

Ethnopharmacology of Medicinal Plants in Treating HIV-Related Opportunistic Infections

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ABSTRACT

The global burden of HIV-related opportunistic infections (OIs) remains a pressing challenge, particularly in low- and middle-income countries. Despite advancements in antiretroviral therapy, the persistent prevalence of these infections underscores the need for alternative strategies. Ethnopharmacology, the study of traditional medicinal practices and their integration into modern medicine offers promising solutions. This review explores the role of medicinal plants in addressing HIV-related OIs, focusing on their antimicrobial, immune-enhancing, and synergistic effects with antiretrovirals. Key medicinal plants such as *Kalanchoe integra* and *Terminalia sericea* have demonstrated potential in managing conditions like Kaposi's sarcoma, herpes zoster, and bacterial infections. Mechanistic insights reveal the ability of these plants to modulate immune responses, reduce microbial loads, and alleviate inflammation. By integrating ethnopharmacological knowledge with clinical research, this study highlights the potential for cost-effective and sustainable treatment options for HIV-related complications. Future research should prioritize clinical validation and explore synergistic therapies to enhance patient outcomes.

Keywords: HIV-related opportunistic infections, Ethnopharmacology, Medicinal plants, Immune modulation, Antiretroviral synergy, Traditional medicine.

INTRODUCTION

The global prevalence of human immunodeficiency virus (HIV)-related opportunistic infections such as tuberculosis, candidiasis, helminth, and cryptosporidium, among others, and the coinfections between HIV and hepatitis viruses are still increasing, lowering the quality of life, especially in low- and middle-income countries. Therefore, accessing highly active antiretroviral therapy is important to improve and raise the life expectancy of HIV-infected individuals, thus making it possible to live longer with the disease. However, opportunistic infection cases are expanding, filtering, and not decreasing in patients undergoing therapy, as well as in other patients admitted to hospitals. This condition will lead to the emergence of drug resistance that could be responsible for death. These circumstances lead us to revisit past experiences in accessing safe, reliable, and cost-effective medicinal compounds derived from plants to treat the said opportunistic infections and other HIV-related complications [1, 2]. In developing countries, particularly in Africa, Latin America, and Asia, local ethnic communities, deprived societies, and forest dwellers still depend on medicinal plant collections for their primary health coverage. Nevertheless, the interactions between HIV-infected patients and the major medicinal plants are quite appreciable. Ethnopharmacology is a scientific study to determine traditional medical science that applies information derived from traditional knowledge. It is closely related to the investigation of plant extracts and their significant supplementary uses and nutrition. Ethnopharmacological research has grown into an early and effective strategy and an alternative development in studies of scientific medicine plans. The purpose of this review is to evaluate past research while introducing an alternative use of medicinal lead compounds derived from plant extracts that have been used in ethnomedical treatments for the many

cooperative infections seen in HIV/AIDS sufferers. What is also extremely significant is to integrate the binary ethnomedical system in the coming urge to manage these opportunistic infections [3, 4].

HIV-Related Opportunistic Infections: Overview

People with HIV are at higher risk for developing certain opportunistic infections. Preventing these infections is an important part of HIV treatment. Even with the use of powerful antiretroviral drugs to suppress HIV, people with very low CD4 cell counts are at increased risk for these types of diseases because the immune system is unable to control the germs. Opportunistic infections might cause any of the following reactions: shortness of breath, general body weakness, fever and cough, night sweats, swelling of the lymph nodes for more than three months, chills, weight loss, prolonged diarrhea, skin rashes, memory loss, and neurological disorders. Today, many people with HIV live longer, stay healthy, and do not exclusively concentrate on one medication treatment, leading to medical progress in the treatment of HIV and HIV-related diseases. These treatments aim to prevent common infections and cancers and prevent disease progression by delaying CD4 cell count drops, allowing patients to keep higher CD4 cell counts after stopping them. The treatment of many HIV-related diseases has been strengthened with plant-based remedies; for centuries, herbal drugs have cured many diseases in African countries, and many of them are still used today [5, 6].

Ethnopharmacology: Concepts and Practices

Ethnopharmacology can be defined as the scientific study of the traditional use of medicinal plants in different cultures. The term means "people's medicine" and integrates pharmacological research with an anthropological perspective of these cultural insights. Ethnopharmacological studies can reveal new pathways and older cultural remedies, all of which are put into a unified traditional knowledge discourse that provides solid evidence of the medicinal properties of plant-based remedies. Practitioners use this traditional knowledge system to carefully look at the scientific literature and consult with healthcare professionals to correlate symptom and disease states, which guide medicinal protocol. People in all regions of the world have learned to use the remedies from plants growing in their environment. Most of our knowledge has come from information passed down from one generation to the next. This kind of trans-generational information and practice accounts for the broad variety of botanical use around the world by many different indigenous and non-indigenous peoples. Several methods have been developed by scientists to gather and record medicinal plants and traditional uses. Ethnobotanical surveys, ethnopharmacologic studies, and detailed phytochemical analyses are among the methods used. Some researchers take special note of the plant's cultural context, i.e., who the healer is, when and how the healer uses the plant, and so on. The many diverse plant remedies being used around the world fit according to set geography and customs tied to those traditions. This dependence is necessary to allow these plant remedies to show good results in the areas where they are used and is part of the sustainability of this small piece of biodiversity [7, 8].

Medicinal Plants Used in Treating HIV-Related Opportunistic Infections

Available evidence has suggested that medicinal plants are of critical importance in managing and treating HIV-related opportunistic infections. Traditional healers in different African communities have been reported to use various plant species to manage or treat these infections. Some of these plant species have been reported to have several pharmacological activities, including, but not limited to, anti-inflammatory, antiplatelet, and antioxidant activities. Practitioners often combine their phytotherapy, multiple drug therapy, and antiviral drugs. Such pharmacological interactions can result in antagonistic, additive, or synergistic effects. Botanists, taxonomists, ethnopharmacologists, pharmacologists, and phytochemists have collaborated on drug discovery and development programs to identify potential herbal drugs. The model for drug development programs in the pharmaceutical and phytotherapy industry, as well as academic or non-government organizations, often focuses their research primarily on only two phases. In the present overview, emphasis has also been given to the assessment of some challenges regarding the integration of the traditional medicine model into the national health system to provide standard care for patients embracing medicinal plants in treating HIV-related opportunistic infections. This chapter discusses 100 plant species used in the management and treatment of HIV-related opportunistic infections. The paper provides scientific evidence showing the anti-HIV activity of some of these plants [9, 10].

PLANT 1

Botanical Classification The plant is known by the Swahili vernacular name "mkakadange." The genus is of the *Evidiieae* plant family. The plant has spreading roots with small herb-like climbing stems that attach to host trees through tendrils. 4.1.2. **Medicinal Uses** The leaves are collected, chewed and then applied to problem areas of the body. A two-year HIV-infected woman, when asked about the leaf, was

silent and kept waiting for other plants to be instructed to stop. When the interview was over, she begged to have the plant, saying that the leaf would stop the itching on her lower limbs. The respondents believe that the leaf is a good antibiotic and that it heals ulcers on the feet. It is also believed to reduce the viral load when ingested. 4.1.3. Ethnopharmacological Investigation The whole plant was collected, and botanically identified, and the samples were submitted for analysis of their chemical components. Powdered samples were extracted in acetone; the acetone was removed by evaporation at room temperature, and the extract was dried in a desiccator to yield 15% crude acetone extract. At low concentrations, the extract did not inhibit the growth of healthy founder cultures of *E. coli*, *Klebsiella aerogenes*, and *Proteus mirabilis* used for drug sensitivity tests. DMSO was used as a negative control, and gentamicin was used as a positive control [11, 12].

PLANT 2

Kalanchoe integra, also known as Mother of Thousands, is used to treat various illnesses. Ethanolic extract of dried leaves of the plant has been shown to inhibit the growth of Kaposi sarcoma cells at concentrations higher than 100 µg/mL. Chrysoeriol derivatives isolated from the plant have shown antibacterial activity and inhibit various skin inflammations. They are also traditionally used in the Cameroonian traditional system of medicine for their blood system strengthening properties. A study showed the immunomodulatory effects of a flavonoid compound isolated from the leaves on macrophage-driven inflammation. Growth and viability of resting and activated macrophages were monitored with the MTT assay after treatment with different concentrations of the product. The treatment of activated macrophages increased the secretion of IL-1 α by 1.9, TNF- α by 2, and IL-10 by 1.8 times. This compound also significantly increased total cell number and viable cell number in treated mice 24 hours after thioglycollate injection. In comparison with the control group, total and viable cell numbers in the peritoneal cavity were increased by 2.5 to 2.9 and 2.6 to 3.0 times, respectively, at a dose of 1 mg/kg. These results indicate that this flavonoid compound enhances macrophage functions [13, 14].

PLANT 3

Terminalia sericea Burch. ex DC. Family: Combretaceae. Ethnopharmacological relevance: *Terminalia sericea* Burch. ex DC. is used by Bapedi traditional healers to treat herpes zoster. Stem bark powder is mixed with water and administered orally. Materials and methods: In vitro, antiviral bioassay-guided fractionation was performed on crude extracts from *T. sericea* stem bark. The use of resazurin as an indicator of cell viability allowed the non-cytotoxic fraction as well as a non-cytotoxic concentration range to be determined. This enabled the non-cytotoxic main compounds to be characterized by means of out-of-column direct bioassays with cytopathic effect CPE inhibition readings, co-chromatography, and TLC-based bioautography. Results: The dichloromethane: methanol fraction showed low inhibition of herpes simplex virions from day 2 up to day 6 post-infection. Main compounds 1 and 2 showed the least toxicity towards both LLC-MK2 cells and Vero monkey kidney cells. These are designated as candidates for further development as non-toxic pharmaceutical products to address kissing disease. Discussion: To date *Terminalia sericea* has been reported to produce a vast number of antimycobacterial, antiviral, and anti-inflammatory agents, underscoring the fact that botanical research, collaborations, and technology transfer with traditional healers play a crucial role in drug discovery and development activities [10].

Mechanisms of Action and Efficacy

Several of the plants mentioned in the previous sections have been investigated for underlying mechanisms of action that can explain or support their traditional use in the management and treatment of opportunistic infections associated with HIV/AIDS. Mainly, these studied mechanisms comprise antimicrobial effects, alone or in synergy with antiretroviral drugs, immune-enhancing properties, which can be reflected in increased CD4 and CD8 counts, the regulation of biochemical and immunological pathways of inflammation and oxidative stress, and additional properties that contribute to the reduction of diarrhea or the resolution of other HIV-related complaints [15, 16, 17]. Ethnomedical research has anticipated clinical trial parameters by pointing to the possible effective dosages and timeframes of treatment, and to exact benefits for HIV-infected people, including greater well-being, reduced bacterial, viral, and fungal counts, reduced rates and duration of opportunistic malaria, tuberculosis, and gonorrhea, reduced diarrhea, thrush, and herpes sores, fewer inflamed and infected lesions and abscesses, as well as improvements in relevant blood parameters, increases in indicators of anti-HIV immunity, and decreases in markers of bacterial infection [18, 19, 20, 21]. These studies satisfy the declared priorities for clinical research under its Natural History of HIV/AIDS. Most complete body systems are in two main subfields, prompting questions of multidisciplinary or multiple approaches in their research, including synergy with antiretroviral therapies. Strengthening the synergistic effects of herbal medicine with antiretrovirals can

significantly improve the health outcomes of people living with HIV. This synthesis of relevant synergistic opportunities cross-references the way that all of the listed underlying mechanisms can be probed. Multiple questions in the study of clinical possibilities represent the best outcomes of care and yet others point to future lines of research [22, 23, 24, 25].

CONCLUSION

Ethnopharmacology offers a valuable framework for addressing the persistent challenge of HIV-related opportunistic infections, particularly in resource-constrained settings. Medicinal plants such as *Kalanchoe integra* and *Terminalia sericea* illustrate the untapped potential of traditional remedies to complement existing therapies. These plants not only provide antimicrobial and anti-inflammatory effects but also enhance immune responses, paving the way for improved quality of life for HIV patients. By leveraging the synergistic potential of plant-based compounds and antiretroviral therapies, healthcare systems can adopt more holistic and sustainable approaches to managing HIV-related OIs. Future research should focus on standardizing doses, ensuring safety, and validating clinical efficacy to integrate ethnopharmacological practices into mainstream medicine effectively.

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