

Exploring the Biochemistry of Medicinal Plants in HIV and Diabetes Management

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ABSTRACT

The global burden of chronic diseases such as HIV/AIDS and diabetes mellitus necessitates the exploration of affordable and effective treatment alternatives. Medicinal plants, long recognized for their therapeutic value in traditional medicine, offer a promising avenue for the development of novel bioactive compounds with minimal side effects. This paper explores the biochemical composition of medicinal plants and their mechanisms of action in managing HIV and diabetes. It provides an overview of key plant-derived secondary metabolites such as alkaloids, flavonoids, saponins, and terpenoids that exhibit antiviral and antidiabetic activities. The integration of ethnomedicinal knowledge with biochemical and pharmacological research has led to the identification of plant-based inhibitors of HIV enzymes and phytochemicals capable of regulating glucose metabolism. Despite substantial progress, challenges persist in standardization, clinical validation, and equitable access. Future directions call for multidisciplinary collaboration to harness the full potential of these natural resources in combating these two major global health challenges.

Keywords: Medicinal Plants, HIV/AIDS, Diabetes Mellitus, Phytochemicals, Bioactive Compounds, Antiretroviral Therapy, Insulin Resistance, Traditional Medicine.

INTRODUCTION

Natural products, including medicinal plants, animal products, and microorganisms, have been reported to possess diverse health benefits for animals, including humans. It is estimated that in developing countries, 80% of the population depends on traditional medicines prepared from plants for the prevention or treatment of diseases. Extracts and compounds derived from these plants have been shown to control and/or prevent diseases through various biological mechanisms [1-5]. Traditional medicine from plant extracts has generally proved to be more affordable, clinically effective, and relatively less adverse than modern drugs. These have paved the road for researchers to investigate the rational quality of these medicinal plants and validated some uses in the treatment of diseases. The application of phytochemical constituents of medicinal plants in the pharmaceutical industry has increased significantly, which can be witnessed through comprehensive research studies published every year. Plant-derived secondary metabolites include steroids, alkaloids, phenolic compounds, essential oils, terpenes, flavonoids, coumarins, saponins, tannins, alkaloidal, and sugar compounds [6-10]. These exhibit a diversity of biological properties beneficial to human beings, such as antiallergic, anticancer, antimicrobial, anti-inflammatory, antidiabetic, renal protective, cardioprotective, and antioxidant activities. Diabetes is a chronic disease resulting from metabolic disorders in the pancreas β -cells. There exist 2 major types. Type 1 diabetes mellitus (T1DM) results from autoimmune destruction of the pancreas β -cells that have an absolute deficiency of insulin production; hence, T1DM patients are required to inject insulin to control blood glucose levels [11-15]. Type 2 diabetes mellitus (T2DM) is caused by a deficiency of

insulin production in response to insulin resistance of the pancreas β -cells. Metformin has been widely used for the therapy of T2DM worldwide. Current medications focus on blood glucose control, which includes α -glucosidase inhibitors and sulfonylurea (SU) classes. Unfortunately, they are expensive and associated with many serious side effects. Traditional medicines are important in management as an alternative treatment. HIV has caused an epidemic that affects millions of people worldwide since the early 1980s. Despite extensive research efforts, a preventative vaccine and curative therapy are still not available for HIV/AIDS. Antiretroviral therapy (ART) is the current standard treatment for HIV infection and has been shown to improve quality of life, but it does not cure the disease [16-21]. Side effects, drug-drug interactions, and high cost are factors that limit their usage. The search for alternative treatment strategies is necessary. In many countries, traditional or folk medicine (TM) is an important resource for healthcare, and is still widely used as a first-line treatment or in combination with conventional medicine [22-24].

Overview of HIV and Diabetes

Diabetes mellitus (DM) is a chronic endocrine disorder due to relative or absolute insulin deficiency or action and causes hyperglycemia. Diabetes affects nearly 230 million people worldwide, and the incidence of the disease is increasing rapidly even in developing countries [25-26]. Alloxan monohydrate induces destruction of insulin secretory β -cells in the pancreas, causing diabetes in experimental animals, which is widely used for the screening of antidiabetic drugs. Insulin is a protein hormone routinely used in the management of diabetics, but it needs critical care while handling, given its tissue destruction with the wrong immunization techniques. There is a global interest in seeking out safe plants that can ameliorate blood glucose levels without exerting any side effects [27-29]. Natural products, more in particular traditional herbal medicine, have played a vital role in developing molecules/lead compounds for different ailments. Out of which, plants that are claimed to be in the management of diabetes and its complications were selected to endorse their validity. Thus, alternatives are needed in developing countries; hence, traditional plants enter into the scope. Generally, these plants can provide a cheap and easily accessible alternative source [30-34]. Reports on the medicinal plants used for the management of diabetes and its complications were compiled using Indian systems of medicine. Both Ayurveda and Siddha systems of medicine swear by their efficacy, and orthodox medicines may find time to recognize them. The usage of herbal plants in the management of diabetes and other metabolic diseases has a considerable popularity in the past decade. OECD guideline # 404 has been meticulously adopted in the present study for evaluation of acute toxicity of medicinal plant extracts on experimental animals, and a popular medicinal plant, *Trichosanthes dioica*, was first time screened for its toxicity in laboratory animals. For the ethanolic medicinal plants cited in the present study, exploration on ethanol, methanol, and hexane extracts is a new concept for discovering potential anti-diabetic drug molecules [35-40].

Medicinal Plants: A Historical Perspective

Plants are vital for human survival, with medicinal drugs capable of preventing or eliminating disease agents. The therapeutic use of plants dates back to the origins of human culture, with knowledge passed down through generations. Indigenous peoples across the Americas, Africa, and Asia developed traditional healing methods long before modern pharmaceuticals [41-43]. The significance of medicinal plants in treating various ailments has been acknowledged for millennia, with records dating to around 3000 B.C. in Egypt. Herbal medicine is among the oldest forms of traditional healing. Throughout history, humans have utilized various plant parts, roots, stems, leaves, barks, flowers, fruits, seeds, and exudates for their healing properties. Research on plants encompasses growth and development, morphology and anatomy, reproductive biology, and ecological impacts, along with economic cultivation aspects, biodiversity conservation, genetic engineering, and essential oil distillation [44-46]. These studies aim to enhance effective and profitable use in the herbal industry, involving complex and diverse experimental approaches. Research efforts often target the isolation of bioactive compounds to expand knowledge and explore their potential in disease treatment and the discovery of novel compounds. Since ancient times, people have employed plant-based remedies in both powder and liquid forms to combat ailments [47-48].

Biochemical Compounds in Medicinal Plants

Medicinal plants have been a source of inspiration for drug discovery over the past decades, with bioactive compounds isolated from them included in the treatment of many diseases, including diabetes and HIV. Bioactive compounds in medicinal plants, some of which are used for the treatment of diabetes and HIV together, are discussed in this article. Biochemical compounds are small organic molecules produced by living organisms, like plants, to improve health by interacting with biological systems such as humans

[49-54]. Biochemical compounds can be divided into two groups, primary and secondary metabolites. Primary metabolites are produced by plants and are involved in the primary physiology of plants and other living organisms. Examples of primary metabolites are carbohydrates, amino acids, fatty acids, lignin, and nucleotides. Plants produce many secondary metabolites for their specific functions and the interaction between plant species and their environment. Some secondary metabolites have specific biochemical activities in humans, which are responsible for their medicinal properties [54-59]. Over 13000 secondary metabolites have been purified and/or isolated from medicinal plants, of which 90% are currently being used as drugs, and studies are being conducted to use the rest. The secondary metabolites of plants can be categorized into various classes of phytochemicals such as alkaloids, flavonoids, terpenoids or essential oils, phenolic compounds, phenylpropanoids, steroids, tannins, saponins, coumarins, quinones, glycosides, thiols, and xanthones. Some of these phytochemicals or substances obtained from them have been purified or isolated as biologically active ones and presently are used for the scientific validation of their folkloric anti-diabetic use. However, this is acknowledged as a challenging one among the other issues due to the complexity of the secondary metabolites and random screening of large numbers of plants or phytochemicals. Nonetheless, several phytochemicals or plant extracts have been screened and shown to be valid for their folkloric anti-diabetic use [60-64].

Mechanisms of Action in HIV Treatment

Human Immunodeficiency Virus (HIV), the causative agent of Acquired Immunodeficiency Syndrome (AIDS), is still a major global health threat. About 37 million people globally are infected with HIV, of which 24 million are in sub-Saharan Africa. Antiretroviral therapy (ART) is a global healthcare achievement for the treatment and management of HIV/AIDS. ART can suppress the HIV viral load to undetectable levels, thereby preventing onward transmission. Single or multiple drugs from different classes with different mechanisms of action are combined in ART treatment regimens to combat the rapid emergence of drug resistance [61-64]. However, despite robust evidence of the public health benefits of ART, there are still continuous challenges facing ART implementation, including patient-to-healthcare provider stigma and discrimination, the pill burden, poverty, ART access inequities, ART adherence challenges, the emergence of drug resistance, and systemic social and structural issues. Antiretroviral therapy (ART) is a combination of antiretroviral (ARV) drugs used for the treatment of HIV-1 infection, in which the objective is to inhibit HIV replication either by blocking viral entry into host cells or by inhibiting one or more steps in the replication cycle of HIV [65-69]. Traditionally, natural products and their derivatives are a major source of new chemical compounds with potential uses as pharmaceuticals. Natural products are structurally diverse and bioactive compounds produced by living organisms. They have played a central and continuous role in drug discovery and development. There are about 12 natural products approved for the treatment of HIV/AIDS, and most recently, two are from medicinal plants, including maramba beans and the stem bark and leaves of *Parkia biglobosa*. These 12 natural products have therapeutic effects via the underlying mechanism of action, including inhibition of HIV attachment to target cells, inhibition of the entry of viruses into cells, inhibition of the reverse transcriptase enzyme, protease inhibitors, and modulation of the immune system [9-10].

Medicinal Plants in Diabetes Management

Plants used in traditional medicine for diabetes treatment contain phytochemicals categorized into flavonoids, terpenoids, alkaloids, phenolic acids, and other compounds. The mechanisms of these phytochemicals in diabetes are discussed based on animal and in vitro studies. Diabetes mellitus, characterized by hyperglycemia from insufficient insulin (Type 1) or insulin action defects (Type 2), poses serious health and economic issues [70-75]. Current oral antihyperglycemic agents, such as sulfonylureas and biguanides, often cause adverse effects like weight gain, cardiovascular issues, hypoglycemia, and gastrointestinal disorders. This has led to a reconsideration of effective traditional plant-based medicines that generally show lower side effects and costs. Almost 2000 plant species have been evaluated for their anti-diabetic potential through screening based on accredited pharmacopoeias. These plants undergo collection, authentication, extraction, and purification processes to prepare crude extracts tested on diabetic models, revealing significant activities and yielding new bioactive compounds. This includes reports of phytochemicals effective against diabetes in both Asian and Western folk medicine. The text emphasizes the need for chemotaxonomy, purification techniques, bioactive compound screening, and new agent identification through both experimental and clinical studies, referencing literature from 2015 to 2019 [76-80].

Case Studies: Successful Applications

HIV/AIDS Management: HIV infection is characterised by the progressive depletion of CD4+ T cells, resulting in progressive immune dysfunction and host vulnerability to opportunistic diseases. The acquired immunodeficiency syndrome (AIDS) may progress in an individual within 5-10 years of infection, resulting in inevitable disease-related death. Antiretroviral therapy (ART) is essential for the effective management of HIV/AIDS. However, drug resistance, adverse side effects, an insufficiency of ART for initiating treatment, high costs of ART, and poverty contribute to the morbidity and the mortality associated with HIV disease. There is thus an urgent need for an effective and affordable cure for HIV infected individuals [81-83].

Diabetes Management: Diabetes is a chronic and debilitating metabolic disorder affecting millions of people worldwide, leading to high blood glucose levels due to a lack of insulin action or synthesis. The most common and serious types of diabetes are type 1 (insulin-dependent) diabetes mellitus (IDDM) and type 2 (non-insulin-dependent) Diabetes mellitus (NIDDM), which respectively account for about 5-10% and 90-95% of diabetes cases [6]. The common symptoms of diabetes are polyuria, polydipsia, polyphagia, and weight loss. Diabetes is usually accompanied by chronic complications, such as cardiovascular disease, kidney failure, and amputation, which are caused by long-term hyperglycemia. Traditional medicinal plants and their active components that are used for the treatment of diabetes have stood as attractive sources for modern antidiabetic drug discovery [84-85].

Challenges in Research and Application

Medicinal plant research often involves collaboration among scientists from different institutions, resulting in the formation of botanical or working groups. This article focuses on a limited number of medicinal plants and the scientific inquiry into isolated compounds, highlighting reasons why some plants receive more attention than others. The saying, "the squeaky wheel gets the grease," illustrates how group dynamics can influence research focuses. Recent discussions at South African biochemistry congresses mentioned studying xanthenes from Myrtaceae, complex herbal teas from the Roussea family, and indigenous legume seed results. A major challenge in initiating new studies is the proximity to diverse cultural communities and the scarcity of documented recipes. Few botanists are inclined to explore Cape Town's less inviting terrains for research. Such a context limits creativity and the capacity for larger, advanced technologies to conduct research. Significant regional differences exist in plants, languages, and resources. Collaborative bottlenecks may arise around specific plants, like the blue roundleaf shrublet or Euphorbia species, where only tribal storytelling informs knowledge. Additionally, the media often amplifies unverified claims from natural product chemists, leading to public curiosity about previously undocumented "miracle plants." For instance, an article discussing potential anti-HIV properties of South African plants sparked outrage among local scientists, as U.S. biochemists gained recognition for plants not yet studied by South African researchers. Indigenous communities and herbal practitioners remain frustrated with slow research progress and inequities in the distribution of treatment benefits [15, 16].

Future Directions in Research

Plant-derived bioactive components include flavonoids, phenolics, alkaloids, terpenes, glycosides, and tannins, drawing interest for new drug sources with unique structures and actions. Many plant products are biologically active, serving as origins or models for synthetic drugs. Several compounds from plant extracts, including glycopeptides, proteins, alkaloids, flavonoids, and tannins, have shown HIV-inhibitory activity. Traditional medicine systems across various countries document the antiviral properties of these plants. Flavonoids notably demonstrate a broad range of inhibitory potency against reverse transcriptase activity and HIV-1 infection. Retroviral and lentiviral enzymes present new targets for developing effective anti-HIV drugs, which also involve host cell proteins interacting with viral proteins. One such protein, the nucleocapsid protein (NC), plays a crucial role in the HIV life cycle, though its interaction mechanisms remain poorly understood. Diabetes, stemming from insulin production deficiency, affects individuals globally and has become a primary focus in 21st-century health research. Anti-HIV properties of plants and proteins show potential for safe, effective human applications. Indigenous knowledge provides valuable bioresources for bioprospecting and in silico studies, assisting medicinal chemists and biologists in discovering novel treatments against HAND [17, 18].

Ethical Considerations in Medicinal Plant Research

Efforts are ongoing internationally to protect the rights of MTS, particularly in access and benefit-sharing, as advised by the Convention on Biological Diversity. Concerns persist regarding the ethics of bioprospecting, specifically that knowledge of MTS may be used without consent, compromising fair

sharing of benefits. Ethical questions arise about recognizing traditional knowledge, obtaining informed consent, and distributing benefits fairly. While various guidelines on ethical medicinal plant research exist, few real-world examples demonstrate their implementation. The newly developed economic botany ethics framework builds on prior codes of ethics and addresses the gaps in conducting ethical medicinal plant research. International standards for bioprospecting primarily focus on pharmaceuticals and biotechnology, but a practical framework for field-based research remains undeveloped. Furthermore, bioprospecting often analyzes biodiversity samples after initial research, where conceptual ethical questions are rarely considered. Consequently, discussions around fieldwork in economic botany often lack coherence, with ethical statements occurring in isolation. Recent presentations and discussions at professional meetings have ignited interest in establishing a practical framework to enhance ethical conduct in medicinal plant research [19, 20].

Cultural Significance of Medicinal Plants

The livelihoods of many communities in this province depend on wild-harvested plants for medicinal use, showcasing their potential for drug discovery. In South Africa, traditional practices utilizing a diverse range of medicinal plants have been established historically. Research has demonstrated their significance as a foundation for modern medicine. Ethnobotanical surveys have documented various medicinal plants among traditional healers in Kauvilwindi, Mapharane, Maralenyena, and Temo in the Mopani District. This herbal knowledge, rooted in generations of indigenous customs, is vital for many tribal communities. Although some South African plants have shown promise in treating ailments like diabetes, formal endorsements of their efficacy in traditional use are insufficient. Despite this, anecdotal evidence confirms the ongoing use of these plants. Ethnomonitoring of treatments for diabetes has been reported in Botswana and Namibia, but no such surveys exist in South Africa. There is an urgent need for ethnobotanical documentation and research into the potential medicinal properties of various species, especially due to forced urbanization leading to a decline in herbal knowledge among younger generations. This information is essential for conservation efforts and corporate responsibility, while also promoting bioprospecting and the discovery of effective medicines to combat diabetes and poverty-related diseases. The Mopani District boasts a rich flora of over 300 species, which has not previously been subjected to bioprospecting. Conservation efforts in other areas have proven beneficial, underscoring the importance of promoting and preserving the ethnomedicine of this region [21-26].

Global Perspectives on Medicinal Plants

Societies worldwide have unique healthcare practices, forming the field of medical anthropology. Indigenous peoples of the Americas historically used plants, animals, and minerals to address physical and spiritual ailments, while African and European botanicals influenced American folk medicine. Current medicines are derived from plant extracts, with some crude forms still used. Alternative medicine, encompassing herbal, folk, traditional, or indigenous practices, has a longstanding presence globally. Countries have studied local medical practices extensively. The resurgence of interest in herbal medicines can be seen as a return to established practices, but concerns arise regarding potential exploitation, safety, and the appropriation of traditional uses by the pharmaceutical industry. Nonetheless, researchers continue to investigate plants' biological mechanisms and active compounds, uncovering health effects. This exploration highlights the symbiotic relationship between science and traditional knowledge, acknowledging that plants offer remedies. Indigenous peoples across the Americas utilized plants to treat ailments long before European influence, while other cultures maintained their botanical customs rooted in folklore and science. Modern pharmaceuticals often trace their origins back to these folk remedies. Ethnobotanists explore the relationships between people and plants, showcasing biocultural diversity. Historical figures who experimented to explain health effects were complemented by herbalists and healers, who typically underwent long apprenticeships. Today's professional folk healers possess extensive libraries of handwritten recipes and case studies, employing a range of tools from dried plants to music and prayer for healing [27, 28].

CONCLUSION

Medicinal plants serve as a critical bridge between traditional knowledge and modern therapeutic innovation, particularly in managing complex diseases such as HIV and diabetes. Their biochemical constituents, including various secondary metabolites, have demonstrated efficacy through diverse mechanisms ranging from inhibition of viral replication in HIV to modulation of insulin secretion and sensitivity in diabetes. While these natural remedies offer a cost-effective and culturally accepted alternative to synthetic drugs, their integration into mainstream healthcare systems requires rigorous scientific validation, clinical trials, and policy support. Overcoming research and application barriers,

including limited bioprospecting infrastructure, intellectual property rights, and regulatory challenges, will be pivotal in fully realizing the therapeutic potential of medicinal plants. Continued interdisciplinary research can facilitate the discovery of novel compounds and promote equitable healthcare access globally.

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