

An Overview of Antiviral Activity of some Medicinal plants of Africa

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Abstract

Owing to numerous problems of controlling viral diseases many African medicinal plants have been screened for their antiviral activity. A review of studies on this shows that 58 plant species had in-vitro antiviral properties against viruses belonging to the families Herpesviridae (20), Flaviviridae (15), Retroviridae (11), Picornaviridae (8), Hepadnaviridae (2) and Paramyxoviridae (2). Some phytochemical compounds isolated from six of the 58 plants showed significant antiviral activity against herpes simplex virus types 1 and 2, coxsackie B type 1, poliovirus type 1, yellow fever virus, dengue virus and human immunodeficiency virus type 1. Further work on the compounds is required for drug development and more plants should be screened for activity not only against members of the Hepadnaviridae and Paramyxoviridae, but including the currently ravaging Ebola virus.

Keywords: Antiviral activity; Medicinal plants; Africa

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Introduction

In spite of the increasing scourge of viral infections the world over, attempts at providing antiviral agents to effectively control them appear to be highly challenging. The difficulty in controlling viral diseases is attributable to the distinct nature and characteristics of the micro-organisms. Viruses obligately depend on their host; hence the antiviral agent must deal with the virus without being inimical to the host. This is compounded by the fact that viruses are functionally and physically integrated into the host cells during replication, hence it is extremely difficult to distinguish special biochemical features suitable for selective attack. Another problem is that certain viruses persist as latent infections and occurring in cryptic form with intermittent flare-ups of clinical diseases [1]. As reported by De Clercq [2] there has been an increasing search for new compounds with antiviral properties owing to the limitations of available antiviral drugs in solving the problem of viral resistance. Therefore the use of plant extracts and phytochemicals as potential sources of antivirals continues to receive the attention of workers [3].

In Africa where some viruses unabatedly cause severe epidemics, workers have drawn attention on the need to screen plants for their antiviral activity. Bessong and Obi [4] published mini-review of South African medicinal plants used in HIV/AIDS management and attempts made to isolate and characterize putative anti HIV-molecules. Omilabu [5] provided a list of plants used ethnomedicinally in the treatment

of viral infections across southwestern Nigeria and highlighted the need to explore the antiviral properties of African medicinal plants. Abonyi et al. [6] writing on plants as sources of antiviral agents included the targets for antiviral activity. In addition they gave a cursory review of some antiviral compounds from higher plants, algae and lichens. Although all of the foregoing publications underscored the importance of antiviral plants, the research efforts of other workers on African plants, which are scattered in the literature were not included in their reviews. This paper provides a detailed compilation of antiviral activity of screened medicinal plants of Africa.

Herpesviridae

There are 8 herpesvirus types that infect humans: herpes simplex viruses 1 and 2, varicella-zoster virus, Epstein-Barr virus, human cytomegalovirus, human herpes virus 6, human herpes virus 7, and Kaposi's sarcoma-associated herpes virus [7]. They are characterized by their ability to establish lifelong persistent infections in their hosts and undergo periodic reactivation causing health problems. Herpes simplex virus 1 and 2 are particularly common with the highest incidence of HSV-1 infection occurring among children 6months -3 years of age. By adulthood, up to 90% of the population has antibodies to HSV-1 while HSV-2 is one of the most prevalent sexually transmitted infections worldwide [8,9].

Kambizi [10] evaluated the antiviral activity of *Aloe ferox* and *Withania somnifera* aqueous extracts on HSV-1 in vitro. The extracts showed detectable activity at 1000µg/ml concentration against the virus in monolayers of Vero cell cultures while aloin components of *A. ferox* showed significant activity at 62µg/ml. Using the aqueous extract of *Helichrysum aureonitens*, [11] reported significant antiviral activity against HSV-1 in human lung fibroblasts in vitro at 1.35µg/ml. Thereafter, they isolated galangin (3, 5, 7-trihydroxy-flavone) as the major antimicrobial compound present in *H. aureonitens* extract. Galangin was later reported [12] to show antiviral activity against HSV-1 at 12 to 47µg/ml concentrations while a comparative assay with kaempferol and quercetin on HSV-1 in

vero cells, showed galangin as the most active [13]. All the foregoing studies were carried out in South Africa.

In Rwanda Central Africa, [14] screened 100 ethnomedicinal plants for antimicrobial properties. They reported that antiviral activity against HSV-1 was promising for eight plant extracts. These were *Clerodendron myricoides*, *Crassocephalum multicorymbosum*, *Dryopteris inequalis* (a fern) *Erythrina abyssinica*, *Glycine javanica*, *Markhamia lutea*, *Rhus vulgaris* and *Euphorbia hirta*. Using vero cells, [15] reported that out of the 19 medicinal plants of Togo, (West Africa) tested ten showed significant activity against HSV. Further studies on the ten plants by [15] showed that the dominant activity in all cases was virucidal. Additionally, the workers reported that the anti-HSV activity of seven most active extracts was enhanced by light especially the ultraviolet (UV) rays. *Adansonia digitata* leaf and root extracts were the most potent of these photosensitizers. Other plants tested were *Conyza aegyptiaca*, *Palisota hirsute*, *Davallia chaerophrioides*, *Sida acuta*, *Ficus ovata*, *Mitracarpus villosus*, *Zanthoxylum zanthoxyloides*, *Harrinsonia abyssinica* and *Paullinia pinnata*.

Picornaviridae

This family includes two major groups of human pathogens: enteroviruses and rhinoviruses. Enteroviruses affecting man include the polioviruses (1-3), coxsackie viruses (CVA1 to 24, CVB1 to 6). Human diseases caused by picornaviruses range from severe paralysis to aseptic meningitis, myocarditis and severe generalized diseases of infants. Hudson [15] reported that methanol extracts of *Adansonia digitata*, *Palisota hirsuta* and *Ficus ovata* showed significant antiviral activity against polio virus. The activity of two polysaccharides isolated from the leaves of *Azadirachta indica*, and their sulfated derivatives, against poliovirus (PV-1) was evaluated by Faccin-Galhardi [16]. They observed that the polysaccharides inhibited the initial stage of viral replication. Also the original polysaccharides had better virucidal effect than their sulfated derivatives at all tested concentrations. According to Sairam [17], a spermicidal fraction of neem (*Azadirachta indica*) oil inhibited the replication of polio virus appreciably. Parida [18] assessed four medicinal

plants for their in vitro potential to inhibit polio virus type 3 (PV-3) replication using vero cells. Ethanolic and aqueous extracts of *Ocimum sanctum* leaves inhibited replication of the virus at 99.9% and 99.68% respectively. Aqueous extract of *Azadirachta indica* and *Allium sativum* as well as ethanolic extract of *Zingiber officinale* did not show significant inhibition of PV-3 replication.

Coxsackieviruses

Vesicular pharyngitis, hand-foot-mouth disease and acute hemorrhagic conjunctivitis are caused by coxsackievirus group A. Myocarditis, pericarditis and severe generalized disease of infants are caused by some group B coxsackie viruses; which are also the most commonly identified agent of viral heart disease in humans [19]. The antiviral and virucidal effect of methanolic extract fraction (NCL-11) of *Azadirachta indica* leaves against coxsackie B group of viruses was tested by Badam [20]. NCL-11 inhibited plaque formation in six antigenic types of coxsackie virus B in vitro at 1000mg/ml concentration after 96 hours. The authors were of the view that NLC-11 was most effective against the virus as a virucidal agent apart from being inhibitory at the early stage of its replicative cycle. Galangin (3, 5, 7 – trihydroxy flavones) the major antimicrobial compound isolated from the aerial parts of *Helichrysum aureonitens* showed significant activity against coxsackie B type 1 (CVB1) at concentrations 12-47µg/ml. [17].

Flaviviridae

The family Flaviviridae has four genera [21]

1. Flavivirus e.g. Yellow fever virus, West Nile virus and Dengue fever virus,
2. Hepacivirus e.g. Hepatitis C virus, and GB virus B
3. Pegivirus e.g. GB virus A, GB virus C and GB virus D
4. Pestivirus e.g. bovine viral diarrhea virus, hog cholera, and classical swine fever.

Members of the family constitute a major cause of disease worldwide. Infection with Hepacivirus frequently cause chronic

liver infection which can lead to scarring of the liver and ultimately to cirrhosis generally apparent after many years [21]. Although most members of the Flaviviridae are transmitted by blood-sucking arthropods, Hepatitis C has no known vector [1].

From Nigeria [22] reported that water leaf extract of *Gossypium hirsutum* inhibited the replication of yellow fever virus (YFV) at a minimum concentration of 0.079mg/ml. That YFV was inhibited at a minimum concentration of 250µg/ml by ethanol extract of *Aframomum melegueta* seeds was also reported by [23]. In another study, Fasola [24] reported that water extract of *Enantia chlorantha* stem bark showed significant antiviral activity against YFV inhibiting the viruses at MICs of 0.025mg/ml when the extract ceased to be cytotoxic to the vero cell line. Vlietinck [14] had reported that the extracts of *Aframomum melegueta* and *Bambusa vulgaris* showed activity against yellow fever virus. Ono [25] demonstrated the antiviral property of sulphated galactomannans extracted from the seeds of two common African plants; *Mimosa scabrella* and *Leucaena leucocephala* against yellow fever virus (Be HIII strain) and dengue virus type 1 (DEN-1).

Dengue fever virus

Although aqueous crude extract of *Azadirachta indica* and its pure compound, azadirachtin were tested in vitro and in vivo, [26] observed that only the aqueous extract showed activity against dengue virus type-2 replication. In vitro antiviral activity of the aqueous extract assessed in C6/36 cloned cells of *Aedes albopictus* larvae showed inhibition in dose dependent manner. Also the maximum non-toxic concentrations of 120-130mg/ml completely inhibited 100-10,000 TCID₅₀ of virus. A confirmation of this finding was the absence of dengue related clinical symptoms in suckling mice and absence of virus specific 511 bp amplicon in RT-PCR.

Hepatitis C virus

Hussein [27] screened 152 methanol and water extracts of parts of 71 medicinal plants of Sudan for their in vitro inhibiting effects on hepatitis C virus (HCV) protease (PR). Thirty-four extracts showed more than 60% inhibition at 1000µg/ml. Of

these, methanol extracts *Acacia nilotica*, *Boswellia carterii*, *Embelia schimperi*, *Quercus infectoria*, *Trachyspermum ammi* and water extracts of *Piper cubeba*, *Q. infectoria* and *Syzygium aromaticum* showed at least 90% inhibition at 100µg/ml.

Retroviridae

Human immunodeficiency virus (HIV), the etiologic agent of acquired immunodeficiency syndrome (AIDS) is a retrovirus and a member of the genus *Lentivirus*. Lentiviruses are non-oncogenic, may be cytotoxic and infect cells of the immune system. Once infected by HIV individuals remain infected for life and if left untreated within a decade, opportunistic infections develop [1]. Globally about 35.3 million people were living with HIV at the end of 2012. Although the burden of the epidemic continues to vary considerably between countries and regions, the sub-Saharan Africa remains most severely affected, accounting for 71% of the global total.

Some medicinal plants of Ethiopia were screened for antiviral activity against HIV-1 and HIV-2 by [28]. They found that the highest selective inhibition of HIV-1 replication was with the acetone leaf extract of *Combretum paniculatum* and methanol leaf extract of *Dodonea angustifolia* which showed selectivity indices of 6.4 and 4.9 respectively. Ali et al. [29] in an evaluation of some medicinal plants of Sudan reported that the leaf extracts of *Combretum hartmannianum* totally inhibited the HIV-1 reverse transcriptase (HIV-IRT) at a concentration of 66µg/ml. Testing the inhibitory properties of some South African plants [30] reported that methanol extract of *Terminalia sericea* leaves strongly inhibited the polymerase (IC₅₀ = 7.3µg/ml) and the ribonuclease N (IC₅₀ = 8.1µg/ml) activities of HIV-1 reverse transcriptase. Another study [4] revealed that out of six South African plants screened, the n-butanol fraction of the methanol root extract of *Bridelia micrantha* was the most active, inhibiting RNA-dependent – DNA polymerization (RDDP) activity of HIV-IRT with an IC₅₀ of 7.3µg/ml. Out of nine plants screened, [31] reported that the strongest inhibition against RNA-dependent-DNA polymerase (RDDP) activity of reverse transcriptase was observed with the methanol stem bark extract of *Peltophorum africanum* (IC₅₀ 3.5µg/ml). Also

methanol root extract of *Combretum molle* was the most inhibitory of the ribonuclease H activity (IC₅₀ 9.7µg/ml).

In another study Magadula and Tewtrakul [32] targeted one of the enzymes, HIV-1 protease (HIV-1 PR) responsible for processing viral proteins into functional enzymes and structural proteins. This was based on the finding of [33] that HIV-1 PR plays a key role in the maturity and infectivity of the virus. Eighteen ethanol extracts from species of *Garcinia* collected in Tanzania were tested for their HIV-1 protease inhibitor properties. Of these, the fruit hulls of *Garcinia semseii* showed the most potent inhibitory activity (IC₅₀ 5.7µg/ml). Also the stem bark extracts of *Garcinia edulis* and *G. kingaensis* had inhibition with IC₅₀ values of 9.2 and 15.2µg/ml respectively. The water and alcohol extracts of *Phyllanthus amarus* blocked HIV-1 attachment and the HIV-1 enzymes, (integrase, reverse transcriptase and protease) to different degrees [34]. In the study, a gallotannin containing fraction and isolated ellagitannins (geraniin and corilagin) were the most potent mediators of the antiviral activities. As a proof of in vivo activity, HIV replication was reduced by more than 30% when plant material was administered orally to volunteers.

Hepadnaviridae

The family includes a group of viruses having DNA polymerase with reverse transcriptase activity. A member of this family, Hepatitis B virus (HBV) causes chronic liver disease which may progress to cirrhosis and eventually hepatocellular carcinoma [35, 36] showed that aqueous extract of *Phyllanthus niruri* inhibited endogenous DNA polymerase of hepatitis B virus (HBV) and bound to the surface antigen of HBV in vitro. Yeh [37] suggested that the aqueous extract of *Phyllanthus amarus* may be helpful in the treatment of hepatitis B virus infection, having inhibited cellular proliferation and suppressed HBsAg gene expression in human hepatoma cell line (HepA2).

Paramyxoviridae

A number of important human diseases are caused by paramyxoviruses. These include mumps and measles which caused 745,000 deaths in 2001 and respiratory syncytial virus

(RSV) which is the major cause of bronchitis and pneumonia in infants and children. The parainfluenza viruses are the second most common causes of respiratory tract disease in infants and children. They can cause pneumonia, bronchitis and croup in children and the elderly. From Nigeria, [23] reported that ethanol leaf extracts of *Bambusa vulgaris* showed antiviral activity by inhibiting measles virus at MIC of 62.5µg/ml while *Aframomum melegueta* inhibited measles virus at MIC of 125µg/ml.

Conclusion

This review shows that an appreciable number of African medicinal plants have antiviral properties. Most of the plants reported had activity against viruses of the Herpesviridae and Flaviviridae families followed by the Retroviridae and Picornaviridae. As the Hepadnaviridae and Paramyxoviridae had the least numbers of plants, more plants are to be screened for activity against notable viruses in these families. Although crude extracts were used in all of the investigations reported, some phytochemical compounds of six plant species were isolated and found to show antiviral activity. Taking cognizance of the increasing scourge of viral infections in Africa more studies are required with a view to harnessing the potentials of African medicinal plants for development of new antiviral agents.

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