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Evaluation of Anti-HIV Activity of Selected Medicinal Plants: A Short Review

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ABSTRACT

Human immunodeficiency virus (HIV) causes the potentially life-threatening and chronic disease called acquired immune deficiency syndrome (AIDS). The main target of this viral disease is to suppress the immune system and make the body unresponsive to external stimuli. According to global health observatory data since epidemic, more than 78 million people were affected by HIV and 39 million people died globally. There were approximately 37.9 million people living with HIV at the end of 2018. Currently, antiretroviral therapy (ART) is available for the control of HIV but has serious associated side effects such as lipodystrophy. Because of the limitations, associated with ART, researchers throughout the world are trying to explore and develop more reliable and safe drugs from natural resources to manage HIV infection. A wide range of medicinal plants have been studied and have reported significant potential against HIV. Medicinal plants contain novel anti-HIV compounds. As it has been well reported that medicinal plants contain various types of phytochemical constituents including alkaloids, flavonoids, phenolic compounds, glycosides, tannins, and saponins, hence the medicinal plants could be potential sources of boosting immune responses, as well as halting the replication of HIV. A literature survey of medicinal plants from PubMed and plant literature database, was carried out to identify the plants with novel antiviral agents reported for the treatment of HIV/AIDS worldwide. Bioactive compounds from plants which play effective roles in the management of AIDS, which have been discussed in this review study. This could pave way for being taken up for active future in vitro and preclinical research studies to qualify as lead anti HIV molecules which is the need of the hour.

KEY WORDS: AIDS, ANTIRETROVIRAL THERAPY, PHYTOCONSTITUENTS, MEDICINAL PLANTS.

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INTRODUCTION

HIV continues to be a major global public health issue, having claimed more than 32 million lives so far. However, with increasing access to effective HIV prevention, diagnosis, treatment and care, including for opportunistic infections, HIV infection has become a manageable chronic health condition, enabling people living with HIV to lead long and healthy lives. There were approximately 37.9 million people living with HIV at the end of 2018.As a result of concerted international efforts to respond to HIV, coverage of services has been steadily increasing. In 2018, 62% of adults and 54% of children living with HIV in low- and middle-income countries were receiving lifelong antiretroviral therapy (ART).(WHO 2019). HIV is a retrovirus that can integrate its DNA into the host genome. The virus enters the host cell and affects the immune system mainly T lymphocytes, monocytes, macrophages and dendritic cells (Salehi et al,.2018).

Its genetic material RNA is made up of nine genes which contain all the instructions to make new viruses. Three of these genes – gag, pol and env – provide the instructions to make proteins that will form new virus particles. The other six genes rev, nef, vif, vpr and vpu, provide code to make proteins that control the ability of HIV to infect a cell, produce new copies of virus or release viruses from infected cells. The HIV-1 binds to the chemokine receptor 5 or the CXC chemokine receptor 4 by interacting with the envelope proteins to gain entry to the host cell (Salehi et al,.2018). Therapies are now available to inhibit various stages of viral infection such as entry inhibitors, reverse transcriptase inhibitors, integrase strand transfer inhibitors and protease inhibitors.Presence of antibody to HIV proteins is well accepted as indicative of HIV infection. Sometimes certain clinical conditions may also result in the presence of false-positive HIV antibody. Serologic tests for HIV includes ELISA, Western blot and HIV p24 antigen assay.

Types and Symptoms

1. Primary infection (Acute HIV): Some people infected by HIV develop a flu-like illness within two to four weeks after the virus enters the body. This illness, known as primary (acute) HIV infection, may last for a few weeks. Possible signs and symptoms include fever, headache, muscle aches and joint pain, rash, sore throat and painful mouth sores, swollen lymph glands, mainly on the neck, diarrhoea, weight loss, cough, night sweats. As the infection progressively weakens the immune system, they can develop other signs and symptoms, such as swollen lymph nodes, weight loss, fever, diarrhoea and cough. Without treatment, they could also develop severe illnesses such as tuberculosis (TB), cryptococcal meningitis, severe bacterial infections, and cancers such as lymphomas and Kaposi's sarcoma (WHO 2019).

2. Clinical latent infection (Chronic HIV): In this stage of infection, HIV is still present in the body and in white blood cells. However, many people may not have any symptoms or infections during this time.

Treatment: Despite challenges, new global efforts have meant that the number of people receiving HIV treatment has increased dramatically in recent years, particularly in resource-poor countries. In 2018, 62% of all people living with HIV were accessing treatment. Of those, 53% were virally suppressed. This equates to 23.3 million people living with HIV receiving antiretroviral treatment (ART) in 2018 – up from 7.7 million in 2010. However, this level of treatment scale up is still not enough for the world to meet its global target of 30 million people on treatment by 2020 (WHO 2019). Significant progress has been made in the prevention of mother-to-child transmission of HIV (PMTCT). In 2018, 82% of all pregnant women living with HIV had access to treatment to prevent HIV transmission to their babies – an increase of more than 90% from 2010.

Antiretroviral Therapy: The combination of drugs used to treat HIV is called antiretroviral therapy antiretroviral therapy (ART). ART is recommended for all people living with HIV, regardless of how long they've had the virus or how healthy they are. More than two dozen antiretroviral drugs has been approved by FDA to treat HIV infection. Different classes of antiretroviral drugs act at different stages of the HIV life cycle. 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) are rcommended for initial regimens (Günthard et al., 2014).

Fostemsavir (entry inhibitor via gp120) and PRO140 (CCR5 monoclonal antibody) are the two additional viral entry inhibitors with novel mechanisms of action that are currently in phase 2 trials (Gravatt et al., 2017). A phase 3 study is currently ongoing (NCT02362503) to determine if fostemsavir is an effective treatment for patients with multidrug-resistant HIV. PRO140 (CytoDyn) is a humanized CCR5 monoclonal antibody with antiviral activity against CCR5-tropic HIV. Based on new evidence assessing benefits and risks, the WHO recommends the use of the HIV drug dolutegravir (DTG) as the preferred first-line and second-line treatment for all populations, including pregnant women and those of childbearing potential (WHO 2019).

Antiretroviral drugs for HIV infection has been classified into the following categories: Multi-class Combination Products, Nucleoside Reverse Transcriptase Inhibitors (NRTIs), Nonnucleoside Reverse Transcriptase Inhibitors (NNRTIs),Protease Inhibitors (PIs), Fusion Inhibitors,Entry Inhibitors—CCR5 co-receptor antagonist and HIV integrase strand transfer inhibitors.

Herbal Medicine In The Treatment Of HIV/AIDS: The use of herbal medicine is increasingly becoming more popular in many countries (Sabde et al., 2011). This practice has continued to be a main source of health care in the rural communities especially in developing

countries, since modern medicine has not been able to reach the majority of the populace. In Africa, traditional herbal medicines are often used as primary treatment for HIV/ AIDS and for HIV-related problems including dermatological disorders, nausea, depression, insomnia and weakness. In North America, commonly used herbal dietary supplements have been found to impede on ARV drug effectiveness. Specifically, garlic supplements (Allium sativum) and St John's Wort (Hypericum perforatum) have been shown to have detrimental effects on the plasma concentrations of saquinavir and indinavir (Piscitelli et al., 2002).

Plants, produce numerous secondary metabolites as evolutionary responses to infections by fungi, nematodes, and other organisms, to avoid herbivory, and to complete for light and space, such as phenolics, glycosides, alkaloids, coumarins, terpenoids, essential oils and peptides. These metabolites have been identified with different biological activities. Some of them play an important role in immune system enhancement, exhibiting antiviral potential, including viral infections associated with Human Immunodeficiency Virus type 1 (HIV-1) and 2 (HIV-2) as genetic variabilities. An increasing number of patients with HIV infection cannot use the currently approved anti-HIV drugs including the reverse transcriptase and protease inhibitors, due to the adverse reactions, particularly liver diseases, that have been reported for antiretroviral drugs.

Some Chinese herbal preparation which consists of 14 plants (*Coptis chinensis, Jasminum officinale, Wolfiporia extensa, Sparganium stoloniferum, Polygonatum odoratum*, and *Scrophularia buergeriana* was investigated during 24 weeks and observed to have increased plasma CD4 count and also showed inhibition of HIV growth.

Table 1a. Plants with proven anti-HIV activity

S. no	Plant Name	Part of the Plant	Family	Assay	Reference
1	*Aegle marmelos*	Leaves Fruits	Rutaceae	p24 antigen assay	Sudeep Sabde, Hardik S. Bodiwala, Aniket Karmase et al., 2011
2	*Adhatoda vasica*	Leaves	Acanthaceae	p24 antigen assay	Sudeep Sabde, Hardik S. Bodiwala, Aniket Karmase et al., 2011
3	*Allium sativum*	Bulbs	Amaryllidaceae	p24 antigen assay	Sudeep Sabde, Hardik S. Bodiwala, Aniket Karmase et al., 2011
4	*Alstonia scholaris*	Stem bark Leaves	Apocynaceae	p24 antigen assay	Sudeep Sabde, Hardik S. Bodiwala, Aniket Karmase et al., 2011
5	*Argemone mexicana*	Leaves	Papaveraceae	p24 antigen assay	Sudeep Sabde, Hardik S. Bodiwala, Aniket Karmase et al., 2011
6	*Asparagus racemosus*	Roots	Asparagaceae	p24 antigen assay	Sudeep Sabde, Hardik S. Bodiwala, Aniket Karmase et al., 2011
7	*Aconitum kusnezoffii*	Aerial	Ranunculaceae	MT-4 cell Assay	L M Bedoya, S Sanchez-Palomino, M J Abad et al., 2001
8	*Anemarrhena asphodeloides*	Rhizoma	Liliaceae	MT-4 cell Assay	Bahare Salehi, Nanjangud V. Anil Kumar, Bilge Sener et al., 2015
9	*Angelica sinensis*	Root	Umbelliferae	MT-4 cell Assay	Carolyn Williams-Orlando., 2017

Continue Table 1

10	*Artemisia caruifolia*	Whole plant	Asteraceae	MT-4 cell Assay	Chao-Mei MA, Norio Nakamura, Masao Hattori., 2001
11	*Andrographis Paniculata*	Leaves	Acanthaceae	MT-4 cell Assay	Mayur M Uttekar, Tiyasa Das, Rohan S Pawar et al., 2012
12	*Azadirachta indica*	Leaves	Meliaceae	Syncytium reduction assay, ELISA, Anti-HIV-1 RT inhibitory activity	David, Pedroza-Escobar Benjamín, Serrano-Gallardo Luis Delia et al., 2017
13	*Areca Catechu*	Seed	Piperaceae	-	Senthil Amudhan, V Hazeena Begum, K. B. Hebba, 2019
14	*Alchornea laxiflora*	Leaf, root, stem	Euphorbiaceae	HIV-1 Integrase inhibitory activity, Cytotoxicity activity	fD.Mnkandhla, M Issacs, F.M. Muganza et al., 2019
15	*Butea monosperma*	Roots Stem Bark	Leguminosae	p24 antigen assay	Sudeep Sabde, Hardik S. Bodiwala, Aniket Karmase et al., 2011
16	*Betula pubescens*	Bark	Betulaceae	anti-HIV-1 integrase assay	Prapaporn Chaniad , Teeratad Sudsai, Abdi Wira Septama et al., 2019
17	*Cassia occidentalis*	Leaves	Fabaceae	p24 antigen assay	Sudeep Sabde, Hardik S. Bodiwala, Aniket Karmase et al., 2011
18	*Catharanthus roseus*	Leaves	Apocynaceae	p24 antigen assay	Sudeep Sabde, Hardik S. Bodiwala, Aniket Karmase et al., 2011
19	*Cissampleos parriera*	Aerial part	Menispermaceae	p24 antigen assay	Sudeep Sabde, Hardik S. Bodiwala, Aniket Karmase et al., 2011
20	*Colchicum luteum*	Bulbs	Colchicaceae	p24 antigen assay	Sudeep Sabde, Hardik S. Bodiwala, Aniket Karmase et al., 2011
21	*Coleus forskohlii*	Aerial part	Lamiaceae	p24 antigen assay	Sudeep Sabde, Hardik S. Bodiwala, Aniket Karmase et al., 2011
22	*Cryptocarya chinensis*	Wood	Lauraceae	HIV growth inhibition assay	Tian-Shung Wu, Chung-Ren Su, Kuo-Hsiung Lee, 2012
23	*Coccinium fenestratum*	Stem bark	Menispermaceae	Integrase and Protease Inhibitor assay	J.J. Magadulai, H.O. Suleiman., 2010
24	*Calophyllum inophyllum*	Bark	Guttiferae	RT Inhibition assay	J.J. Magadulai, H.O. Suleiman., 2010
25	*Cinnamomun aromiticum*	Bark	Lauraceae	MT-4 cell Assay	Franklin Nyenty Tabe, Nicolas Yanou Njintang, Armel Hervé Nwabo Kamdje et al., 2015
26	*Cynanchum chinense*	Root	Asclepiadaceae	MT-4 cell Assay	Jian Tao, Jing Yang, Chaoyin Chen et al., 2011
27	*Cynomorium songaricum*	Stem	Cynomoriaceae	MT-4 cell Assay	Suvdmaa Tuvaanjav, Han Shuqin, Masashi Komata et al., 2016

Continue Table 1

28	*Dracocephalum rupestre*	Whole plant	Labiatae	MT-4 cell Assay	Qi Zeng, Hui-Zi Jin, Jiang-Jiang Qin et al., 2010
29	*Dryopteris crassirhizoma*	-	Aspidiaceae	MT-4 cell Assay	Ji Suk Lee, Hirotsugu Miyashiro, Norio Nakamura et al., 2008
30	*Embelica ribes*	Fruits	Primulaceae	p24 antigen assay	Sudeep Sabde, Hardik S. Bodiwala, Aniket Karmase et al., 2011
31	*Embellica officinalis*	Fruits	Phyllanthaceae	p24 antigen assay	Sudeep Sabde, Hardik S. Bodiwala, Aniket Karmase et al., 2011
32	*Erodium stephanianum*	Whole plant	Geraniaceae	MT-4 cell Assay	Chao-mei Ma, Norio Nakamura, Hirotsugu Miyashiro, 2002
33	*Eugenia jambolona*	Bark	Myrtaceae	-	Richa Sood, D Swarup, S Bhatia, D D Kulkarni et al., 2012
34	*Garcinia indica*	Leaves	Clusiaceae	MT-4 cell Assay	J.J. Magadulai, H.O. Suleiman., 2010
35	*Garcinia cambogia*	Leaves	Clusiaceae	Integrase and Protease Inhibitor assay	J.J. Magadulai, H.O. Suleiman., 2010

Table 1b. Plants with proven anti-HIV activity

S. no	Plant Name	Part of the Plant	Family	Assay	Reference
1	*Gentiana scabra*	Root	Centianaceae	MT-4 cell Assay	Bahare Salehi, Nv Anil, Bilge Sener et al., 2018
2	*Gossampinus malabarica*	Flower	Bombacaeae	MT-4 cell Assay	J A Wu, A S Attele, L Zhang et al., 2001
3	*Gymnadenia conopsea*	Root	Orchidaceae	MT-4 cell Assay	Xiaofei Shang, Xiao Guo,Yu Liu et al., 2017
4	*Glycyrrhiza glabra*	Glcyrrhyrine	Fabaceae	OKM-1, MT-4 cells	Cristina Fiore, Michael Eisenhut, Rea Krausse et al., 2008
5	*Glycyrrhiza glabra*	Roots	Fabaceae	p24 antigen assay	Sudeep Sabde, Hardik S. Bodiwala, Aniket Karmase et al., 2011
6	*Gentiana scabra*	Root	Centianaceae	MT-4 cell Assay	Bahare Salehi, Nv Anil, Bilge Sener et al., 2018
7	*Lygodium japonicum*	Spore	Schizaeaceae	MT-4 cell Assay	Xavier-ravi Baskaran, Antony-varuvel Geo Vigila, Shou-zhou Zhang et al., 2018
8	*Madhuca indica*	Bark	Sapotaceae	p24 antigen assay	Sudeep Sabde, Hardik S. Bodiwala, Aniket Karmase et al., 2011
9	*Morinda citrifolia*	Leaves	Rubiaceae	MT-4 cell Assay	P. Selvam, N. Murugesh, M. Witvrouw et al., 2009
10	*Moringa oleifera*	Leaves	Moringaceae	Vector based antiviral assay	Nworu CS, Ezeifeka GO, Ebele Okoye et al., 2013

Continue Table 1b

11	*Myrianthus holstii*	Root	Urticaceae	Synctia Formation assay	Michael J. Currens, Lewis K. Pannell, and Michael R. Boyd et al., 2000
12	*Ocimum sanctum*	Leaves	Lamiaceae	RT Inhibition assay, Gp120 Binding Inhibition assay	Kun Silprasit, Supaporn Seetaha, Parinya Pongsanarakul et al., 2011
13	*Oldenlandia diffusa*	Whole plant	Rubiaceae	MT-4 cell Assay	Bahare Salehi, Nanjangud V. Kumar, Anil Bilge Sener et al., 2018
14	*Polygonum divaricatum*	Whole plant	Polygonaceae	MT-4 cell Assay	Yu Zhong, Yoshiyuki Yoshinaka, Tadahiro Takeda et al., 2005
15	*Papaver somniferum*	Seeds	Papaveraceae	p24 antigen assay	Sudeep Sabde, Hardik S. Bodiwala, Aniket Karmase et al., 2011
16	*Piper longum*	Fruit	Piperaceae	p24 antigen assay	Sudeep Sabde, Hardik S. Bodiwala, Aniket Karmase et al., 2011
17	*Phyllanthus amarus Schum*	Leaves	Phyllanthaceae	RT assay	F Notka, G R Meier, Ralf Wagner, 2003
18	*Phyllanthus emblica*	Fruit	Phyllanthaceae	p24 production assay	M Estari, L Venkanna, D Sripriya et al., 2012
19	*Pelargonium sidoides*	Root	Geraniaceae	HIV-1-cell attachment assays	Markus Helfer, Herwig Koppensteiner, Martha Schneider et al., 2014
20	*Rubia cordifolia*	Roots	Rubiaceae	p24 antigen assay	Sudeep Sabde, Hardik S. Bodiwala, Aniket Karmase et al., 2011
21	*Rhaponticum uniflorum*	Root	Compositae	MT-4 cell Assay	Hai-Li Liu,Yue -Wei Guo, 2008
22	*Rubia cordifolia* L	Root	Rubiaceae	MT-4 cell Assay	Yuanyuan Sun, Xuepeng Gong, Jia Y Tan et al., 2016
23	*Rauwolfia serpentina*	Roots	Apocynaceae	p24 antigen assay	Sudeep Sabde, Hardik S. Bodiwala, Aniket Karmase et al., 2011
24	*Papaver somniferum*	Seeds	Papaveraceae	p24 antigen assay	Sudeep Sabde, Hardik S. Bodiwala, Aniket Karmase et al., 2011
25	*Piper longum*	Fruit	Piperaceae	p24 antigen assay	Sudeep Sabde, Hardik S. Bodiwala, Aniket Karmase et al., 2011
26	*Phyllanthus amarus Schum*	Leaves	Phyllanthaceae	RT assay	F Notka, G R Meier, Ralf Wagner, 2003
27	*Salacia oblonga*	Leaves	Celastraceae	Integrase and Protease Inhibitor assay	J.J. Magadulai, H.O. Suleiman., 2010
28	*Salvia miltiorrhiza*	Roots	Lamiaceae	MTT assay, Virus neutralization assay	Ibrahim S Abd-Elazem, Hong S Chen, Robert B Bates et al., 2002
29	*Silybum marianum*	-	Asteraceae	MT-4 cell Assay	Ching-Hsuan Liu, Alagie Jassey,
30	*Scorzonera glabra*	Root	Compositae	MT-4 cell Assay	Hsin-Ya Hsu et al., 2019 Chao-mei Ma, Norio Nakamura, Hirotsugu Miyashiro et al., 2002

Continue Table 1b

31	*Scutellaria barbata*	Whole plant	Portulacaceae	MT-4 cell Assay	Zi-Long Wang, Shuang Wang,
32	*Stellera chamaejasme*	Root	Thymelaeaceae	MT-4 cell Assay	Yi Kuang et al., 2018 Min Yan, Yan Lu, Chin-Ho Chen et al., 2015
33	*Stephania cepharantha*	Root, Tuber	Menispermaceae	MT-4 cell Assay	Chao-mei Ma 1, Norio Nakamura, Hirotsugu Miyashiro et al., 2002
34	*Sterculia scaphigera*	Seed	Sterculiaceae	MT-4 cell Assay	Moshera Mohamed El-Sherei, Alia Ragheb, Mona Kassem et al.,2016
35	*Tinospora cordifolia*	Stem bark	Menispermaceae	p24 antigen assay	Sudeep Sabde, Hardik S. Bodiwala, Aniket Karmase et al., 2011
36	*Terminalia sericea*	Leaves	Combretaceae	MTT assay	M A Chauke, L J Shai, M A Mogale et al., 2016
37	*Withania somnifera*	Roots	Solanaceae	p24 antigen assay, Gp120 Binding Inhibition assay	Sudeep Sabde, Hardik S. Bodiwala, Aniket Karmase et al., 2011
38	*Withania somnifera*	Roots	Solanaceae	p24 antigen Gp120 assay, Binding Inhibition assay	Sudeep Sabde, Hardik S. Bodiwala, Aniket Karmase et al., 2011

Cytotoxicity of Anti-HIV Phytochemicals: Cytotoxic evaluation is very important and integral part of research involving discoveries of new and potent antiviral drugs. A novel formulation with potent antiviral activity have to be proven as not having any toxicity effects and cytotoxicity assays in a suitable cell culture system are only a part of primary step in this direction. For the purpose of testing, different plants active principals have to be extracted with suitable solvents. The list of commonly used solvents for extraction purpose is summarized in Table 2. Treating cells with these phytochemicals can result in a variety of cell fates. The cells may undergo necrosis, in which they lose membrane integrity.

Table 2. Solvents used for active components extraction

Water	Ethanol	Methanol	Chloroform	Di-chloro methanol	Ether	Acetone
Anthocyanins	Tannins	Anthocyanins	Terpenoids	Terpenoids	Alkaloids	Flavanols
Starches	Polyphenols	Terpenoids	Flavonoids		Terpenoids	
Tannins	Polyacetylenes	Saponins			Coumarins	
Saponins	Flavanol	Tannins			Fatty acids	
Terpenoids	Terpenoids	Xanthophyllines				
Polypeptides	Sterols	Totarol				
		Lactones				

Cytotoxicity can also be monitored using the MTT or MTS assay. This assay measures the reducing potential of the cell using a colorimetric reaction. Viable cells will reduce the MTS reagent to a colored formazan product. Tetrazolium salts are reduced only by metabolically active cells. Thus, 3-(4, 5-dimethylthiazol-2- yl)-2, 5-diphenyltetrazolium bromide (MTT) can be reduced to a blue colored formazan32. A similar redox-based assay has also been developed using the fluorescent dye, resazurin. In addition to using dyes to indicate the redox potential of cells in order to monitor their viability, researchers have developed assays that use ATP content as a marker of viability (Riss et al., 2004). Adenosine triphosphate (ATP) that is present in all metabolically active cells can be determined in a bioluminescent measurement. The bioluminescent method utilizes an enzyme, luciferase, which catalyses the formation of light from ATP and luciferin. The emitted light intensity is linearly related to the ATP concentration (Weyermann et al.,2005). Neutral red (3- amino-m-dimethylamino-2-methylphenazine hydrochloride) has been used previously for the identification of vital cells in cultures. This assay quantifies the number of viable, uninjured cells after their exposure to toxicants; it is based on the uptake and subsequent lysosomal accumulation of the supravital dye, neutral red. Quantification of

the dye extracted from the cells has been shown to be linear with cell numbers, both by direct cell counts and by protein determinations of cell populations (Weyermann et al., 2005).

Future Perspectives: In vitro studies of many plant phytoconstituents can be evaluated for various anti-viral activities including anti-HIV activity and COVID-19. Further studies can be carried out to know the mechanism of drug inhibition in virus. Synthetic drugs are proved to cause side effects. However, more exploratory research to prove the efficacy of medicinal plants including plant - drug interactions and their mechanism of action has to be explored so that plant compounds can be used to treat various viral infections including deadly COVID-19.

CONCLUSION

Many plant species have been investigated for anti-HIV potential and has shown promising activity. Azidothymidine, the first drug that was approved in the fight against AIDS in the 1980s, still a main component in the medication mix commonly prescribed to HIV patients today. But new research have found a plant-derived chemical compound that is much more effective than azidothymidine. The chemical compound is called "patentiflorin A" and is derived from a medicinal plant found in East Asia: Justicia gendarussa. Hence, plant based source drugs are non-toxic and work effectively unlike synthetic drugs. Many synthetic medicines are being used in the treatment of AIDS. Various medicinal plants or plant-derived natural products has offered alternatives to expensive medicines in future.

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