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REVIEW ARTICLE

Antiviral Activity of Indigenous Medicinal Plants in Kenya and Their Potential Role in Managing Viral Infections: A Systematic Review

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Abstract

Background: The use of indigenous medicinal plants to manage viral diseases such as human immunodeficiency virus (HIV)/acquired immune deficiency syndrome (AIDS), Herpes, Hepatitis, and measles is a global practice, especially in sub-Saharan Africa and southern Asia. During the COVID-19 pandemic, reliance on traditional remedies increased significantly. However, concerns remain regarding the scientific validation of efficacy, dosage and safety of these remedies.

Objective: To systematically summarise the available scientific evidence on the antiviral properties of Kenyan medicinal plants and highlight those suitable for further pharmacological research and development.

Methods: A systematic search was conducted in Google Scholar and PubMed using Boolean combinations of keywords: "antiviral," "activity," "herbal," "plant," and "Kenya." Eligible sources included original research articles, conference papers, and abstracts that assessed antiviral activity through in vitro, in-vivo, or clinical methods.

Results: Eighteen studies met the inclusion criteria. Of the 54 plant species evaluated, 28 exhibited antiviral activity against six viruses: human immunodeficiency virus (HIV) (14 plants), herpes simlex virus (HSV) (9), measles virus (MV) (5), human cytomegalovirus (HCMV) (4), hepatitis B virus (HBV) (3), and dengue virus (DV) (1).

Conclusion: Several Kenyan medicinal plants show promising antiviral properties. Further research is needed to investigate their mechanisms of action, toxicity/safety, and dosaging to support their integration into evidence-based healthcare.

Keywords: Medicinal Plant, Antiviral Activity, Cytotoxicity, Mechanism of Action , Herpes Simplex Virus, Hepatitis B Virus, Human Cytomegalovirus, Dengue Virus, Measles Virus, Human Immuno-defficiency Virus.

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Introduction

Herbal medicine has played a central role in healthcare in Kenya since the precolonial era, when traditional practices were the primary method for treating human and animal ailments [1]. Today, more than 1,200 plant species are used by various Kenyan communities for their perceived therapeutic effects [1,2]. The continued reliance on these remedies is driven by accessibility, affordability, cultural acceptance, and the belief in their safety, efficacy, and low

tendency to promote drug resistance [3,4].

The World Health Organisation (WHO) recognised the importance of traditional medicine in global health during the 1978 Alma-Ata Declaration and has since encouraged its integration into national healthcare systems to support universal health coverage [5]. However, WHO emphasises the importance of validating these products through rigorous scientific assessment of their safety, efficacy, and quality before integration into routine care.

Despite their widespread use, many traditional medicines in Kenya are prepared under unhygienic conditions, often without standardised dosages or quality controls. As a result, the potential for contamination, toxicity, adverse reactions, or treatment failure remains a significant concern [1,6-8]. With increased reliance on herbal medicine during viral outbreaks (e.g COVID-19), there is a need to evaluate the antiviral properties, safety margins, and dosage parameters of Kenyan medicinal plants consumed to treat viruses through robust laboratory research.

Viral agents such as human immunodeficiency virus (HIV), herpes simlex virus (HSV), measles virus (MV), human cytomegalovirus (HCMV), hepatitis B virus (HBV), and Dengue virus (DV) are associated with diseases that cause significant morbidity and mortality globally which is disproportionately higher within the WHO African region. According to WHO, an estimated 40.8 million people globally are living with HIV of which 65% are in Africa [1,9,10].

The infection severity of HIV is only managed through administering antiretroviral therapy (ART). However, the virus develops resistance to even the most potent ART[11]. ART-resistance rapidly renders conventional treatment for HIV ineffective thereby increasing disease burden. This creates the need for new homegrown treatment options that will be effective, accessible, and affordable. Isolation of natural compounds from medicinal plants and testing them for antiviral properties against the virus could lead to a breakthrough in new HIV drug discoveries.

The prevalence of HSV-1 is higher in Africa compared to other regions. In Africa, over 90% of the population acquire HSV-1 infections orally by the age of 15 years [12]. A steep increase in prevalence of HSV-2 was observed by age, with figures ranging from 10% in 13- to 14-year-olds, 28% in 15- to 19-year-olds, to 70% among the 20- to 24-year-olds in Kenya. The HSV infections are managed by antiviral drugs of which acyclovir nucleoside analog is the drug of choice. The resistance of HSV to acyclovir is an emerging concern in clinical management of HSV-associated diseases [13,14]. Human-cytomegalovirus (HCMV) belongs to the same family of herpesviruses with HSV. HCMV has a significant global prevalence at 60-90% sero-prevalence [15] and is one of the leading causes of congenital infections posing high risk of health complications, morbidity, and mortality to immunocompromised populations such as people with HIV/AIDS, organ transplant recipients, and those with developing fetuses. A Kenyan study involving pregnant women reported a CMV seropositivity of 77.3% and 28% IgG and IgM, respectively10 Just like HSV, HCMV infections have no cure but antiviral drugs such Ganciclovir, Valganciclovir, Foscarnet, and Cidofovir are administered to manage symptoms. The virus has however shown resistance to these drugs thereby hampering its clinical management efforts [15]. To overcome the clinical impacts of herpesviruses' drug resistance, medicinal plants form a promising source for bioactive compounds that could be useful in new drug development.

Hepatitis B virus (HBV) is an endemic disease in Africa causing complications like liver cirrhosis and hepatocellular carcinoma. In 2019 alone, 80,000 new HBV infections and over 40,000 HBV-associated mortalities were experienced in the WHO African region [16]. The prevalence of HBV in Kenya is generally high (6.025%) [17]. There is no cure for HBV. The available antiviral agents for HBV including Tenofovir and Entecavir only manage disease severity and prevent liver damage by suppressing viral replication. However, HBV has been reported to exhibit resistance to these medications. Drug resistance in addition to lack of an effective cure creates the need for new drug development.

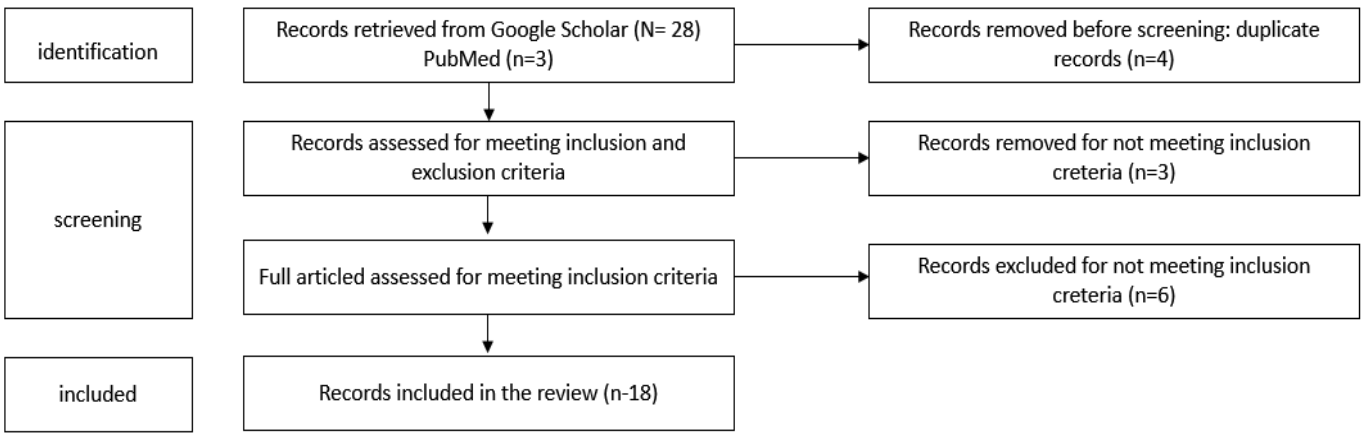

Figure 1: Flow diagram of included studies

Table 1: Risk of bias for in-vitro studies

Study	Sequence Generation	Baseline Characteristics	Allocation Concealment	Random Housing	Researcher Blinding	Random Outcome Assessment	Outcome Assessor Blinding	Incomplete Outcome Data	Selective Reporting	Other Bias
[32]	Negative	Positive	Positive	Positive	Unclear	Positive	Negative	Positive	Positive	Positive
[31]	Negative	Positive	Positive	Positive	Unclear	Positive	Negative	Positive	Positive	Positive
[27]	Negative	Positive	Positive	Positive	Negative	Positive	Negative	Positive	Positive	Positive
[35]	Negative	Positive	Positive	Positive	Negative	Positive	Negative	Positive	Unclear	Unclear
[23]	Negative	Positive	Positive	Positive	Unclear	Positive	Negative	Unclear	Unclear	Unclear
[24]	Negative	Positive	Positive	Positive	Unclear	Positive	Negative	Negative	Unclear	Unclear
[25]	Negative	Positive	Positive	Positive	Unclear	Positive	Negative	Positive	Positive	Unclear
[29]	Negative	Positive	Positive	Positive	Unclear	Positive	Negative	Positive	Positive	Unclear
[26]	Negative	Positive	Positive	Positive	Negative	Positive	Negative	Unclear	Negative	Unclear
[39]	Negative	Positive	Positive	Positive	Negative	Positive	Negative	Unclear	Negative	Negative
[22]	Negative	Positive	Positive	Positive	Negative	Positive	Negative	Unclear	Negative	Negative
[30]	Negative	Positive	Positive	Positive	Negative	Positive	Negative	Unclear	Negative	Negative
[33]	Negative	Positive	Positive	Positive	Negative	Positive	Negative	Positive	Unclear	Negative
[38]	Negative	Positive	Positive	Positive	Negative	Unclear	Negative	Positive	Positive	Unclear
[35]	Negative	Positive	Negative	Unclear	Negative	Negative	Negative	Unclear	Unclear	Unclear
[26]	Negative	Positive	Negative	Unclear	Negative	Negative	Negative	Unclear	Negative	Negative
[22]	Negative	Positive	Negative	Positive	Negative	Unclear	Negative	Unclear	Negative	Negative
[37]	Negative	Positive	Positive	Positive	Negative	Unclear	Negative	Unclear	Negative	Positive

Table 2: Risk of bias for in-vivo studies

Study	Sequence Generation	Baseline Characteristics	Allocation Concealment	Random Housing	Researcher Blinding	Random Outcome Assessment	Outcome Assessor Blinding	Incomplete Outcome Data	Selective Reporting	Other Bias
[35]	Negative	Positive	Negative	Unclear	Negative	Negative	Negative	Unclear	Unclear	Unclear
[26]	Negative	Positive	Negative	Unclear	Negative	Negative	Negative	Unclear	Negative	Negative
[22]	Negative	Positive	Negative	Positive	Negative	Unclear	Negative	Unclear	Negative	Negative
[37]	Negative	Positive	Positive	Positive	Negative	Unclear	Negative	Unclear	Negative	Positive

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Table 3: Cytotoxicity Profiles of Antiviral Active Medicinal Plants

Plant Species	Plant Parts	Extract Type and Safety Data		Cell Culture/Animal Model	Comments	Reference
		Solvent	Cytotoxicity/Toxicity			
Chrysanthemum cinerariaefolium (Pyrethrum)	Flower	Methanol	CC50= 42.23 ± 0.32(µg/ml)	Vero E6 Cells	Methanol extract more cytotoxic	31
		Water	CC50= 249 ± 8.4(µg/ml)			
	Flower	Both Water and Methanol extracts	LD50=2000mg/Kg	Mice	Non-cytotoxic in in-vivo	36
Dichrocephala integrifolia (Kuntze)	Leaves	Water	CC50 >100 (µg/ml)	Vero E6 Cells; Female Swiss albino mice	Methanol extract of flower moderately cytotoxic. All extracts non-toxic to mice at 300-2000mg/kg dose	35
		Methanol	CC50 >100 (µg/ml)			
	Flower	Water	CC50 >100 (µg/ml)			
		Methanol	CC50 = 71.31± 2.65 (µg/ml)			
	Stem Bark	Water	CC50 >100 (µg/ml)			
		Methanol	CC50 >100 (µg/ml)			
	Roots	Water	CC50 >100 (µg/ml)			
		Methanol	CC50 >100 (µg/ml)			
Acacia mellifera (Vahl Benth)	Roots	Methanol	CC50 >100 (µg/ml)	SNU-182 Cell line	Non-cytotoxic	24
Moringa oleifera	Leaves	Water	CC50= 1965.23 ± 10.26µg/mL	Vero cells	Non-cytotoxic	28
	Leaves	Methanol	CC50= 1622.10±11.98µg /mL			
Garcinia buchanii	Stembark		CC50>500(µg/ml)	Vero Cells	Non-cytotoxic	22
Caesalpinia decepetala	Whole root	Water	CC50>500(µg/ml)	Vero Cells	Non-cytotoxic	22
Prunus Africana	Roots	Water	CC50 <100 (µg/ml)	SNU-182 Cell line	Non-cytotoxic	24
	Stembark	Water	CC50 >100 (µg/ml)	Human embryonic lung fibroblast cells (HEL)	Non-cytotoxic	33
Plumeria alba	Latex		50% of latex cause 100% reduction of cells	Vero E6 Cells	More than 2.5% concentration is cytotoxic. 1.5mg/ml concentration cause cell lysis	26
Melia azedarach	Leaves	DCM/MEOH	Concentration above 0.5mg/ml cause cell lysis	Vero E6 cells	Moderately Cytotoxic at concentration>0.5mg/ml	26
	Stembark	Water	CC50 >80 (µg/ml)	Human embryonic lung fibroblast cells (HEL)	Non-cytotoxic	33
Croton dichogamus	Aerial parts	DCM:MEOH	CC50= 4.70 ± 0.26 µg/mL	Human T-lymphocytic MT-4 cells (ARP-120)	Cytotoxic	34
Croton megalocarpus	Leaves	DCM:MEOH	CC50=27.7 ± 0.65 µg/mL	Human T-lymphocytic MT-4 cells (ARP-120)	Cytotoxic	34
	Stembark	DCM:MEOH	CC50= 3.27 ± 0.12 µg/mL	Human T-lymphocytic MT-4 cells (ARP-120)	Cytotoxic	
Croton macrostachyus	Stembark	Water	CC50>500(µg/ml)	Vero Cells	Non-cytotoxic	22
	Leaves	DCM:MEOH	CC50= 0.008 ± 0.00 µg/mL	Human T-lymphocytic MT-4 cells (ARP-120)	Leaf extract Most cytotoxic among the 3 Croton genus reported to have anti-HIV activity	34
	Stembark	DCM:MEOH	CC50= 45.9 ± 0.12 µg/mL	Human T-lymphocytic MT-4 cells (ARP-120)		
Rhus natalensis	Stembark	Methanol	No toxicity at concentration≤1µg/ml	Vero cells; U937 cells	Non-cytotoxic	39

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Table 3: Cytotoxicity Profiles of Antiviral Active Medicinal Plants (cont'd)

Plant Species	Plant Parts	Extract Type and Safety Data		Cell Culture/Animal Model	Comments	Reference
		Solvent	Cytotoxicity/Toxicity			
Carissa edulis	Rootbark	Water	CC50>100 µg/ml	Human embryonic lung fibroblast cells (HEL)	Non-cytotoxic	33
Olinia rochetiana	Stembark	Methanol	No toxicity at concentration≤1 µg/ml	Vero cells; U937 cells	Non-cytotoxic	39
Scutia myrtina	Stembark	Methanol	No toxicity at concentration≤1 µg/ml	Vero cells; U937 cells	Non-cytotoxic	39
Warbugia ugandensis	Leaves	DCM/MEOH	Concentration above 0.5mg/ml cause cell lysis	Vero E6 cells	Cytotoxic at concentration>0.5mg/ml	26
	Stembark	Methanol	No toxicity at concentration≤1 µg/ml	Vero cells; U937 cells	Toxic when the concentration increases.	39
Albizia amara	Stembark	Methanol	No toxicity at concentration≤1 µg/ml	Vero cells; U937 cells	Toxic when the concentration increases.	39
Rhamnus prinoides	Stembark	Methanol	No toxicity at concentration≤1 µg/ml	Vero cells; U937 cells	Non-cytotoxic	39

The measles virus infects over 30 million children causing 1 million deaths a year in developing countries. Kenya reported 597 cases in 2020, an increase of 158 cases from those reported in 2019. The infection is a leading cause of blindness at 15,000-60,000 cases per year globally with Africa experiencing a disproportionately higher disease burden [18]. Simillarly, the dengue viral infection is currently putting half of the global population at risk of dengue-associated disease. It is estimated that about 100-400 million dengue infections occur globally every year. Kenya has had sporadic outbreaks of dengue the latest reported in Wajir, Malindi, Kilifi, and Mombasa, on the Kenyan Coast in 2017 [19]. The disease is endemic in over 125 countries where it continues to cause a significant burden of dengue fever and dengue hemorrhagic fever[20]. There is no pharmacological cure for both dengue and measles viruses. As the search for effective treatments for these viruses continue, medicinal plants can be considered as a good source for phyto-compounds that could be investigated as potential anti-measles and anti-dengue drugs.

This systematic review is aimed at synthesising evidence of antiviral efficacy, safety, and dosaging of Kenyan medicinal plants to support their safe, effective and evidence-based use in healthcare.

Methodology

We conducted this review in accordance with PRISMA 2020 guidelines [21]. We conducted a systematic search of PubMed and Google Scholar using predefined Boolean search strategies. The search terms were structured into three main concept groups: antiviral activity, medicinal plants, and geographic focus (Kenya), and were combined using appropriate Boolean operators as follows:

("antiviral" OR "antiviral activity" OR "antiviral efficacy" OR "antiviral effect")

AND ("medicinal plant" OR "herbal medicine" OR "traditional medicine" OR "phytotherapy" OR "herbs")

AND ("Kenya" OR "Kenyan")

Full database-specific search strategies are provided in Supplementary File 1. No date or language restrictions were applied. The final search was conducted on 23rd July 2024.

Eligibility Criteria

We included primary studies (in vitro, in vivo, or clinical) evaluating antiviral activity of indigenous Kenyan plant species as extracts or isolated compounds. Studies conducted outside Kenya were eligible if they investigated Kenyan indigenous species. We excluded reviews, ethnobotanical surveys without pharmacological data, modelling/in-silico-only studies (unless paired with laboratory data), and studies lacking antiviral outcomes. Exclusion of ethnobotanical surveys and reviews was decided following a unanimous decision by authors that their inclusion could introduce biases and redundancy in

data reporting.

Study Selection

Two reviewers independently screened titles/abstracts and then full texts against the criteria. Discrepancies were resolved by discussion or third-reviewer adjudication. Non-English articles were machine-translated (Google Translate) and verified by a second reviewer for data items; uncertainties were flagged during extraction.

Study Selection Results

The search identified 31 records. After deduplication, 30 records were screened by title/abstract; 25 full-text articles were assessed for eligibility; 18 studies met inclusion criteria and were included in the qualitative synthesis[22-39]. Reasons for full-text exclusion are detailed in Supplement 2.A PRISMA 2020 flow diagram is provided in Figure 1.

Risk of Bias (RoB) Assessment

Two reviewers (John Kirema and Raphael Lwembe) independently assessed risk of bias. We used SYRCLE's RoB tool for in vivo studies and a modified SYRCLE-based checklist for in vitro studies, adapted from previous studies[40]. Both tools assess 10 domains in the following order: sequence generation, baseline characteristics, allocation concealment, random housing, researcher blinding, random outcome assessment, outcome assessor blinding, incomplete outcome data, selective reporting, and other sources of bias. These domains were used to evaluate potential risks of selection, performance, attrition, detection, reporting, and other biases across both in vivo and in vitro studies. The RoB assessments were tabulated, and each domain was classified as low risk ("positive"), high risk ("negative"), or unclear risk where insufficient methodological information was available to permit judgment. Any disagreements between the two reviewers were resolved through discussion and consensus or, where necessary, through consultation with two additional investigators (B.I. and S.N.). All authors reviewed the final RoB judgments to ensure consistency and accuracy. The results of the RoB assessment were considered during interpretation of the overall strength and reliability of the evidence.

Data Extraction

Data were extracted using a Cochrane-compliant form developed collaboratively by all investigators. The form was created in Microsoft Word and adapted to include relevant components of the Cochrane template specific to this review. Extracted items included study identifiers (title, authors, and references), study design and eligibility, methodological characteristics, risk of bias (RoB), intervention details, outcome assessment methods, key findings, and authors' main conclusions.

In addition, plant-specific data were extracted, including species, plant part used, extract type (aqueous or organic solvent), study model (*in vitro*, *in vivo*, or *in silico*), virus type, measures of antiviral activity, and reported toxicity outcomes.

Two reviewers (R.L. and J.K.) independently performed data extraction to ensure accuracy and consistency. Discrepancies were resolved through discussion and consensus or, when necessary, by consultation with two additional investigators (B.I. and S.N.).

The findings were synthesized narratively and organized according to plant species and viral targets. A narrative synthesis approach was adopted due to substantial heterogeneity across the included studies in terms of study design, plant species, extraction methods, viral targets, and outcome measures, which precluded meaningful quantitative analysis.

Results

Risk of Bias Assessment

The RoB assessments for every publication included in our current review are included in Tables 1 and 2 below. For all publications related to in-vitro studies, the Modified SYRCLE RoB tool revealed a high risk of three categories of bias including selection, performance and detection biases. These results are consistent with findings by Sanchez-Fernandez study[41] which reported significant bias risks associated with selection and detection in in-vitro studies. Selection bias in these studies is contributed by the overall lack of sequence generation methods. The baseline characteristics of the control versus intervention groups (Culture cells) are similar since they are prepared in same laboratory environment, a factor that buffers selection bias impact. Performance and detection bias in our included in-vitro studies are caused by poor blinding when introducing the intervention in the experimental phase and when selecting the cells to examine first between the control and intervention groups. Blinding can be improved by ensuring the assessor is unaware of which group is the control or intervention thereby giving the two groups equal chance for selection during outcome assessment. Simillarly, the SYRCLE RoB for in-vivo studies indicated high risks of performance, detection, and selection biases influenced by poor randomization of research animals, compromised animal grouping and selection methods, and poor blinding of the whole experiment process.

Risk of Bias Assessment

The risk of bias (RoB) assessments for all included studies are presented in Tables 1 and 2. Overall, the included studies exhibited several methodological limitations, with

Table 4: Antiviral activity of Indigenous medicinal plants against HSV-1 in Kenya.

Plant Species, Local name	Parts Assessed	Solvent used for extraction	Study type	Activity	Ref
Chrysanthemum cinerariaefolium (Pyrethrum)	Flower	Methanol	In-vitro	Active with (IC50= 1.69 µg/ml)	31
Chrysanthemum cinerariaefolium (Pyrethrum)	Flower	Water	In-vitro	Active with (IC50= 23.21 µg/ml)	36
Chrysanthemum cinerariaefolium (Pyrethrum)	Flower	Methanol	Invivo	Active at (10 mg/kg, 25 mg/kg)	36
Chrysanthemum cinerariaefolium (Pyrethrum)	Flower	Water	Invivo	Active at (50 mg/kg)	36
Dichrocephala integrifolia (Kuntze)	Leaves	Methanol	In-vitro	Active with (IC50=63.95±5.36) in Pre-treatment method.	35
Dichrocephala integrifolia (Kuntze)	Flower	Methanol	In-vitro	Active with (IC50= 86.20±7.56) using Post-Treatment Strategy	35
Dichrocephala integrifolia (Kuntze)	Stem Bark	Methanol	In-vitro	Active with (IC50=54.45±3.45) using Pre-treatment method	35
Dichrocephala integrifolia (Kuntze)	Leaves	Water	In-vitro	Active with (IC50=86.20±7.56) using Pre-treatment Method	35
Dichrocephala integrifolia (Kuntze)	Leaves	Water	In-vitro	Active with (IC50=82.44±7.92) using Post-treatment strategy	35
Dichrocephala integrifolia (Kuntze)	Flower	Methanol	In-vitro	Showed Virucidal activity with (IC50=45.27±2.41)	35
Dichrocephala integrifolia (Kuntze)	Leaves	Methanol	In-vitro	Showed Virucidal activity with (IC50=30.53±4.51)	35
Dichrocephala integrifolia (Kuntze)	Roots	Water	In-vitro	Showed virucidal activity with (IC50= 0.333±1.23)	35
Acacia mellifera (Vahl) Benth)	Stembark	DCM and methanol	Invitro	Betulin Compound highly active at 50 µg/ml. Low activities at concentration between 1-10 µg/ml.	29
Moringa oleifera	Leaves	Water	In-vitro	Active with (IC50= 627.29± 0.33) using Post-infection treatment strategy	28
Moringa oleifera	Leaves	Water	In-vitro	Active with (IC50 of 695.10±0.28) using pre-infection treatment strategy	28
Moringa oleifera	Leaves	Methanol	In-vitro	Active with (IC50=1350.61) using post-infection treatment strategy	28
Moringa oleifera	Leaves	Methanol	In-vitro	Active with (IC50=2427.83 ± 0.23) using pre-infection treatment strategy.	28
Garcinia buchanii	Stembark	Water	In-vitro, in-vivo	Active (IC50) at 20µg/mL.	22
Caesalpinia decepetala	Root	Water	In-vitro	Active IC50 at 80µg/mL.	22
Carissa edulis (Forssk.) Vahl	Rootbark	Diethyether and pure methanol	In-vitro	Lupeol showed activity with (EC50 at 2.98 µg/ml-4.2 µg/ml).	38
Carissa edulis (Forssk.) Vahl)	Rootbark	Diethyether and pure methanol	In-vivo	Lupeol showed activity at 20.0 µg/ml with a delayed onset of infections at ($p \leq 0.05$ test vs. control)	38
Prunus Africana	Stembark	Water	In-vivo	Active at a dose of 250 mg/kg.	37
Acacia mellifera	Stembark	Water	In-vivo	Active at a lower dose of 250 mg/kg.	37
Plumeria alba	Plumeria alba latex	Hexane	In-vitro	Active at 1mg/ml with 0.5 log units viral yield reduction.	26
Plumeria alba	Plumeria alba latex	DCM	In-vitro	Active at 1mg/ml with 0.75 log units viral yield reduction.	26
Plumeria alba	Plumeria alba latex	Ethyl-acetate	In-vitro	Active at 1mg/ml with 1.5 log units viral yield reduction	26

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the most common concerns observed in domains related to selection bias, performance bias, and detection bias.

Among the in vitro studies, the modified SYRCLE-based assessment indicated a predominantly high or unclear risk of bias in domains related to sequence generation, researcher blinding, and outcome assessment. In particular, most studies did not report methods of sequence generation, contributing to potential selection bias. Although baseline characteristics of control and intervention cell cultures were generally comparable due to standardized laboratory conditions, lack of randomization procedures remained a concern. Additionally, blinding during intervention administration and outcome assessment was often absent or insufficiently reported, increasing the likelihood of performance and detection bias.

Similarly, the SYRCLE assessment of in vivo studies revealed frequent concerns related to sequence generation, allocation procedures, blinding, and outcome assessment. Many studies did not clearly describe randomization of experimental animals or blinding of investigators, which may have introduced bias in group allocation and outcome measurement.

Overall, these findings indicate that although several studies reported promising antiviral activity, the reliability of the evidence is limited by methodological weaknesses. Therefore, the findings of this review should be interpreted with caution, particularly where conclusions are based on studies with high or unclear risk of bias.

Summary of Included Studies

Approximately half of the included studies focused on *Herpes simplex virus type 1* (HSV-1), likely reflecting its biosafety level 2 (BSL-2) classification, which facilitates research in resource-limited settings. Overall, 18 studies evaluated 54 Kenyan medicinal plant species, of which 28 demonstrated antiviral activity against six viruses: *Human immunodeficiency virus* (HIV), HSV, measles virus, *Human cytomegalovirus* (HCMV), *Hepatitis B virus* (HBV), and dengue virus, as summarized in Tables 1–3.

Several plant species exhibited broad-spectrum antiviral activity. Notably, *Carissa edulis*, *Prunus africana*, *Melia azedarach*, *Rhus natalensis*, and *Acacia mellifera* demonstrated activity against multiple viral targets, including HBV, HCMV, HIV-1, HSV-1, and measles virus (Table 4). Most studies were conducted *in vitro*, with only five incorporating *in vivo* models [22,26,36-38]. This predominance of preclinical evidence, together with the generally high or unclear risk of bias identified across several methodological domains, limits confidence in the overall strength of the evidence.

The observed antiviral activity may be partly attributed to the presence of bioactive phytochemicals such as flavonoids, tannins, alkaloids, and terpenoids, although detailed phytochemical characterization was inconsistently reported across studies.

Overall, the strength of evidence was judged to be low to moderate, reflecting the predominance of *in vitro* studies, limited *in vivo* validation, and methodological limitations identified in the risk of bias assessment.

A structured comparison of antiviral activity across included studies indicates that several plant extracts demonstrated strong *in vitro* activity, with reported IC_{50} or EC_{50} values generally ranging from less than 5 µg/mL for anti-HIV activity to approximately 1.69–23.21 µg/mL for anti-HSV activity, depending on plant species and extraction method. However, differences in experimental models, extract preparation, and outcome reporting limited direct quantitative comparison across studies [22,26,36-38].

Toxicity Profiles of the Active Plants

Toxicity or cytotoxicity data were reported for 19 of the 28 plant species identified as having antiviral activity (Table 3). Overall, while the majority of active plants had some form of safety evaluation, nine species lacked any reported toxicity data. These included *Maytenus buchananii*, *Maytenus senegalensis*, *Maytenus heterophylla*, *Erythrina abyssinica*, *Azadirachta indica*, *Leptotrichilia* spp., *Carica papaya*, *Myrica salicifolia*, and *Grewia mollis*. The absence of safety data for these plants limits interpretation of their potential therapeutic relevance.

Among the studies that reported toxicity, assessments were primarily conducted using cell culture models or animal studies. However, in some cases, antiviral activity was evaluated without accompanying cytotoxicity testing, particularly in studies employing *in silico* approaches or enzyme-based assays such as reverse transcriptase inhibition [27,30]. Additionally, some studies focused on isolated compounds rather than crude extracts, which may reduce the presence of toxic impurities [25,29].

Variability in cytotoxicity profiles across plant extracts may be influenced by differences in phytochemical composition, extraction methods, and experimental models. This highlights the importance of standardized extraction procedures and comprehensive toxicity evaluation in future studies.

Overall, although several plants demonstrated promising antiviral activity, incomplete toxicity data for some species necessitates cautious interpretation of their potential for therapeutic application.

The included studies exhibited substantial heterogeneity in terms of plant species investigated, plant parts used, extraction methods, experimental models (*in vitro* vs. *in vivo*), viral targets, and outcome measures. This variability limited the ability to directly compare findings across studies and precluded quantitative synthesis, such as meta-analysis. Consequently, the findings were synthesized narratively, and comparisons of antiviral activity across studies should be interpreted with caution.

Discussion

This review highlights the antiviral potential of Kenyan medicinal plants. Notably, *Croton dichogamus*, *Croton megalocarpus*, *Croton macrostachyus*, and *Rhus natalensis* demonstrated strong activity against *Human immunodeficiency virus type 1* (HIV-1), with reported IC_{50} values below 5 µg/mL. Several other species also exhibited notable activity against *Herpes simplex virus* (HSV) and measles virus. However, the observed findings should be interpreted in the context of potential publication bias, methodological variability, and uneven research focus across plant species.

Despite these promising findings, confidence in the overall evidence remains limited. The risk of bias assessment indicated that many studies had high or unclear risk across key methodological domains, particularly in sequence generation, blinding, and outcome assessment. Furthermore, the majority of the evidence was derived from *in vitro* studies, with only a few *in vivo* investigations and no clinical trials. These limitations reduce the certainty of the evidence and increase the likelihood that reported antiviral effects may be overestimated. Accordingly, the findings of this review should be interpreted as preliminary and hypothesis-generating rather than definitive evidence of therapeutic efficacy.

a. Indigenous Medicinal Plants for Herpes Viruses Treatment in Kenya

Acyclovir remains the first-line treatment, increasing reports of resistance pose a growing challenge to effective HSV management [42]. In this context, medicinal plants represent a promising source of novel antiviral agents. For instance, extracts of Chrysanthemum cinerariaefolium demonstrated potent anti-HSV-1 activity: methanol extracts inhibited 50% of plaques at 1.69 µg/mL in vitro, while aqueous extracts achieved comparable inhibition at 23.21 µg/mL[31]. In vivo, both extracts delayed HSV-1 progression in mice at doses of 10 mg/kg and 50 mg/kg, respectively[36]. Several other Kenyan medicinal plants including *Dichrocephala integrifolia*, *Acacia mellifera*, *Garcinia buchananii*, *Caesalpinia decapetala*, *Prunus africana*, and *Plumeria alba* have also demonstrated strong anti-HSV-1 activity [22,26,29,35,37]. Notably, *D. integrifolia* exhibited direct virucidal properties [35], while Chrysanthemum cinerariaefolium exhibited remarkable potency through both pre-and-post treatment infection methods. Pure compound, Lupeol obtained from *Carissa edulis* showed activity against both wild type and acyclovir resistance HSV-1 (EC50 at 2.98 µg/ml for 7401H HSV-1, 3.66 µg/ml for APr 7401H HSV-1 and 4.2 µg/ml for the TK–B2006 HSV-1) [38].

The findings on *Carissa edulis* potency against acyclovir-resistance HSV-1 suggest that Lupeol could be exhibiting a different mechanism of action from acyclovir. The compound could be acting by blocking adsorption receptors thereby preventing viral attachment or by preventing synthesis of viral structural components once the virus has entered the cells. Virucidal properties of *D. integrifolia* suggest a similar mechanism of action while the findings on *Chrysanthemum cinerariaefolium* efficacy in both pre-and-post treatment experiments suggest the potential for a multi-action mechanisms of some extracts. Besides blocking cell receptors to prevent viral attachment, the other mechanisms of action could include hindering some steps in replication cycle once the virus has entered the cell. The multi-directional action mechanisms could be associated by the presence of polyphenols such as tannins and tannic acids previously reported to act against HSV-2 by preventing viral attachment and inducing production of cytokines and chemokines that interfere with replication[43]

b. Indigenous Medicinal Plants for Hepatitis B Virus Treatment in Kenya

Several Kenyan medicinal plants including *Carissa edulis*, *Prunus africana*, and *Acacia mellifera* have demonstrated in vitro anti-HBV activity [24]. Among them, aqueous extracts of *C. edulis* demonstrated the highest level of viral inhibition (12.15%), whereas *P. africana* and *A. mellifera* exhibited lower inhibition rates of 5% and 2.15%, respectively [24]. These findings were supported by real-time PCR, which confirmed sustained antiviral effects at concentrations ranging from 31.25 to 125 µg/mL. Reported EC_{50} values of 331.6 and 295.0 µg/mL suggest potential antiviral efficacy. Phytochemical screening of *Carissa edulis* have shown the presence of polyphenols such as tannins, flavonoids, steroids, glycosides, lignins, coumarins, and terpenoids [44]. Screening of *Prunus africana* reveals its richness in flavonoids, phenols, quinones, steroids, coumarins, saponins, alkaloids, tannins, and terpenoids [45]. Simmilar phyto-compounds including phenolics, cardiac glycosides, alkaloids, steroids, flavonoids, sapponins, tannins ,and terpenoids are found in *Acacia mellifera* [46].

The presence of flavonoids from these plants could be responsible for their anti-HBV activity. Previous studies have shown that certain types of plant-derived flavonoids such as epigallocatechin and epigallocatechin-3-gallate (EGCG) that is abundant in green tea exhibits antiviral action against HBV by blocking attachment receptors, hindering DNA synthesis and replication, and suppressing gene expression[47]. Other flavonoids such as betulinic acid and baicalin have been shown to act against HBV in a similar manner of inhibiting HBV RNAs and cutting viral replication pathway thereby limiting chances of producing new virions [47]. The flavonoids present in *Carissa edulis*, Prunus africana, and *Acacia mellifera* could be responsible for their antiviral efficacy. The extracts probably have similar mechanisms of action of blocking entry and interfering with pathways for development of viral structural components like other flavonoids.

c. Indigenous Medicinal Plants for Measles Virus Treatment in Kenya

The measles virus, a highly contagious RNA virus belonging to the Paramyxoviridae family, remains a major cause of childhood morbidity and mortality worldwide [48]. An in vitro evaluation of 13 Kenyan medicinal plants identified four species - *Rhus natalensis*, *Albizia amara*, *Olinia rochetiana*, and *Warburgia ugandensis;* that exhibited significant measles virus neutralization activity [39]. Among them, *O. rochetiana* and *W. ugandensis* demonstrated the highest potency, achieving 107.3 and 98.0 neutralization units, respectively, relative to 293.5 observed in human serum. Both extracts achieved 50% neutralization of measles viral particles at concentrations as low as 0.1 µg/mL. In addition, *R. natalensis* and *A. amara* demonstrated notable 17-fold increases in neutralization capacity. Furthermore, *Rhamnus prinoides* and *Scutia myrtina* were found to reduce viral yield in U937 cell cultures. The mechanisms of action of these extracts could be through blocking viral entry into the cell. This could be due to the presence of saponins and amyrin-acetate which have previously demonstrated significant binding affinity with the 5e4v-receptor proteins of the measles virus in an in-sillico model[49]. Saponins and amyrin-acetate are key phyto-compounds present in *Warbugia ugandensis* and *Olinia rochetiana* [50,51].

These plants are traditionally used by the Maasai community in Kenya as dietary additives for children, a practice that may contribute to measles protection. The convergence of their traditional use with demonstrated antiviral activity underscores the need for further research to isolate and characterize active phyto-compounds for potential therapeutic development.

d. Indigenous Medicinal Plants for Human Cytomegalovirus Treatment in Kenya

Human cytomegalovirus (HCMV), a β-herpesvirus, is globally prevalent with seropositivity rates ranging from 60% to 90%, and poses serious health risks to immunocompromised individuals, neonates, and transplant recipients [52]. Given the absence of a licensed vaccine, the exploration of plant-derived antivirals has gained considerable attention. Root bark extracts of *Maytenus heterophylla* yielded pristimerin, a compound that demonstrated potent anti-HCMV activity (IC_{50} = 0.53 µg/mL), effectively inhibiting viral replication without compromising cell viability [25]. Mechanistic studies using Western blot analysis confirmed reduced amount of immediate early (IE) antigen including the expression of immediate-early (IE2) viral antigens [25]. In addition, aqueous extracts of *Carissa edulis*, *Prunus africana*, and *Melia azedarach* displayed in vitro anti-HCMV activity, with EC_{50} values ranging from 40 to 80 µg/mL [33]. The findings from Western blot show that Pristimerin could be acting by hindering the synthesis of vital viral components (IE2 antigens) thereby blocking infectivity and replication.

Two similarities can be identified in the treatment of HCMV versus HSV-1. First, two of the plants, *Carissa edulis* and *Prunus africana* found to be active against HCMV are also active against HSV-1. Secondly, both HCMV and HSV-1 belong to the same class of herpes viruses. Their similarities in pathogenesis and replication cycles suggests that phytochemicals present in *Carissa edulis* and *Prunus africana* could be exhibiting similar mechanisms of action on HCMV and HSV-1.

Collectively, these findings underscore the potential of Kenyan medicinal plants as promising sources for developing alternative antiviral therapies against HCMV, particularly for high-risk populations.

e. Indigenous Medicinal Plants for Dengue Virus Treatment in Kenya

Among Kenyan medicinal plants, *Carica papaya* leaf methanol extracts have demonstrated notable anti-dengue potential in a silico docking study which identified 5,7-dimethoxycoumarin and quercetin as key bioactive compounds with strong binding affinity to the DENV-2 NS5 protein [27]. Subsequent in vitro experiments demonstrated that silver nanoparticle formulations containing these compounds effectively inhibited DENV-2 replication, with an IC_{50} of 9.20 µg/mL [27]. By binding with the NS5 protein, the compounds 5,7-dimethoxycoumarin and quercetin blocks the ability of the virus to attach to the host receptor proteins thereby stoping the replication of the viral RNA.

These findings suggest that *Carica papaya*, a plant widely cultivated and traditionally used in Kenya, holds a significant promise as a source of novel plant-based dengue therapeutics.

f. Indigenous Medicinal Plants against HIV-1 in Kenya

Kenyan medicinal plants have demonstrated promising anti-HIV-1 activity, particularly through inhibition of the viral reverse transcriptase enzyme, which is essential for viral replication. Several species including *Maytenus buchananii*, *Maytenus senegalensis*, *Acacia mellifera*, *Erythrina abyssinica*, *Azadirachta indica*, *Leptotrichilia sp.*, *Melia azedarach*, *Myrica salicifolia*, *Prunus africana*, *Grewia mollis*, and *Rhus natalensis* have shown significant reverse transcriptase inhibition capacity in vitro [23,30]. The Croton plant genus seems to be a promising source for anti-HIV drugs. From *Croton macrostachyus*, compounds such as lupenone, lupeol acetate, and betulin have exhibited potent anti-HIV-1 effects, with IC_{50} values below 5 µg/mL, possibly through interactions with viral envelope proteins [32]. Dichloromethane (DCM)-methanol extracts from *Croton dichogamus* and *Croton megalocarpus* inhibited more than 70% of HIV-induced cytopathic effects at low IC_{50} concentrations (0.05 + 0.03 µg/mL) [34].

The antiviral activity observed in several Kenyan medicinal

plants may be partly attributed to their phytochemical composition. For example, *Carissa edulis* has been reported to contain a wide range of bioactive compounds, including polyphenols such as tannins, flavonoids, glycosides, coumarins, lignins, steroids, and terpenoids[38]. Similarly, *Prunus africana* contains flavonoids, phenols, quinones, alkaloids, saponins, tannins, and terpenoids, while *Acacia mellifera* has been shown to contain phenolics, flavonoids, alkaloids, cardiac glycosides, steroids, saponins, tannins, and terpenoids [24]. These classes of compounds are well known for their antiviral, antioxidant, and immunomodulatory properties, and may contribute to the observed inhibition of viral replication through mechanisms such as interference with viral entry, replication, or protein synthesis.

The overall strength of evidence in this review was assessed qualitatively based on study design, consistency of findings, availability of toxicity data, and risk of bias. Most of the included evidence was derived from *in vitro* studies, with only a limited number of *in vivo* investigations and no clinical studies. In addition, several studies demonstrated high or unclear risk of bias across key methodological domains.

Based on these factors, the overall confidence in the evidence was judged to be low to moderate for most plant–virus combinations. Higher confidence was observed where findings were supported by both *in vitro* and *in vivo* data with reported toxicity assessments. However, in many cases, the absence of toxicity data and methodological limitations reduced the reliability of the findings. Therefore, the evidence should be interpreted cautiously and considered preliminary.

Although structured summaries of antiviral activity were considered, the substantial heterogeneity across included studies—including differences in plant species, plant parts used, extraction methods, viral targets, experimental models, and outcome measures—limited the feasibility of detailed quantitative comparison or tabulation. Consequently, a narrative synthesis approach was retained as the most appropriate method for summarizing the available evidence. This heterogeneity also limits direct comparability across studies and reduces confidence in drawing generalized conclusions.

Furthermore, variability in reported antiviral activity may be influenced by differences in extraction methods, as solvent polarity determines the types of phytochemicals extracted. Aqueous extracts are more likely to yield polar compounds such as phenolics and flavonoids, whereas organic solvents, including methanol or dichloromethane:methanol mixtures, may extract a broader range of bioactive constituents such as terpenoids and other lipophilic compounds. However, because most included studies did not perform detailed phytochemical characterization or standardization, the relationship between chemical composition, extraction method, and antiviral activity remains suggestive rather than definitive. Despite these encouraging findings, the precise mechanisms of action and pharmacodynamic properties of these medicinal plants remain poorly understood. Current evidence is largely limited to *in vitro* studies, underscoring the need for well-designed *in vivo* and clinical investigations to validate their therapeutic potential. In addition, the generally high or unclear risk of bias across several included studies further limits confidence in the reliability of the findings.

The study selection approach, which excluded publications with substantially overlapping findings to reduce redundancy, may also have introduced selection bias and potentially limited the comprehensiveness of the evidence base.

Finally, although several medicinal plants demonstrated antiviral activity, the absence of toxicity data for a number of species limits their translational potential. Safety evaluation is a critical component of drug development, and the lack of cytotoxicity or *in vivo* toxicity data makes it difficult to assess therapeutic windows and potential adverse effects. Therefore, plants without toxicity data should be interpreted cautiously, and further studies are required to establish their safety profiles before any consideration of clinical application.

Conclusion

Several indigenous Kenyan medicinal plants demonstrate promising antiviral activity against viruses such as *Human immunodeficiency virus* (HIV), *Herpes simplex virus* (HSV), *Hepatitis B virus* (HBV), *Human cytomegalovirus* (HCMV), measles virus, and dengue virus. However, the current evidence base is predominantly preclinical, with most findings derived from *in vitro* studies, limited *in vivo* validation, and no clinical trials.

The overall strength of evidence is low to moderate and is further constrained by methodological heterogeneity, high or unclear risk of bias, and incomplete toxicity data for several plant species. Consequently, these findings should be interpreted cautiously and regarded as preliminary.

Future research should prioritize well-designed pharmacological, toxicological, and clinical studies to validate these findings, establish safety profiles, and identify bioactive compounds responsible for antiviral activity. In particular, standardization of extraction methods, detailed phytochemical characterization, and comprehensive toxicity evaluation will be essential to advance these plants toward therapeutic application.

Overall, while Kenyan medicinal plants represent a valuable resource for antiviral drug discovery, further rigorous investigation is required before their potential clinical utility can be established.

Recommendations

Further research should expand screening of Kenyan medicinal plants for antiviral properties, safety and cytotoxicity, isolate active compounds, and clarify their mechanisms of action. Emphasis on multi-virus testing and

toxicity assessment is needed. Strengthening partnerships among researchers, traditional practitioners, and pharmaceutical developers will support drug discovery and sustainable use of indigenous resources.

Future Perspectives

Future research should prioritise in-vivo testing of antiviral plant compounds, integrating ethnobotany, molecular biology, and pharmacology. Collaboration between academia, traditional healers, and industry is essential to develop and clinically validate novel antiviral drugs from indigenous plants for global health impact.

Author contributions

RLM, JK, BI, JWL, SN, AM and JKN designed the study, interpreted the data, and wrote the main manuscript text. All authors reviewed the final manuscript.

Conflict of interest

The authors state no conflict of interest.

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