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PLANT AS A SOURCE OF NATURAL ANTIVIRAL AGENTS: A REVIEW OF THEIR ANTIVIRAL ACTIVITY

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Abstract

Medicinal plants have been extensively used to treat a variety of infectious and non-infectious ailments. As the number of viral infections and in particular resistant viral strains increasing, current remedies need to be upgraded and brought into line with the discovery of new antiviral agents to combat persistent viral infections Nature has already conferred on us a wide variety of antiviral remedies in the form of herbs, they are characterized with a broad antiviral spectrum. Several plants could offer a rich reserve for drug discovery of infectious diseases, particularly in an era when the latest separation methods are available on one hand, and the human population is dared by a number of emerging infectious diseases on the other hand. Of importance, a variety of medicinal plants have shown promise effect to treat a number of viral infections, and some of them have broad-spectrum antiviral activity. Among several other ailments, viral infections, particularly infections connected with human immunodeficiency virus type 1 (HIV-1) and 2 (HIV-2), influenza virus, hepatitis B virus, viruses causing respiratory infections, severe acute respiratory syndrome (SARS) virus and newly emerging infectious viruses have challenged mankind survival. Viral infections affect about three to five million patients every year. While frequently used antivirals often show limited effectiveness and sometimes may have serious adverse effects. This article describes potential antiviral properties of medicinal plants against a diverse group of viruses, and suggests screening the potential of plants possessing broad-spectrum antiviral effects against emerging viral infections.

Keywords: *Infectious, antiviral agents, viral infections, adverse effects, broad-spectrum.*

Introduction

Viruses are obligate intracellular parasites that have evolved genetic variation, transmission, and replication, and have the ability to persist within the host for short or long period of time [1]. Medicinal plants are the Nature's gift to human beings to help them pursue a disease-free healthy life, regarding treatment of the diseases and role in preserving health [2]. Nature has already bestowed on us a wide variety of antiviral remedies in the form of herbs, they are characterized with a broad antiviral spectrum [3] Natural products have proved to be an important source of lead molecules and many extracts and compounds of plant origin with antiviral activity have been reported [4]. The pandemic of several infectious viral diseases have been reported till date and newer ones are occurring frequently during recent years that forced the scientific community to investigate less toxic antiviral phytomolecules instead of using nucleic acid analogues, protease inhibitors or other toxic synthetic molecules as antiviral therapeutics [1]. Due to the high prevalence of viral infections for which there are no specific treatment and the constant appearance of new resistant viral strains, the development of novel antiviral agents is essential [5]. Recent studies have reported the inhibitory effects of medicinal plant extracts on the replication of several viruses, such as HIV, hepatitis B virus, viruses causing respiratory infections, influenza virus, severe acute respiratory syndrome (SARS) virus and many others [6-11]. Moreover, recent studies showing antiviral potential of plant extracts against viral strains resistant to conventional antiviral agents have challenged the modern drug discovery practices, and deem a very careful look toward exploring natural antiviral components of medicinal plants [12]

This review was designed to highlight the antiviral effects of the medicinal plants available in different regions and countries and suggests screening the potential of plants possessing broad-spectrum antiviral effects against emerging viral infections.

Methods

A search (till July 2020) was done in the following databases: PubMed, Springer, Science Direct, MedLine, Scopus, and Google Scholar with the keyword "Natural Antiviral Agents", pairing with 'phytochemicals', 'biological activities/effects', or 'pharmacological activities/effects'. No language limitations were forced. Articles were evaluated for the data about the concentrates or divisions and separated mixes of the plant or its parts, fixation or portion (course of organization), test frameworks, results or conceivable system of activity, and last end. Incorporation and avoidance criteria of confirmations found in databases have been given as follows.

Inclusion criteria:

1. Studies carried out in vitro, ex vivo or in vivo with or without using experimental animals, including humans and their consequent tissue and cells;

2. Studies with or without recommending activity mechanisms;

3. Studies with extracts without phytochemical analysis, but having biological activities;

4. Studies with extracts, with phytochemical analysis, but having no report for biological activities.

Exclusion criteria:

1. Duplicate of any data and titles and/or abstracts not meeting the inclusion criteria

Results & Discussion

Antiviral activity of Colombian medicinal plant extracts:

The aqueous extract from Beta vulgaris, the ethanol extract from Callisia grasilis and the methanol extract Annona sp. showed some antiherpetic activity with acceptable therapeutic indexes (the ratio of CC50 to EC50). These species are good candidates for further activity-monitored fractionation to identify active principles [13]

Antiviral properties from plants of the Mediterranean flora:

Antiviral activity was found in the extract obtained from the branches of Daphne gnidium L. against human immunodeficiency virus type-1 (EC50 ¼ 0.08 mg/mL) and coxsackievirus B5 (EC50 ¼

0.10mg/mL). Other relevant activities were found against BVDV, YFV, Sb-1, RSV and HSV-1. Interestingly, extracts from Artemisia arborescens L. and Rubus ulmifolius Schott, as well as those from D. gnidium L., showed activities against two different viruses. This extensive antiviral screening allowed us to identify attractive activities, offering opportunities to develop lead compounds with a great pharmaceutical potential [14]

Antiviral screening of British Columbian medicinal plants:

The extracts of Rosa nutkunu and Amelunchier alnifoliu, both members of the Rosaceae, were very active against an enteric coronavirus. A root extract of another member of the Rosaceae, Potentillu urgutu, completely inhibited respiratory syncytial virus. A Sumbucus rucemosu branch tip extract was also very active against respiratory syncytial virus while the inner bark extract of Oplopunux horridus partially inhibited this virus. An extract of Ipomopsis uggregutu demonstrated very good activity against parainfluenza virus type 3. A Lomatium dissectum root extract completely inhibited the cytopathic effects of rotavirus [15].

Antiviral activities of Colombian medicinal plant extracts of the Euphorbia genus:

Forty-seven plant extracts of 10 species of the genus Euphorbia (Euphorbiaceae) used by Colombian traditional healers for the treatment of ulcers, cancers, tumors, warts, and other diseases, were tested in vitro for their potential antitumour (antiproliferative and cytotoxic) and antiherpetic activity. Five of the 47 extracts (11%) representing 3 out of 10 Euphorbia species (30%) exhibited antiherpetic action; the highest activity was found in the leaf/stem watermethanol extracts from E. cotinifolia and E. tirucalli.[16]

Screening of Brazilian medicinal plants for antiviral activity against rotavirus:

Brazilian medicinal plants traditionally used for the treatment of diarrhoea were investigated for their in vitro antiviral activity against the simian rotavirus SA11. Among different species studied, Byrsonima verbascifolia, Eugenia dysenterica, Hymenaea courbaril and Myracrodruon urundeuva showed potential activity against rotavirus and are worthy of further study. The present study corroborates ethnopharmacological data as a valuable source in the selection of plants with antiviral activity and to some extent validates their traditional uses [17].

In vitro antiviral activity of plant extracts from Asteraceae medicinal plants:

B. gaudichaudiana and B. spicata OE (organic extracts) were active against PV-2 and VSV. T. absinthioides OE was only active against PV-2. The corresponding three AE aqueous extracts (AE) were active against HSV-1. B. gaudichaudiana extracts (OE and AE) were the most selective ones with selectivity index (SI) values of 10.9 (PV-2) and >117 (HSV-1). For this reason, both extracts of B. gaudichaudiana were selected to characterize their antiviral effects [5].

Antiviral activity of the Indian medicinal plant extract, Swertia chirata against herpes simplex viruses:

Swertia plant crude extract (1gm/mL) at 1:64 diluti plaque formation at more than 70% level. HSV antigen expression and time kinetics experiments conducted by indirect immunofluorescen revealed a characteristic pattern of small foci of single fluorescent cells in Swertia extract treated HSV-1 infected cells at 4 hours post infe drug inhibited viral dissemination. Infected cell cultures treated with Swertia extract at various time intervals, tested by PCR, failed to sho 12, 24-72 hours. HSV-1 infected cells treated with Acyclovir (antiviral drug) did not show any amplification by PCR [18]

Antiviral activity of medicinal plant Nepeta nuda:

Nepeta nuda subsp. nuda L. is a valuable medicinal plant well-known for its various therapeutic properties. Studies revealed that methanol and chloroform extracts derived from N. nuda propagated in vivo and in vitro possess clear antiviral activity. The CHV (chloroform extract from native plant) and CHR (chloroform extract from laboratory propagated plant), such as the methanol native extract MEV, exerted a strong inhibitory effect against the replication of HSV type 1 and type 2 in MDBK cells. The extract CHV suppressed the first steps of replicative cycle of HSV type 2 [19].

Antiviral properties of supercritical CO2 extracts from Oregano and Sage:

The antiviral properties of supercritical CO2 extracts obtained from oregano and sage were evaluated against the herpes simplex virus type 1 at different stages during virus infection. All of the extracts tested presented a moderate extracellular direct virucidal activity, although a pre-treatment of Vero cells, with 10 µg/mL of sage extracts before virus addition, inhibited 70% of the virus infection. Carvacrol and thymol could be pointed out as the compounds responsible for the antiviral activity found in oregano supercritical extracts; meanwhile, borneol, camphor, and 1,8-cineole could be proposed as antiviral compounds in supercritical sage extracts [20].

Antiviral activity of commercially available medicinal plants on suid and bovine herpes viruses:

The following species were tested: Mikania glomerata, Cymbopogon citratus, Equisetum arvense, Peumus boldus, Solanum paniculatum, Malva sylvestris, Piper umbellatun and Solidago microglossa. The extracts from Peumus boldus and Solanum paniculatum showed antiviral activity against SuHV-1 with 98% of inhibition. The extract of Peumus boldus also showed activity against BoHV-1 with 99% of inhibition [21].

Antiviral activity of medicinal plants of Nilgiris:

Three plant extracts Hypericum mysorense, Hypericum hookerianum and Usnea complanta exhibited significant antiviral activity against Herpes simplex virus (HSV) at a concentration nontoxic to the cell line used. The extracts of Melia dubia, Cryptostegia grandiflora and essential oil of Rosmarinus officinalis showed partial activity at higher concentrations [22].

Antiviral activity of phenanthrenes from the medicinal plant Bletilla striata against influenza A virus:

Influenza represents a serious public health concern. The emergence of resistance to anti-influenza drugs underlines the need to develop new drugs. Twelve phenanthrenes were isolated and identified from B. striata. This study showed that phenanthrenes 1, 2, 3, 4, 6, 9, 10, 11, and 12 significantly inhibited the viruses in vivo, with inhibition rates of 20.7, 79.3, 17.2, 34.5, 34.5, 34.5, 44.8, 75.9, and 34.5%, respectively. In Madin-Darby canine kidney (MDCK) models, the phenanthrenes did not show significant antiviral activity when administered as pretreatment, while phenanthrenes 2, 3, 4, 6, 7 10, and 11 exhibited inhibitory activities as simultaneous treatment with 50% inhibition concentration (IC50) ranging from 14.6 ± 2.4 to 43.3 ± 5.3 µM [23].

In vitro evaluation of novel antiviral activities of medicinal plants extracts against hepatitis B virus:

Guiera senegalensis (dichloromethane extract, IC50=10.65), Pulicaria crispa (ethyl acetate extract, IC50=14.45), Coccinea grandis (total ethanol extract, IC50=31.57), Fumaria parviflora (hexane extract, IC50=35.44), Capparis decidua (aqueous extract, IC50=66.82), Corallocarpus epigeus (total ethanol extract, IC50=71.9), Indigofera caerulea (methanol extract, IC50=73.21), Abutilon figarianum (dichloromethane extract, IC50=99.76) and Acacia oerfota (total ethanol extract, IC50=101.46) demonstrated novel anti-HBV activities in a time- and dose-dependent manner. Further qualitative phytochemical analysis of the active extracts revealed the presence of alkaloids, tannins, flavonoids and saponins, which are attributed to antiviral efficacies [24].

Antiviral activity of eight commonly used medicinal plants in Taiwan:

In this study, B. variegata and D. caudatum were found to possess a broad spectrum in antiviral activity whereas G. max had little effect in inhibiting HSV and ADV infections. The saponins of G. max are found to inhibit the replication of HSV, human cytomegalovirus, influenza virus and HIV type-1 in vitro. A. hypogaea was shown to inhibit HSV-2 infection but not HSV-1 and ADV infections. During our study, there were three extracts that suppressed ADV infection but not HSV infection; these are A. pavonia, D. triforum and P. sativum [25].

Iraqi medicinal plants with antiviral effect:

Ethanol extract from the rhizome of Adiantum capillus-veneris exerted in vitro antiviral activity

against vesicular stomatitis virus. Ethanolic extract of Agrimonia eupatoria was reported to be active against Columbia SK virus. The inhibitory activity of an aqueous extract of the aerial parts (stems and leaves) of Agrimonia eupatoria against HBsAg release against hepatitis B virus (HBV) was investigated. Three neolignan glycosides extracted from the ethanolic extract of the root bark of Ailanthus altissima exhibited moderate in vitro inhibitory effect on tobacco mosaic virus replication whereas the methanolic stem bark extract of Ailanthus altissima showed potent anti-HIV activity. Extracts of Cordia myxa were tested for their anti–HIV–1 activity using the syncytia formation assay. All the extracts showed a weak anti–HIV–1 activity. The essential oils of Cuminum cyminum showed antiviral activities against herpes simplex virus 1 (HSV-1). Anti-influenza viral activities of quince fruits phenolic extract was studied. Quince phenolics showed anti-influenza viral activity on the hemagglutination inhibition test. Clerodendrum inerme showed antiviral activity against Hepatitis B virus with ED50 value of 16 mg/ml. A novel 10 kDa protein with anti-HIV-1 reverse transcriptase (RT) inhibitory activity was isolated from leaves of Canna indica L. Aqueous, ethanol and methanolic extracts of Caesalpinia crista showed complete inhibition of paramyxovirus and highly significant inhibitory activity of orthomyxovirus. Glycyrrhiza glabra extracts and glycyrrhizic acid inhibited the replication of several viruses included Epstein-Barr virus, Herpes simplex virus, Hepatitis A virus, Hepatitis B virus, Hepatitis C virus, Human cytomegalovirus, Human immunodeficiency virus, Influenza virus, SARS coronavirus and Varicella zoster virus. Esculetin (6,7-dihydroxycoumarin) isolated from dried stem bark from mature trees of Fraxinus ornus, and its diacetate exhibited a marked inhibitory effect on Newcastle disease virus replication. Gossypol has been reported to possess antiviral properties against enveloped viruses, including HIV-1, HSV-2, influenza, and parainfluenza [26].

In vitro antiviral activity of Brazilian Cerrado plant extracts against animal and human herpesviruses:

The Brazilian savanna known as "Cerrado" is very rich in medicinal plants that are used by the local population for treatment of several illnesses. The results showed that all plant extracts: Banisteriopsis variabilis, Byrsonima intermedia, Campomanesia xanthocarpa, Erythroxilum deciduum, Lacistema hasslerianum, Ocotea pulchella, Stryphodendron adstringens and Xylopia aromatica presented antiviral activity against at least one herpesvirus. Furthermore, it was observed a direct anti-herpes effect of extracts from B. variabilis and B. intermedia in non-toxic concentrations against all herpesviruses [27].

Investigations on the antiviral activities of medicinal plants of TOGO:

Studies were done on the antiviral activities of 10 species of Togolese medicinal plants, previously shown to possess activity against herpes simplex virus (HSV) shown in Table 1. The dominant activity in all cases was virucidal (direct inactivation of virus particles), although Adansonia digitata extracts also appeared to have intracellular antiviral activities as well, which could indicate the presence of multiple antiviral compounds, or a single compound with multiple actions [28].

In Vitro studies of some medicinal plants extracts for antiviral activity against Rotavirus:

In this study, we investigated in vitro antiviral activity of aqueous extracts of some medicinal plants including, garlic bulbs (Allium Sativum), ginger rhizomes (Zingiber officinale), pomegranate peel (Punica granatum) and Lemongrass leaves (Cymbopogon citratus) against rotavirus. The results showed (Figure 1) that the dilutions of crude extracts of Allium sativum gave mean inhibition percentage for rotavirus of 73.33% while Zingiber officinale gave 68.33%, Cymbopogon citrates gave 67.33% and Punica granatum gave 65% inhibited. All plants extract showed antiviral activities but statistically no significant differences of antiviral activity were found among these plant extracts. These findings suggested that the anti-rotaviral activity might be owing to the presence of various compounds such as flavonoids, terpenes, polyphenolic derivatives and other compounds that have been documented to possess antiviral properties [29]

Antiviral activity of some Indian traditional medicinal herbs:

The focus of the present review is particularly on Indian medicinal herbs and plants used to treat viral diseases, which are cheap and easily accessible since viral infections can be one of the biggest nightmares for Medical Practitioners and patients. List of Some Selected Medicinal Herbs under screening for Anti-viral properties based on Traditional Knowledge Documentation shown on Table 2. [30].

Antiviral activity of different medicinal plants against Newcastle Disease Virus:

Newcastle Disease (ND) is a highly contagious viral disease that has a tremendous negative impact on the poultry industry worldwide. Plant extracts were prepared from five different medicinal plants and applied against Newcastle Disease Virus (NDV) to evaluate the antiviral replication in Specific Pathogen-Free (SPF) chicken embryos. Some plant extracts showed a complete inhibition of NDV evidenced by the absence of embryo deaths, the absence of HA titer and viral RNA in the allantoic fluid. These plant extracts were from Moringa peregrina (leaves), Acacia cyanophylla (leaves), Eucalyptus camaldulensis (fruits) and Pistacia atlantica (leaves and stems). Other plant extracts showed partial inhibition of NDV, such as Ceratonia siliqua (leaves) and Eucalyptus camaldulensis (leaves) [31].

Novel antiviral agents: a medicinal plant perspective

In view of the signification number of plant extracts that have yielded positive results it seems reasonable to conclude that there are probably numerous kinds of antiviral agents in these materials. Further characterization of the active ingredients will reveal useful compounds. Some of these compounds belong to a wide range of different structural classes, e.g. coumarins, flavonoids, tannins, alkaloids, lignans, terpenes, naphtho- and anthraquinones, polysaccharides, proteins and peptides. Others may turn out to be identical to, or structurally related to, the antivirals, which are illustrated in Table 1. There may also be novel phytochemicals. Although large numbers of new compounds have been isolated from medicinal plants only some have been marketed as pharmaceutical products. Some compounds have been or are undergoing various phases of clinical trials [32]. Table 3. Showed the summary of the mechanism of the most active antiviral compound from numerous medicinal plants.

Antiviral activity of some Nigerian medicinal plant extracts:

This study examined plant extracts of Nigerian medicinal plants species, used by the Hausa and other tribes of Northern Nigeria, for symptoms possibly indicative of viral illness were found to have antiviral activity. Some of the traditional medicinal uses recorded for the plant species which these extract were derived from are given in Table 4. Given the pressing need for new antiviral agents and the inherent limitations of in vitro antiviral testing for such agents, the results of this screening were promising. It is possible that the elucidation of the active constituents in these plants may provide useful leads in the development of antiviral therapeutics [33].

Conclusion

The results of the present investigation provide further evidence of the importance of ethnopharmacology as a guide to the screening for biologically active plant material. Altogether, the evidence presented in this work supports the notion that medicinal plants have promising therapeutic potential, especially in the case of herb products against viral infections. Further research on the mechanisms by which phytochemicals exhibit their antiviral effect will allow the developing of successful target-specific drug delivery systems. Considering vast range and complexity of bioactive molecules or phytochemicals present in plants, a strong unrelenting and persistent approach is needed to explore unknown phytoconstituents with potent antiviral activities.

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Table 1. Summary of species with antiviral activity

Plant tested	Minimum Antiviral Activity (g/ml)		
	Herpes simplex	Sindbis	Polio
Asteraceae *Conyza aegyptiaca* (L.) Aiton	500	250	500
Bombacaceae (root-bark) *Adansonia digitata L*	125	250	250
(leaves)	<62.5	250	-
Commelinaceae *Palisota hirsuta* (Thunb.) K. Schum.	<62.5	500	250
Davalliaceae *Davallia chaerophylloides* (Poir.) Steud.	500	-	-
Malvacae *Sida acuta* Burm. f.	250	-	-
Moraceae *Ficus ovata* Vahl	125	-	250
Rubiaceae *Mitracarpus villosus* (Sw.) DC.	125	-	500
Rutaceae *Zanthoxylum zanthoxyloides* (Lam.) Zepernick & Timler	500	-	-
Simarubaceae *Harrisonia abyssinica* Oliv	250	-	-
Sapindaceae *Paullinia pinnata* L	125	-	-

- , no detectable activity at 500 g/ml

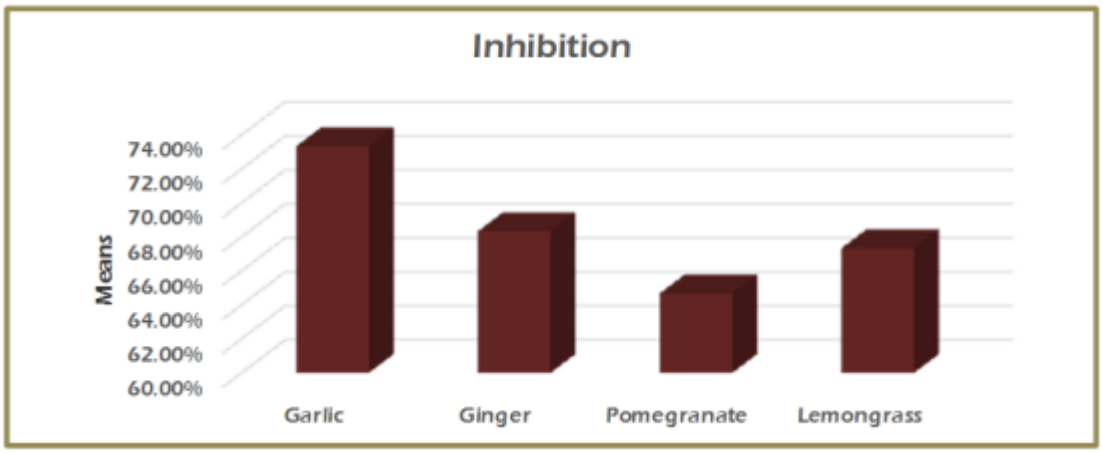

Figure 1. Means inhibitory effect of the studied plant extracts on rotavirus SA-11 on MA-104 cell line

Table 2. List of Some Selected Indian Medicinal Herbs traditionally used for Anti-viral properties

Sl. No.	Common name	Local name	Botanical name	Family name	Parts use	Medicinal use(s)
1	Onion	Lehsan	*Allium sativa*	Liliacea	Bulb	Measles, poliomyelitis, herpes
2	Aloe vera	Kumari, Ghirita	*Aloebarbadensis*	Liliacea	Flowers	Influenza
3	Devil tree	Vishagni	*Alstonia venenata*	Apocyanaceae	Roots	Measles
4	Joseph's coat;	Bhaji	*Amaranthus tricolor*	Amaranthaceae	Leaf	Human tumors caused by viruses
5	Custerd apple	Sarifa	*Annona reticulata*	Annonaceae	Leaf	Influenza, Measeles
6	Andamanesee bowstring plant	Indian - Mallow	*Anodendron paniculatum*	Apocyanaceae	Leaf	Hepatitis
7	Margosa	Neem	*Azadirachta indica*	Meliaceae	Seed,leaf	Herpes, Measeles, chicken pox
8	Indian pennywort	Brahmi	*Bacopa monnieri*	Scrophulariaceae	Leaf,seed	Herpes, HIV
9	Butterfly tree	Kaniar	*Bauhinia purpurea*	Caeselpiniacece	Leaf,Aerial part	Herpes
10	Asiatic penn-ywort, gotukola	Jal Brahmi,	*Centella asiatica*	Apiaceae	Root	Herpes, influenza
11	Nettle-leaved goosefoot	Bathua	*Chenopodium murale*	Chenopodiaceae	Whole plant	Herpes, Hepatitis
12	Henna plant	Mehendi	*Lawsonia inermis*	Lythraceae	Leaf	Poliomylitis, Measles
13	Ginger	Adrak	*Zinger officinale*	Zingiberaceae	Rhizome	Poliomylitis, Measles
14	Mango	Aam	*Magnifera indica*	Anacardaceae	Stem bark	Jaundice
15	Bamboo	Bash	*Banbusa vulgaris*	Poaceae	Leaf	Measles
16	Bitterguard	Karela	*Momordica charantia*	Curbitaceae	Whole plant	Jaundice, Yellow fever
17	Maize	Makai	*Zea mays*	Poaceae	Flower	Chickenpox
18	Tobacco	Tambaku	*Nicotiana tabacum*	Solanaceae	Leaf	Poliomylitis
19	Heliotrope	Siriyari	*Helitropium indiucm*	Boraginuceae	Leaf	Measles
20	Guava	Amrud	*Psidium guajava*	Myrtaceae	Stem bark	Jaundice
21	Korina, frake	Limba	*Terminalia superb*	Cobretaceae	Stem bark	Yellow fever

Table 3. Summary of the mechanism of the most active antiviral compound from medicinal plants

Class of compound	Mechanism virus target	Example of plant source
Furyl compounds: furocoumarins and furanochromones	DNA and RNA genomes. Interactions required long-wave ultraviolet (UVA, 300–400 nm)	Rutaceae and Umbelliferae (Apiaceae)
Alkaloids constitute: b-carbolines, furanoquinolines, camptothecin, atropine, caffeine, indolizidines swainsonine, castanospermine, colchicines, vinblastine	DNA and other polynucleotides and virions proteins. In some interactions are enhanced by UVA	Rutaceae, *Camptotheca acuminate*, *Atropa belladona* (L.), *Swainsona canescens*, *Astragalus lentiginosus*, *Castanospermum australe*, *Aglaia roxburghiana*
Polyacetylenes (polyines)	Membrane interaction. Phototoxic activity frequently requires UVA	Asteraceae, Apiaceae, *Campanulaceae Panax* ginseng (Korean ginseng roots), *Bidens sp*., *Chrysanthemum sibiricum*
Polysaccharides	Blocking virus binding	*Achyrocline flaccida*, *Bostrychia montagnei*, *Cedrela tubiflora*, *Prunella vulgaris*, *Sclerotium glucanicum*, *Stevia rebaudiana*, Rhizophora mucronat
Thiophenes	Membrane interaction. Phototoxic activity frequently requires UVA	Aspilia, *Chenactis douglasii*, *Dyssodia anthemidifolia*, *Eclipta alba*, *Eriophyllum lanatum*
Flavonoids: amentoflavone, theaflavin, iridoids, phenylpropanoid glycosides, agathisflavone, robustaflavone, rhusflavanone, succedaneflavanone, chrysosplenol C, morin, coumarins, galangin (3,5,7-trihydroxyflavone), baicalin	Blocking RNA synthesis. Exhibited HIV-inhibitory activity	*Agastache rugosa*, *Euphorbia grantii*, *Barleria prionitis*, *Calophyllum cerasiferum*, *Cal. inophyllum*, *Cal. teysmannii*, *Camellia sinensis*, *Garcinia multiflora*, *Helichrysum aureonitens*, *Maclura cochinchinensis*, *Markhamia lutea*, *Monotes africanus*, *Pterocaulon sphacelatum*, *Rhus succedanea*, *Scutellaria baicalensis*, *Selaginella sinensis*, *Sophora moorcroftiana*, *Sophora tomentosa*, *Tephrosi sp*

Terpenoids: sesquiterpene, triterpenoids (moronic acid, ursolic acid, maslinic acid and saponin)	**Membrane-mediated mechanisms. Inhibition of viral DNA synthesis**	***Acokanthera sp., Anagallis arvensis* (Primulaceae), *Cannabis sativa, Geum japonicum, Glycyrrhiza glabra, Glycyrrhiza radix, Glyptopetalum sclerocarpum, Gymnema sylvestre, Maesa lanceolata, Olea europa, Quillaja saponaria, Rhus javanica, Strophanthus gratus***
Lignans Podophyllotoxin and related lignans (cyclolignanolides), such as the peltatins Dibenzocyclooctadiene lignans such as schizarin B and taiwanschirin D	Blocking virus replication Blocking HBV replication	*Amanoa aff.* Oblongifolia, *Juniperus communis*, *Justicia procumbens*, *Podophyllum peltatum* *Kadsura matsudai*
Miscellaneous phenolic compounds anthraquinone chrysophanic acid, caffic acid, eugeniin, hypericin, tannins (condensed polymers), proanthocyanidins, salicylates and quinines (naphthoquinones, naphthoquinones and anthraquinones in particular aloe emodin)	Inhibition of viral RNA and DNA replication	*Aloe barbadensis*, *Aster scaber*, *Cassia angustifolia*, Dianella longifolia, *Euodia roxburghiana*, *Geum japonicum*. *Hamamelis virginiana*, *Hypericum sp.*, *Melissa officinalis*, *Phyllanthus myrtifolius*, *Phyllanthus urinaria*, *Punica granatum*, *Rhamnus frangula*, *Rhamnus purshianus*, *Rheum officinale*, *Rhinacanthus nasutus*, *Shepherdia argentea*, *Syzgium aromatica*, St. John's wort.

Table 4. Antiviral action, cytotoxicity and effective concentration of some medicinal plant extracts from Nigeria

Plant species	Cytotoxicity (mg/100 ml)	Viruses							Dilution factor
		Poliovirus	Astrovirus	HSV 1	Equine HSV	Bovine parvovirus	Canine parvovirus	Effective Concentration (mg/ml)	
Anogeissus schimperi	NT	++++	++++	++	++	-	-	2	2
Bauhinia thonningii	NT	++++	++++	++++	+++	+++	+++	1	3
Anacardium occidentale	NT	++++	++++	++++	++++	++++	++++	1	3
Butyrospermum parkii	200	++	++	-	-	-	-	1	2
Boswelia dalzielii	NT	++++	++++	++	++	+++	+++	1	3
Dichrostachys glomerata	NT	++++	++++	++++	++++	+++	+++	1	3
Ziziphus mucronata	400	+++	+++	-	-	-	-	2	3
Detarium senegalensis	400	+++	+++	+++	++	++	++	2	2
Lannea humilis	100	++	++	+	+	-	-	1	3
Sterculia setigera	NT	++++	++++	++++	++++	++++	++++	1	3

++++, Total inhibition; +++, 75% inhibition; ++, 50% inhibition, +, B50% inhibition; –, no inhibition; NT, not cytotoxic at 400 mg/100 ml