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Review on the Impact of HIV their Early History and Reason Behind the Outbreaks.

Kanawade Vaishnavi[1], Tordmal Vishakha[2]

[1] UG Student, Guide[2]
Vidya Niketan College of Pharmacy Bota

ABSTRACT :

Since the onset of the epidemic, approximately 70 million individuals globally have been infected with the human immunodeficiency virus (HIV), with the majority residing in sub-Saharan Africa. Significant advancements have been made in HIV treatment through the use of antiretroviral drug combinations. Nevertheless, the emergence of drug resistance to these anti-HIV medications poses a challenge, and numerous individuals living with HIV experience adverse effects or lack sufficient access to the available therapies. Consequently, there is an urgent need to identify new anti-HIV agents to enhance our existing treatment options and to offer therapeutic alternatives for populations with limited resources or access to effective treatments. Natural products derived from plants continue to be a valuable source for the discovery of novel medicines, including anti-HIV compounds. This review provides an overview of various plants that have demonstrated anti-HIV properties, both in vitro and in vivo.

KEYWORDS: HIV, drug, discovery, pharmacognosy, antiviral, acquired immune deficiency syndrome, infected

INTRODUCTION :

The World Health Organization estimates that more than 75 million individuals worldwide have been infected with the human immunodeficiency virus (HIV), with around 37 million currently living with the infection[1]. The recognition of Acquired Immune Deficiency Syndrome (AIDS) began in the United States around 1981, primarily due to a rise in cases among adult males, particularly within the gay community in cities such as San Francisco and New York. These cases were characterized by immune system suppression, Pneumocystis carinii pneumonia, and Kaposi's sarcoma[2,3,4]. Presently, it is estimated that approximately 26 million of these individuals reside in Africa, with 3.3 million in the Americas, 3.5 million in Southeast Asia, 2.4 million in Europe, 360,000 in the Eastern Mediterranean, and 1.5 million in the Western Pacific[5].

HIV is the causative agent of AIDS, and transmission occurs through the exchange of viral particles typically found in the blood, semen, and vaginal fluids of an infected person to an uninfected individual, with condom use being a primary preventive measure [2,3,6]. Vertical transmission is another mode of infection, where the virus is passed from an infected mother to her child during pregnancy, childbirth, or breastfeeding. While HIV significantly contributes to global morbidity and mortality, the sub-Saharan region of Africa bears the highest burden, accounting for approximately 70% of the 37 million HIV cases, despite representing only 21% of the global population. Notably, men and women in Africa are disproportionately affected by this disease compared to other racial groups[5,8].

A total of ten nations in southern and eastern Africa, namely South Africa (25%), Nigeria (13%), Mozambique (6%), Uganda (6%), Tanzania (6%), Zambia (4%), Zimbabwe (6%), Kenya (6%), Malawi (4%), and Ethiopia (3%), collectively represent approximately 80% of the HIV-positive population [2,3]. In many of these countries, the highest prevalence of HIV is observed among specific demographics, including men who have sex with men, intravenous drug users, individuals in prisons and other confined environments, sex workers, and transgender individuals. Notably, in sub-Saharan Africa, the predominant mode of HIV transmission is heterosexual intercourse, with a significant incidence of vertical transmission affecting children. Consequently, women in Africa are disproportionately impacted, constituting around 58% of the total population living with HIV, and they also represent the largest number of children living with HIV as well as the highest rates of AIDS-related fatalities[5].

HISTORY:

At the end of 2009, 68% of the 330,000 Zambians needing antiretroviral therapy (ART) were Receiving it and a third of all health facilities in the [9] country was able to offer treatment . Despite this impressive progress, Zambia's ART programmeis like a candle in the wind as it battles to glimmer Against the inevitable possibility of dying from another form of AIDS- 'Acquired Income Deficiency Syndrome'. There are concerns that the country's free public sector ART programme is not sustainable due its heavy reliance on donor funds. Besides funding, access to treatment in Zambia is challenged

by inadequacy of the healthcare system, which suffers from high patient numbers, lack of physical space and infrastructure, and attrition of 2,3 health workers . Notably, there is a critical shortage of doctors. In 2006, there were only about 646 Doctors; this was under a third of the doctor-patient ratio recommended by the World Health 2 Organization (WHO) .

The World Health Organization (WHO) recommended that traditional healers be included in 6 National responses to HIV/AIDS . As early as 1989, WHO had already voiced the need to evaluate ethnomedicines for the management of HIV/AIDS:

In this context, there is need to evaluate those elements of traditional medicine, particularly medicinal plants and other natural products that might yield effective and affordable therapeutic agents. This will require a systematic approach 7In the past, the screening and development of natural products and chemically synthesized compounds have been developed as medication for HIV infections. [10–14] With marine species Comprising approximately one-half of the total global biodiversity, the sea offers an enormous resource for novel compounds. [15] Moreover, very different kinds of substances have been procured from Marine organisms because they are living in a very exigent, competitive, and aggressive surrounding; Very different in many aspects from the terrestrial environment, a situation that demands the production of quite specific and potent active molecules. The marine environment serves as a source of functional Materials, including polyunsaturated fatty acids (PUFA),polysaccharides, minerals and vitamins, Anti-oxidants, enzymes, and bioactive peptides.[16,17]

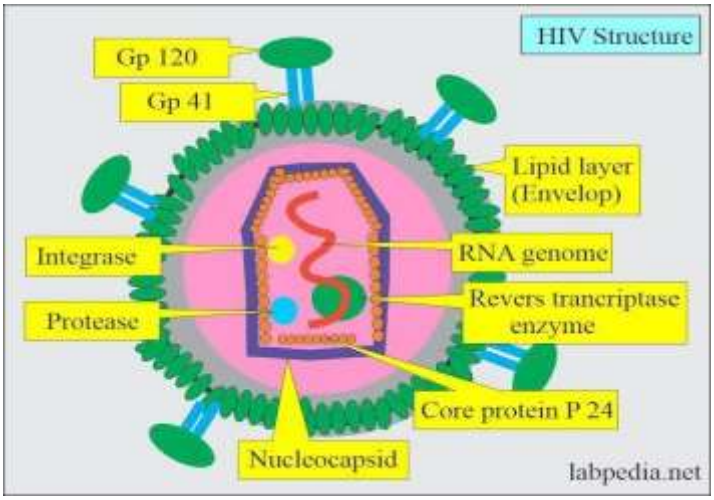

Fig .Structure of HIV

The ribonucleoprotein particle is encapsulated by a capsid made up of a capsid protein (CA), p24. The capsid environment also contains other viral proteins such as integrase and reverse transcriptase. It also contains a wide variety of other macromolecules derived from the cell including tRNAlys3, which serves as a primer for reverse transcription.[19] The major HIV proteins associated with the envelope are gp120/41, these functions as the viral attachment proteins.

Types of HIV:

Two major types of HIV have been identified so far,[20]

HIV-1:

It is the cause of the worldwide epidemic and is most referred to as HIV. It is a highly variable virus, which mutate readily. There are many different strains of HIV-1, which can be classified according to groups and subtypes; M and O. Within group M, there are currently known to be at least ten genetically distinct subtypes which are A to J.

HIV-2:

In addition, Group O contains another distinct group of heterogeneous viruses. HIV-2 is less pathogenic and occurs rarely; it is found mostly in West Africa.

HIV INFECTIONS MECHANISM :

HIV begins its infection by binding to the CD4 receptor on the host cell. 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 reverse transcriptase is necessary to catalyze this conversion of viral RNA into DNA. Once the genetic material of HIV has been changed into DNA, this viral DNA enters the host cell nucleus where it can be integrated into the genetic material of the cell. The enzyme integrase catalyzes this process. Once

the viral DNA is integrated into the genetic material of the host, it is possible that HIV may persist in a latent state for many years. This ability of HIV to persist in certain latently infected cells is the major barrier to eradication or cure of HIV[21]

Objective :

The goal of the current study is to provide empirical evidence that several plants possess anti-HIV active compounds, help refocus the attention of researchers towards the study of herbal plants with anti-HIV activity, and re-inspire public and research interest in the use of plants with anti-HIV properties.

This goal was approached through the following objectives:

- To search the literature for research articles that document plants with anti-HIV properties;
- To document the taxonomic families and species of plants with anti-HIV properties, their active ingredients, and modes of action against HIV.

Pathophysiology-

The HIV virus is classified as a retrovirus, capable of integrating a DNA copy of its viral genome into the DNA of host cells. It gains entry into the cell by binding to receptors present on the surface of T lymphocytes (with activated T lymphocytes being the primary targets), as well as monocytes, macrophages, and dendritic cells[1,22]. The entry process involves HIV-1 attaching to either the chemokine receptor 5 or the CXC chemokine receptor 4 through interactions with its envelope proteins. Following the fusion and uncoating of the virus, the single-stranded RNA is reverse transcribed into HIV DNA, which is subsequently integrated into the host's DNA. The integrated HIV DNA is then transcribed into viral mRNA, which is transported to the cytoplasm for translation into viral Gag, Gag-Pol, and Nef polyproteins. These polyproteins are later cleaved during the assembly and maturation of new virions, either at the cell surface or after the release of the viral particles. Current therapeutic strategies target various stages of this process, including entry inhibitors, reverse transcriptase inhibitors, integrase strand transfer inhibitors, and protease inhibitors [23,24].

Pathogenesis:

This virus infects CD4+ cells and the CCR5 or CXCR4 chemokine receptor. The Presence of infection in CD4+ cells shows that the patient's immune system is impaired. In 1996,a cohort study found that the viral load in the plasma could predict the course of HIV infection within 6 to 12 months, and that at this point, the CD4+ count verified the disease severity. During the early stages of infection, more than half of the CD4+ cells decline. When the number of these cells falls, the disease advances from acute to chronic. CD4+ T lymphocytes are reduced in the gut during HIV infection, and helper cells generate interleukins to keep the mucosal barrier intact. [23,24]

Symptoms of AIDS:

There is no clearly defined symptom in HIV infected person in initial stage, however, have a flu-like illness within a month or two after exposure to the virus. This illness may include: rash fever, headache, tiredness and enlarged lymph nodes (glands of the immune system easily felt in the neck and groin). More persistent or severe symptoms may not appear even for 10 years or more after HIV enters the body in adults, or within 2 years in children born with HIV infection. This period of "asymptomatic" infection varies greatly in everyone. Even during the asymptomatic period, the virus is actively multiplying, infecting, and killing cells of the immune system. Other symptoms often experienced from months to years before the onset of AIDS include:

· Lack of energy

· Anorexia

· Fatigue

· Frequent fevers and sweats

· Persistent or frequent yeast infections (oral or vaginal)

· Persistent skin rashes or flaky skin

· Pelvic inflammatory disease in women that does not respond to treatment

· Short-term memory loss

· Weight loss

Mode of Transmission:

- **Infected Blood**

HIV spread through contact with infected blood. HIV is transmitted through transfusions of contaminated blood or blood components.HIV is frequently spreading among users by the sharing of needles or syringes contaminated with very small quantities of blood from someone infected with the virus.

- **Mother & Baby**

During pregnancy and childbirth, women can pass HIV to their unborn children. HIV can also be passed from mother to child through breast milk. The likelihood that a kid may contract HIV can be considerably decreased if the mother uses specific medications while she is pregnant.

- **Infections Transmitted Sexually**

A person may be more likely to contract HIV having intercourse with infected partners if they have syphilis, genital herpes, chlamydia infection, gonorrhea, or bacterial vaginosis

Stages of HIV Infection.

There are basically four stages of HIV infection:

State of Health Carrier:

A carrier is a person who has a disease but exhibits no clinical symptoms, yet is nonetheless able to spread it to other individuals. The only safe practice at this time is to assume that anyone who has the virus can spread it to others.

Lymphadenopathy Syndrome (LAS)

"Disease of the lymphatic system" is what lymphadenopathy is. Swollen lymph nodes are one of the main indicators of lymphadenopathy. Undoubtedly, any infection, like the flu, makes the lymph nodes enlarge, but this swelling subsides soon. When a person has HIV, this nodal swelling may last for months without showing any other symptoms of a transient viral condition. As a result, Persistent Generalized Lymphadenopathy (PGL) is another name for lymphadenopathy.

Diagnoses:

Acute HIV infection is characterized by symptoms such as fever, general malaise, lymphadenopathy, rash, and myalgias. Additionally, severe complications, including meningitis, have been reported[22,26].. The detection of the HIV virus in the bloodstream is typically measured by assessing the viral RNA load. During the acute phase of infection, plasma levels of HIV RNA reach their peak, and there is a correlation between the viral load and the severity of symptoms. Certain theories suggest that the characteristics of the virus and the viral load play a role in regulating viral replication and pathogenicity. Consequently, both the viral genotype and the host influence clinical outcomes and the progression of the disease[22]. HIV establishes a dormant or latent infection within memory CD4+ T cells, which possess a stem-cell-like ability for self-renewal, complicating efforts for complete eradication. If these cells remain viable, the HIV virus can reactivate and replicate once its DNA has integrated into the host's chromatin. While antiretroviral therapy (ART) can prevent the infection from spreading to new cells, it does not eliminate the infection once the viral DNA has successfully entered a target cell. Due to limited host clearance mechanisms and the penetration of antiretroviral drugs, lymph nodes can act as reservoirs for viral reactivation in patients who stop or interrupt their therapy. Some studies suggest that ART may need to be maintained for several decades before the viral reservoir diminishes to a minimal level.[25].

Treatment :

Although HIV was recognized early in the 1980s, there is still no cure or an effective vaccine for HIV infection, but there have been some significant advances in treatment, control, and prevention. [27] The introduction of anti-retroviral agents and highly active antiretroviral therapy (HAART) in 1996 significantly reduced the morbidity and mortality of HIV/AIDS. Antiretroviral therapy is currently recommended for all adults with HIV. Recommendations for initial regimens include two nucleoside reverse transcriptase inhibitors (nrtis; abacavir with lamivudine or tenofovir disoproxil fumarate with emtricitabine) and an integrase strand transfer inhibitor, such as dolutegravir, elvitegravir, or raltegravir; a nonnucleoside reverse transcriptase inhibitor (efavirenz or rilpivirine) or a boosted protease inhibitor (darunavir or atazanavir) [28]. There are additional regimens available.

Although HIV was initially discovered in the early 1980s, there is still no cure or vaccine that can effectively stop HIV infection [27]. But there have been substantial advancements in management, treatment, and prevention. With the approval of highly active antiretroviral therapy (HAART) and other antiretroviral drugs in 1996, the morbidity and mortality of HIV/AIDS significantly decreased. All HIV-positive people are currently advised to take antiretroviral drugs. Recommendations for initial regimens include two nucleoside reverse transcriptase inhibitors (nrtis; abacavir with lamivudine or tenofovir disoproxil fumarate with emtricitabine) and an integrase strand transfer inhibitor, such as dolutegravir, elvitegravir, or raltegravir; a nonnucleoside reverse transcriptase inhibitor (efavirenz or rilpivirine) or a boosted protease inhibitor (darunavir or atazanavir). [28] There are more regimens accessible. The disease is now a chronic, treatable condition rather than a deadly one because of the decline in morbidity and mortality [1,5,29,30]. It is interesting to note that the increased survival rate has led to an ageing HIV/AIDS population, which has created a whole new set of problems. These problems include a higher prevalence of chronic diseases in this population, such as cardiovascular and pulmonary diseases, malignancies, and even a special set of comorbidities that are now known as HIV-associated Non-AIDS (HANA) conditions, and a higher incidence of comorbidities. The cornerstone of HIV treatment and prevention continues to be antiretroviral drugs. [35] Anti-retroviral therapy (ART) is currently advised for all HIV-infected individuals with detectable virus, regardless of CD4 cell count, as soon as possible after diagnosis to halt disease progression, improve clinical outcomes, including lowering AIDS-associated events and non-AIDS-related events, and reducing all-cause mortality and transmission [35]

All HIV-infected people with detectable plasma virus should receive treatment with recommended initial regimens consisting of an integrase strand transfer inhibitor (insti) plus two nucleoside reverse transcriptase inhibitors (nrtis). These recommendations are supported by large randomized controlled clinical trials. Anti-retroviral medications suppress HIV and stop the spread of new HIV infections when administered correctly. With these treatment plans, it has been hypothesized that adult HIV-positive patients' survival rates may approach those of adult HIV-negative patients. [35]

Recent therapy for HIV :

Histone deacetylase (HDAC) inhibitors, gene therapies, broadly neutralizing anti-HIV antibodies, immune modulation strategies, and innovative medications that block HIV entry through new mechanisms have been highlighted in a recent review focusing on HIV therapies currently undergoing phase 2 clinical trials. [36] These emerging treatments are designed to serve as alternatives to existing combination antiretroviral therapies and to provide options when treatment regimens are disrupted. The preliminary effectiveness of these developing medications has shown variability in initial trials. Each of these innovative therapies holds the promise of addressing existing gaps in available antiretroviral treatments, ultimately enhancing health outcomes for individuals living with HIV[90].

Natural & Herbal products for HIV

Many civilizations use plant-based remedies, and many cutting-edge pharmaceutical medications have their roots in plants. There are other plants that can treat deadly conditions like cancer. There is a claim that herbal medicines succeed when allopathic ones fail. According to some reports, herbal treatments are so effective that they can even eliminate the need for surgery. Ayurveda is the name given to herbal medicine in India. Herbs have been employed in this type of therapy to treat all ailments.[37]

Although effective, ART does have serious side effects, which are particularly noticeable in patients receiving long-term care. In addition, the formation of multidrug resistance limits the effectiveness of current medicines [38] ,necessitating the development of new drugs and novel targets to address the problem of the body's HIV reservoirs and achieve the goal of the complete eradication of HIV and AIDS. Cells that are still latently infected are the biggest obstacle to eliminating HIV-1. The molecular basis for HIV latency persistence has been elucidated during the past ten years, and as a result, several medications that can selectively reactivate latent proviruses without causing polyclonal T cell activation have been found [39]It's interesting to note that vorinostat and other histone deacetylase (HDAC) inhibitors can activate latently infected cells' transcription of the HIV gene. In a spreading-infection assay, vorinostat has been shown to increase CD4+ T cell susceptibility to HIV infection in a dose- and time-dependent manner. It does not enhance viral fusion with cells, but it does increase reverse transcription, nuclear import, and integration, and it increases viral production. A "shock and-kill" approach to eliminate HIV latent reservoirs is currently being researched clinically with HDAC inhibitors, specifically vorinostat [39] .Since new drugs will be needed for the management of HIV, the World Health Organization (WHO) has suggested the that ethnomedicines and other natural products should be systematically Tested against HIV as they may yield effective and more affordable therapeutic agents (World Health Organization [40,41]. Interestingly, a significant amount of work in this area was performed in the 1990s, particularly investigations of natural products with activities against HIV-1 reverse transcriptase, HIV-1 and -2 proteases and integrases (extensively reviewed by Kurapati et al). [42]. The natural products calanolides (coumarins), ursolic and betulinic acids (triterpenes), baicalin (flavonoid), polycitone A (alkaloid), lithospermic acid (phenolic compound) have been proposed as promising candidates for anti-HIV agents [42]. However, most of these studies are in vitro, and too few investigations have been performed in vivo or in human studies. In terms of clinical data, a meta-analysis assessed 12 clinical trials involving 881 patients with AIDS to determine the efficacy of traditional Chinese medicines (TCM).been carried out in human research or in vivo. In order to analyse the effectiveness of traditional Chinese medicines (TCM), a meta-analysis of 12 clinical studies including 881 patients with AIDS was conducted. The findings demonstrated that when compared to a placebo, TCM therapies were linked with a considerably lower plasma viral load. According to this study, TCM treatments considerably outperformed a placebo in terms of lowering plasma viral loads and raising CD4+ T lymphocyte counts in AIDS patients. TCM therapies were associated with improved symptoms in a greater percentage of patients with fewer adverse effects, but they were significantly less successful in lowering viral load when compared to traditional Western medication [43]. Therefore, natural items and conventional pharmaceuticals have a lot of potential for treating HIV infections and symptoms, although in vivo and human research are lacking[90].

Medicinal plants used to treat HIV/AIDS-

For a range of viral and non-infectious illnesses, drugs made from natural resources, such as medicinal plants, have remained the preferred treatment. According to numerous reports, medicinal plants can treat HIV/AIDS with little to no side effects. Herbs not only affect viral particle replication but also act as immunomodulators and immune stimulants since they can be a source of antioxidants and nutraceutical components. Numerous plants having anti-HIV properties have been identified in the literature.

Sr no.	Medicinal plants	Family	Active constituents	Mechanism of action	Reference
1.	Andrographis paniculata	Acanthaceae	Aqueous extracts of leaves	Inhibits HIV protease and reverse transcriptase	44
			Diterpene lactones (andrograph olide)	Inhibit cell-to-cell transmission, viral replication, and syncytia formation in HIV-infected cells	45

2.	Acer okamotoanu m	Aceraceae	Flavonoid gallate ester	Anti-HIV-1 integrase activity	46
3.	Lentinus edodes (Berk.) Singer	Agaricaceae	Sulfated lentinan	Prevents HIV-induced cytopathic effect	47
4.	Galanthus nivalis L. Hippeastrum hybrids	Amaryllidac eae	Plant lectins: G. nivalis agglutinin (GNA), Hippeastrum hybrid agglutinin (HHA), and monocot mannose-bin ding lectins (MBLs) Stops spread of HIV among lymphocytes ; most prominent anti-HIV activity is found among	Stops spread of HIV among lymphocytes ; most prominent anti-HIV activity is found among MBLs; GNA has specificity for terminal α(1-3)-linked mannose residues; HHA recognizes both terminal and	48
			MBLs; GNA has specificity for	internal α(1-3)- and α(1-6)- linked mannose residues	
5.	Rhus succedanea L.	Anacardiace ae	Biflavonoids , robustaflavo ne and hinokiflavon e	Inhibits HIV-1 reverse transcriptase	49
6.	Ancistroclad us korupensis	Ancistroclad aceae	Michellamin es A and B	Inhibits reverse transcriptase, cellular fusion and syncytium formation	59
7.	Polyalthia suberosa	Annonaceae	Lanostane-ty pe triterpene, suberosol	Anti-HIV replication activity	51
8.	Lomatium suksdorfii	Apiaceae	Suksdorfin	Suppresses HIV-1 viral replication	52
9.	Agardhiella tenera (J. Agardh) F. Schmitz	Areschougia ceae	Sulfonated polysacchari des	Inhibits HIV cytopathic effect 21 180	53

10.	Achyrocline satureioides (Lam.) DC (Marcela);	Asteraceae	Dicaffeoylquinic acids: 3,5-dicaffeoylquinic acid, and 1-methoxyoxalyl-3,5-dicaffeoylquinic acid	Irreversible inhibition of HIV-1 integrase	54
	Arctium lappa (Burdock)		Wedelolactone, a coumarin derivative; orobol (an isoflavone derivative)	Inhibits HIV-1 replication; blocks cell-to-cell transmission of HIV-1	55
11.	Arnebia euchroma (Royle) Jonst	Boraginaceae	Monosodium and monopotassium salts of isomeric caffeic acid tetramer	Inhibits HIV replication	56
12.	Humulus lupulus	Cannabaceae	Xanthohumol	Inhibits HIV-1-induced cytopathic effects	57
13.	Celastrus hindsii	Celastraceae	Celasdin B	Anti-HIV replication activity	58
14.	Tripterygium wilfordii Hook F	Celastraceae	Diterpene lactones (nortripterifordin)	Inhibits HIV replication	59
15.	Callophyllum	Clusiaceae	Cordatolide A and B	Inhibits HIV-1 replication	60
	cordato-oblongum		(+)-calanolide A	Inhibits cytopathic effects of HIV-1	61
	Marila laxiflora		Laxoflorano ne	Inhibits reverse transcriptase	62
	Symphonia globulifera		Guttiferone A	Inhibits cytopathic effects of HIV	63
	Hypericum perforatum L.		Hypericin, 3-hydroxy lauric acid		
16.	Combretum molle R.Br. ex G.Don	Combreataceae	Gallotannin	Inhibits HIV-1 reverse transcriptase	65

	Terminalia chebula		Gallic acid and galloyl glucose	Inhibits HIV reverse transcriptase and integrase	66
17.	Vatica astrotricha	Dipterocarpaceae	6,8-diprenylaromadendrin and 6,8-diprenylkaempferol	Inhibits HIV-1 entry and replication	67
18.	Peltophorum africanum Sond.	Fabaceae	Gallotannin	Inhibits HIV-1 reverse transcriptase	68
19.	Swertia franchetiana	Gentianaceae	Flavonone-x anthone glucoside	Inhibits HIV-1 reverse transcriptase	69
20.	Inonotus obliquus	Hymenochaetaceae	Water-soluble lignins	Inhibits HIV-1 protease	70
21.	Garcinia speciosa	Hypericaceae	Protostane,garcisaterpenes A and C	Inhibits HIV-1 reverse transcriptase	71
22.	Sideritis	Lamiaceae	Sulfonated	Anti-HIV	72
	akmanii		polysaccharides; linearol	replication	
23.	Detarium microcarpum	Leguminosae	Catechins 1-5	Inhibit HIV-1 reverse transcriptase activity in a non-specific way	73
24.	Magnolia spp.	Magnoliaceae	Neolignans e.g. magnolol 1 and honokiol 2	Antioxidant; induces apoptosis in tumor cells, weak anti-HIV-1 activity	74
25.	Stephania cepharantha	Menispermaceae	Cepharanthine	Inhibits HIV replication	75
26.	Musa acuminata	Musaceae	BanLec, a jacalin-related lectin	Blocks HIV entry, hence is a good microbicide; potent inhibitor of HIV-1 replication	76

27.	Myrothamnu s flabellifolius (Welw.)	Myrothamna ceae	Polyphenols, gallotannins, 3,4,5-tri-O- galloylquinic acids	Polyphenols protect cell membranes against free radical-induc ed damage; gallotannins have anti-burn properties; 3,4,5-tri-O-galloylquinic acids have anti- HIV reverse transcriptase activity	77
28.	Flammulina velutipes (Curt.: Fries) Singer	Physalacriac eae	Velutin	Inhibits HIV-1 reverse transcriptase	78
29.	Phytolacca Americana L	Phytolaccace ae	Pokeweed antiviral protein (PAP)	Broad spectrum microbicide	79
30.	Crataegus pinatifida	Rosaceae	Uvaol and ursolic acid	Inhibits HIV-1 protease	80
	Geum japonicum		Maslinic acid	Inhibits HIV-1 protease	80

About 28 different chemical compounds were known to be active against HIV reverse transcriptase and replication. Some of these HIV reverse transcriptase inhibitors included:

bioflavonoids from Rhus suc c edanea[49] , michellamines from Ancistrocladus korupensis[50] ,

lanostane-type triterpenes from Polyalthia suberosa[51] , suksdorfin from Lomatium suksdorfii[52], caffeic acids from Arnebia euchroma [56] ,celasdin B from Celastrus hindsii[58] , calanolide A from Callophyllum cordato-oblongum[61] , gallotannin from Combretum molle[65] , flavonone-xanthone glucoside from Swertia franchetiana[68] , protostanes from Garcinia speciosa [70] , catechins from Detarium microcarpum[72] , cepharanthine from Stephania cepharantha [74], galloyquinic acids from Myrothamnus flabellifolius [76], velutin isolated from Flammulina velutipes[77] , oleanolic from Xanthoceras sorbifolia [81], nigranoic acid from Schisandra sphaerandra [82], triterpene lactone fromKadsura lancilimba , and harmine isolated from About 28 different chemicals were identified to block HIV reverse transcriptase and replication. Biflavonoids from Rhus suc c edanea[49], michellamines from Ancistrocladus korupensis[50], lanostane-type triterpenes from Polyalthia suberosa[51], suksdorfin from Lomatium suksdorfii[52], caffeic acids from Arnebia euchroma[56], celasdin B from Celastrus hindsii[58] ,Symplocos setchuensis .Symplocos setchuensis was used to isolate Kadsura lancilimba and harmine.

Flavonoid gallate ester from Acer okamotaanum of the Aceraceae family [46], dicaffeoylquinic acids from Achyrocline satureioides of the Asteraceae family [22], and curcumin from Curcuma longa in the Zingiberaceae family [86] were three of the identified active substances that were known to be HIV integrase inhibitors. Six active compounds were found to be HIV protease inhibitors: water-soluble lignins from Inonotus obliquus [69], uvaol and ursolic acid from Crataegus pinatifida [79] ,maslinic acid from Geum japonicum , limonin and nomilin from Citrus spp.[88] , camellia-tannin H from Camellia japonica [85], and curcumin [86] , which was also shown to be active against HIV-1 integrase[86].

Two active compounds were found to inhibit syncytia formation, a property of HIV that makes infected and healthy CD4 cells to fuse and form one giant cell with as many as 500 nuclei. Syncytia- inhibiting compounds included: diterpene lactones [13], and michellamines Aand B [50]. Seven plant compounds prevented HIV-induced cytopathic e ff e c t: sulfated lentinan [47] , sulfona t Ed polysaccharides [53], xantholhumol [57] , (+)-calanolide A [61], guttiferone A[63] , palicourein[62] , and nitidine [89] . Magnolia spp [73] . and the Namibian resurrection plant Myrothamnus flabellifolius [76]were found to have anti-oxidant properties.

Inhibiting the development of syncytia, a characteristic of HIV that causes healthy and infected CD4 cells to combine and create a massive cell with up to 500 nuclei. Among the substances that prevented syncytia were michellamines A and B [50] and diterpene lactones [13] . Seven plant compounds—sulfated lentinan [47], sulfonated polysaccharides [53], xantholhumol [57], (+)-calanolide A [61], guttiferone A [63], palicourein [62], and nitidine [89]—prevented

HIV-induced cytopathic effects. Anti-oxidant capabilities have been discovered in Magnolia spp. [73] and the Namibian resurrection plant Myrothamnus flabellifolius. [76]

Marketed Preparations-

IMMUN-UP herbal capsule for HIV/AIDS treatment. (Plastic Jar with 30 Capsule Pack).

Doses:

three times a day, one capsule. (For a patient in very poor condition, such as AIDS in its latter stages)

In the case of all other patients, take one capsule twice daily. 50 capsules in a plastic jar, KAMILARI PLUS

It is an extremely uncommon mixture of virocidal and immunostimulant natural substances. The medicine HOO-IMM PLUS is used treat hepatitis as well as HIV, and it has the greatest 98% inhibition rate. These medications boost the body's CD4 treat hepatitis as well as HIV, and it has the greatest 98% inhibition rate. These medications boost the body's CD4 lymphocytes, lower the RNA viral load count, limit viral replication, stimulate, and maintain overall physiological activity, and increase CD4 lymphocytes. It works to strengthen the immune system and is employed in HIV/AIDS patients' opportunistic infection therapy and prevention.

MATERIALS AND METHODS :

1) Species collection

The medicinal herbs and oriental medicine were donated by OBM Lab., LTD. in Daejeon, Korea, and were identified at Daejeon University. Hanbat National University's Laboratory of Natural Products Chemistry is home to the species' vouchers (HNU-03011–HNU-03014).

2)Cells and virus

Cell lines used in this study (C8166, MT4, Hela CD4 cloned6, and HIV-1IIIB/H9) were maintained in RPMI-1640 supplemented with 10% heat inactivated newborn calf serum (Gibco). The cells used in all experiments were in log-phase growth. HIV-1IIIB was

obtained from the culture supernatant of H9/HIV-1IIIBcells. HIV-1 A102 (NIH AIDS Research & ReferenceReagent Program, US) –resistant to AZT was used for the initial infection of the MT4 cells. The 50% HIV-1 tissue culture infectious dose (TCID50) of the virus preparation was determined in the relevant target cells using standard techniques.

3)Cytotoxicity assay

The cellular toxicity of extracts on MT4 cells was assessed by WST-1 method was used. The cells were incubated with 0.5 mM of WST-1 solution containing 20 mM of 1-methoxy PMS (Dojindo, Japan) at 37 ℃ for 2 h. The production of WST-1 formazan was measured by a microplate reader at 450 nm. The cytotoxicity of inhibitors was calculated as the relative rate of WST-1 formazan production to that of the dox- treated cells. The cytotoxic concentration that caused the reduction of viable cells by 50% (CC50) was calculated from dose–response curve.

By using the WST-1 method, the cellular toxicity of extracts on MT4 cells was evaluated. 20 mM of 1-methoxy PMS (Dojindo, Japan) was added to 0.5 mM of WST-1 solution, which was added to the cells and incubated for 2 hours at 37 ℃. Using a microplate reader, the formation of WST-1 formazan was quantified at 450 nm. The relative rate of WST-1 formazan synthesis to that of the dox-treated cells was used to calculate the cytotoxicity of the inhibitors. The dose-response curve was used to determine the cytotoxic concentration (CC50) that resulted in a 50% reduction in viable cells.

4)ELISA for HIV-1 p24 antigen

The p24 release test (Vironostika, BioMerieux Co., Metherland) was used to gauge the impact of extracts on HIV-1 replication in vitro. Microelisa strip wells were coated with anti-HIV-1 p24 core antigen antibodies. In order to destroy HIV-1 virions found in test samples, disruption buffer is added. All samples were incubated at 37°C for 60 min (100 l in each well). 100 l of an anti-HIV-1 (human) conjugate labelled with horseradish peroxidase (HRP) was added to each well after washing with diluted phosphate-buffered saline (PBS), and each well was then incubated at 37°C for 60 min. After cleaning the plates, 100 l of tetramethylbenzidine substrate in urea peroxide solution was applied to each well, and the plates were then incubated for 30 minutes at room temperature. The colour reaction was finally stopped 100 l of 1M sulfuric acid are then added. The ELISA reader read the absorbance of each well at 450 nm in 15 minutes. The dose-response curve was used to calculate the EC50, or concentration, required to halve the expression of the p24 antigen

5)Inhibition assay of recombinant HIV -1 RT activity The effect of the crude extracts on reverse transcription was assessed using a non-radioactive HIV-RT colorimetric ELISA kit from Roche Diagnostics, Germany. The kit's recommended approach was A well was filled with 2 ng of the enzyme, and the reaction was allowed to sit there for two hours at 37°C. At 0.2 mg/ml, extracts were tested[87]

Conclusion -

HIV-caused acquired immunodeficiency syndrome is an illness that suppresses the immune sy. Due to the rapid spread of the infections, the syndrome is an illness that suppresses the immune system. Due to the rapid spread of the infections, the expensive expense of treatment, and the increased risk of transmission of other STDs & AIDS, acquire immunodeficiency syndrome is currently garnering significant attention. The current AIDS symptomatic therapy options are highly expensive. Many AIDS patients are turning to complementary medical practises such Unani, Chinese, Ayurvedic, and homoeopathy for relief. Research is being done to find herbs that have been utilised for treating AIDS for a very long period and their active ingredients that are active against sexually transmitted diseases, such as the human immunodeficiency virus, with the goal of offering an efficient strategy for the treatment and prevention of this disease. The use of medicinal plants has a long history and is common in both industrialized and developing nations.

PAIDS can be treated rationally with herbal medication. Alkaloids, sugars, coumarine, flavonoids, lignin, phenolics, proteins, quinines, xanthenes, phospholipids, and tannins are only a few of the plant-derived compounds that inhibit HIV at different stages of its life cycle. Plant bodies and plant-derived microbicides are two recent HIV preventive strategies. In order to treat AIDS, herbal medicines can be produced that are both effective aaffordable.

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