Phytochemical compounds with HIV-1 reverse transcriptase inhibition activity – A review

Suleiman Danladi[*1], Adeniyi Ayinde Abdulwahab[1], Zainab Iman Sani[1], Nazifi Auwalu Abubakar[1]

[1]Department of Pharmaceutical and Medicinal Chemistry, Faculty of Pharmaceutical Sciences, Bayero University Kano

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**Corresponding Author: Suleiman Danladi; sdanladi.phc@buk.edu.ng*

Abstract

HIV/AIDS is a global public health issue, exacerbated by the inaccessibility of combination antiretroviral therapy (cART) in some regions. In such settings, herbal therapy can serve as affordable and effective alternative treatment option. Numerous scientific studies have affirmed the inhibitory effects of medicinal plants on several targets in the HIV life cycle, including the HIV type-1 reverse transcriptase (HIV-1 RT) enzyme. To obtain relevant information on the HIV-1 RT inhibition profiles of these medicinal plants, we conducted a literature search for peer-reviewed papers in various scientific databases including PubMed, Scopus, and Google Scholar on bioactive compounds with HIV-1 RT inhibition. We found 60 different plant species distributed across 24 families and reported their respective geographical distribution, specific parts used, bioactive compounds and HIV-1 RT inhibitory profiles. The family Lamiaceae has the highest number of plants (n=10, 16.7%) with HIV-1 RT inhibitory activity. The classes flavonoids, terpenoids and polyphenolic compounds were found to have the highest number of HIV-1 RT inhibition activity. Herbal therapy is an indispensable treatment option for HIV/AIDS, particularly in many low- and middle-income countries and other

resource-constrained settings with limited access to cART.

Keywords: Phytochemical compounds, HIV-1, reverse transcriptase enzyme, medicinal plants.

Introduction

The human immunodeficiency virus (HIV) is a positive-sense, single-stranded, enveloped ribonucleic acid (RNA) virus that is classified within the Lentivirus genus of the Retroviridae family (Mandal et al, 2020). Transmission of this virus occurs through the exchange of bodily fluids such as semen, blood, breast milk, and vaginal secretions from HIV-positive individuals. It can also be transmitted from mother to child during pregnancy and childbirth (WHO, 2024). HIV infection alters the body's immune system, causing Acquired Immunodeficiency Syndrome (AIDS), a major global health emergency that predisposes patients to various infections and malignancies (Mandal *et al*., 2020; Mandhata *et al*., 2023; Yashi and Ravi, 2023; Narayan *et al*., 2013). HIV has two subtypes: HIV type 1 (HIV-1) and HIV type 2 (HIV-2) (Bekut *et al*., 2018; Mandhata *et al*., 2023; Yashi and Ravi, 2023). Compared to HIV-2, HIV-1 has a higher incidence rate and is more fatal. The RNA-dependent DNA polymerase (RDDP) and ribonuclease H (RNase H) that makeup HIV type 1 reverse transcriptase (HIV-1 RT) combine to transform viral genomic single-stranded RNA into double-stranded DNA, which is subsequently incorporated into the host cell's DNA (Chinsembu, 2019). The inhibition of HIV-1 RT through the use of combination antiretroviral therapy (cART) in clinical settings continues to be the cornerstone of human immunodeficiency virus treatment. These include the Nucleoside Reverse Transcriptase Inhibitors (NRTIs) and the Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs) (Bekut *et al*., 2018). NNRTIs are agents that block HIV-1 reverse transcription via an allosteric

mode of action by binding to HIV-1 RT at a location different from the DNA polymerase active site of the enzyme. NRTIs on the other hand act as prodrugs and become phosphorylated into the active form in the host cell to inhibit replication of the virus (Chinsembu, 2019; Patel and Zulfiqar, 2024).

According to the World Health Organization (WHO) 2023 HIV report, over 82 million people have been infected with HIV, of which approximately 37 million are still alive and living with the infection (WHO, 2024). Moreover, it has been reported that 530,000 people were living with HIV in the eastern Mediterranean; 2.3 million in the western Pacific, 3.1 million in Europe; 4.0 million in the Americas; 4.0 million in Southeast Asia; and 26.0 million in Africa (WHO, 2024).

Access to efficient HIV prevention, diagnosis, treatment, and care has posed a serious challenge to the management of HIV infection (Narayan *et al*., 2013; Bekut *et al*., 2018; Mandhata *et al*., 2023; Yashi and Ravi, 2023). In addition, the development of resistance, toxicity, lack of curative effect and limited availability of cART therapy have significantly diminished the success of drug treatment (Bessong *et al*., 2005; Narayan *et al*., 2013; Prinsloo *et al*., 2017). Consequently, the WHO, the Joint United Nations Programme on HIV/AIDS (UNAIDS) and the Global Fund might not achieve the Sustainable Development Goal target 3.3 of ending the HIV epidemic by 2030, particularly given the increasing incidence of this epidemic in low-middle-income countries with limited access to cART therapy (Mandal *et al*., 2020; WHO, 2024).

Several studies have shown that medicinal plants have the potential to be used as HIV-1 RT inhibitors. Recent research has shown an increasing interest in extracting phytochemicals from plants to inhibit the activity of HIV through interruption of its life cycle by targeting the HIV-1 RT pathway

(El-mekkawiy *et al*., 1995; Hisayoshi *et al*., 2015; Esposito *et al*., 2016). According to a case series published by Wang *et al*., 2017, AIDS patients treated with either a unique formula of herbal therapy alone or a combination of herbal and antiretroviral therapies for a period of 5-8 years had low to undetectable viral loads. Similarly, a cohort study showed that AIDS patients treated with a 16-herb formula for a period of 14 days to 9 months had 8-year survival rates compared with 5-year survival rates of AIDS patients treated with cART for 0- 60 months (Zhao *et al*., 2014).

Given the aforementioned, it is evident why there is a continuous need to find affordable, effective, and safe medications with minimal side effects and strong anti-HIV properties. This review aims to comprehensively summarise existing research on plants and phytochemical compounds that demonstrate inhibition of HIV-1 reverse transcriptase as anti-HIV agents. By addressing these gaps, we aspire to contribute to the expanding body of literature that underscores the potential of phytochemicals as alternative treatments in the battle against HIV/AIDS.

Methods

A literature search for peer-reviewed papers was conducted on PubMed, Scopus, Google Scholar, and Web of Science databases using the key terms “phytochemical compounds”, “HIV-1”, and “reverse transcriptase inhibitors”. Supplemental data were obtained from reputable websites such as World Health Organization website. The inclusion criteria include only papers that discussed medicinal plants with anti-HIV-1 RT activities and were published in English from 1989- 2025**.** Exclusion criteria include papers which document phytochemical compounds that inhibit HIV integrase, HIV protease, and fusion of HIV envelope and CD4 cell membrane. Additionally, papers published in languages other than English were not considered in this study. From the studies

identified, the plant families, species, class, geographical distribution, part used, and principal bioactive compound(s) were recorded. Finally, the anti-RT activity profiles for bioactive compounds were reported as half maximal inhibitory concentration (IC50), inhibitory dose (ID50), median effective dose (ED50), effective concentration (EC50), therapeutic index (TI) and percentage inhibition of RT.

Results and discussion

In this study, we reported medicinal plants and bioactive compounds that were found to have anti-HIV-1 RT activity. Table 1 shows various plant species, genera, geographical distribution, specific parts used, bioactive compounds and HIV-1 RT inhibitory profiles of 60 different plant species distributed across 26 families. The family Lamiaceae has the highest number of plants (n=10, 16.7%) with HIV-1 RT inhibitory activity (Figure 1).

Table 1: Medicinal plant products with HIV-1 reverse transcriptase inhibition activity

Plants	**Family**	**Plant Distribution**	**Plant of part used**	**Class**	**Bioactive Compound(s)**	**Reverse transcriptase inhibitory profiles**	**Reference**
Nelumbo nucifera	Nymphaceae	South Africa	Leaves	Alkaloid	Coclaurine, norcoclaurine, liensinine, neferine and isoliensinine	Coclaurine (EC50=0.8 μg/mL, TI >125), and norcoclaurine (EC50 <0.8 μg/mL, TI >25). Isoliensinine neferine and liensinine, showed EC50 values <0.8 μg/mL.	Kashiwada *et al*., 2005
Schisandra chinensis	Schisandraceae	China	Fruits	Alkaloids	Schizandrin B	Schisandrin B displayed strong inhibition of RDDP function of HIV-1 RT.	Xu *et al*., 2015
Calophyllum inophyllum L.	Clusiaceae	Malaysia	Leaves	Coumarins	Inophyllum B Inophyllum P	Inophyllums B (IC50=38 nM) Inophyllum P (IC50 =130 nM)	Patil *et al*., 1993
Ferula sumbul	Apiaceae	Mediterranean region to Central Asia	Herb	Coumarins	pabulenol	EC50 <0.10 mg/ml, IC50 >100 mg/ml	Zhou *et al*., 2000

Lagerstroemia speciosa	Lythraceae	Malaysia	Leaves and stems	Polyphenol	Gallic acid	IC50 = 1 to 25 µg/ml	Nutan *et al*., 2013
Anogeissus acuminata	Combretaceae	Bangladesh, Burma, Cambodia, India, Thailand, and Vietnam	Stems	Lignans	**Anolignans A**	IC5=106.0 pg/ml	Rimando *et al*., 1994
Phyllanthus niruri	Euphorbiaceae	Taiwan	Whole plant	Phenolic compound	Repandusinic acid	ID50= 0.05 µM	Ogata *et al*., 1992
Celastrus hindsii	Celastraceae	Taiwan	Dried stem	Terpene	Celasdin B	EC50= 0.8 µg/ml	Kuo and Kuo, 1997
Kadsura lancilimba	Schizandraceae	Indigenous to southern China	Stems and roots	Terpene	Lancilactone C	EC50= 1.4 µg/mL, TI> 71.4	Chen *et al*., 1999
Swertia franchetiana	Gentianaceae	China	Whole plant	Xanthone	Swertifrancheside	ED50=30.9 µg/ml	Wang *et al*., 1994
Excoecaria agallocha	Euphorbiaceae	Australia	Twigs and barks	Terpenoid	Phorbol	Phorbol ester 1 (IC50 6nM).	(Erickson *et al*., 1995)

Euphorbia myrsinites	Euphorbiaceae	Turkey	Root	Terpenoid	15-O-acetyl-3-O-butanoyl-5-O-propionyl-7-Onicotinoylmyrsinol	IC50= 80 µg/ml	Oksüz *et al*., 1995
Cowania Mexicana	Rosaceae	USA	Leaves	Terpenoid	Cucurbitacin F	23,24-Dihydro-cucurbitacin F (EC50=0.8µg/ml), 15-oxo-cucurbitacin F (EC50 = 0.3µg/ml) and 15-oxo-23,24-dihydro-cucurbitacin F (EC50 = 2.5 µg/ml)	Konoshima *et al*., 1994
Tripterygium wilfordii Hook.	Celastraceae	China	Root	Terpenoid	Tripterifordin	EC50= 1 µg/ml	Chen *et al*., 1995
Maprounea Africana Muell.	Euphorbiaceae	Tanzania	Root	Terpenoid	1-β-hydroxymaprounic acid, 3-p-hydroxybenzoate	Both 1-β-hydroxymaprounic acid and 3-p-hydroxybenzoate Inhibit have IC50 of 3.7 µM	Pengsuparp *et al*., 1994
Szigium claviforum	Myrtaceae	Taiwan	Leaves	Terpenoid	Betulinic acid,	Betulinic acid (EC50= 1.4 µM, IC50 =13 µM).	(Fujioa *et al*., 1994)

					Platonic acid	Platonic acids(EC50 = 6.5 μM, IC50 = 90 μM	
Houttuynia cordata	Saururaceae	Japan	Aerial parts	Terpenoid	Lauryl aldehyde, capryl aldehyde	Lauryl aldehyde, capryl aldehyde exhibited moderate anti-viral activity against HVS-1 with ED50 (%w/v) of 0.0008 and 0.00038 respectively	Hayashi *et al*., 1995
Chrysanthemum morifolium	Compositae	China	Flowering heads	Flavonoid	Acacetin-7-O-β-galactopyranoside	Acacetin-7-O-β-galactopyranoside (EC50=8 μM, IC50=37 μM).	Hu *et al*., 1994
Buchenavia capitata	Combretaceae	Dominican Republic	Leaves	Flavonoid	Buchenavianine	IC50 =5.7 μM	Beutler *et al*., 1992
Kummerolvia striata	Fabaceae	China	Herbs	Flavonoid	Apigenin-7-O-β-D-glucopyranoside	50% inhibitory concentration (IC50) of HIV-RT treated by PFA and Suramin were 0.2 mumol and 19.9 mumol, respectively.	Tang *et al*. 1994
Lomatium suksdorfii	Umbelliferae	Washington state	Fruit	Coumarin	Suksdorfin	EC50= 2.6 +/- 2.1 μM	Lee *et al*., 1994

Euphorbia jolkini	Euphorbiaceae	Japan	Whole plant	Tannin	Putranjivain A	IC50 = 7.9 +/- 1.2 µM	Cheng *et al*., 2004
Hyssop officinalis	Lamiaceae	Eastern Europe	Leaves	Tannin	Caffeic acid	Caffeic acid showed 71 to 60% RT inhibition	Kreis *et al*., 1990
Ipomoea cairica	Convolvulaceae	Botswana, Swaziland and tropical africa	Above ground parts	Lignan	**Arctigenin,** trachelogenin	Both compounds showed 80-90% RT inhibition	Schröder *et al*., 1990
Andrographis paniculata Nees	Acanthaceae	Indonesia	Leaves	Diterpene lactone	Andrographolide	EC50= 4.2-175 g/ml	Otake *et al*. 1995
Justicia gendarussa Burm.f.	Acanthaceae	Vietnam	Stem and root	Arylnaphthalide lignans (ANL) glycosides	Justiprocumins A and B Patentiflorin A	90% RT inhibition	Zhang *et al*., 2017
Parthenium hysterophorus L.	Asteraceae	India	Leaves	Polyphenol	fumaric acid, caffeic acid and vanillic acid	40% of RT inhibition	Kumar *et al*., 2013
Centratherum	Asteraceae	South africa	Leaves	Sesquiterpene	Germacranolide	IC50 = 72.8 g/ml	Chukwujek

punctatum Cass.				lactones			wu *et al*., 2014
Vernonia stipulacea Klatt	Asteraceae	South Africa	Root	Polyphenol	Gallic acid, dicaffeoyl acids, and chlorogenic acid.	IC50 = 350 g/ml for methanol extract	Prinsloo *et al*., 2018
Artemisia annua L.	Asteraceae	South africa, tanzania, cameroon, germany, mozambique	Leaves/flowers	Sesquiterpene lactones	Artemisinin	EC50= 20.9 g/ml, IC50= 1.0–48.0 g/ml)	Lubbe *et al*., 2012
Petasites japonicus F.Schmidt	Asteraceae	Japan	Flower buds	Sesquiterpenes	Fukinone and eremophilenolides	EC50= 1–2 g/ml	Hisayoshi *et al*., 2015
Onopordum illyricum L.	Asteraceae	Italy	Aerial parts at the flowering stage	Flavonoid	Luteolin, apigenin, and 1,5-dicaffeoylquinic acid	Luteolin (IC50 =12.8 M), 1,5-dicaffeoylquinicacid (IC50= 16.9 M) and apigenin (IC50=59.6 M)	Sanna *et al*., 2018
Alnus firma	Betulaceae.	South America,	Leaves	flavonoids	**Luteolin**	IC50=60 mM	Sati *et al*.,

Siebold & Zucc.		China					2011
Humulus lupulus Thunb.	Cannabinaceae	China	Hop cones	Prenylatedchalcone flavonoid	Xanthohumol	EC50 = 0.50 g/m, TI = 10.8	Wang *et al*., 2004
Maytenus buchananii (Loes.) R.Wilczek	Celastraceae	Cameroon	Whole plant	Favonoids	**Quercetin**	EC50 = 1.38 µg/mL	Tebou *et al*., 2017
Calophyllum brasiliense Cambess	Clusiaceae	Mexico	Leaves	Triterpenes	Calanolides B and C	Calanolides B and C (IC50 = 20.2 g/ml)	César *et al*., 2011
Vismia cayennensis (Jacq.) Pers. Clusiaceae	Clusiaceae	New York	Leaves	Anthraquinones, prenylated benzophenones	Vismiaphenone D	EC50 = 11 g/ml	Fuller *et al*., 1999
Terminalia chebula Willd. ex Flem.	Combretaceae	Egypt	Fruit	Phenol	Gallic acid, chebulagic acid and chebulinic acid	IC50 ≤50 g/ml	El-Mekkawy *et al*., 1995

Anogeissus acuminata (Roxb. ex DC.) Wall. ex Guillem. & Perr.	Combretaceae	Bangladesh, Burma, Cambodia, India, Thailand, and Vietnam	Stem	Lignan	**Anolignan A** and B	Anolignan A and B showed IC50 of 106.0 g/ml and 1072 g/ml respectively	Rimando *et al*., 1994
Mallotus philippensis (Lam.) Mull.Arg.	Euphorbiaceae	India, SriLanka, southern China, and throughout Malesia to Australia	Stem bark	Phloroglucinol derivative	mallotojaponin	Ki = 6.1 M	Nakane *et al*., 1991
Croton echinocarpus Baill.	Euphorbiaceae	Brazil	Leaves	Alkaloids	Corydine and norisoboldine	Corydine and norisoboldine displayed IC50 values of 356.8 g/ml and 153.7 g/ml respectively.	Ravanelli *et al*., 2016
Bridelia	Euphorbiaceae	South Africa	Root	Flavonoids,	Gallic, ellagic acids	IC50 of 7.3 g/ml	Pascal *et*

micrantha Baill.				tannins, friedelin, phenolic derivatives	and caffeic acid		*al*., 2006
Peltophorum africanum Sond.	Fabaceae	South Africa	Bark	Pentacyclic triterpenoid	Betulinic acid	IC50 = 3.5 g/ml	Mulaudzi *et al*., 2011
Detarium microcarpum Leguminosae	Leguminosae	Africa	Methanol extract/ whole plant	Catechins	(−)epicatechin 3-gallate	IC50 = 0.5 g/ml	Moore and Pizza, 1992
Psoralea corylifolia L.	Fabaceae	southern Africa, North America, South America and Australia	Seed	Prenylated chalcone of the class flavonoid	Isobavachalcone,	56.26% inhibition of RT at 100 g/m	(Kuete and Sandjo, 2012)
Salvia officinalis L.	Lamiaceae	Tokyo	Herbs	Pentacyclic triterpenoid	Oleanolic acid	IC50 = 1.6–2.0 g/ml,	Watanabe *et al*., 2000
Thymus	Lamiaceae	Japan	Herbs	Terpene	P-cymene and -	ED50 = 7.6 g/ml; EC50 = 31	Yamasaki

serpyllum L.					terpinene	g/ml	*et al*., 1998
Mentha spicata L.	Lamiaceae	Algeria	Leaves	Phenolics, Phenolics, Cyclic polyol.	Gallic acid, caffeic acid quinic acid	EC50 = 31 g/ml	Ben *et al*., 2018
Mentha longifolia (L.) L.	Lamiaceae	Morocco	Whole plant	Monoterpenes	Pinene, pinene, and limonene	Up to 90% inhibition of RT	Amzazi *et al*., 2003
Melissa officinalis L.	Lamiaceae	Mediterranean, Central Asia	Leaves and herbs	Polyphenol	**Rosmarinic acid**	EC50 = 16 g/ml, ED50 = 1.6 g/ml	Bekut *et al*., 2018
Ocimum basilicum L.	Lamiaceae	Pakistan	Aerial parts	Terpene	Linalool	IC50 16.4 = µg/mL	Kwee and Niemeyer, 2003
(Perilla frutescens (L.) Britt.	Lamiaceae	Japan, China, and other Asian countries.	Leaves	Polyphenol	2,2-diphenyl-1-picrylhydrazyl	IC50= 29 µg/ml	Saita *et al*., 2012
Scutellaria baicalensis Georgi	Lamiaceae	China	Root	Flavones	Baicalein	Inhibited HIV-1 RT activity by 90% at 2µg/mL	Zhao *et al*., 2016

Hoslundia opposita Vahl	Lamiaceae	Subsaharan Africa	Various plant parts	Flavonoid	5,7-dimethoxy-6-methylflavone	Inhibited HIV-1 reverse transcriptase enzyme by 52% at 100µg/ml	Said, 2017
Lagerstroemia speciosa L.	Lythraceae	India	Leaves and stems	Polyphenols	Gallic acid ellagic acid	IC50= 0.19 µg/ml IC50= 73 µg/ml	Nutan *et al*, 2013
Marcetia taxifolia Triana	Melastomataceae	Amazonas State of Venezuela	Aerial parts	Flavonoid	Myricetin myricetin 3-rhamnoside myricetin 3-(6-rhamnosylgalactoside)	IC50= 7.6 µM IC50 = 10.6 µM IC50 =13.8 µM	Ortega *et al*., 2017
Myrothamnus flabellifolia Welw.	Myrothamnaceae.	South Africa, Africa	Stems and leaves	Polyphenolic compound	3,4,5-tri-O-galloylquinic acids	IC50= 34 M	Brar *et al*., 2018
Eugenia hyemalis Cambess.	Myrtaceae	Nueva Colombia, Cordillera, Paraguay.	Whole plant, minus roots	Phenolic glycoside	Arbutin - Galloylarbutins (hyemalosides A–C)	Hyemalosides A–C have IC50= 1.46, >18, and 1.19 M, respectively	Bokesch *et al*., 2008
Rheum palmatum	Polygonaceae	China	Dried roots	Phenols	Sennoside A and sennoside B	Sennoside A and B showed IC50 = 1.9 M and 2.1, respectively for	Esposito *et al*., 2016

L.,						RNase H, and IC50 = 5.3 M and 2.1 M for RDDP respectively.	
Prunus africana (Hook.f.) Kalkman	Rosaceae	Ethiopia, South Africa, Nigeria, Madagascar.	Stem and root barks	phenolic compound	Ferulic acid	97% inhibition of RT enzyme	Rukunga *et al*., 2002

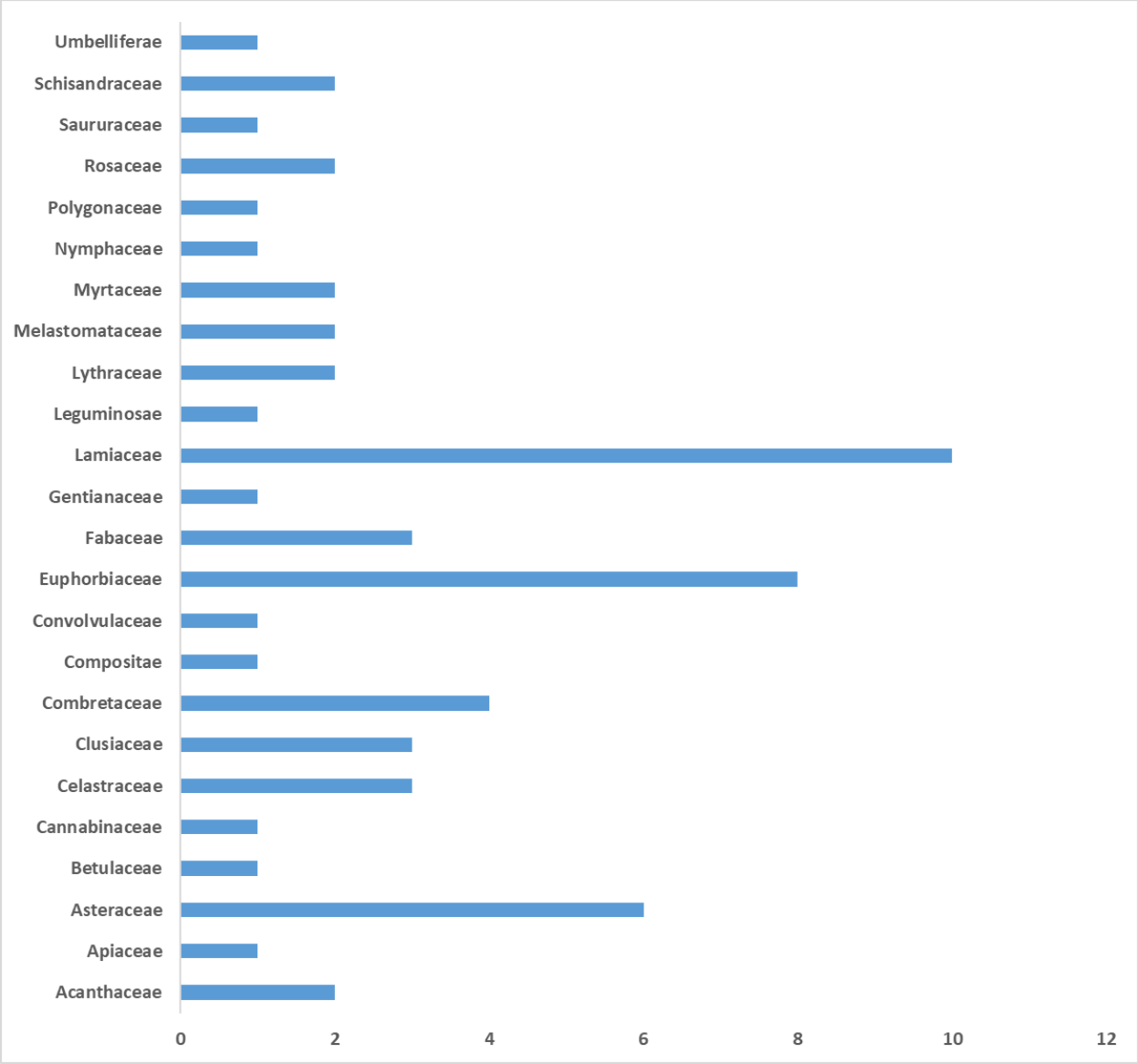

Fig. 1. Percentage frequency distribution of anti-HIV-1 RT plant species across families.

The part of the plant employed for anti-HIV-RT activity varies with each plant, as shown in the Table 1.0, and may include leaves, fruit, herbs, seeds, stems, twigs, aerial parts, inflorescence, underground parts and in some cases the whole plant. Flavonoids, terpenoids and polyphenolic compounds were found to have the highest number of HIV-1 RT inhibition activity (Table 1.0). The report of this study indicated that the anti-HIV-RT

activity of medicinal plants can be attributed to their phytochemical constituents.

Regarding the HIV-1 RT inhibition profiles, compounds found to have minimal IC50 values included 38-130 nM for inophyllum B and inophyllum P isolated from *Calophyllum inophyllum L*., 1 to 25 µg/ml for gallic acid isolated from Lagerstroemia speciosa, 1.4 µg/mL Lancilactone C isolated from *Kadsura lancilimba,* 3.7 µM for both 1-β-hydroxymaprounic acid and 3-p-hydroxybenzoate isolated from *Maprounea Africana Muell.* EC50 values included <0.8 µg/mL for coclaurine and isoliensinine isolated from *Nelumbo nucifera,* 1 µg/ml for tripterifordin isolated from *Tripterygium wilfordii Hook.,* 1.4 µM for betullinic acid isolated from *Szigium claviforum,* 8 µM for acacetin-7-O-β-galactopyranoside isolated from *Chrysanthemum morifolium*, and 1.38 µg/mL for quercetin isolated from *Maytenus buchananii.*

Several reports have shown that phytochemical compounds from various medicinal plants have significant activity against HIV-1 RT and can serve as novel scaffold for the further development of anti-HIV drugs (Fuller *et al*., 1999; Lubbe *et al*., 2012; Prinsloo *et al*., 2018; Sanna *et al*., 2018) . The effects of baicalein and baicalin as potent anti-HIV agents have received significant attention. Baicalen was reported to inhibit HIV-1 RT by 90% and HIV-1 protease by 91.1% at concentrations of 2 µg/mL and 200 g/ml, respectively (Ono *et al*., 1989). Additionally, baicalein inhibits HIV-1 integrase, a key enzyme in the lifecycle of the virus, by binding to the hydrophobic area of the HIV-1 integrase catalytic core domain and inducing a change in conformation (Ahn *et al*., 2001). Bisbenzylisoquinoline alkaloids such as liensinine, negferine, and isoliensinine isolated from the leaves of *Nelumbo nucifera,* were tested for anti-HIV activity in a structure-activity study and have

shown to have significant anti-HIV activity, with EC50 values less than 0.8lg/mL and TI values less than 9.9, 8.6, and 6.5, respectively (Kashiwada *et al*., 2005). Schisandrin B and Deoxyschizandrin have been reported to possess selective inhibition of the HIV-1 RT associated DNA polymerase activity (Xu *et al*., 2015).

Gallic acid and ellagic acid were evaluated for their cytotoxicity and anti-HIV activity using in vitro reporter gene-based assays. Both compounds (Gallic acid and ellagic acid) showed promising anti-HIV activity by inhibiting reverse transcriptase and HIV protease, respectively. As a result, they were considered to be potential candidates for the development of topical anti-HIV-1 drugs (Nutan *et al*., 2013). Two phytochemical compounds isolated from *Cowania mexicana*; 23,24-Dihydro- cucurbitacin F, 15-oxo-cucurbitacin F and 15-oxo-23,24-dihydrocucurbitacin have shown inhibitory activity against HIV-1 replication in H9 cells with EC50 values of 0.8, 0.3, and 2.5 μg/ml, respectively (Konoshima *et al*., 1994).

According to the "Status Report on Progress Towards the 2015 Targets on Access to Antiretroviral Therapy in Africa" published by the UNAIDS, only 20% of the population in at least 14 African nations that were eligible for antiretroviral therapy under the 2013 WHO criteria were receiving treatment as of December 2012 (UNAIDS, 2013). The Global Plan Towards the Elimination of New HIV Infections among Children and Keeping Their Mothers Alive program also reported that only 9 out of the 21 sub-Saharan African countries considered for special interventions, 75% or more of the children qualified for cART under the 2010 WHO guidelines were not receiving antiretroviral treatment in 2012 (Chinsembu, 2019). This shortfall underscores the urgent need to accelerate the research, discovery, development and integration of medicinal plants with anti-HIV properties into the

healthcare care system as an adjunct to conventional antiretroviral therapy. This approach can help bridge the gap in access to cART in many low- and middle-income countries and other resource-constrained settings.

The Sondashi Formula (SF2000) was tested in HIV-positive human subjects in Zambia and found to increase CD4 counts and reduce viral loads. Similarly, Phase II clinical studies of calanolide A have been initiated by Sarawak MediChem Pharmaceuticals in order to evaluate the long-term anti-HIV efficacy of calanolide A in combination with other anti-HIV medicines as well as the long-term durability of such medication combinations (Narayan *et al*., 2013). Further, a pilot study regarding the use of α-Zam herbal concoction (composed of Nigella sativa and honey) for the treatment of six HIV-positive patients in Nigeria showed a remarkable outcome as evidenced by a notable improvement in the patients' clinical manifestations and laboratory findings (Onifade *et al*., 2013).

Although herbal therapy has shown promise in treating HIV infection, there are still several barriers preventing its widespread use. Most of the data reported in this study are from in-vivo and in-vitro studies with few clinical trials demonstrating a drawback in extrapolating the results obtained to a large patient population. Additionally, while the phytochemical compounds with HIV-1 RT inhibition activity were identified, further studies are required to establish the appropriate dosage form, dose and frequency of administration of herbal therapy for optimal therapeutic outcomes.

Conclusion

The paper summarized families, genera, and species of plants with anti-HIV-RT activity including the specific part of the plant used, plant distribution, and reverse transcriptase inhibitory profile of each principal bioactive

constituent. It also presented the significance of herbal therapy as an alternative treatment option, particularly in many resource-limited settings with little or no access to cART. Most of the studies reported in this paper are in-vitro analyses and a few human studies. Therefore, a well-designed clinical trial is recommended to further confirm the antiretrovral properties of these compounds.

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Declaration of interest

The authors declare that there is no conflict of interest. The authors alone are responsible for the accuracy and integrity of the paper content.

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