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A REVIEW ON HIV DISEASE ALONG WITH HERBAL ADVANCEMENT IN IT.

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ABSTRACT

HIV(Human Immunodeficiency Virus) is retrovirus which infects our immune system cell and impairs their function. There are 2 subtypes of virus: HIV-1 and HIV-2 from which the HIV-1 is more common. It is one of the most common sexually transmitted infection. This disease affects women as well as men. Infection progresses in 3 stages and worsens the symptoms and results in reduced life span of patient. The global burden of HIV is large, leaving over 38.4 million [33.9-43.8 million] people were living with HIV at the end of 2021. Stem cell therapy are viable treatment choice for people suffering from a wide range of illness and injuries. . Plant derived microbicide and plant bodies are some of new approach for prevention of HIV. So, herbal medicines can be developed as a safe effective and economical alternate for AIDS.

Keywords: -

HIV, Herbal Drugs, Stem Cell therapy, Palmae, Rosaceae.

INTRODUCTION

HIV (Human immunodeficiency virus) is retrovirus; it infects our immune system cell, and impairs their function. Virus cause infection that leads to worsen the immune system, result in immune deficiency.[1]

- **HIV**

H-It infects only human beings and also transmitted between humans not from animals. It is not transmitted from bites of mosquitoes, bats or any other species.

I-The body has immune system whose function is to protect our body from germs, infections etc. But a person suffering from HIV has inability to fight against diseases. However, immune system becomes deficient.

V-Virus is a small, simplest thing which is in inactive form outside the body and becomes active when it goes inside human body.

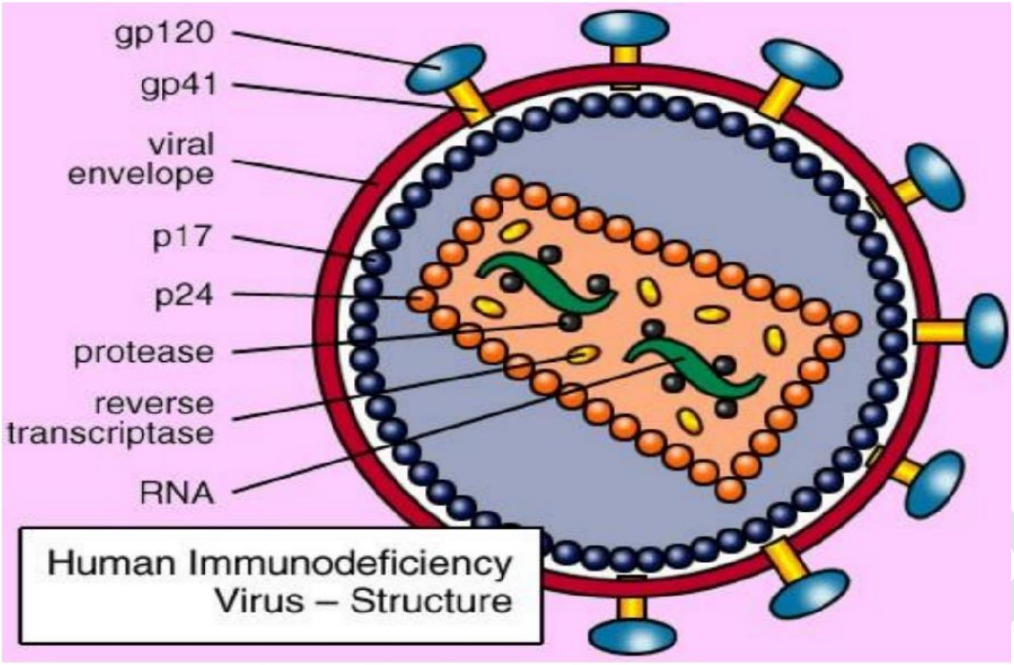
HIV is a virus that causes AIDS. Normally, our body has immune system that attack viruses and bacteria. Immune system has white blood cells which protect us from infections. White blood cells contain CD4+ cells which is also known as helper cells or T cells. [2] The immune system helps body to fight off infection. As a result of this body is more likely prone to other infections and cancer which further prove fatal.[3]

- **Origin of Disease**

Scientists believe that the HIV infection was transmitted from a type of chimpanzee in West Africa to humans. SIV (Simian immunodeficiency virus) is the chimpanzee version of immunodeficiency virus. It is believed that this virus was transferred and mutated to HIV in humans when they hunted SIV infected chimpanzee foe meat and came in contact with its blood. Likely the very first case of infection with HIV-1

type in human was detected in 1959 from the blood sample of a man in Kinshasa, Democratic Republic of Congo. The genetic analysis of blood sample suggested that the person may be infected with virus in the late 1940s or early 1950s. [4]

Figure no. 1- Structure of HIV Virus



Structure of HIV virus

Gp120 The 120 in its name comes from its molecular weight. It is essential for virus entry into the cells as it plays vital role in attachment to specific cell surface receptors.

GP41

It is a subunit of the envelope protein complex of retroviruses including human immuno deficiencies virus. It is family of enveloped viruses that replicate in host cell through process of reverse transcriptase. It targets a host cell.

Viral envelope

It is envelope through which virus binds. P17 Viral core is made from protein. It is bullet shaped. Three enzymes required for HIV replication are reverse transcription, integrase and protease.

P24

P24 is component of HIV capsid.

Protease

It is a retroviral aspartyl protease that is essential for life cycle of HIV, the retrovirus that caused AIDS. This enzyme cleaves newly synthesized polyproteins at appropriate place to create nature protein components of infectious HIV virion.

RNA

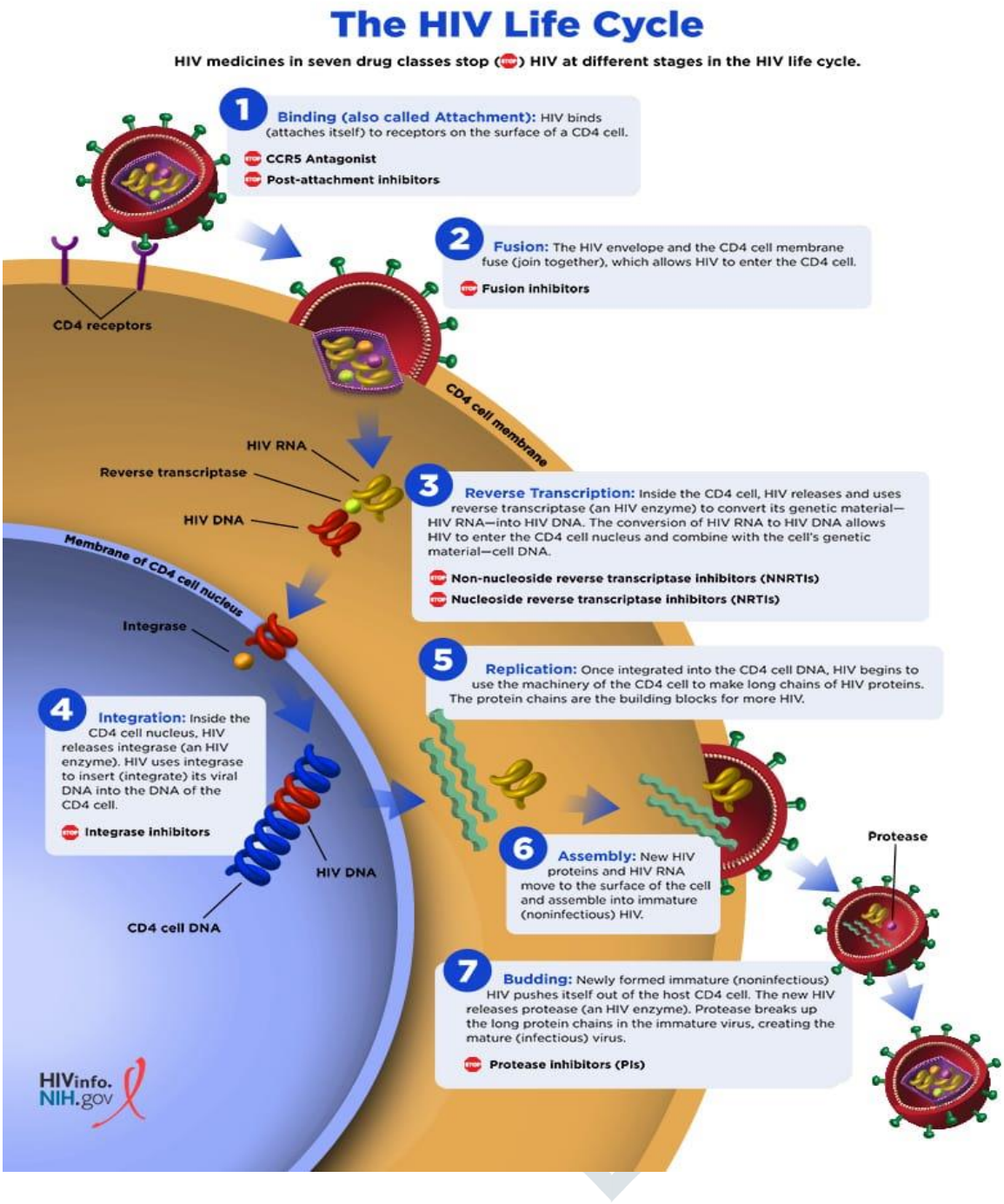
All organisms including most viruses store their genetic material on long strands of DNA. Retrovirus is exception because their genes are composed of RNA.[5]

Types

There are two types of HIV.

- HIV 1
- HIV 2

HIV 1 is the more virulent easily transmit. HIV majority caused by HIV 1 while HIV 2 is less transmit and it is mostly confined to west Africa. HIV 2 is also called as non-progresses which mean the chance of progression into AIDS is less.[6] HIV-1 is most commonly found in affected people. About 95 percent people infected with HIV have HIV-1 infections. It (HIV-1) is easily transmitted as compared to the latter one (HIV-2). Though HIV-1 and HIV-2 are both retroviruses that similarly affect body's immune system, they vary in their genetic composition. A study revealed that their genome had only 55 percent similar identity. This means that not all tests and treatments can work for both types of HIV.[7]



[8]

How is HIV spread

The spread of HIV from person to person is called HIV transmission. HIV is spread only through certain body fluids from a person who has HIV. These body fluids include:

- Blood
- Semen
- Pre-seminal fluid
- Rectal fluids
- Breast milk

HIV transmission is only possible through contact with HIV-infected body fluids. In the United States, HIV is spread mainly by: Having anal or vaginal sex with someone who has HIV without using a condom or taking medicines to prevent or treat HIV Sharing injection drug equipment (works), such as needles or syringes, with someone who has HIV The spread of HIV from a woman with HIV to her child during pregnancy, childbirth, or breastfeeding is called perinatal transmission of HIV.You cannot get HIV by

shaking hands or hugging a person who has HIV. You also cannot get HIV from contact with objects, such as dishes, toilet seats, or doorknobs, used by a person with HIV. HIV is not spread through the air or water or by mosquitoes, ticks, or other blood-sucking insects.[9]

How can a person reduce the risk of getting HIV?

- To reduce your risk of HIV infection
- Use condoms correctly every time you have sex
- Limit your number of sexual partners and
- Never share injection drug equipment [10]

Causes

It is caused by sexual contact from one person to another person.

When someone becomes infected with HIV the virus weakens and damages their body's defence are used to slow down the diseases so you stay healthier for long time. There is no medicine to get rid of diseases.

system (the immune system) so that it cannot fight off infections.

It is cause by:

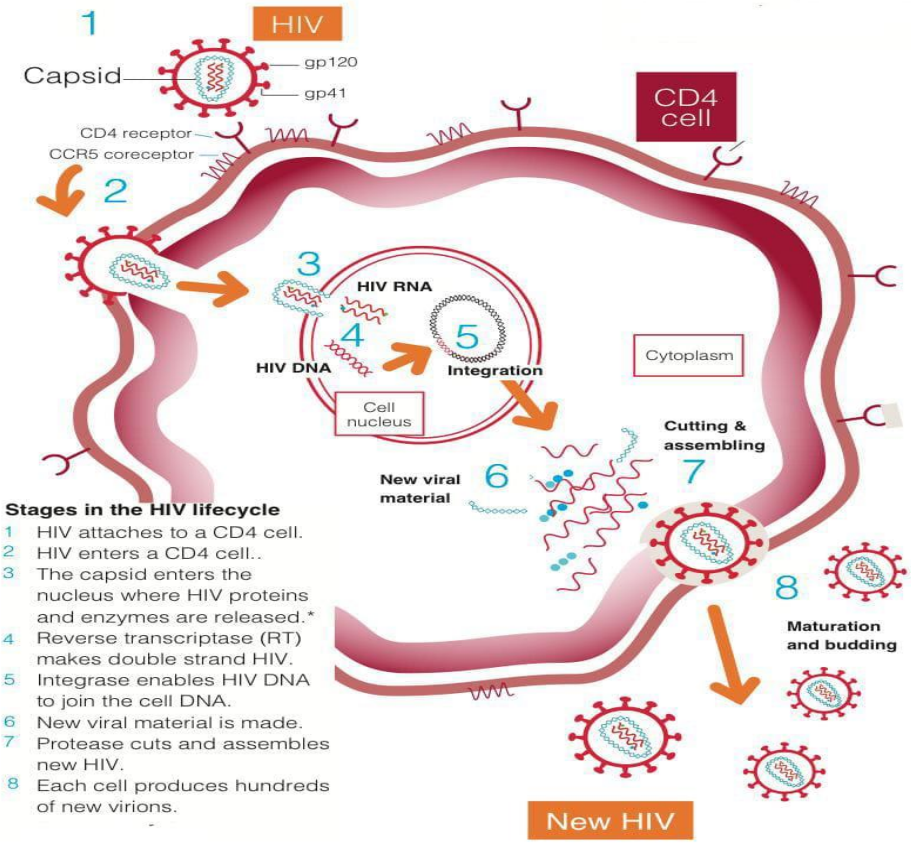
a). Sharing drug needles or syringes.

b). Sexual contact including oral, vaginal or oral who is HIV positive.

c). Having other sexually transmitted diseases such as syphilis, herpes, and gonorrhoea seem to increase the risk of being infected by HIV during unprotected sexual contact with infected partner.

d). Babies can be infected by an HIV-positive mother during pregnancy, birth and breast feeding.[11]

HIV Infection Mechanism



[12]

CD4 is present on the surface of many lymphocytes, which are a critical part of the body's immune system. It is now known that a co-receptor is needed for HIV to enter the cell. Following fusion of the virus with the host cell, HIV enters the cell. The genetic material of the virus, which is RNA, is released and undergoes reverse transcription into DNA. An enzyme in HIV called revers discomforting illness. His or her everyday

activity may be restricted and he or she is probably manifesting bouts of illness that require short-term or long-term medical treatment in and out of the hospital.[13]

Stages of Infection

There are 3 stages of infections and severity increases as the stage of disease increases.

Stage 1 (Acute HIV infection)
Stage 2 (Chronic infection)
Stage 3 (Acquired immunodeficiency syndrome)

Stage 1: Acute HIV Infection

The earliest stage of infection is called as acute HIV, and generally develops within 2 to 4 weeks after the patient is infected with HIV virus. In this very first stage infection the virus multiplies and spreads rapidly throughout the body. The HIV starts to attack and destroy the infection-fighting CD4 cells. This gradually collapses the immune system.

Stage 2: Chronic HIV Infection

This is the second stage of HIV infection also named as asymptomatic HIV or clinical latency. In this second stage of infection, the virus is in state of continuous multiplication but at very low levels. If the ART not given to patient is this stage, the stage may advance to AIDS in about 10 years (may be more or less depending on immune system of patient).

Stage 3: AIDS

The third stage is actually called AIDS and is the most severe stage of HIV infection. In this stage, the HIV has severely damaged the immune system and the body is unable to fight to the opportunistic infections. People with HIV are diagnosed with AIDS when their CD4 count is less than 200 cells/mm. Once the person is diagnosed with AIDS, they have a high viral load and can transmit disease to others very easily. Without treatment a person with AIDS typically survives for up to 3 years.[14]

Symptoms of Disease

Many people who are living with HIV have no obvious signs
and symptoms at all. Recent evidence shows that between 70% to 90% of people who become infected with HIV experience flu-like symptoms within a few weeks after infection. The most common symptoms are a fever, a rash and a severe sore throat all occurring at the same time. These symptoms in an otherwise healthy person may indicate recent
HIV infection.

HIV infected patients may get yeast infections (oral or vaginal) that do not go away or that occur often. Frequent and severe herpes infections that cause mouth, genital, or anal sores are also common. Herpes zoster (shingles) is more likely to occur in infected patients. Other pulmonary infections (pneumonia) or so called atypical mycobacterial infections can be serious for your loved one. Women may get pelvic inflammatory disease that does not respond to treatment. The virus may attack the nervous system (nerves, spinal cord or brain) and produce a variety of symptoms ranging from tingling in the feet and trouble walking to memory disturbances.[15]

Symptoms of the disease vary according to the stage of infection. Symptoms according to the stage of disease are mentioned below:-

Symptoms of Stage 1

1. Headache
2. Fatigue
3. A red rash that doesn't itch
4. Sore throat
5. Swollen lymph nodes

These symptoms are very similar to flu and are usually compared with it. The symptoms appears after 2-6 weeks after infection and vanishes after a week. If they are left untreated, the disease progresses to second stage.

Symptoms of Stage 2

After the person advances to the second stage of HIV infection, seroconversion process takes place and patient often feel better. In the second stage, patient may not show any other symptoms nearly for 10 years or even more (depending upon the health background of patient) But, the virus will still be active and continue to infect new cells of body. The virus also continues to replicate itself and risk of transmission is present during this stage. If ART is not given to patient overtime, HIV will continue to severely damage the immune system.

Symptoms of Stage 3

1. Being tired all the time
2. Fever that lasts for merely about 10 days
3. Night sweats
4. Weight loss with no obvious reasons
5. Shortness of breath
6. Severe long-lasting diarrhoea
7. Purplish spots on your skin
8. Swollen lymph nodes in your neck and groin region
9. Yeast infections in your mouth, throat, vagina.

These symptoms are treated and medication is given to increase the life span of the patient.[16]

Transmission

HIV is transmitted principally in three ways: By sexual contact, by blood through transfusion, blood products or contaminated needles or by passage from mother to child. Although homosexual contact remains a major source of HIV within the United States, "hetero sexual transmission is the most important means of HIV spread worldwide today." Treatment of blood products and donor screening has essentially eliminated the risk of HIV from contaminated blood products in developed countries, but its spread continues among intravenous drug users who share needles. In developing countries, contaminated blood and contaminated needles remain important means of infection. Thirteen to thirty-five percent of pregnant women infected with HIV will pass the infection on to their babies; transmission occurs before as well as during birth. Breast milk from infected mothers has been shown to contain high levels of the virus also. HIV is not spread by the fecal-oral route; aerosols; insects; or casual contact, such as sharing household items or hugging. The risk to health care workers is primarily from direct inoculation by needle sticks. Although saliva can contain small quantities of the virus, the virus cannot be spread by kissing. HIV is transmitted primarily by sexual contact (both heterosexual and male to female);

HIV can be transmitted from an infected person to another through:

- Blood (including menstrual blood),
- Semen,
- Vaginal secretions,
- Breast milk.[17]

Diagnosis Of The Disease

HIV is most commonly diagnosed by testing your blood or saliva for antibodies to the virus. Unfortunately it takes time for your body to develop these antibodies-usually up to 12 week. A newer type of test that checks for HIV antigen, a protein produced by the virus immediately after infection, can quickly confirm a diagnosis soon after infection. Following are the tests for detection of HIV AIDS:

- **Home Tests**

The home access expert test is approved by US FDA and is sold in pharmacies. It is the only approved home test kit.

- **Tests To Tailor Treatment**

If you receive a diagnosis of HIV/AIDS, several types of tests can be done. These tests include:

- **CD4 count**

CD4 cells are a type of white blood cell that's specifically targeted and destroyed by HIV.

- **Drug resistance**

This blood test determines whether the strain of HIV you have will be resistant to certain anti-HIV medications.[18]

- **Antigen/Antibody testing**

Antigen can show positive test within few days of infection but immune system requires time to produce antibodies to infection and hence my require time (2-6 weeks) to be positive. Hence a combination of Antigen/Antibody test may take 2- 6 weeks to show positive results after exposure to virus.

- **Antibody tests**

These tests look for antibodies to HIV in blood or saliva. Most rapid HIV tests, including self-tests done at home, are antibody tests. Antibody tests can take 3 to 12 weeks after you're exposed to become positive.

- **Nucleic acid tests (NATs)**

These tests look for the actual virus in your blood (viral load). They also involve blood drawn from a vein. If you might have been exposed to HIV within the past few weeks, your health care provider may recommend NAT. NAT will be the first test to become positive after exposure to HIV.[19]

- **Viral load test**

The amount of HIV in blood is measured using viral load test. This test is generally used to monitor treatment progress and also is helpful in detecting early HIV infections. The three technologies which measure HIV
viral load with same basic principle are:

1. Branched DNA (bDNA)
2. NA (nucleic acid) sequence based amplification
3. Reverse transcription PCR

- **ELISA Test**

ELISA (enzyme-linked immunosorbent assay) is used to detect the presence of HIV infection. After getting positive result of ELISA test, usually western blot test is administered to confirm the infection. Though ELISA test may show negative result, but if patient thinks that there may be HIV infection present, he/she should again get tested after one or three months. ELISA is a very sensitive to HIV infection, but antibodies are not produced immediately after infection so one may test negative within few weeks after being infected. Although, you may get negative test results, the level of virus present is high and you will be at risk of transmitting infection.

- **Saliva Tests**

By using a cotton pad, saliva is obtained from the inside of patient's cheek. It is placed in vial and submitted for testing. Results are usually available within 3 days and positive results are confirmed with blood tests.[20]

Herbal Drugs For HIV

use Human Immuno Deficiency virus (HIV) and Acquired Immune Deficiency syndrome is necessary due to is wide spread infection throughout the world.

India has more than 30000 plant species and most of them have medicinal properties. even as on today more than 50% marketed drug products are obtained from natural source only.

Over the last two-decades notable progress has been made in research of natural drugs for the treatment of HIV. There is no cure for HIV but many drugs are available to control the HIV virus. such treatment is known as antiretroviral therapy.

HIV can be diagnosed by testing blood for antibodies to the virus, but it is time consuming and takes about 12 weeks, and hence not practisable for immediate**.**

- **Herbal drugs which are used to reduce the severity of HIV are:**
    1) Sutherlandia frutescens
    2) Hypoxis hemerocallidea (African potato)

3) Hypericum perforate[21]

Herbal Remedies For HIV

Remedies derived from plants are common to many cultures and a number of advanced pharmaceutical drugs were derived from plants. There are herbs that can heal dangerous disease such as Cancer too. Sometimes it is said that where allopathic fails, herbal remedies work. Herbal remedies are said to work to such an extent that they can even do away with the need for the surgery. In India the medicine of herbs came to be known as Ayurveda. This form of medicine has used herbs to cure all forms of disease.[22]

Plants for Anti HIV activity

Sr. No.	Family/Species	Active Constitutents	Mechanism of Action
1.	**Palmae** Areca catechu	Seed extract, procyanidin, arecatanin B1	HIV protease inhibition.
2.	**Rosaceae** Crataegus pinatifida	Uvaol and ursolic acid	Inhibitory activity against HIV-1 protease.
3.	**Malvaceae** Gossypium spp	Gossypol	Inhibiton of giant cell formation of HIV-infected cells.
4.	**Physalacriaceae** Flammulina velutipes	Velutin	Inhibition of HIV-1 reverse transcriptase.
5.	**Apocyanaceae** Rauwolfia serpentina	Papaverine	Inhibition of HIV reverse transcriptase and HIV cell growth.

[23]

Treatment

Antiretroviral drugs are used to treat HIV. These are the drugs active against human immunodefiency virus (HIV) which is retrovirus. They are useful in prolonging and improving a quality of life.

In a standard antiretroviral therapy commonly called as ART is combination of at least 3 antiretroviral (ARV) drugs which is intended for maximal suppression of HIV virus in the body. Antiretroviral treatment is the best option for long lasting viral suppression and, subsequently, for reduction of morbidity and mortality. Effective treatment returns to near normal the turnover rates of both CD4+ and CD8+ T-cell populations. Antiretroviral drugs are classified as following:

❖ **Nucleoside reverse transcriptase inhibitors (NRTIs):**

Zidovudine (AZT), Didanosine, Lamivudine, Tenofovir.

❖ **Nonnucleoside reverse transcriptase inhibitors:**

Nevirapine, Delavirdine, Efavirenz.

Protease inhibitors:

- **Nucleoside analogue reverse transcriptase inhibitors**

(NRTIs) were the first type of drug available to treat HIV infection in 1987. When HIV infects a cell, it copies its own genetic code into the cell's DNA, and the cell is then programmed to create new copies of HIV. To reproduce, HIV must first convert its RNA into DNA using the enzyme reverse transcriptase. These inhibitors act like false building blocks and compete with the cell's nucleosides, thereby preventing DNA synthesis**.**

- **Non nucleoside reverse transcriptase inhibitors** (NNRTIs)

started to be approved in 1997. These also interfere with HIV's ability to infect cells by targeting reverse transcriptase. In contrast to nucleoside analogue reverse transcriptase inhibitors, non nucleosides bind directly to the enzyme.[23]

❖ **Protease inhibitors (PIs)**

inactivate HIV protease, another protein that HIV needs to make copies of itself.

Examples include atazanavir (Reyataz), darunavir (Prezista) and lopinavir/ritonavir (Kaletra).

❖ **Integrase inhibitors**

work by disabling a protein calledintegrase, which HIV uses to insert its genetic material into CD4 T cells.

Examples include bictegravir sodium/emtricitabine/tenofovir alafenamide fumarate (Biktarvy), raltegravir (Isentress), dolutegravir (Tivicay) and cabotegravir (Vocabria).

- ❖ **Entry or fusion inhibitors**

block HIV's entry into CD4 T cells.

Examples include enfuvirtide (Fuzeon) and maraviroc (Selzentry). treatment side effects.

Treatment side effects can include:

- Nausea, vomiting or diarrhea
- Heart disease
- Kidney and liver damage
- Weakened bones or bone loss
- Abnormal cholesterol levels
- Higher blood sugar
- Cognitive and emotional problems, as well as sleep problem [24]

Marketed Preparations

IMMUN-UP

Herbal Capsule for treatment of HIV/AIDS. (30 capsule pack in plastic jar).

Doses

- One capsule three times a day. (For patient with very weak health – i.e. last stage of AIDS)
- One Capsule two times a day (for all other patient)

KAMILARI PLUS (50 capsule pack in plastic jar)

It is a very rare combination of various herbal ingredients which are virocidal and immuno stimulant**.**

HOO-IMM PLUS

HOO-IMM PLUS drug are used not only in the treatment of HIV but also hepatitis and has recorded the highest inhibition rate of 98%. These drugs inhibit viral multiplication, increase CD4 lymphocytes cells in the body, decrease the RNA viral load count, stimulate and sustain general physiological activity. It restores the immune system and is used for the treatment and prophylaxis of opportunistic infections in HIV/AIDS patients.[25]

HIV Technology

The term 'technology' is used to encompass medical technologies such as HIV treatment, but also other 'technologies' of health care, including psychosocial and social interventions and communications media applied to moderating HIV's impact and to preventing HIV transmission. HIV technologies of the biomedical kind have become a focus in the research and policy literature. Policy frameworks advocate for close attention to the relationship between HIV treatment and prevention (Global HIV Prevention Working Group, 2008: 6) (see also Mykhalovskiy, this volume) and an address to 'psychosocial' factors (UNAIDS, 2009b), as well as integration between HIV and other health and social policy initiatives, around for instance TB, drug use, and gender-based violence (UNAIDS, 2009a).[26]

Pharmacokinetic

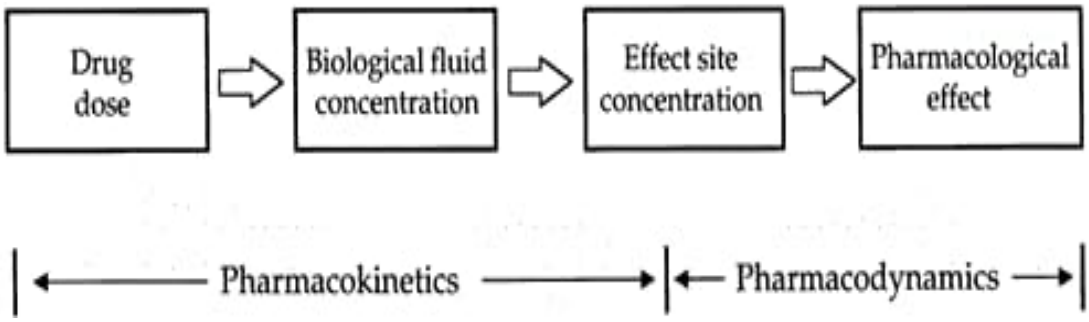
Pharmacokinetics is the study of how a drug is absorbed, distributed, metabolized, and eliminated from the body; it is what the body does to a drug or toxin.[27] The PK of an agent is performed in a controlled setting where all study individuals are taking the same dose at the same time each day, with the same food/fluid requirements and without any known agents that could produce a drug–drug interaction. In addition, studies are often performed in healthy, non-HIV-infected volunteers, and until recently, many have been performed with few, if any, female participants. Even when evaluated under these conditions, agents can display wide interpatient variability.[28]

In early HAART, manipulation of drug exposures through the use of therapeutic drug monitoring showed promise by improving viral responses and/or minimizing drug toxicities. [29-31] However, with the advent of low-dose ritonavir boosting, the levels of PIs are substantially increased to well above the concentrations needed to inhibit wild-type HIV, even when the wide interpatient variability is taken into account.

Pharmacodynamic

Pharmacodynamics is the study of drug concentration and effect relationships. whereas pharmacodynamics describes what the drug does to the body.[32] The general relationship between pharmacokinetics and

pharmacodynamics in figure. Several factors are important with respect to pharmacokinetic and pharmacodynamic relationships. First, a given dose of a drug does not always produce the same blood concentration. Although other factors are involved, this variability in blood concentrations is primarily a result of between-patient differences in drug absorption and clearance. Second, variability in blood concentrations leads to variability in concentrations at the site of action. Consequently, variability at the site of action ultimately contributes to heterogeneity in response to therapy.



General relationship between pharmacokinetics and pharmacodynamics

This relationship may occur because the analytical techniques used to detect low drug concentrations might not be available and high concentrations are avoided to prevent toxicities. In the case of therapy for HIV infection, technology to quantify very low levels of plasma HIV RNA may not have been used or available, which would prevent the absolute magnitude of change from being observed, thereby limiting the data set to the linear range of values.[33]

Stem cell therapy

The stem cells can be transformed into a wide range of specialized functional cell types. [34,35] In response to injury or maturation, those same stem cells can propagate in massive quantities.[36] Adult, embryonic, and induced pluripotent stem cells are examples of stem cell-based therapies.[37,38] The stem cells, due to their capability to distinguish the specific cell types requisite for a diseased tissue regeneration, can provide an effective solution, while tissue and organ transplantation are considered necessary.[39]

The sophistication of stem cell-based treatment interventions, on the other hand, probably leads researchers to seek stable, credible, and readily available stem cell sources capable of converting into numerous lineages. As an outcome it is critical to exercise caution when selecting the type of stem cells to be used in therapeutic trials. [40,41]

CONCLUSION

HIV prevention programs have focused primarily on developing risk reduction interventions for those at high risk for becoming infected with HIV. In 1999, a review of 55 state and city applications to the CDC for funds for HIV prevention programs demonstrated that only 18 (32.7%) listed HIV-infected individuals as a priority population for HIV prevention programs. Although there are millions of people in the United States at "behavioral risk" for HIV infection, transmission can occur only from people who are infected with the virus. Plant derived microbicide and plant bodies are some of new approach for prevention of HIV. So, herbal medicines can be developed as a safe effective and economical alternate for AIDS. .Stem cell therapy are also viable treatment choice for people suffering from a wide range of illness and injuries.

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