africa due to existing poverty, illiteracy and overall ignorance.

Acquired immunodeficiency syndrome (AIDS)³⁻⁴ is a chronic, potentially life-threatening condition caused by the human immunodeficiency virus (HIV). By damaging your immune system, HIV interferes with your body's ability to fight the organisms that cause disease. Without medication, it may take years before HIV weakens your immune system to the point that you have AIDS.

HIV/AIDS cannot be cured, however several drugs can significantly decrease the disease's development. In many affluent countries, these medications have decreased AIDS-related fatalities. Thus, HIV-positive individuals who are not taking treatment will find it increasingly difficult to fend against infections and illnesses. If HIV is not treated, it could take up to 10 or 15 years for the immune system to become so badly compromised that it is unable to fight itself. The rate at which HIV spreads, however, varies according to factors like age, health, and background. HIV is a virus that causes the disease known as AIDS.

HIV, a retrovirus, gradually undermines the immune system, which protects the human body from disease. This illness is contagious in HIV treatment initially began with monotherapy; later, patients were given various medications as part of regimens that required them to take 11–16 tablets daily. Tenofovir, Lamivudine, and Efavirenz in a single fixed dose or Zidovudine, Lamivudine, and Nevirapine twice daily are now the mainstays of treatment. The key issues of toxicity, resistance, and adherence still exist. We require long-acting depot medications that are effective for both treatment and prevention and have fewer side

effects. In many regions of the world, AIDS and HIV infection have reached epidemic levels. Given the complexity of the virus infection cycle and the targets for antiretroviral drug administration.

Guideline for Initiation of Anti Retroviral Drugs

Different guidelines exist for the treatment of HIV/AIDS which mainly include Centre for Disease Control (CDC), World Health Organization (WHO), British HIV association (BHIVA), and HIV clinical guidelines programme, New York and World Health Organization (NACO), India. Though ART is recommended for all HIV-infected individuals in most of the guidelines, regardless of CD4 count, NACO India is yet to implement this policy. ART is also recommended for HIV-infected individuals to prevent HIV transmission. Patient education and counselling is very important before initiating ART to overcome the challenges with the improper use of ART and to maximize the benefits.

Current Situation

Currently, 16 antiretroviral drugs are approved for treatment of HIV infection. However, even the best currently available regimens pose challenges with regard to adherence, toxicity, antiviral activity, and resistance. New drug development thus confronts the need for improved convenience and tolerability, reduced toxicity, and improved activity against both wild-type and drug-resistant viruses. Other goals of drug development include improved drug penetration into viral reservoirs (eg: genital tract and central nervous system) and exploitation of additional viral targets with the aims of achieving additive or synergistic effects with drugs from existing classes, reducing or preventing viral resistance, and improving treatment options in cases of drug resistance.

Major Goals of Antiretroviral Drugs

1. Maximal and durable suppression of viral load.
2. Restoration and/or preservation of immunologic function.
3. Reduction of HIV-related morbidity and mortality.
4. Improvement of quality of life of HIV infected persons.
5. Prevention of Mother to Child Transmission (PMTCT).
6. Providing Post Exposure Prophylaxis (PEP).
7. Minimise adverse effects of the treatment.
8. Prevent onward transmission of HIV.

These objectives are accomplished by using a well-tolerated, long-lasting treatment regimen that is taken religiously in order to completely limit viral replication for as long as possible. The CD4+ lymphocyte count typically rises with extended viral suppression, which is accompanied by a recovery of pathogen-specific immune activity. This significantly lowers the risk of HIV-related morbidity and mortality for the majority of patients. It is still unknown if immune function will ever fully recover to normal. Patients who adhere successfully to ART have a near-normal life expectancy, according to long-term cohort studies.

Basic Facts about HIV

1. The earlier HIV is diagnosed; the sooner treatment can start – leading to better long term health. So regular testing for HIV is important.
2. HIV cannot be transmitted through sweat, saliva or urine.
3. Using male condoms or female condoms during sex is the best way to prevent HIV.
4. HIV is a sexually transmitted infection (STI).
5. If you inject drugs, always use a clean needle and syringe, and never share equipment.
6. If you are pregnant and living with HIV, the virus in your blood could pass into your baby's body, or after giving birth through breastfeeding.
7. Taking HIV treatment virtually eliminates this risk.

CLASSIFICATION ANTIRETROVIRAL DRUG ⁵⁻¹⁴

This classification does not represent all the ARV drugs described above, these are the drugs currently recommended by guideline development team for the use. Depending on the mechanism of action, ARVs are categorized into following classes:

1. Nucleoside and nucleotide analogs (NRTI).
 - A. Nucleoside reverse transcriptase inhibitors.
 - B. Nucleotide reverse transcriptase inhibitors.
2. Non-nucleoside reverse transcriptase inhibitors (NNRTIs).
3. Protease inhibitors (PIs).
4. Integrase inhibitors.
5. Fusion inhibitors.
6. Pharmacokinetic enhancers.

The role of the antiretroviral treatment for prevention of HIV transmission has also been demonstrated. This underlines the need of ensuring access to quality treatment for all people living with HIV. The development of current ART guidelines is based on two fundamental principles of HIV care- to provide standardized treatment regimens and to promote more than 95% adherences to the regimens. This will ensure effective antiretroviral therapy with minimal possibilities of resistance development to ARV, and reduce chances of further HIV transmission.

Nucleoside/Nucleotide Reverse Transcriptase Inhibitors

The first effective class of antiretroviral drugs was the Nucleoside analogues. These are structural analogues of nucleosides and mimic the DNA building blocks there by stopping the viral replication process. The resulting DNA is incomplete and cannot create new virus. Nucleotide analogues work in the same way as nucleosides. All nucleoside analogs have been associated with lactic acidosis as their common side effects. For the details of individual ARV of this class, refer the **Table 1**.

S.No	Generic Name	Dose	Adverse effects
1	Zidovudine	300 mg twice daily.	Anaemia, Neutropenia, Bone Marrow Suppression, Gastro Intestinal Intolerance, Headache, Insomnia, Myopathy, Skin and Nail Hyper Pigmentation.
2	Lamivudine	150 mg twice daily or 300mg once daily.	Headache, Diarrhoea, Nausea, Vomiting, Minimal Toxicity.
3	Tenofovir	300 mg once daily.	Asthenia, Headache, Diarrhoea, Nausea, Vomiting, Flatulence Renal Insufficiency.
4	Abacavir	300 mg twice daily or 600mg once daily.	Hypersensitivity Reaction, Fever, Rash, Fatigue, Nausea, Vomiting, Anorexia, Respiratory and Cardiac Problems.
5	Emtricitabine	200 mg once daily.	Diarrhoea, Headache, Nausea, Rash, Skin Discoloration, Hepato Toxicity or lactic acidosis.

Table 1: List of Nucleoside/Nucleotide Reverse Transcriptase Inhibitors.

The simplification of HAART regimens has been a high priority for many years. As the number of effective drugs increases, so does the number of possible effective regimens. The trend toward fixed-dose combinations and once-daily dosage forms of many antiretroviral drugs has provided welcome relief to patients. Not only is their medication burden simplified, but, as a consequence of improved adherence to therapy, they should experience better control of HIV and thus reduced morbidity. The search for new, more effective drugs with pharmacokinetic properties that permit once-daily dosing continues and should contribute to the improved outlook for HIV-infected patients.

Non-Nucleoside Reverse Transcriptase Inhibitors

All of these drugs prevent HIV-1 replication by non-competitively inhibiting reverse transcriptase (RT). This group is not active against HIV-1 strains in group O, HIV-2 or animal retroviruses. HIV-1 group O viruses are usually not encountered outside West and Central Africa; they are reportedly most common in Cameroon. Each of the NNRTIs is metabolized to some degree by the cytochrome P450 (CYP) system of enzymes, mainly by CYP3A4, and glucurono conjugation. In addition, they elicit variable effects on other medications, acting as either inducers or inhibitors of drugs metabolized by CYP.

Non-nucleoside reverse transcriptase inhibitors (NNRTIs) stop HIV production by binding onto reverse transcriptase and preventing the conversion of RNA into DNA. These are called "non-nucleoside" inhibitors because they are not nucleoside analogues and act by physically blocking the reverse transcriptase. For the details refer the **Table 2**.

S.No	Generic Name	Dose	Adverse effects
1	Nevirapine	200 mg once daily for 14 days followed by 200 mg twice daily.	Hepatitis, Hepatic Toxicity; Skin Rash, Stevens Johnson Syndrome.
2	Efavirenz	600 mg once daily.	CNS Symptoms, Insomnia, Confusion, Hallucinations, and Personality Change.
3	Rilpivirine	25mg once daily.	Blistering Skin, Redness or Swelling of Eyes, Insomnia, Confusion.

Table 2: List of Non-Nucleoside Reverse Transcriptase Inhibitors.

Protease Inhibitors

Protease inhibitors work at the last stage of the viral reproduction cycle. These drugs prevent HIV from being successfully assembled and released from the infected CD4 cell. For the details of individual ARV of this class refer the **Table 3**.

S.No	Generic Name	Dose	Adverse effects
1	Lopinavir	200mg Twice daily.	Diarrhoea, Nausea, Vomiting, Abnormal Lipid Profiles, Glucose Intolerance.
2	Saquinavir	1000mg Once daily.	Diarrhoea, Nausea, Vomiting, Headache, Photosensitivity.
3	Atazanavir	300mg Once daily.	Hyperbilirubinemia, Lipid Problem, Hyperglycaemia.
4	Darunavir	600mg or 800mg Twice daily.	Diarrhoea, Nausea, Vomiting, Headache, Abnormal Lipid Profiles, Skin Rash.
5	Ritonavir	50 mg Twice or 100mg Once daily.	Diarrhoea, Nausea, Vomiting, Abnormal Lipid Profiles, Glucose Intolerance.
6	Tipranavir	250mg Twice or 500mg Once daily.	Joint pain or Stiffness, Diarrhoea, Headache. Throat Tightness, Redness or Swelling of Eyes, Insomnia, Confusion.

Table 3: List of Protease Inhibitors.

Integrase Inhibitors

An enzyme found in HIV (and other retroviruses). HIV uses integrase to insert (integrate) its viral DNA into the DNA of the host CD4 cell. Integration is a crucial step in the HIV life cycle and is targeted by a class of antiretroviral (ARV) HIV drugs called integrase strand transfer inhibitors (INSTIs). By blocking integrase, integrase inhibitors prevent HIV from multiplying and can reduce the amount of HIV in the body, refer Table 4.

S.No	Generic Name	Dose	Adverse effects
1	Raltegravir	400mg Twice daily	Diarrhoea, Nausea, Vomiting, Headache, Insomnia.
2	Dolutegravir	50mg Once or Twice daily	Diarrhoea, Nausea, Vomiting, Headache, Abnormal Lipid Profiles, Skin Rash.

Table 4: List of Integrase Inhibitors.

Fusion Inhibitors

Entry inhibitors, also known as fusion inhibitors, are a class of antiretroviral drugs, used in combination therapy for the treatment of HIV infection. This class of drugs interferes with the binding, fusion and entry of the HIV virions to a human cell. By blocking this step in HIV's replication cycle, such agents slow the progression from HIV infection to AIDS, refer the Table 5.

S.No	Generic Name	Dose	Adverse effects
1	Maraviroc	150mg Twice or 300mg Once daily.	Nausea, Upper Stomach Pain, Loss of Appetite, Dark Urine, Jaundice.
2	Enfuvirtide	90mg Twice daily.	Constipation, Diarrhoea, Rapid Heart Rate, Nausea, Abnormal Lipid Profiles, Skin Rash.

Table 5: List of Fusion Inhibitors.

Pharmacokinetic Enhancers

A pharmacokinetic enhancer is used to boost the effectiveness of another drug. When the two drugs are given together, the pharmacokinetic enhancer interferes with the breakdown of the other drug, which allows the drug to remain in the body longer at a higher concentration. Pharmacokinetic enhancers are used in HIV treatment to increase the amount of other HIV medicines in the blood, refer the Table 6.

S.No	Generic Name	Dose	Adverse effects
1	Cobisistat	150mg Once daily.	Nausea, Constipation, Diarrhoea, Loss of Appetite, Skin Rash.

Table 6: List of Pharmacokinetic Enhancer.

MECHANISMS OF ACTION:

Infectious diseases are well known since ancient time to human civilisation. Infectious disease are caused due to different microorganisms (bacteria, viruses and fungi).¹⁵ Viral structure is simple and consists of a protein coat, nucleic acid, viral enzymes and, sometimes, a lipid envelope, unlike the complex structure of fungi, helminths and protozoa. Additionally, viruses use the host's cellular machinery for replication, hence are obligate intracellular pathogens. Such characteristics create the difficulties in developing drugs with selective toxicity against viruses.¹⁶ Viruses are ultra microscopic agents having either DNA or RNA as the genetic material and are known to cause variety of diseases in humans, animals and plants. The fight between humans and viruses is continuous process, as both will adopt different strategies to fight against each other. Antiviral drugs development is a tedious process involving many stages such as target identification and screening, lead generation and optimisation, clinical studies and the drug registration, etc.¹⁷ Dynamic antiviral drug development is a pressing need, as viral infections have caused millions of human fatalities worldwide over the course of human civilisation. The approval of first antiviral drug 'idoxuridine' in June 1963 has opened a new era in antiviral drug development. Since then, number of drugs with antiviral potential have been developed for clinical use for the treatment of millions of human beings worldwide. Antiviral drugs are a class of medicines particularly used for the treatment of viral infections. Specific antiviral drugs are used for treating specific viruses just like the antibiotics for bacteria. Antiviral drugs, unlike the most antibiotics, do not destroy their target pathogens; rather inhibit their development. As the viruses use the host's cells to replicate, hence makes it difficult to design a safe and effective antiviral drug. Therefore, it is difficult to find the drug targets that would interfere with the virus without damaging the host's cells. Furthermore, the major complications in developing anti-viral drugs and vaccines are because of viral variation.¹⁸ One of the important ways of finding antiviral drugs is the computer based drug discovery and for this approach nelfinavir is an example discovered in the 1990s for the treatment of human immunodeficiency virus (HIV) infection. In spite of modern tools and stringent measures for the quality control only a few antiviral drugs are getting approved for the use of human either due to the side effects or resistance to antiviral drugs. With increase in the awareness about the viruses, their mechanism of infection and the rapid evolvement of novel strategies and techniques for antiviral will speed up the novel antiviral drugs development.¹⁹ The current scenario all over the world indicates that continuous emergence of microbial threats at an accelerating pace, mainly due to unprecedented climate change and globalisation.

DNA virus

Viruses such as poxviruses, herpes, adenoviruses and papilloma viruses usually contain doublestranded DNA, leaving single-digit DNA. DNA virus enters the cell centre and leads to new viruses

RNA virus

RNA viruses include influenza, measles, mumps, colds, meningitis, polio, retroviruses (AIDS, T-cell leukaemia), arena viruses, all considered, single descriptor RNA (ssRNA). RNA virus does not enter the cell centre (in addition to the cold virus contamination this season). Viral RNA is then used to make a DNA copy of the viral RNA, which is organised by the host genome followed by a retroviruses.

Steps of viral infections

Viral DNA enters a host cell, replicates there, and releases new viruses as a result of viral infection. Viral attachment, invasion, uncoating, replication, assembly, and release are the six phases of viral replication. The steps of the virus life cycle, emphasising the virus's entry and escape, are detailed here.

The viral DNA or RNA is then incorporated into the host cell's genetic material, causing it to replicate the viral genome. The virus attaches to a host cell and injects its genetic material into the host cell during the attachment and penetration stage. During this phase of the virus life cycle, the uncoating, replication, and assembly occur.

- The freshly generated viruses are discharged by the host cell either by waiting cell death or by budding off through the cell membrane.^{20,21}

Valacyclovir

Valacyclovir, L-valyl ester from acyclovir, is also available in oral form. After swallowing, drug is immediately changed to acyclovir by the substance valacyclovir hydrolase in the digestive tract and liver. The original bioavailability is three to several times that of acyclovir. Valacyclovir has proven exceptional in treatment of pollution obtained by the herpes simplex virus and varicella-zoster virus and in prophylaxis against cytomegalovirus.

Penciclovir

Penciclovir is basically like ganciclovir, in contrast only by replacing the methylene connection for oxygen either in the non-cyclic ribose portion of the particle. Its digestive component and activity are similar to acyclovir, so again, it is only a DNA chain terminator that is bound. The inhibitory effect of in vitro penciclovir on herpes simplex 1 and 2 types and varicella-zoster infection is alike to acyclovir. Now, it has claimed only as topical plan for the treatment of cold sores. Intravenous preparations are considered as treatment formucocutaneous herpes in immunocompromised patients²¹.

Antiviral drugs and COVID-19

The worldwide outbreak of COVID-19 virus infection is associated with the unavailability of specific drug(s) to combat with this viral infection. To date, nearly 10 million people are infected and about 500,000 people die worldwide due to COVID-19 viral infection. To find the solutions for this viral infection, great efforts have been made and are continued to develop vaccines, small molecule drugs or monoclonal antibodies that can prevent the infection spread to avoid the expected human, social and economic devastation related to this infection. Several FDA approved drugs have been reported in the literature and in hospitals during clinical trials to treat or reduce the COVID-19 severity.

Remdesivir (GS-5734)

Remdesivir is a novel antiviral drug originally used for treating Marburg virus and Ebola virus infections and this drug was developed by Gilead Sciences. The chemical formula of remdesivir is C₂₇H₃₅N₆O₈P with a molecular mass of 602.6 g/mol. This is a prodrug of a nucleotide analogue metabolised intracellularly to adenosine triphosphate analogue inhibiting the viral RNA polymerases. It acts as an inhibitor of RNA dependant RNA polymerase and its characteristics and pharmacokinetics have been studied in MERSCoV and SARSCoV infections²². This drug causes decline in the replication of viral genome and its production due to the alterations in the viral exonuclease function and disturbed proof reading. It can be recommended to prevent the disease progression severity in COVID-19 patients since it prevents the replication of the virus. To confirm its therapeutic potential against COVID-19, double blind randomised clinical trials with such patients are underway in phase 3. In vitro studies have shown that in addition to its efficacy against COVID-19 in epithelial cells of the human airways, remdesivir has virologic as well as clinical efficacy in a non human primate model. Remdesivir has broad spectrum antiviral activity against several virus family members including the coronaviruses for example.

Antagonistic impacts of antiviral drugs

Because infections involve intracellular pathogens that have cellular capacity, cynics once accepted that no specific inhibitor of viral reproduction could be found. This confidence was strengthened by the disappointments of the first antivirals like idoxuridine and cytarabine essential, and moderately late with fialuridine. Fortunately, drugs have been developed that affect viral replication to a greater extent than cells. All antiviral drugs, whether alone or not, can have effects and some are unexplained, such as thrombotic microangiopathy linked to valacyclovir in patients with immunodeficiency syndrome²³.

Virus inactivating agents

Some compound operators have been performed which use a fairly attractive antiviral movement by straight disabling infection. Calcium elenolate, a monoterpene gained from corrosive liquid concentrates hydrolysed from various pieces of the olive tree, uses a virucidal effect in vitro against a variety of RNA and DNA infections, clearly by communicating with the protein layer of the infecting molecule. In a creature study, intranasal administration reduced yields of parainfluenza infection without significant adverse effects. Human preparations with this compound have only demonstrated viability if treatment is started immediately after infection. Certain dihydroisoquinolines have shown an inactivating effect on influenza A and B infections and parainfluenza

infections; these infections had a strong antiviral effect in cell culture and were later found to have a moderate effect in animal tests. The mixtures have in any case been neglected in order to obtain the antiviral effect required in humans.

Restraint of viral attachment, entrance and uncoating

Because the infection first contaminated a eukaryotic cell, certain general stages of the disease process occur that can be spots of outbreak by potential antiviral drugs. At these stages, the contaminating virion binds to receptors on the cell film, enters the cell layer and once in the cell's cytoplasm, the virion's protein layer is emptied and the viral nucleus corrodes the substance.

Contact or viral adsorption was the least viable site to attack antiviral agents, without discovering substances that were still dynamic enough to warrant a clinical trial. The sulfated polysaccharide is thought to communicate with infectious particles, thereby reducing the rate of cell binding in vitro. Affected infections include encephalomyocarditis, reverberation, flu, dengue fever and rabies²⁴. A moderate effect in vivo has also been observed against dengue infection in mice. Heparin, an unfavourably charged mucopolysaccharide, clearly forms a non-infectious complex with a herpes infection that prevents it from being secreted into the host cell. An action against herpes infection was observed both in vitro and in the analysis of creatures, in the latter case a heparin infusion was injected into the skin of the rabbit before or as a whole. Because of the ionic concept of communication, in all respects, heparin would have an impressive degree of non-specificity.

INHIBITORS OF ENZYMES ASSOCIATED WITH VIRIONS

DNA polymerases

Countless substances accept antiviral movement due to the inhibition of DNA polymerases associated with virions. Antivirals of this type can be widely collected in pyrophosphate analogues and analogues of conventional nucleoside polyphosphates. This latter collection is regularly distinguished in the sweet portion of the particle or in the particles of purine or pyrimidine, although hardly in both. There are two interesting mixtures in main classification: trisodium phosphonoformate (PF An) and trisodium phosphonoacetate (PA).

RNA polymerases

Various substances are recognised to prevent DNA and RNA-mediated RNA polymerase in vitro, and this activity is repeatedly believed to be responsible for antiviral activity. For example, in a careful report, Ericsson et al. reported that a very important class of malaria, ribavirin triphosphate (RTP), is a potent antioxidant that promotes RNA polymerase. The polarisation of viral polymers is strong for ATP and GTP, but not for UTP or CTP. RNA interference polymers have been identified as more complex than guanine-containing dinucleotides, and Plotch and Krug have shown that ApG or GpC is inserted at the 5' end of the AcG gene.

Viral neuraminidase

There are different views on the work of virion associated neuraminidases, but whether they are infiltrated or agglomerated, the severity of influenza side effects increases among volunteers and increases the immune response to neuraminidase against plasma. Concentration is declining. 2-Deoxy-2,3-dehydro-N-trifluoroacetylneuramine caustic is an inhibitor of influenza infection.

INHIBITORS OF THE TRANSLATIONAL PROCESSES OF VIRAL MRNA

mRNA translation

This suggests that the interpretation of various mRNAs in the wheat germ range is restricted to 7-methylguanosine-5'-monophosphate (m7-GMP). However, guanosine nucleotides are released rapidly upon entering the 7-methyl collection or other methyl collections. Not enough, surprisingly, m7-GMP suppresses RNA interpretation of satellite tobacco spoilage infections in the wheat germ range.

Early viral polypeptide chains

Parafluorophenylalanine (pFPhe) was first used in 1951 in a simple, non-corrosive manner and along these lines has been shown to have broad spectrum antiviral activity against RNA and DNA infections.

Inhibitors of the synthesis of viral DNA

Many exacerbations that inhibit the binding of viral DNA occur either by direct blocking of the polymerase (and were hidden by previous regions), while, on the other hand, due to the impedance in the previous binding or binding. Square DNA replication or in collaboration with the layout, which ultimately makes defective material work²⁵.

Fused to DNA.

The fusion of 5-IldU with viral DNA instead of thymine and its subsequent delicacy and distortion of this DNA were investigated, and an extensive variety of halogenated deoxy pyrimidine nucleosides was rather widely illuminated. The fusion of these substances can lead to non-functional DNA along these lines that destroy the nose of genetic data.

Inhibitors of non-viral enzymatic processes involved in DNA synthesis

Among the procedures that can change the proportion or volume of DNA mixtures, antiviral specialists mainly influence the estimates of thymidylate synthetase and deoxynucleoside triphosphate pools either directly or bypassing. Countless deoxyuridine subsidiaries show incredible barriers to synthetic TMP.

Inhibitors of the biosynthesis and assembly of viral glycoprotein

Both DNA and RNA infections include membranes with glycopeptides integrated into the infection, recommended by another possible direction of antiviral drugs. Influenza infections include hemagglutinin spikes. This is an important part of the envelope glycoprotein of the infection and is suitable for connecting infectious molecules with their cellular receptors. Another important part of the influenza infection film is chemical neuraminidase (N-Acetylneuraminic Acid Glycohydrolase).

Adverse effects of antiretroviral therapy for HIV infection

There is evidence that the major adverse events associated with use of the drugs were anaemia for NRTIs and changes in the plasma lipid profile for NNRTIs and PIs. In one case, NNRTIs were also associated with gynaecomastia and PIs were linked to the development of anaemia in post-partum women. Also, the use of new drugs, such as CCR5 binding inhibitors, has been found to lead to changes in markers of liver damage such as alanine aminotransferase (ALT).

Adverse effects of the combination Abacavir/Lamivudine + Raltegravir was similar in relation to those of Tenofovir/Emtricitabine + Raltegravir, for which no patient discontinued the treatment due to hypersensitivity and presented a superior increase in the percentage of HDL compared to the other combinations.

The subclass of PIs was represented by the largest number of studies showing adverse effects caused by continuous use. Most of these adverse effects were related to the Lipidaemia caused by the drugs. However, the use of Indinavir/ritonavir was associated with the occurrence of higher rates of renal, gastrointestinal and dermatological problems than combinations including Saquinavir/Ritonavir. Furthermore, when the effects of different concentrations of Indinavir/Ritonavir (800/100 and 400/100 mg) twice daily for 48 weeks were investigated, it was found that discontinuation because of intolerance, interruption and adverse effects occurred more frequently at the higher dosage.

When the effects of Tipranavir (500 mg)/ritonavir (100 or 200 mg) or Lopinavir (400 mg)/ritonavir (100 mg) were investigated for 48 weeks, use of Tipranavir with the higher ritonavir concentration was found to result in a higher frequency of adverse effects compared with the other combinations, with these effects being mainly gastrointestinal symptoms and grade 3–4 elevations in cholesterol levels. Similarly, in a study examining different combinations of PIs boosted with ritonavir, it was demonstrated that use of Darunavir (800 mg)/Ritonavir (100 mg) resulted in higher low-density lipoprotein (LDL) cholesterol concentrations than the other combinations investigated. However, the use of Atazanavir (300 mg) + Ritonavir (100 mg) resulted in a greater increase in plasma triglyceride levels.

The coadjutant effects of Ritonavir with other drugs are currently poorly understood.

CONCLUSION:

New antiretroviral drugs are necessary to make antiretroviral therapy more practical, bearable, secure, and antiviral-active. Promising agents in both new and established classes are being created (HIV entry and HIV integrase inhibitors). Additional viral life cycle stages, such as viral uncoating and viral assembly, as well as other enzymes should and can be the target of future drug development. Along with current and upcoming antiretroviral medicines, the use of other immune therapies, such as interleukin-2 and therapeutic HIV vaccines, may be possible. Combination medications are projected to surpass monotherapy as the main strategy of treating viral infections in the future as a result of the lessons learnt from the HIV experience. Effective combination medicines involve a range of targets and/or more fundamental mechanisms of action. Numerous brand-new medications have been created, and many more are currently being developed. However, the emerging infectious disorders brought on by viruses like COVID-19 continue to be a problem. Additionally, the failure of medications in human trials is a general phenomenon that needs to be understood and addressed. The advent of numerous new technologies is predicted to produce the positive outcomes. The expanding understanding of viruses and the quickly evolving techniques and methods offer a better assistance in the development of new medications with antiviral activity.

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