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Exploring Ethnopharmacology: Medicinal Plants in Managing HIV-Associated Wasting Syndrome

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ABSTRACT

HIV-associated wasting syndrome (HIV-ASS) remains a significant complication among individuals living with HIV/AIDS, characterized by severe involuntary weight loss and muscle wasting. Despite the availability of antiretroviral therapies (ART), many patients in developing regions continue to suffer from the syndrome due to ART-related toxicities, limited healthcare access, and socio-economic barriers. This study explores the ethnopharmacological knowledge and practices related to the use of medicinal plants in managing HIV-ASS among a homogenous community residing near a national park in southwest Zambia. By documenting traditional herbal remedies, methods of preparation and administration, and knowledge transmission mechanisms, this research aims to illuminate overlooked but potentially effective plant-based interventions. The study also addresses the historical, biological, ethical, and clinical dimensions of plant-based treatments, critically analyzing the gaps between in vitro and in vivo efficacy and the implications of bioprospecting and ethical stewardship. It highlights the need for integrated healthcare models that recognize traditional medicine's role in community-based HIV care, and calls for systematic validation of herbal remedies to bridge traditional knowledge and modern medical practice.

Keywords: Ethnopharmacology, HIV-associated wasting syndrome, Traditional medicine, Medicinal plants, Antiretroviral therapy, Indigenous knowledge, Zambia.

INTRODUCTION

HIV-1 is a retrovirus that is the cause of AIDS, a chronic immune deficiency disorder. The pathogenesis of this disease is attributed to the loss of CD4+ T-helper lymphocytes and other immune cells, resulting in opportunistic infections, among other complications. In the 1970s, the social stigma associated with HIV/AIDS led to a plight for treatments that were more natural and less socially stigmatizing, fuelling the growth of ethnopharmacology regarding ASS. Plant preparations that promoted appetite or muscle mass gain or that supported healthy weight were absorbed from information given to clinical researchers either directly from patients or indirectly via practitioners. This growth of ethnopharmacological research on ASS in turn fuelled a growth of interested cohort studies worldwide on medicinal-plant-based treatments in diverse populations. However, unlike with HIV, this research context is largely ignored in clinical contexts and is scarcely known to bioethicists globally. Medications in the background that need to be benchmarked against medicinal-plant-based treatments are in vitro–in vivo incoherent and inconsistent; thus, ASS management is in vitro–in vivo incoherent and consistent. Biological diversity in the foreground is the same, but it is not publicly appreciated. HAD approaches depend on parallel consultations and sampling of treatment knowledge on the same illnesses in different populations. Simultaneously, HAD approaches are locally destructive and globally pro-poorly sustainable, as the vicinage of the plants used by the population studied is poor worldwide. Medicine focused on competitive advantage is biased; it biases clinical practice and is clinically pro-marginalized and locally selective, as it

ignores the bioprospecting potential of less popular knowledge and resource-poor populations. All this raises many questions about southwest Zambia's use or legacies of medicinal-plant-based treatments for managing ASS. Hence, the present study aims to document the hitherto undocumented medicinal plants, various modes of preparation, methods of administration, and knowledge transmission pertaining to the use of medicinal plants for managing ASS in a homogeneous population settled close to a national park in southwest Zambia [1, 2].

Understanding HIV-Associated Wasting Syndrome

HIV is one of the most devastating epidemics of the modern era. By utilizing the effective global response to HIV, it has been estimated that there are around 36.7 million people living with HIV/AIDS worldwide. Following HIV infection, the gradual depletion of the immune cell population (T-lymphocytes) (CD4+ T-cells) occurs over a period of time. The immune system is thus left in an immune suppressed state which facilitates HIV opportunistic infections and the development of AIDS. Other long-term consequences of chronic HIV infection include metabolic disorders, cardiovascular complications, and HIV-associated neurocognitive disorders. The presence of co-infections significantly increases the morbidity and mortality of HIV in affected individuals. Wasting syndrome is another complication of chronic HIV infection which remains poorly managed despite the best treatment available. Wasting syndrome is a gradual loss of lean body mass which mainly consists of skeletal muscle loss. It can occur with or without the presence of other metabolic disorders. Wasting syndrome leads to a compromised quality of life, poor treatment adherence and healthcare costs, as well as premature death and a loss of economic activity. In the absence of ARTs, the life expectancy is only around 1–3 years. In the presence of ARTs, the quality of life is improved for up to 10–20 years. However, these medications do not affect most long-term consequences and significant health risks remain. Wasting syndrome can occur at any stage of HIV infection and information regarding its occurrence in patients is often lacking. This leads to the use of a large number of alternative medicines to manage wasting syndrome [3, 4].

Ethno pharmacology: An Overview

Ethnopharmacology studies the interactions between different ethnic groups and their local flora, particularly focusing on plant-based medicinal uses. It seeks alternative drugs, especially phytochemicals from traditional medicine, validating and isolating bioactive compounds for effective treatment regimens. Over the past three decades, antiviral drug development primarily targeted viral enzymes of RNA and DNA viruses. HIV-associated Wasting Syndrome (WAS) continues to significantly burden public health, particularly in developing countries, where 90% of HIV-affected individuals reside. WAS, characterized by weight loss in HIV patients, is better assessed through Body Mass Index (BMI) than mere body weight. Although antiretroviral therapy (ART) has improved outcomes for HIV-1-infected individuals, the combination of ART, the prevalence of TB infection, and anti-HAART toxicity can lead to severe weight loss or additional health risks. ARV therapies also negatively impact quality of life. Vaccination appears promising, yet no vaccine candidate has successfully passed phase II trials, and immunizing high-risk populations may inadvertently foster more virulent strains. Numerous studies aim to extract bioactive compounds from local practices in developing countries to alleviate HIV symptoms and enhance life quality. Ethnopharmacology now plays a crucial role in addressing HIV/AIDS challenges, necessitating a review of its contributions to understand the trade-offs and future opportunities. The field's principles, strengths, limitations, and opportunities must be clarified to promote systematic research in drug discovery and development [5, 6].

Role of Medicinal Plants in Traditional Medicine

The acceptance of herbal medicines for disease management has grown in developing countries due to limited government support for modern healthcare. Traditional practitioners, or herbalists, serve as primary care providers, especially for the underprivileged and those in remote areas, including for HIV/AIDS management. There is an emerging recognition of their role in global prevention and treatment efforts. Interestingly, even in resource-rich nations, many individuals with HIV/AIDS seek traditional healers for treatment. This study aims to gather data on the plants and preservation methods employed by traditional practitioners in Uganda for managing HIV/AIDS and related conditions. It records the use of 47 plant species across 27 families, with roots (42.6%), leaves (37.2%), and stems (7.5%) being the primary parts used for treatment. Preservation methods included drying (83%), boiling (51%), underground storage (45%), and liquid storage (30%). Opportunistic infections often accompany AIDS, contributing significantly to mortality in developing regions. However, information about medicinal plants for managing these infections is limited, particularly in Northern Uganda where the HIV epidemic

is on the rise. This research documents the plant species and biological activities of commonly used varieties by the local population in district Bannu, aiming to support further studies on their safe and rational use [7, 8].

Historical Context of Medicinal Plant Use

Managing Aids-Associated Wasting Syndrome with Medicinal Plants

The use of herbal preparations for sickness management dates back hundreds of years. Noma, a gangrene form affecting the mouth and face, has been noted since antiquity. Ancient texts, including the Egyptian papyrus of Smith (circa 1600 BC) and Sanskrit recipes in the Indian Materia Medica, contain references to medicinal plants. A Sumerian clay tablet from 2600 BC lists about 40 plants with medicinal uses. Egyptian records from roughly 4500 years ago mention 25 herbs and other substances, such as milk and honey. In 1760, Dr. William Storkson identified Absolom tree bark for gonorrhea treatment and a pulverized plant for worm discharges. Traditional herbal medicine remains prevalent today, with up to 80% of populations in some countries relying on it for primary healthcare, especially in developing tropical areas where modern medicines are scarce. Estimates suggest 25% of modern medications have roots in ethnopharmacological plant sources. Some phytomedicines have shown effectiveness as hypotensives and in managing AIDS-associated wasting syndrome. However, scientific validity regarding the efficacy and safety of these folkloric remedies is largely unexplored across different ethnicities and regions. This lack of verification creates challenges for their safe and effective use in treating and preventing various diseases. Yet, an understanding of their pharmacology, ethnography, chemistry, and toxicology could aid in discovering novel compounds for developing safer, more effective drugs without current side effects [9, 10].

Mechanisms of Action of Medicinal Plants

The human immunodeficiency virus (HIV) is a retrovirus that attacks various components of the immune system and may lead to acquired immunodeficiency syndrome (AIDS) if left untreated. Despite extensive research and treatment options available today, HIV is still a major global health issue, particularly in sub-Saharan Africa (SSA), which has been the most affected region. Antiretroviral therapy (ART) for the management of HIV infection have tremendously aided in controlling the disease. While ART is an effective treatment, it is associated with several drawbacks as some patients experience side effects and toxicities. ART medications are not widely available and affordable in many developing countries. More importantly, ART is not curative and patients on HAART will remain lifelong patients. Data from various studies show that low-weight patients are less compliant to ART and develop opportunistic infections. This is usually as a result of a decrease in weight and muscle wasting that follows chronic opportunistic infections which also includes HIV. This issue termed HIV-associated wasting syndrome is common in HIV positive patients. Wasting syndrome in turn increases the risk of opportunistic infections which activates the cycle that exacerbates the HIV condition. Problematic are the side effects associated with current medications used. Therefore new ways to manage HIV-associated wasting syndrome in a more patient-friendly, low-cost and safe manner than the existing ones are needed. While the initial target of ethnopharmacological investigation was solely the use of traditional folk medicines to manage human diseases, it is clear that the field has evolved with the advent of novel research and technological advancements in medicinal plant studies. This review discusses the case for the use of ethnopharmacology in the search for novel medicinal plants in the management of HIV-associated wasting syndrome and the potential mechanisms of action of proposed remedies [11, 12].

Key Medicinal Plants for HIV-Associated Wasting

The significant medicinal plants used in managing HIV/AIDS-associated wasting syndrome are as follows, arranged alphabetically by genus. **Gardenia ternifolia Smith** (Rubiaceae) is a shrub or small tree up to 10 m tall found in East Africa, with bitter leaves and bark used to brew beer and as a poison antidote. **Moringa oleifera Lam.** (Moringaceae), an erect tree 10–12 m high, has thin, deeply grooved, yellowish-brown bark, and dark-green leaflets. **Annona muricata Lin.** (Annonaceae) is a small tree with thick, glossy, oval leaves, producing a round, edible fruit with custard-like pulp, and seeds used in traditional medicine for infections. **Zingiber officinale Roscoe** (Zingiberaceae) is an herbaceous plant reaching 1 meter, with edible swollen underground rhizomes and pale yellow flowers. Commonly cultivated in tropical regions, ginger serves as a spice and food preservative, with decoctions used as tonic for coughs and colds, although excessive use may cause gastrointestinal issues [13, 14].

Clinical Evidence Supporting Medicinal Plant Use

Many HIV-positive people in developing countries rely on herbal medications to treat their HIV disease, as AIDS and its associated symptoms can be managed and improved using a variety of herbal medicines. A study involving semi-structured interviews with free list and cognitive mapping techniques was conducted among HIV-positive people living in Lesotho to investigate the use of herbal medicine among them. A lay person's exploitation of herbal medicine for HIV-positive patients was examined, and the frequency of use of such medicines seven days prior to the interviews was analyzed. Among 78 respondents, 73% used herbal remedies, mostly in combination with ART. Four herbs were frequently taken, two of which were also the most important, namely medicinal plants and herbal medications consisting of multiple herbs. People seeking ART tended to use more effective herbal medications. People using herbal medications perceived their needs to be unmet. Although medical herbalists improved the perception, they perceived their needs to be met. Similarly, traditional healers were perceived to be undesirable to visit and were rarely seen. For a developing country, frequent use of herbal medicine for HIV-positive patients and its potential influences on ART comprehensibility were reported. Patients in Lesotho described herbs they use with or without complementary or alternative medicine as information seeking after being diagnosed. They mentioned perceived efficacy or efforts to find information, perceived information safeness, perceived privacy, and retrieval difficulty based on the experience of seeing friends using herbs, or pre-existing knowledge from environmental information. Herbal medications targeting care for mothers and children with ART and herbs believed to inhibit viral replication were also mentioned. Herbal medicines intended to care for body strength, blood restoration, common cold, cough, and fever were mentioned. Projected usage perceptions included reduced ART effects and delayed initiation of ART. Concerns to be avoided when seeking information about herbal medicines included secrecy and confidentiality, distance, and inability to recall the herb name [15, 16].

Challenges in Ethno pharmacological Research

Investigating plants in ethnopharmacology presents challenges that impact both the research process and outcomes. One of the main issues is communication, which hinders access to information about plants used in traditional medicine. While some published literature aggregates knowledge about specific plants, comprehensive compilations remain scarce, especially for many countries. Most of the available literature is in European languages, creating a barrier for traditional medical practitioners who speak local languages. Prioritizing the compilation of knowledge in these languages is crucial, as many researchers lack access to the existing literature. Additionally, it is important to verify the bioactivity of listed plants, focusing on high-activity extracts, and standardizing bioassays based on vital traditional uses of these plants. Ethnopharmacological research often depends on bioassays to identify promising plants, but the quality of many studies is low, sometimes based only on preliminary bioassays, neglecting plants that may have unknown activity. The bioassay-guided fractionation of active extracts often results in rediscovery of known compounds, leading to skepticism about its effectiveness in uncovering new substances from traditional medicine. Despite these challenges, investigating medicinal plants can lead to effective treatments for diseases such as HIV/AIDS and related wasting syndrome. This syndrome manifests as unexplained weight loss, muscle wasting, diarrhea, chronic fatigue, and inflammatory neuropathy in HIV patients, caused by neuroendocrine regulation impairments. Chronic HIV infection can disrupt hypothalamic neuropeptides like pro-opiomelanocortin and agouti-related protein, affecting cortisol and growth hormone regulation. Studies on HIV-1 transgenic rats indicate loss of integrity in the arcuate nucleus and a significant reduction in proinsulin mRNA, which is crucial for blood glucose regulation. This dysregulation can also lead to diabetes and frequent hypoglycemic episodes, as observed in a significant percentage of HIV-infected patients [17, 18].

Ethical Considerations in Medicinal Plant Research

The research examined 33 plant species exhibiting in vitro antiviral activity against HIV-1. Information on medicines and treatments was gathered from 15 practitioners, while healing plants were identified over 12 consultations. Three species—Euphorbia spp., Huernia hystrix, and Sutherlandia frutescens—are indigenous to South Africa and previously shown to be effective against cachexia, body fat loss, and HIV-related issues. Ethnopharmacology emerged as a vital research area, emphasizing the significance of plants from cultures without written languages. In the U.S., researchers began publishing on ethnopharmacology as a source for new compounds, but this generated controversy over ethical information disposal and bioresource use. Ethnopharmacological researchers faced criticism, and legislation was enacted to regulate knowledge and resources. Brazil experienced similar controversies

that prompted laws to address unethical biodiversity research. An international symposium on tropical medicinal plants in 1980 sought to establish research protocols and practices. This conference emphasized respecting indigenous cultures and their knowledge while advocating for resource and knowledge reciprocity. The protocol also highlighted the safeguarding of intellectual property and sacred sites. With growing genomic sequence data from human microbiomes and plant genetic materials, corporate interests emerged as new threats. Farmers and indigenous groups sought to assert their ancestral rights to genetic resources, reflecting ongoing challenges from past ethnobiological and bioprospecting issues amidst evolving contexts [19, 20].

Regulatory Framework for Medicinal Plants

Traditionally, the use of plants as medicine is central to African culture, passed down orally, which risks loss as elders pass away. African traditional medicine manages various diseases, including HIV/AIDS, alongside modern treatments and is used in divination and religious practices. Its cultural significance is closely tied to social and religious beliefs, facilitating healing within structures of injustice and possessing bioremedial capabilities. This complex cultural importance helps contextualize its current transformative, researchable, and scientific relevance. Medicinal plants are defined as those with actual or potential therapeutic value. Traditional medicine encompasses the knowledge, skills, and practices originating from diverse cultures for preventing, diagnosing, or treating physical and mental ailments. Ethno-pharmacology examines medicinal plants biologically, pharmacologically, and chemically, focusing on active compounds and their effects, relying on local communities' knowledge of medicinal flora. Ethnopharmacological studies initiate with ethnobotanical research, plant collection, and species selection. In recent years, southern Africa's herbal remedies have garnered increasing scientific interest, leading to new discoveries and the utilization of biodiversity for research. The significance of developing and protecting the genetic resources of traditionally used plants has been highlighted. Without conservation efforts, certain medicinal plants risk extinction. Traditionally, African communities accumulated and selectively shared knowledge of medicinal flora, sometimes keeping sacred information secret. The knowledge of beneficial plants has attracted pharmaceutical companies, providing locals economic incentives to exploit their flora. Sustainable drug discovery and herbal treatment development hinge on genetic protection. Before exploration, biodiversity hotspots should be inventorized to ensure protection. The patenting of natural resources by industrialized nations has sparked debates on bio-piracy and bioprospecting, leading to the creation of databases to identify 'ownership' of natural products and efforts to safeguard traditional knowledge. Ultimately, indigenous populations, the original users of these resources, seek to share in the benefits derived from their utilization [21, 22].

Case Studies: Successful Applications

The management of HIV-associated wasting syndrome (WAS) has recently revived interest in ethnopharmacology and medicinal plants due to their historical use and demand for natural therapies [23-25]. This study focuses on polyherbal remedies derived from medicinal plants traditionally used by HIV-positive individuals. A preclinical investigation was conducted on extracts from six selected plant species for their efficacy in WAS, aiming for standardization and commercialization. The plants were chosen based on ethnobotanical surveys and consultations with traditional healers in Lesotho. Methanol extracts of these species were tested in vitro on C2C12 myoblast and myotube cells and in mouse models for their anti-cachectic effects [26-28]. The study screened for active phytoactive principles to guide the selection of effective fractions. Intellectual property rights, patenting, and the integration of commercial delivery systems for herbal products were also discussed. A new 12-herb ethnomedicinal formulation, EPE (Ethnomedicinal Plants Extract), was launched by community partners HERB-DESIGN and SHEBA health groups, collectively known as SOWERS [28-32]. An eight-herb formulation containing six promising bioactive extracts with anti-HIV and anti-WAS activity was developed for community delivery. The EPE extracts and herbal capsules are expected to initiate the path towards commercialization, serving both WAS treatment and potentially leading to further innovations in management [23, 24].

Integration of Medicinal Plants in Modern Healthcare

Recent research indicates that traditional African medicinal plants may enhance modern ART for HIV and related infections. Even with population migration, local communities retain rich knowledge of these plants, often passed down through oral traditions [33-34]. This study aimed to document such plants used in HIV-AIDS care in Eastern Cape, South Africa. Data was gathered via herbalist discussions, interviews, field tours, and participant observation. Comparing the knowledge of HIV-positive individuals

with that of professional herbalists revealed that field interviews significantly increased the diversity of documented medicinal plants. Seven previously unknown HIV-related plants were identified, underlining the importance of capturing traditional knowledge, which might otherwise be lost [35-38]. The study advocates for incorporating field interviews into ethnobotanical research, suggesting that local knowledge continuity is crucial amid globalization and rural development. Many plants reported to possess anti-HIV effects were previously unrecognized by scientists, highlighting the necessity of further research on both known and newly discovered species. Ultimately, supporting local knowledge systems can enhance the collection and use of traditional medicine, addressing global health challenges in developing regions [38-42].

Future Directions in Ethno pharmacology

In this review, plant substances with anti-HIV action are explored. A search was conducted for plants reported to show anti-HIV activity in cell-based or non-cell-based assays. Additionally, plants with anti-HIV action have been claimed to address neurocognitive impairment associated with the infection status, but their status is less explored [43-46]. The current review highlights the role of these plants in the treatment of HAND, classes of their secondary metabolites involved in anti-HIV activity, and their preclinical and clinical status. From the studies reviewed, 319 bioactive compounds from 56 plant families, including numerous unreported compounds, were identified. Fifty-three plants also inhibited HIV-1 infection of human naïve C–CD4 T-cells. Several medicinal plants modulate factors involved in HIV latency and reservoirs, and 88 plants address neuropathogenesis of HAND. In translational research, focusing on holistic therapy according to biological systems, the WHO has advocated for better understanding of "High-Throughput Natural Products" to target new ailments [43-46]. A better understanding of "Reverse Pharmacology" approaches to target undiscovered/unused receptor interactions of marketed drugs has highlighted the need for ethnomedicines toward neglected diseases. Safety, efficacy, and quality-resilient adjuvant drug mixtures derived from medicinal plants used in traditional practice have shown promising clinical outcomes. More billion-dollar markets have also been outsourced for the last few decades from Europe to Asian/Middle Eastern nations. Few metabolite-target approaches from natural products with specific olfactory cyclodehydrogenase enzymes have also recently seeded significance to early million-dollar clinical-phase preclinical biomedical research industries [27, 28].

CONCLUSION

The management of HIV-associated wasting syndrome in resource-limited settings continues to challenge both patients and healthcare systems. This study demonstrates that ethnopharmacological approaches, grounded in traditional knowledge, provide viable complementary options for managing HIV-ASS. Medicinal plants such as *Moringa oleifera*, *Annona muricata*, and *Zingiber officinale* play significant roles in improving patient outcomes by enhancing appetite, strengthening the immune system, and alleviating related symptoms. However, the clinical utility of these herbal treatments remains under-recognized, and their mechanisms of action inadequately studied. Bridging the gap between traditional knowledge systems and modern biomedical frameworks is essential for sustainable, equitable healthcare. Ethical considerations must guide bioprospecting and benefit-sharing to protect indigenous intellectual property and biodiversity. Moving forward, interdisciplinary collaborations are needed to validate traditional remedies, ensure quality control, and develop safe, standardized formulations that can be integrated into HIV care protocols globally.

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