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Review Article

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How Herbal Drugs Works as an Adjuvant Therapy in HIV Related Opportunistic Infections-A Review on Previous Reviews of Litterateur and Researches

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Abstract

Herbal medicine use is becoming very popular in many countries especially in the western world, where public health safety has become a concern, especially its concomitant use with orthodox medicine. The devastating impact of HIV/AIDS pandemic coupled with the severe shortage of health personnel has compelled patients to develop coping mechanisms by adopting alternative sources of primary health care, one of which has been the use of herbal therapies. An integration of herbal medicine into the current medical curriculum will enable future physicians to communicate better with their patients on this evolving healthcare system. The aim of this paper is to stimulate public health concern among physician who are sometimes uncertain about the safety of herbs especially when used concomitantly with regular orthodox (ART) medications. This review briefly examines the role of herbal medicine as a second line of treatment and management in HIV/AIDS. It is hoped that this review will provide important and relevant information that will help policy makers to put in place control measures against the abuse of herbal therapy.

Keywords: ART; Herbal medicine; HIV; Opportunistic infections; TIMH

Objective

The purpose of this review was to survey and assess the quantity and quality of published, English-language literature on botanicals or herbal medicines for HIV/AIDS treatment and care. Met analysis was neither intended nor possible due to the diversity of herbal practices, therapies, and outcome measures in the extant literature. Quality scoring, such as assigning Jadad scores, was not performed, since this was intended to be a descriptive review.To identify studies on HIV/AIDS and TIMH, MEDLINE, Embassy, BIOSIS, NCBI, CINAHL, clinical trials.gov, or Ayurvedaor unani or siddha or naturopathy or homeopathy or yoga, and some African and middle east studies have been taken into account and catalog were searched using the following keyword (use of herbal medicines) in HIV/AIDS. Most of the articles were extracted from research gate after full request for the article download from the authors. Only studies in English were reviewed. Bibliographies of review and other relevant articles were searched for relevant Indian literature, as well as a bibliography of Indian medicine and unani system of medicine and several easily accessible Indian journals.

Study collection or picking up of material

We examined studies focused on the impact of herbal drugs on HIV/AIDS *in vivo*, *in vitro* and in clinical studies. Studies that met the following inclusion criteria: English language, peer-reviewed literature, published after the first case reported of HIV in the world. Randomized controlled trials, experimental studies,

observational studies, descriptive studies, and reviews of HIV and TIMH were included, while ethnographic literature was excluded. Two reviewers independently screened the titles and abstracts of all of the literature collected through the searches. If both reviewers agreed that the abstract was relevant, the full article was accessed and a second phase of screening was conducted. All studies passing these screening phases were included in the full descriptive review. The majority of articles were excluded because they were not based on actual research studies and were not in English only few of those were relevant and met the inclusion criteria described above.

Introduction

About the use of traditional medicine

HIV/AIDS pandemic is currently the most socio-economic challenge that is facing the world at large as it affects mostly the young and economically productive population. A study has shown that majority of people living with HIV/AIDS are susceptible to fungal and bacterial opportunistic infections that result from immunosuppression and treatment of such infections is therefore one of the areas that traditional health services for the control of the disease is prevalent. The World Health Organization (WHO) estimates that 4 billion people (80% of the World's population) use herbal medicines for some aspect of primary healthcare [1-7]. Traditional herbal use has been reported to be common among individuals with moderate and advanced HIV disease [8]. In Africa, traditional herbal medicines are often used as primary treatment for HIV/ AIDS and for HIV-related problems including dermatological disorders, nausea, depression, insomnia and weakness [9]. The use of traditional herbal medicine by AIDS patients after HIV diagnosis was noted in a study in Uganda. Despite a paucity of evidence on effectiveness and the possibility of serious side effects, some African ministries of health currently promote traditional medicines for the treatment of HIV and associated symptoms. In the case of South Africa, the Ministry of Health is actively promoting the use of traditional medicines with antiretroviral treatments [10]. Two principal African herbal compounds used for HIV/AIDS treatment in sub-Saharan Africa include *Hypoxishemerocallidea* (African potato-an immune stimulant) and *Sutherlandia*. These two herbal remedies are currently recommended by the South African Ministry of Health for HIV management.It is found promoting the use of traditional medicines with antiretroviral treatments [10]. Two principal African herbal compounds used for HIV/AIDS treatment in sub-Saharan Africa include *Hypoxishemerocallidea* (African potato-an immune stimulant) and *Sutherlandia*. These two herbal remedies are currently recommended by the South African Ministry of Health for HIV management.

Traditional medicine as a complementary health care to modern medicine in HIV+

There are some challenges to collaboration between traditional herbal medicine and orthodox medicine especially in the developing countries mainly due to shortage of mutual trust and appreciation between the two health system, limited availability of training in basic preventive medicine, palliative care for traditional herbal healer, lack of meaningful referral between conventional health providers and traditional herbal healers, exclusion of traditional healing methods from the training curricula of doctors and traditional healers fear of losing their treatments secrets to scientists and researchers . A patient's level of knowledge about HIV disease, a belief that ART is effective and prolongs life and recognition that poor adherence may result in viral resistance and treatment failure all impact negatively upon a patient's ability to adhere. Beliefs about the medications (including traditional) themselves also play a role in adherence. Patients who report low confidence in the efficacy of the medications and perceive minimal benefits resulting from ART are less likely to be adherent. It is estimated from other studies that at least 30% of patients on ART will use any form of traditional complementary and alternative medicine. Because the exact level of risk and/or benefits resulting from traditional herbal medicine-antiretroviral-drug co-therapy amongst AIDS 7 patients are largely unknown, the concerns raised about herb-ARV drug interactions, communication between patients and physicians about herbal medicine is valuable in enabling physicians to address issues of potential herb-drug interactions and ensuring appropriate medical care [7]. Treatment of diseases using traditional remedies is an age old art which has been confined into the backstage due to access to western biomedicine, adequate education, employment opportunities and economic growthHuman immunodeficiency virus (HIV) is the virus that causes AIDS. When a person becomes infected with HIV, the virus attacks and weakens the immune system. As the immune system weakens, the person is at risk of getting life-threatening infections and cancers. When that happens, the illness is called AIDS. Once a person has the virus, it stays inside the body [2]. The genetic material of the AIDS virus, or HIV-1, is formed by ribonucleic acid (RNA), and encodes several proteins that allow it to penetrate the human cells and reproduce within them [1]. HIV infection is required to develop AIDS, the actual definition of AIDS is the development of a low CD_4 cell count (<200 cells/mm^3) or any one of a long list of complications of HIV infection ranging from a variety of so-called "opportunistic infections," cancers, neurologic symptoms, and wasting syndromes [3]. Many people have no symptoms when they are first infected with HIV. Acute HIV infection progresses over a few weeks to months to become an asymptomatic HIV infection (no symptoms). This stage can last 10 years or longer. During this period, the person might have no reason to suspect they have HIV, but they can spread the virus to others. If they are not treated, almost all people infected with HIV will develop AIDS. Some people develop AIDS within a few years of infection. Others remain completely healthy after 10 or even 20 years. People with AIDS have had their immune system damaged by HIV. They are at very high risk of getting infections that are uncommon in people with a healthy immune system. These infections are called opportunistic infections. These can be caused by bacteria, viruses, fungi, or protozoa, and can affect any part of the body. People with AIDS are also at higher risk for certain

cancers, especially lymphomas and a skin cancer called Kaposi sarcoma. Symptoms depend on the particular infection and which part of the body is infected. Lung infections are common in AIDS and usually cause cough, fever, and shortness of breath. Intestinal infections are also common and can cause diarrhoea, abdominal pain, vomiting, or swallowing problems. Weight loss, fever, sweats, rashes, and swollen lymph glands are common in people with HIV infection and AIDS [2].

Life expectancy with the classical treatment

More people than ever are living with HIV, largely due to greater access to treatment (UNAIDS, 2011). The classical treatment with ARTs has been effective in prolonging the lives of HIV-positive patients who would have eventually progressed to stages III and IV of AIDS. However, the drugs do not cure the infection; they only apprehend the progression of the condition. These drugs are also potentially toxic and have significant adverse side effects which can result in lack of adherence. An alteration of blood drug levels and/or development of drug-resistant strains of the virus are therefore highly possible, thus undermining effective treatment and posing public health risks and challenges. These have made it necessary and essential to investigating all alternatives to formal HIV/AIDS treatment [11].

Use of Traditional medicines to manage opportunistic infections

It has been estimated from various studies that at least 30% of PLWA on ARTs utilize any form of TM and colleagues assessed the use of TCAM by 618 HIV patients in three public hospitals in KwaZulu-Natal, South Africa and found that 51.3% relied on traditional therapies. In Kabarole District, Western Uganda, Langlois- observed among 137 AIDS patients, that 63.7% had used TM after diagnosis to manage the opportunistic infections and to boost the immune system. Herbal medicines and pharmaceutical drugs use was reported by 32.8% of AIDS patients studied 44 individuals with moderate or advanced HIV disease attending a workplace clinic providing ARTs in South Africa. They observed that 32% were using TM, most frequently African potato and aloe vera. According to 7.7% among HIV-infected patients on ARTs in Pretoria, South Africa, used traditional health care based on a self-reported survey on use of TCAM and over-the-counter medicines by HIV patientsinterviewed 388 HIV-patients in a study of impact of herbal drug use on adverse drug reaction profiles of patients on ARTs in Zimbabwe and found that 98.2% of participants were using at least one herbal drug together with ARTs. Two indigenous herbs, *Musakavakadzi* and *Peltoforumafricanum* were identified to reduce the occurrence of adverse drug events. Further, ARTs recipients have been reported to use herbs to alleviate some of the negative side effects of ART drugs such as nausea and diarrhea found that 44.3% of PLWA sample reported mixed use of marijuana for therapeutic and recreational purposes [11,12].

Concomitant herbal preparations use with ART

Herbal preparations are commonly used by HIV/AIDS on ARV. So long as they are safe and effective, herbal preparations may be considered more advantageous for developing countries as they are relatively cost-effective, more accessible and widely accepted by local populations. Evaluation of traditional healers' role in the management of HIV is need and should be considered with urgency. Mechanisms that will enable the THs to be part of ARTs programmers and administration ought to be explored. However, concomitant herbal medicines use with ARTs may have the potential for drug interactions and should be discussed routinely in ARTs counseling sessions. An evaluation of the potentials of traditional remedies to interact with ARTs may be helpful in improving the clinical outcome of HIV patients. The clinical staff involved in ART dispensary and delivery need to inquire ardently about natural products that patient may use outside the regimen of ARTs, either self-administrated or obtained from TH. Further research option is suggested to investigate efficacy and safety of use of traditional therapies by PLWA and the pharmacological interactions between ARTs and herbal preparations. The need to identifying the potential risks, benefits, and interaction or non-interaction associated with concomitant ARTs and herbal preparations use is also recommended. In British Columbia, found among HIV patients that major reasons for TCAM use were to improve energy level, to supplement dietary intake and to enhance immune response. A survey found in USA that the most common treated conditions by traditional, complementary and alternative medicines were anxiety and or fear, depression, pain and neuropathy. Contrary to our results, other studies report that TM is used to alleviate some of the negative side effects of ARV drugs including nausea/ vomiting, anemia, dizziness, insomnia, pain, skin rash, weight loss, diarrhea and higher degrees of suffering. Only a few (3.0%) of the participants believed that they could cure HIV with TM. This is not different from reports of previous surveys. Found that 4.1% of 618 HIV infected South Africans claimed that TCAM could cure HIV. A study reported in Canada that 9% of study participants believed that it was possible to cure HIV solely with the use of TCAM [11].

Natural coumarins which are endowed with the ability to inhibit HIV

alternative approaches, including herbal therapies, long-term screening of plant extracts, particularly anti-infective or immune modulating medicinal herbs, and structural modifications of lead compounds, have been attempted. A number of articles discussing anti-HIV activity of herbs [13,14] suggest a variety of chemically disparate molecules, produced by plant species show similar effect. The replicative cycle of HIV is comprised of several steps that may be targets for chemotherapy. These steps are: (1) Viral adsorption to the cell membrane; (2) Fusion between the viral envelope and cell membrane, (3) Uncoating of viral nucleocapsid, (4) Reverse transcription of viral RNA to proviral DNA, (5) Integration of proviral DNA to the host cell genome, (6) DNA replication, (7) Transcription of proviral DNA to RNA, (8) Translation of viral mRNA, (9) Maturation of the viral precursor proteins by proteolysis, myristoylation, and glycosylation and (10)

Assembly, budding and release of newly formed virions. Step 4 -a key and unique one in replication of retroviruses is catalysed by the virion enzyme reverse transcriptase (RT). Another target of research is step 9, particularly blocking the HIV protease (PR). Therefore, the majority of chemotherapeutic strategies focus on the development of retroviral enzyme inhibitors. Various coumarins have been shown to inhibit, in cell culture, one or more retroviral enzymes. (+)-Calanolide A, (+)- [10R, 11S, 12S]-10,11-trans-dihydro-12-hydroxy-6,6,10,11- tetramethyl-4-propyl-2H,6H-benzo[1,2- b:3,4-b':5,6 b"]tripyran-2-one, is a novel nonnucleoside RT inhibitor (NNRTI) with potent activity against HIV-115,16,17. The compound was first isolated from a tropical tree (Calophyllumlanigerum) in Malaysia17 potent activity against HIV-115,16,17. The compound was first isolated from a tropical tree (Calophyllumlanigerum) in Malaysia. Previous *in vitro* studies have demonstrated the protective activity of (+)-calanolide A to established cell lines and primary human cells against a wide variety of HIV-1 isolates. Hizi A. et al18. studying the effect of calanolide A on HIV replication, has found that the compound specifically inhibited DNA polymerase activity of HIV-1 RT but had no effect on RNase H activity. Calanolides A and B were found protective against HIV-1 replication and cytopathicity, but were inactive against HIV-2. Calanolide A was active against a number of HIV-1 resistant strains emerging after nucleoside and non-nucleoside RT inhibitors. Soulattrolide, a coumarins isolated from Calophyllumteysman- nii latex, was found a potent inhibitor of HIV-1 RT, Chinese herbal medicines and subsequent structural modification of discovered leads could provide new, effective, and less toxic drug candidates. Two series of compounds demonstrated anti-HIV effect: the triterpene derivatives DSB and DSD, developed from betulinic acid, isolated from Syzigiumclaviflorum and the coumarin derivative DCK, developed from suksdorfin. As already mentioned, the pyranocoumarinsuksdorfin [(3'*R*,4'*R*)-3'-acetoxy-4'-(isovaleryloxy)- 3',4'-dihydroseselin] inhibited HIV replication.

Study conducted to screen medicinal plants for their anti HIV activity19

Tuberaria lignose

Family: Cistaceae, Parts used: Aerial parts. Study: has reported that extracts of *Tuberarialignosa* exhibits anti-HIV activity in an *in vitro* MTT assay. The compound isolated was ellagitannin enriched fraction that was isolated first time in this plant. And he reported that ellgitannin is HIV-1 reverse transcriptase inhibitor. This ellagitannin enriched fraction showed anti-HIV activity in MT-2 infected cells

Calendula officinalis

Family: *Asteraceae,* Parts used: Flowers and leaves. Study: A study conducted in 1978 indicated that chloroform extract of *Calendula officinalis* has HIV replication inhibitory activity in acutely infected lymphocytic MOLT-4 cells *in vitro*with IC50 of 0.4mg/ml and they have reported the anti-HIV activity of extracts from *Calendula officinalis* flowers. Extract was tested for its efficacy to inhibit replication of human immunodeficiency virus type 1 (HIV-1). Organic and aqueous extract was used for study. Both were non-toxic to human lymphocytic Molt-4 cells. Potent antiviral activity was exhibited by organic extract in an *in vitro* MTT/tetrazolium-based assay. This study indicated that organic extract from *Calendula officinalis* flowers has anti-HIV-1 reverse transcription (RT) activity.

Palicourea condensate

Family: Rubiaceae, Part used: Leaves. Study: has reported a novel anti-HIV activity. It was found that it is able to inhibit the *in vitro* cytopathic effects of HIV-1RF infection of CEM-SS cells. Although the mechanism of action is not yet understood, however, the plausibly suggesting reverse transcriptase as a potential mechanism of action.

Kadsuralancilimba

Family: Schizandraceae, Parts used: Stems and roots. Root and stem of this plant is used to treat HIV and other associate disorders. Lancilactone C and related triterpenes are found in *Kadsuralancilimba*. Lancilactone inhibited replication of HIV.

Symplocossetchuenensis

Family: Symplocaceae, Parts used: Bark. Study: has reported the anti-AIDS agents, anti-HIV activity of harman, an anti-HIV principle from *Symplocossetchuensis* and its derivatives. A study conducted byIshida *et al* (2001)., *Symplocossetchuensis* has two compounds named Matairesinol (1) and harman (5). These compounds were found active against replication of HIV in H9 lymphocyte cell.

Control over the disease after being used with herbal therapies28

Studies in South Africa have shown that herbal remedies are good supplements to antiretroviral therapy because of their immune boosting properties [15-20]. A study in western Uganda found that 38% of HIV positive patients used traditional medicines and antiretroviral drugs at the same time for the management of HIV infection [21], and the major reasons for use of traditional medicines were perceived additional efficacy, improvement in quality of life, and a feeling of control over the disease. The most commonly used herbal remedies in Southern Africa are *Hypoxishemerocallidea* (common name: African potato), and *Sutherlandia* [21]. many studies have identified adverse events associated with use of herbal remedies. In Sweden, the most common adverse reactions attributed to use of complementary medicines were skin rashes (urticaria, exanthema, and dermatitis) [22]. The most common complementary medicines associated with these adverse events were coneflower, gingko leaf, and Siberian ginseng [22]. Other studies have shown that garlic can cause allergic reactions such as contact dermatitis, and generalized urticuria. Garlic also has the potential to induce cytochrome P450 enzymes and consequently reduce the effectiveness of ARVs [23].

In a clinical study, garlic was shown to reduce pharmacokinetic concentrations of Saquinavir in plasma [24].

Quality of life in patients taking herbal remedies with ARV28

One of the major goals of antiretroviral therapy is to improve QOL among HIV-infected individuals, in part by reducing the incidence of opportunistic infections and delaying progression to AIDS. Some studies suggest that the use of complementary and alternative medicines (CAMs) is one way that persons living with HIV/AIDS can feel they are in control of their lives and illness. Therefore, patients can feel confident about their livelihood and wellbeing [25]. In Thailand, use of herbal medicines by HIV positive patients was associated with better mental health outcomes [26]. Some studies have shown that patients use herbal remedies because of the personal knowledge that such alternatives are available [27-29]. A research article entitled as the impact of herbal remedies on adverse effects and quality of life in HIV-infected individuals on antiretroviral therapy published in The Journal of Infection in Developing Countries. February 2011 have had quested for the adverseoutcomes of herbal remedies collateral with ARV. The data which we have assessed shows

Development of rash and abdominal pain were the most common adverse events experienced by patients taking herbal remedies together with antiretroviral drugs. This is consistent with other studies which have shown that some herbal remedies cause certain types of skin rashes when used alone [22,23] and our study shows that these skin rashes become more prominent among individuals taking antiretroviral drugs and herbal remedies at the same time. Patients reported experiencing peripheral neuropathy with Concomitant use of herbal remedies and ARV. Abdominal pain and rash were the only adverse events significantly associated with herbal drug use during antiretroviral therapy. Other adverse events assessed in the study did not have a significant association with use of herbal remedies during antiretroviral therapy. *Moringaoleifera* has been identified as an offending agent responsible for abdominal pains found *moringa* to have significant inhibitory effects on CYP3A4, which results in the elevation of plasma levels of drugs metabolized by this pathway. Nevirapine and Efavirenz are both metabolized via the cytochrome P450 enzyme pathway. Thus a potential interaction exists between the NNRTIs with *moringa*. Nevirapine and Efavirenz are both documented as causing abdominal pains (BNF, 2007). There is therefore potential that the abdominal pains may be due to elevated NVP/EFV levels while a patient is on *moringa*. The difference in the ADR profiles in this study is an indicator of potential drug-herb interactions. Herbs contain a mixture of naturally occurring phytochemicals which may be substrates for enzymes or transporters that act on drugs, potentially inhibiting the drugs' metabolism or transportation. These processes can result in altered drug absorption. In Uganda, there are over 1 million people with HIV/AIDS.When advanced, this disease is characterized by life-threatening opportunistic infections.As the formal health sector struggles to confront this epidemic, new medicines from traditional sources are needed to complement control efforts. Many plant species identified in this survey belonged to the families Asteraceae and Euphorbiaceae, which are well recognized for their medicinal value in Uganda. These plants are widely distributed in nature and chances of TMPs experimenting with them are high. The disagreement (or the very low ICF) in plants reported by different TMPs may be explained by the fact that TMPs treated the AIDS conditions and opportunistic infections rather than HIV infection per se. For example, *Mangiferaindica, Erythrinaabyssinica*, W*arburgiasalutaris* and *Eucalyptus sp* which were identified in this survey, are medicinal plants recognized for treatment of coughs and some opportunistic infections in HIV/AIDS present with cough. The underlying cause of the clinical disorders seen in HIV/AIDS patients is the progressive loss of CD_4 positive T-cell lymphocytes in blood. These cells are important because they mediate immune responses and their depletion is associated with opportunistic infections. With increasing access to ARVs in Uganda, an important consideration is the potential for interactions between TM and ARVs when they are administered concurrently. Some classes of ARVs have great potential for unwanted herbal-drug interactions and some African medicinal plants have shown potential forunfavorable drug-herbal interactions with ARVs in laboratory studies [30-32].

Use of natural coumarins in neurocognitive disorders in HIV31

Nature has always been considered a basis for providing resources that can be used to fight off infections and treat diseases. Among these resources there have been findings of medicinal plants that have anti- HIV properties with low levels of toxicity. For the management of HIV/AIDS, in 1989 the World Health Organization (WHO) had declared the necessity to assess ethno medicines and other natural products. Individuals infected with HIV have conditions of fluctuating degrees of impairment of cognition and associated functioning and can develop HIV-associated neurocognitive disorders. Invasion and replication of HIV Fr in the brain parenchyma is accomplished by brain perivascular macrophages, endogenous microglia, and some astrocytes that are infected and can initiate the neuro pathogenesis of HAND. Immune activation of resident glia and neuro inflammation are associated with this infection and neuronal injury.

Ameliorating Effects of *Withaniasomnifera* (Ashwagandha) Root Extract on HIV-Associated Neurocognitive Disorders31

A medicinal plant that has many therapeutic properties such as antioxidant and immunomodulatory properties, memory enhancer, nerve tonic and anti stressis *Withaniasomnifera* (L.) Dunal, also known as 'ashwagandha' (ASH)or 'Indian ginseng' and has had a significanttupsurgein pharmacological studies in the recent years. In cultured neurons and in rodents injected with Aβ 25-35, neurite outgrowth has been induced by withanolides IV and withanolides extracted from the roots. Root extracts from this species have also

been shown to significantly reduce the number of hippocampal degenerating cells in the brains of stressed rodents and were neuro-protective in animal models of Parkinson's disease. Accumulation of oligomers and β-amyloid peptides(Aβ), behavioural deficits and plaque pathology have been up turned in the brains of old and middle-aged APP/PS1 Alzheimer's disease trans genic mice with the oral dispensation of a semi- purified extract of the root of *W. Somnifera* mainly involving withanosides and withanolides.

Nigella sativa concoction induced sero-reversion in HIV patient-32

Nigella sativa had been documented to possess many therapeutic functions in medicine but the least expected issero-reversion in HIV patient which is very rare despite extensive therapy with highly active HAART. This case presentation is to highlight the complete recovery and sero-reversion of adult HIV patient after treatment with nigella sativa concoction. The patient presented to the herbal therapist with history of chronic fever, diarrhoea, weight loss and multiple papular pruritic lesions of 3 months' duration. Examination revealed moderate weight loss, and the laboratory tests of ELISA (Genscreen) and western blot (new blot 1 & 2) confirmed sero-positivity to HIV infection with pre-treatment viral (HIV-RNA) load and CD_4 count of 27,000 copies/ml and CD_4 count of 250 cells/ mm^3 respectively. The patient was commenced on *Nigella sativa* concoction 10mls twice daily for 6 months. He was contacted daily to monitor side-effects and drug efficacy. Fever, diarrhoea and multiple pruritic lesions disappeared on 5^{th}, 7thand 20^{th}day respectively on *Nigella sativa* therapy. The CD_4 count decreased to 160 cells/ mm^3 despite significant reduction in viral load (≤1000 copies/ml) on 30^{th}day on *N. sativa*. Repeated EIA and Western blot tests on 187^{th}day on *Nigella sativa* therapy was sero-negative. The post therapy CD_4 count was 650cells/ mm^3 with undetectable viral (HIV-RNA) load. Several repeats of the HIV tests remained sero-negative, aviraemia and normal CD_4 count since 24 months without herbal therapy. This case report reflects the fact that there are possible therapeutic agents in *Nigella sativa* that may effectively control HIV infection

Conclusion

Nature has always been considered a basis for providing resources that can be used to fight off infections and treat diseases. Among these resources there have been findings of medicinal plants that have anti- HIV properties with low levels of toxicity. For the management of HIV/AIDS, in 1989 the World Health Organization (WHO) had declared the Necessity to assess ethno medicines and other natural products. Medicinal effects of plants incline to stabilize physiological function and fix the fundamental cause of the condition. The many medicinal plants identified in this survey that are used to manage the numerous ailments occurring in HIV/AIDS patients, need to have their value in the therapeutic management of HIV/AIDS-related opportunistic infections investigated. Recently, there has been a sustained bio prospective effort to isolate the active leads from plants and other natural products for treatment of HIV and management of AIDS and also screening of plants based on ethnopharmacological data enhances the ability of discovering novel anti-HIV compounds. Indigenous knowledge of medicinal plants further provides leads toward therapeutic concept, thereby accelerating drug discovery. Thus, it is essential to explore for new antiretroviral agents which can be combined with or substitute the present resource of drugs against HIV. The patient presented to the herbal therapist with history of chronic fever, diarrhoea, weight loss and multiple papular pruritic lesions of 3 months'duration. Examination revealed moderate weight loss, and the laboratory tests of ELISA (Genscreen) and western blot (new blot 1&2) confirmed sero-positivity to HIV infection with pre-treatment viral (HIV-RNA) load and CD_4 count of 27,000 copies/ml and CD_4 count of 250 cells/ mm^3 respectively. The patient was commenced on *Nigella sativa* concoction 10mls twice daily for 6 months. He was contacted daily to monitor side-effects and drug efficacy. Fever, diarrhoea and multiple pruritic lesions disappeared on 5^{th}, $7^{th}$and 20^{th}day respectively on *Nigella sativa* therapy. The CD_4 count decreased to 160 cells/ mm^3 despite significant reduction in viral load (≤1000 copies/ml) on 30^{th}day on *N. sativa*. Repeated EIA and Western blot tests on 187th day on *Nigella sativa* therapy was sero-negative. The post therapy CD_4 count was 650cells/ mm^3 with undetectable viral (HIV-RNA) load. Several repeats of the HIV tests remained sero-negative, aviraemia and normal CD_4 count since 24 months without herbal therapy. This case report reflects the fact that there are possible therapeutic agents in *Nigella sativa* that may effectively control HIV infection and it might be the main goal of unani physicians to carry out effective description of research of this concoction over HIV patients.

References

1. https://www.sciencedaily.com/releases/2013/11/131128103951.htm
2. https://medlineplus.gov/ency/article/000594.htm
3. http://www.medicinenet.com/human_immunodeficiency_virus_hiv/page2.htm
4. http://www.medicinenet.com/human_immunodeficiency_virus_hiv/page3.htm
5. https://aidsinfo.nih.gov/understanding-hiv-aids/fact-sheets/19/73/the-hiv-life-cycle
6. https://www.aids.gov/hiv-aids-basics/just-diagnosed-with-hiv-aids/understand-your-test-results/cd4-count/
7. Orisatoki RO and OguntibejuOO (2010) The role of herbal medicine use in HIV/AIDS treatment, , Archives of clinical microbiology 1: 3-3.
8. Langlois-Klassen D1, Kipp W, Jhangri GS, Rubaale T (2007) Use of traditional herbal medicine by AIDS patients in Kabarole District, Western Uganda. Am J Trop Med and Hyg 77: 757-763
9. Hodgson TA and Rachanis CC (2002) Oral fungal and bacterial infections in HIV-infected individuals: an overview in Africa. J Oral Dis 8: 80-87.
10. Manfredi R andChiodo F (2000) The effects of alternative treatments for HIV disease on recommended pharmacological regimens, Int J Antimicrobial Agents 13: 281-285.

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11. Gyasi RM, Tagoe-Darko E, Mensah CM (2013) Use of Traditional Medicine by HIV/AIDS Patients in Kumasi Metropolis, Ghana: A Cross-sectional Survey by et al, American International Journal of Contemporary Research Pp:3.

12. I. Kostova, Raleva S, Genova P, Argirova R (2014) Recent Advances in the Discovery and Development of Plant-Derived Natural Coumarins and their Analogues as Anti Human Immunodeficiency Virus-Type 1 (HIV-1) Agents, Biotechnology & Biotechnological Equipment 19: 16-22.

13. Lee KH and Morris-Natschke SL (1999) Recent advances in the discovery and development of plant-derived natural products and their analogs as anti-HIV agents. Pure Appl. Chem 71: 1045-1051.

14. Vlietinck AJ, De Bruyne T, Apers S, Pieters LA (1998) Plant-derived leading compounds for chemotherapy of human immunodeficiency virus (HIV) infection. Planta Med 64: 97-109.

15. Kashman Y, Gustafson KR, Fuller RW, Cardellina JH, McMahon JB, et al. (1992) The calanolides, a novel HIV-inhibitory class of coumarin derivatives from the tropical rainforest tree, Calophyllumlanigerum. J. Med. Chem 35: 2735-2743.

16. Terri C, Ruckle JL, Dwain Tolbert D, Giltner J, David A, et al. (2001) Safety and Pharmacokinetics of Single Doses of (+)-Calanolide A, a Novel, Naturally Occurring Nonnucleoside Reverse Transcriptase Inhibitor, in Healthy, Human Immunodeficiency Virus-Negative Human Subjects. Antimicrobial Agents and Chemotherapy 45: 1379-1386.

17. Xu ZQ, Jenta TR, Flavin MT (2000) Calanolides, the naturally occurring anti-HIV agents. CurrOpin Drug DiscovDevel 3: 155-166.

18. Hizi A, Tal R, Shaharabany M, Currens MJ, Boyd MR, et al. (1993) Specific inhibition of the reverse transcriptase of human immunodeficiency virus type 1 and the chimeric enzymes of human immunodeficiency virus type 1 and type 2 by nonnucleoside inhibitors.Antimicrob. Agents Chemother 37: 1037-1042.

19. Daniyal M, Akram M, Hamid A, Nawaz A, Usmanghani K, et al. (2006) Comprehensive review on treatment of HIV.Pak. J. Pharm. Sci 29: 1331-1338.

20. Tshibangu KC, Worku ZB de Jongh MA, van Wyk AE, Mokwena SO, Peranovic V (2004) Assessment ofeffectiveness of traditional herbal medicine in managing HIV/AIDS patients in South Africa. East Afr Med J 81: 499-504.

21. Langlois-Klassen D, Kipp W, Jhangri GS, Rubaale T (2007) Use of traditional herbal medicines by AIDS patients in Kabarole District, Western Uganda. Am J of Trop Med and Hyg 77: 757-763.

22. Jacobsson I, Jonsson AK, Gerden B, Hagg S (2009) Spontaneously reported adverse reactions in association with complementary and alternative medicine substances in Sweden. Pharmacoepidemiol Drug Saf 18: 1039-1047.

23. Borrelli F, Capasso R, Izzo AA (2007) Garlic (*Allium Sativum L*): Adverse effects and drug interactions in humans. MolNutr Food Res 51: 1386-1397.

24. Piscitelli SC, Burstein AH, Welden N, Gallicano KD, Falloon J (2002) The effect of garlic supplements on the pharmacokinetics of Saquinavir. ClinInf Dis 34: 234-238.

25. Foote-Ardah CE (2003) The meaning of complementary and alternative medicine practices among people with HIV in the United States: strategies for managing everyday life. Sociol Heal Ill 25: 481-500.

26. Sugimoto N, Ichikawa M, Siriliang B, Nakahara S, Jimba M, et al. (2005) Herbal medicine use and quality of life among people living with HIV/AIDS in northeastern Thailand. AIDS Care 17: 252-262.

27. Josephs JS, Fleishman JA, Gaist P, Gebo KA (2007) Use of complementary and alternative medicines among a multistate, multisite cohort of people living with HIV/AIDS. HIV Med 8: 300-305.

28. Bepe N, Madanhi N, Mudzviti T, Gavi S, Maponga CC, et al. (2011) The impact of herbal remedies on adverse effects and quality of life in HIV-infected individuals on antiretroviral therapy J Infect Dev Ctries 5: 048-053.

29. Monera TG, Wolfe AR, Maponga CC, Benet LZ, Guglielmo J (2008) *Moringaoleifera*leaf extracts inhibit 6 beta-hydroxylation of testosterone by CYP3A4. J Infect Dev Ctries 2: 379-383.

30. Lamorde M, Tabuti JR, Obua C, Kukunda-Byobona C, Lanyero H, et al. (2010) Medicinal plants used by traditional medicine practitioners for the treatment of HIV/AIDS and related conditions in Uganda.J Ethnopharmacol 130: 43-53.

31. Kurapati KRV, Atluri VS, Samikkannu T, Garcia G, Nair MPN (2015) Natural Products as Anti-HIV Agents and Role in HIV-Associated Neurocognitive Disorders (HAND): A Brief Overview.Front Microbiol 6: 1444.

32. Onifade AA, Jewell AP, Adedeji WA (2013) *Nigella Sativa* Concoction Induced Sustained Seroreversion in HIV Patient. Afr J Tradit Complement Altern Med 10: 332-335.

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