



ALTERNATIVE MEDICINES FOR THE MANAGEMENT OF AIDS FROM NATURE A REVIEW

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ABSTRACT

The acquired immunodeficiency syndrome (AIDS) is caused by human immunodeficiency virus (HIV) infection which leads to severe suppression of immune functions where CD4+ cell count falls below 200 cells/ μ l. AIDS is a real threat to the health of mankind and the search for effective therapies is still of great importance. Antiretroviral therapy for the treatment of AIDS is costly and many limitations are associated with antiretroviral therapy. Hence, herbal medicines are frequently used as alternate medicines by individuals living with HIV. Numerous plant-derived compounds have been evaluated for inhibitory effects on HIV replication and many have been found to inhibit different steps in HIV replication cycle. The aim of this review is to give an idea for herbal medicines which are used to inhibit HIV.

Keywords: AIDS, Antiretroviral therapy, Alternative medicine, HIV.

INTRODUCTION

AIDS is one of the most dangerous and a pandemic [1] disease which is present over a large demographic area of the world. It has a great impact on society such as an illness, a source of discrimination [2] and economic condition of people. AIDS is the most serious infectious disease and actively spreading worldwide among humankind. Women living in lower income countries are particularly at risk as extreme poverty [3] and other structural factors such as gender inequities, lack of education and violence reduce their ability to control health outcomes or access HIV-related information and services. Human immunodeficiency virus infection/acquired immune deficiency syndrome (HIV/AIDS) is a disease of the human immune system [4] caused by infection with human immune deficiency virus. AIDS is called when a person infected with HIV has a CD4+ count of less than 200 cells/ μ L. Prevention of HIV infection primarily through safe sex, male circumcision [5], use of diaphragms [6], substance abuse treatment, condom [7] use, use needle exchange [8] programs are key strategies to control the spread of disease and may lead to a near-normal life expectancy. AIDS therapy may require the use of a combination of agents that exhibit synergistic antiviral [9] effects to prevent the emergence of drug-resistant HIV mutants. The combination of three or more drugs reduces the viral load to undetectable levels and results in the prolonged survival of treated patients. A phytotherapeutic approach [10] to modern drug development can provide many valuable drugs from traditional medicinal plants. A large number of plant-derived substances [11] have been described that exhibit anti-HIV activity, e.g. alkaloids, polysaccharides, lignans, flavonoids, coumarins, and terpenes. There is a need for the discovery of novel therapeutic strategies. One of the strategies has been to identify anti-HIV compounds from natural sources, particularly from plants [12]. Traditional medicine has served as a source of alternative medicine, new pharmaceuticals and healthcare products. Herbal medicines provide rational means for the treatment of many diseases that are obstinate and incurable in other systems of medicine. These are gaining popularity because of several advantages such as often fewer side effects, better patient tolerance, relatively less expensive and acceptance due to a long history of use. Medicinal effects of plants tend to normalize physiological function and correct the underlying cause of the disorder. Plants are often less prone to the emergence of drug resistance. Due to all these advantages, plants continue to be a major source of new lead compounds. A large number of active agents is available for the symptomatic treatment of STDs and

AIDS. The emergence of drug resistant strains and dose-limiting toxic effects has complicated the treatment of these infectious diseases. Extracts of plants and phytochemicals have been shown to possess activity against sexually transmitted pathogens and may be a good source of new active agents [13]. The present review gives an idea about alternative medicine of AIDS.

Acquired immunodeficiency syndrome (AIDS)

AIDS is a clinical syndrome resulting from infection with HIV that causes profound immune suppression. It is a complex multifactorial disease associated with immunodeficiency and autoimmune inflammation. HIV produces gradual effects on the body's defense mechanisms thereby leading to cancers and opportunistic infections [14] involving multiple systems of the body such as immune, gastrointestinal, genitourinary, endocrine, dermatologic and nervous systems. Symptoms [15] associated with AIDS include persistent fever, night sweat, weight loss (wasting syndrome), headache, lymphadenopathy, skin rashes, short term memory loss, cough, shortness of breath, seizure, painful swallowing, vision loss, fatigue, diarrhea, thrush, recurrence of varicella zoster virus infection, kaposi's sarcoma, pneumocystis carinii pneumonia, cryptococcal meningitis, candida esophagitis, toxoplasma encephalitis and disseminated atypical mycobacterial infection. HIV is transmitted by sexual contact [16,17], Parenteral transmission [18], Vertical transmission [19,20], exposure to infected body fluids or tissues and from mother to child during pregnancy.

TM/CAM

The World Health Organization defines traditional medicine (TM) as diverse health practices, approaches, knowledge and beliefs incorporating plant, animal and mineral based medicines, spiritual therapies, manual techniques and exercises applied singularly or in combination to maintain well-being as well as to treat diagnose or prevent illness. TM is a comprehensive term that refers to forms of medicine long established in a country whether developed or developing. Health care practices that are not part of country's own tradition and that are not well established within the country's conventional health care system are often referred to as complementary and alternative medicine (CAM). Alternative medicine exists in all cultures to some degree and terms such as traditional medicine, indigenous medicine or folk medicine etc. are used to describe such practices. These medicines date back hundred or even thousands of years depending on the country and culture concerned. Because two-thirds of the world's

population (mainly in the developing countries) relies entirely on such traditional medical therapies, the World Health Organization has declared its intention actively to encourage traditional medicine worldwide to fulfill their various goals.

TM/CAM therapies are considered medication based if they use herbal medicines, animal parts, minerals or homeopathic remedies. Herbal medicines include herbs, herbal materials, herbal preparations and finished herbal products that contain therapeutic active ingredients that are plant based. Hence, CAM [21] is defined as a group of diverse medical and health care systems, practices and products that are not generally considered part of conventional medicine for example acupuncture herbal medicine, osteopathy, homeopathy, massage etc. There are more than 100 systems of alternative medicines still in practice all over the world. Every country, region or area has its own traditional system of health and medical care such as for the Chinese it is acupuncture; for the French magnetic healing; for the Germans Heilpraxis; for the English - Herbalism, for India - Ayurveda; for the Muslim countries - Unani; for the southern part of the country - Siddha; for Japan - shiatsu etc. The most popular forms of alternative medicine are Ayurveda, Homoeopathy, Unani, Siddha, Naturopathy, Yoga therapy, Acupuncture, Acupressure, Magneto therapy, Shiatsu, Herbalism, Meditation, Aromatherapy, Bach Flower Remedies, Gem therapy, Chromotherapy, Hydropathy, Diet Therapy and Reiki. People living with HIV/AIDS (PLWHA) often choose complementary and alternative medicine (CAM) to complement or replace conventional treatment. TM/CAM usage is widespread. For example according to WHO up to 80% of people in Africa and Asia use TM as part of their primary health care, in China traditional herbs make up 30 to 50% of total medicine consumption and 90% of Germans, 70% Canadians and 50% of Swedes have used a natural remedy at some time [22].

Alternative medicines for AIDS

By taking good diet and micronutrient supplements patient has improved health condition. There are some advantages of vitamin A supplementation in children that reduces mortality and improves growth. There is an improvement of a health condition to lactating mothers when a multivitamin supplement [23] is given. Evidence for supplementation with selenium is mixed with some tentative evidence of benefit. Dietary intake of micronutrients at RDA levels by HIV-infected adults is recommended by the World Health Organization. The WHO further states that several studies indicate that supplementation of vitamin A, zinc, and iron can produce adverse effects in HIV positive adults. There is insufficient evidence to recommend or support the use of medical cannabis to try to increase appetite or weight gain.

Herbal medicines provide rational means for the treatment of many diseases that are obstinate and incurable in other systems of medicine. These are gaining popularity because of several advantages such as often fewer side effects, better patient tolerance, relatively less expensive and acceptance due to a long history of use. Medicinal effects of plants tend to normalize physiological function and correct the underlying cause of the disorder. Medicinal plants [24] are renewable in nature, unlike the synthetic drugs that are obtained from non-renewable sources of basic raw materials such as fossil sources and petrochemicals. Cultivation and processing of plants often are environment-friendly unlike the pollution by chemical industry. Cultivation of medicinal plants can also be a source of income for poor families. Many of the medicinal plants are locally available, especially in developing and underdeveloped countries. Also, plants are often less prone to the emergence of drug resistance. Due to all these advantages, plants continue to be a major source of new lead compounds [25]. Herbal compounds are used for the treatment of HIV/AIDS which are given below. Some plant species which are used for AIDS are represented in Table 1.

Table 1: Plant species used to treat and manage AIDS [26-28]

| Species name | Family | Growth habit | Part(s) used | Pharmacological activity |
|------------------------------------|------------------|--------------|---------------------|---|
| <i>Allium sativum</i> L. | Amaryllidaceae | Herb | Bulb | HIV-1 reverse transcriptase[29] |
| <i>Mangifera indica</i> L. | Anacardiaceae | Tree | Bark/leaves | Inhibits HSV-1 and 2 replication[30] |
| <i>Artemisia annua</i> L. | Asteraceae | Shrub | Leaves | Anti-HIV activity[31] |
| <i>Raphanus sativus</i> L. | Brassicaceae | Herb | Leaves | Anti viral activity[32] |
| <i>Carica papaya</i> L. | Caricaceae | Tree | Leaves/roots/seeds | Anti HIV-1 activity[33] |
| <i>Cleome gynandra</i> L. | Cleomaceae | Herb | Leaves | Anti-HIV activity[34] |
| <i>Cucurbita maxima</i> L. | Cucurbitaceae | Climber | Leaves | Anti-HIV activity[35] |
| <i>Euphorbia tirucalli</i> L. | Euphorbiaceae | Shrub | Leaves | Anti-HIV activity[36] |
| <i>Dichrostachys cinerea</i> L. | Fabaceae | Shrub | Leaves | Inhibits HIV-1 reverse transcriptase[37] |
| <i>Ocimum basilicum</i> L. | Lamiaceae | Herb | Leaves | Inhibits HIV-1 reverse transcriptase[38] |
| <i>Azadirachta indica</i> A. | Meliaceae | Tree | Leaves | Inhibits HIV-1 replication and protease[39] |
| <i>Moringa oleifera</i> Lam. | Moringaceae | Shrub | Leaves/seeds | Anti HIV activity[40] |
| <i>Eucalyptus globules</i> Labil. | Myrtaceae | Tree | Leaves | Anti HSV-1 and 2 activity[41] |
| <i>Ximenea Americana</i> L. | Oleaceae | Shrub | Bark/root | Inhibits HIV-1 replication[42] |
| <i>Passiflora edulis</i> Sims | Passifloraceae | Climber | Leaves | Anti HSV-1 activity[43] |
| <i>Citrus lemon</i> L. | Rutaceae | Tree | Leaves/roots/fruits | Anti HIV-1 activity[44] |
| <i>Solanum americanum</i> L. | Solanaceae | Shrub | Leaves | Anti viral activity[45] |
| <i>Aloe vera</i> L. | Xanthorrhoeaceae | Herb | Leaf sap/leaves | Anti HSV-2 activity[46] |
| <i>Bulbine alooides</i> L. Wild | Xanthorrhoeaceae | Herb | Leaves/roots | Anti-HIV activity[37] |
| <i>Zingiber officinalis</i> L. | Zingiberaceae | Herb | Bulb | Anti HIV-1 activity[47] |
| <i>Momordica foetida</i> Schumach | Cucurbitaceae | Herb | Leaves | Anti HIV activity[48] |
| <i>Euphorbia hirta</i> L. | Euphorbiaceae | Herb | Leaves/roots | Inhibits HIV-1,2 reverse transcriptase[49] |
| <i>Jatropha curcas</i> L. | Euphorbiaceae | Shrub | Leaves | Anti HIV activity[24] |
| <i>Ricinus communis</i> L. | Euphorbiaceae | Shrub | Roots | Inhibits HIV-1 reverse transcriptase[50] |
| <i>Abrus precatorius</i> L. | Fabaceae | Climber | Bark/leaves/roots | Inhibits HIV-1 reverse transcriptase[51] |
| <i>Albizia amara</i> | Fabaceae | Tree | Leaves | Inhibits HIV-1 reverse transcriptase[52] |
| <i>Cajanus cajan</i> | Fabaceae | Herb | Stem | Antiviral activity[53] |
| <i>Erythrina abyssinica</i> DC | Fabaceae | Tree | Bark/root | Inhibits HIV-1 replication[39] |
| <i>Peltophorum africanum</i> Sond | Fabaceae | Tree | Bark/root | Inhibits HIV-1 reverse transcriptase[50] |
| <i>Ptilostigma thonningii</i> | Fabaceae | Tree | Bark/root | Anti HIV, HSV-1 and 2 activity[54] |
| <i>Bridelia micrantha</i> | Phyllanthaceae | Tree | Bark/root | Inhibits HIV-1 reverse transcriptase[50] |
| <i>Flueggea virosa</i> | Phyllanthaceae | Shrub | Leaves/roots | Inhibits HIV-1 reverse transcriptase[55] |
| <i>Phyllanthus reticulatus</i> | Phyllanthaceae | Shrub | Leaves | Inhibits HIV-1 reverse transcriptase[56] |
| <i>Securidaca longipedunculata</i> | Polygalaceae | Tree | Bark/leaves | Inhibits HIV-1 replication[57] |
| <i>Rumex nepalensis</i> | Polygonaceae | Herb | leaves | Anti HIV activity[58] |
| <i>Kigelia africana</i> | Bignoneae | Tree | Bark/fruit | Inhibits HIV-1 reverse transcriptase[39] |
| <i>Garcinia livingstonei</i> | Clusiaceae | Tree | Bark/roots | HIV-1 protease inhibitory activity [59] |
| <i>Garcinia buchananii</i> Bak. | Clusiaceae | Tree | Bark/roots | HIV-1 protease inhibitory activity [59] |

| | | | | |
|--|--------------|------|-------------------|---|
| <i>Olea europaea</i> L. | Oleaceae | Tree | Bulb | Anti-HIV activity[60] |
| <i>Areca catechu</i> Linn. | Palmae | Tree | Seed | HIV-1 protease inhibitory activity [61] |
| <i>Syzygium guineense</i> (Willd) | Myrtaceae | Tree | Bark | Inhibits HIV-1 reverse transcriptase[62] |
| <i>Combretum hartmannianum</i> Schweinf. | Combretaceae | Tree | Bark/leaves/ stem | Inhibits HIV-1 reverse transcriptase [63] |

Anti-HIV agents of natural origin

Drugs affecting adsorption and penetration

Many natural products have been used which inhibit binding of the virus between glycoprotein of virus coat and CD4 receptor. Hence, reduce the activity of the virus.

Phenolic compounds [64]

Detarium microcarpum Guill and Perr.(Caesalpinaceae) contains flavonoid,epicatechin-3-O- gallate which blocks the binding of gp-120 to CD4.It is very common to other tannins and also inhibits reverse transcriptase.

Polysaccharides

Heparin, carrageenan, dextran sulphate and compounds of sulphated polysaccharides obtained from species of algae (Gigartaceae and Solieriaceae) inhibit HIV replication by blocking the absorption of virus particles to the cell.Several sulphated polysaccharides obtained from seaweeds like *Nothogenia fastigiata*,*Aghardiella tenra* inhibit virus adsorption process[65].

Glycoalkaloids

Glycoalkaloids bind between CD4 and gp-120 hence interfere in the synthesis of glycoproteins [66].*Castanospermine* is an indolizidine alkaloid found in *Castanospermum australe* A.(Fabaceae) which inhibits α glucosidase. *Castanospermine* acts synergistically with zidovudine against HIV-1 and HIV-2.

Pseudomonas exotoxin

Isolation of hybrid protein consisting of human recombinant CD4 combined with toxins such as *pseudomonas* exotoxin [67] produces anti-HIV agents as a result of interaction between CD4 and gp-120.

Protein

Cynovirin N, a protein from cyanobacteria (blue-green algae) irreversibly inactivates HIV and aborts cell to cell fusion and transmission of HIV.

Drugs affecting reverse transcription and integration

Many flavonoids [64] such as amento flavones,quercetin and scutellarin have shown to inhibit reverse transcriptase of some RNA tumour viruses as well as HIV.Digallic acid is a potent inhibitor of HIV reverse transcriptase which affects DNA polymerase. A macrocyclic ellagitannin such as oenothin B isolated from *Oenothera erythrosepala* (Onagraceae) inhibits both viral absorption and reverse transcription.Lignanoides obtained from *Ipomoea cairica* (Convolvulaceae) namely arctigenin and trachelogenin were identified as important inhibitors of HIV replication. Calanolide A is a coumarin derivative isolated from a tropical tree *Calophyllum lanigerum* (Clusiaceae) and inhibits HIV-1 reverse transcriptase. Among other natural substances anti-HIV activity include psychtrine,phloroglucinol derivatives,calanolides,curcumin,dicaffeoyl quinic acid,dicaffeoyl artartaric acid and L chicoric acid. A Chinese herbal medicine *Scutellaria baicalensis* (Lamiaceae) and its isolated compounds baicalein and baicalin inhibit replication of HIV.

Drugs affecting transcription and replication

Papaverine [68] an alkaloid obtained from poppy *Papaver somniferum* (Papaveraceae) inhibits HIV replication.Oleanolic acid has anti HIV activity which is obtained from many plants such as *Rosa woodsii*,*Prosopis glandulosa*, *Phoradendron juniperinum*, *Syzygium claviflorum*, *Hyptis capitata* and *Ternstroemia*

gymnanthera.Epigallocatechin,theasinensin D, and 8 C ascorbyl are most potent inhibitors of HIV replication which is obtained from tea.

Drugs affecting post translational modifications

A complex ester namely Didemnaketal of *Didenum* species possess some HIV protease inhibiting property, but its potential is limited due to low potency and instability.

Drugs affecting viral assembly and viral release

The mannose specific lectins from plants e.g. *Galanthus*,*Hippeastrum*,*Narcissus*,*Epipactis helleborine*(Orchidaceae) and *Listera ovate*(Orchidaceae) and N acetyl glucosamine from *Urtica dioica* (Urticaceae) can be targeted to inhibit virus cell fusion process.Two aromatic polycyclic diones hypericin and pseudohypericin found in plants of family Hypericaceae have potent anti retroviral activity[69].

CONCLUSION

CAM is still often used to address these complex health and social issues associated with living with HIV/AIDS including stress reduction, relieving side-effects and symptoms, and boosting the immune system. It is important that conventional clinicians are aware of CAM use and where appropriate discuss its use with their patients both to improve the practitioner-patient relationship and adherence to ART and to identify potential safety issues. Practitioners therefore need to have up-to-date knowledge regarding CAM use. The plant species have the potential to be developed as anti-HIV agents. While there are still gaps in the phyto chemistry and pharmacological studies conducted so far which need to be bridged in order to exploit the full medicinal potential of these species. It is still very clear that these plant species have tremendous potential for the future. This inventory will assist future workers on the selection of herbal plants to evaluate for phytochemical safety and pharmaceutical efficacy. There is also need for more research on the active compounds of these herbal medicines, some of which have pharmacological activities. Herbal medicines can be developed as a safe, effective and economical alternative to drugs presently approved for symptomatic treatment of AIDS.

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