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The Potential of Medicinal Plants in Preventing Diabetes-Related Complications in Malaria Patients

Nalongo Bina K.

Faculty of Medicine Kampala International University Uganda

ABSTRACT

Diabetes mellitus and malaria represent significant and often overlapping public health challenges, particularly in developing regions. The dual burden of these conditions can exacerbate metabolic dysfunction and immune compromise, making management increasingly complex. Modern pharmacological treatments often carry undesirable side effects and may not be effective in addressing complications arising from co-infection. This review examines the potential of medicinal plants with dual antidiabetic and antimalarial properties to mitigate diabetes-related complications in malaria patients. Drawing from traditional knowledge and emerging scientific evidence, the paper highlights key phytochemicals with hypoglycemic and immunomodulatory properties. Specific plants such as *Azadirachta indica*, *Morus alba*, and *Commiphora molmol* are discussed for their biochemical efficacy in improving glycemic control and combating Plasmodium infection. Through an integrative lens, the study emphasizes the importance of preserving ethnobotanical knowledge, promoting sustainable harvesting, and encouraging further clinical trials to validate plant-based therapies. This synergistic approach may offer a cost-effective and culturally appropriate strategy to reduce the burden of chronic and infectious diseases simultaneously.

Keywords: Medicinal Plants, Diabetes Mellitus, Malaria, Phytochemicals, Traditional Medicine, Antidiabetic Agents.

INTRODUCTION

Diabetes is a chronic condition that has become a public health concern as one of the main causes of morbidity and mortality. Diabetes is extremely associated with obesity and has become an epidemic globally, especially in less developed countries. There are about 537 million people aged 20-79 years who are now living with diabetes, and the number is expected to rise to 643 million by 2030 and 783 million by 2045. The complication of diabetes is a major public health concern. Long-term unregulated diabetes can lead to severe and devastating complications that include microvascular, macrovascular, and other complications. Malaria in diabetics is a clear indication of a vicious cycle wherein diabetes puts patients at risk of getting malaria, and getting malaria worsens the diabetes condition. People with diabetes are at particularly high risk of severe malaria and related mortality. Furthermore, hyperglycemia impairs innate immunity and T-cell populations against malaria, while malaria infection reduces the insulin level and increases blood glucose level, all adding to the severity of hyperglycemia. Though modern medicines have made promising strategies to manage chronic diseases such as diabetes and malaria, many traditional herbal medicines used since time immemorial have no adverse effects in comparison. Various antidiabetic plants have been used since antiquity in folkloric treatments for diabetes. On the other hand, many medicinal plants having bioactive compounds have been empirically used for the alleviation or prevention of diabetes-related diseases. These plants serve as a source of active phytomolecules for the management of diabetes complications in malaria patients. Despite advancements in modern pharmaceutical science, the interest in evaluating various medicinal plants, especially for their bioactive phytomolecules and pharmacological activities, remains ever-increasing, even today [1, 2].

Understanding Diabetes and Malaria

Diabetes Mellitus (DM) is a chronic metabolic disorder that leads to high blood glucose levels (hyperglycemia) resulting from defects in insulin production, secretion, or action. There are two general forms of DM: Type 1 diabetes (insulin-dependent diabetes mellitus (IDDM), juvenile diabetes, or early-onset diabetes), which is due to autoimmune destruction of the insulin-producing β-cells that results in an absolute insulin deficiency, leading to hyperglycemia, and Type 2 diabetes (non-insulin-dependent diabetes mellitus (NIDDM), maturity-onset diabetes, or sporadic diabetes), which is characterized by insulin resistance, relative insulin deficiency, and often a progressive secretory defect to maintain glucose homeostasis. DM is a complication of childhood infectious diseases such as malaria, diarrhea, and measles, and poses a serious public health challenge. In developing countries, it is crucial to ensure the safety of recovery and prevention from the development of these chronic complications of childhood infections. Plant-derived drugs have been a significant source of medicinal agents since ancient times and remain a major source of drugs. Various plants and their phytoconstituents are extensively used as remedies for various ailments. Malaria is responsible for the majority of infectious disease-related mortality in children less than 5 years of age in sub-Saharan Africa, while an important cause of infectious disease-related morbidity and mortality among children aged less than 5 years globally. Understanding the malaria pathophysiology, particularly secondary complications following recovery from acute malaria, is crucial in realizing the burden of malaria, solving the problem, and improving the well-being of recovered malaria patients. Malaria is a generally tropical disease caused by protozoan parasites of the genus Plasmodium, which are transmitted to hosts via the bite of infective female Anopheles mosquitoes. The four species of Plasmodium infecting humans are P. falciparum-less virulent but responsible for malaria in America and Papua New Guinea, P. vivax, P. malariae, and P. ovale, and the former two are noteworthy as they cause hypnozoite-associated relapsing malaria-associated morbidities and mortalities [3, 4].

Pathophysiology of Diabetes

Diabetes mellitus (DM) is a group of metabolic disorders identified by high blood glucose levels over a prolonged period. The cardinal signs of diabetes include polyuria, polydipsia, and polyphagia. DM is characterized by both a reduction in insulin secretion and insulin resistance. Major chronic diabetes complications include diseases of the eye, kidney, nervous system, heart, and blood vessels .5. The main types of DM are type 1 DM (T1DM) and type 2 DM (T2DM). T1DM, also known as juvenile diabetes, is characterized by the loss of ß-cells of the pancreas. T2DM is because either the pancreas does not secrete enough insulin, or the body's cells do not respond to insulin adequately. DM has long been considered a substantial health problem, as it leads to life-threatening complications such as cardiovascular death and residual disability. Prediabetes is a state of hyperglycemia above normal but not sufficient for a diagnosis of T2DM. It is associated with increased risk of cardiovascular diseases, diabetes, and mortality [6, 7].

Malaria's Impact on Diabetes

Diabetes is one of the leading chronic diseases worldwide and often results in serious complications, including heart disease, retinopathy, nephropathy, neuropathy, and foot ulcers, leading to lower limb amputations. It is important to prevent diabetes and its complications to improve the quality of life, productivity, and life expectancy 5. This review discusses the role of plants in preventing diabetes-related complications. Diabetes-related complications are commonly classified into two major classes: microvascular complications, which are characterized by capillary endothelial injury in target organs due to chronic hyperglycemia resulting in retinopathy, nephropathy, and neuropathy, and macrovascular complications due to large blood vessel lesions leading to the shortening of lifespan. Development of diabetes-related complications is multifactorial and generally involves chronic hyperglycemia, oxidative stress, inflammation, and the disruption of glucose homeostasis 8. Biguanides, insulin secretagogues, alpha-glucosidase inhibitors, and thiazolidinediones are commonly used as drugs to improve glycemic control in diabetes. However, the side effects of the existing drugs raised a strong demand for the development of alternative conservation and sustainable management resources. Medicinal plants have been used for treatment for thousands of years. Various search engines and databases can be used to track down biomass sources of relevant compounds. While depletion of conventional medicine resources is acute and immediate, loss of traditional medicine resources is more gradual and involves developmental issues. Celebrating the effectiveness of medicinal plants to prevent hazardous diseases will enhance global awareness of the importance of preserving their genetic resources through education and poverty alleviation [9, 10].

Medicinal Plants: An Overview

Plants have been used in medicine to treat many diseases for thousands of years. Traditional healers treat 70-95% of the diseases in developing countries. Folks still rely on local herbal vendors for the prevention and treatment of various diseases, including neurological disorders, skin problems and cosmetics, obesity, and related metabolic disorders. Many species of plants have been used for medicinal purposes throughout history and have yet to be studied pharmacologically and/or toxicologically. Malaria is one of the serious public health problems, with over 41% of the world population at risk of malaria, primarily in Sub-Saharan Africa. Malaria and diabetes mellitus (DM) are both metabolic disorders, but the relationship between them is controversial. Commiphora molmol (myrrh), Mangifera indica (mango), Morus alba (white mulberry), and other plants have shown in vivo anti-diabetic activity. Hyperglycemia is responsible for many complications of diabetes. Traditional medicine is widely used to prevent DM and related complications. Some plants are widely consumed and over-exploited through traditional medicine. So it is essential to take cognizance of those plants in combating DM and its complications. The potential of plants in preventing or treating DM and its complications in malaria patients has been reviewed. In India alone, 1700 plants are recognized as ethnomedicinally relevant for treating diabetes. Almost 800 plants were reported to have antidiabetic effects. Besides, traditional plant medicines are used all over the world for diabetic presentations, which may offer a natural key to uncover a critical anticipated medication for the future. Compounds derived from plants used in phytomedicine may provide remedies for metabolic disorders, such as type II diabetes (T2DM). Galega officinalis L. has been used since the early period in Europe aimed at treating symptoms associated with T2DM. Its hypoglycemic and insulin-sensitizing potential is related to its guanidine compound (galegine). A related compound, the biguanide metformin molecule, was later developed and is still broadly utilized in antidiabetic treatment. Several natural compounds have been identified with their different mechanisms to treat diabetic hyperglycemia [11, 12].

Medicinal Plants' Action Mechanisms

Around the world, malaria is one of the major health problems. the fall in glucose level can also result in an anti-hyperglycemic way in patients presenting with concomitant diabetes mellitus in a malarial attack. Inappropriate treatment of either condition may worsen prognosis and produce life-threatening consequences. However, during concomitant infection of malaria and diabetes, the use of anti-diabetic agents to regain glucose levels is a big problem. Some risks can rapidly reach and deteriorate within a few hours, and may be life-threatening. In this regard, the use of traditional medicinal plants that possess both antidiabetic and antimicrobial activity may help. The medicinal plants that have hypoglycemic activity may restore the aberrant glycemic level and other parameters related to diabetes, whereas hawthorn leaf, chrysin, and green tea have +%%79, -+91, and −+91% efficacy against malaria, respectively. Some of these traditional plants, for example, hawthorn leaf, artichoke leaf, cinnamon leaf, thyme leaf, wild thyme leaf, chrysin, green tea, mucuna pruriens, and neem leaf, have some pharmacologically active compounds such as catechin, quercetin, and flavonoids. These classes of compounds can hinder glucose transporters (GLUTs), which are a catalyst for concurrently lowering anti-diabetic and blood glucose levels. These agents also improve insulin sensitivity of muscles, fat, and other insulin-controlled tissues through diverse and molecule-specific abrogation of serine/threonine protein kinases (PK) cascade by phosphorylation. Chalcone and catechin can improve hepatic glycogenesis [13, 14].

Key Medicinal Plants for Diabetes Management

From ancient times, medicinal plants have played a big role in human health. These plants are used in a wide range of ailments as folk medicine. Therefore, medicinal plants and their derived natural products have gained great interest for their importance as a major source of drug development. Even today, the WHO recommends scientific investigation of traditional plants for the discovery of new drugs. Approximately 50 % of modern drugs are of plant origin or inspired by phytochemical structures. Medicinal plants account for 25% of modern drugs. Medicinal plants are identified as a group of plants used to treat different ailments as medication. The plant surroundings provide a variety of unexplored biota. Many bioactive compounds from plant extracts have been isolated so far and used as drugs in modern medicine. More than 50 bioactive compounds have been isolated from plants for diabetes management. In this review potential plant bioactivity to control diabetes and prevent diabetes complications is summarized. Type II diabetes mellitus is the most common metabolic disorder prevalent in the world so far. Today, a variety of modern drugs are available for diabetes control after being developed from animal models and plant extracts. But these drugs have, for obvious and legal reasons known as well as unknown side effects. Herbal medicines are attracting greater attention for the

treatment of diabetes with their naturally occurring ingredients. Such medicines potentially have a variety of medicinal activities. Hypoglycaemia as well as anti-diabetic bioactive compounds isolated from medicinal plants [15, 16].

Role of Medicinal Plants in Malaria Treatment

Presently, the use of medicinal plants is increasingly gaining popularity as an alternative resource to conventional medicines for malaria treatment. Naturally produced toxic phytochemicals are the precursors of modern drugs with diverse biofunctions such as artemisinin, quinine, ephedrine, vincristine, taxol, camptothecin, and curcumin. Medicinal plants used in malaria treatment mainly belong to the Asteraceae, Apocynaceae, Euphorbiaceae, Fabaceae, and Rutaceae families. Antimalarial prescriptions include herbs (fresh or dried), powders, soft/hard tablets, decoction, tincture, infusion, lotion, and vaporization. Roughly two-thirds of respondents prepared single-plant remedies, while others preferred polyherbal formulations. Before typical use, the remedy was prepared by boiling, grinding, crushing, soaking, or steeping. When necessary, other additives such as jucoja leaves, tea leaves, rice, sugar, salt, and alcohol were mixed in. Indications for use were typically fever, chills, malaise, myalgia, gastrointestinal distress, or splenomegaly. Medicinal plants used widely in the treatment of diabetes in various parts of the world indicate the traditional knowledge base of herbal medicine. In the Middle East, plants such as Solanum tuberosum, Convolvulus erectus, Acacia gerrardii, Cinnamomum cassia, and Salvia trilobata are used in treating diabetes. Some plants, such as Plantago psyllium, Silybum marianum, and Avena sativa, are traditionally used for the treatment of diabetes in Europe. In Asia, plants such as Cichorium intybus, Azadirachta indica, and Salacia oblonga display hypoglycemic activity and are used in Andhra Pradesh (India) as antidiabetic agents. In other parts of the world, especially South America and Africa, this information on the use of plants in the control of diabetes is scant. In Africa, plants such as Gymnosporia montana, Croton macrostachyus, and Gardenia lucida are used in South Africa, but no evidence of scientific investigation exists. Further studies employing the use of biological systems in these countries may discover more previously unknown plants possessing valuable pharmaceutical properties [17, 18].

Clinical Evidence and Case Studies

Numerous studies highlight the anti-diabetic efficacy of medicinal plants investigated in this study. The Nirjharini leaves paradigm mentions clinical trials with participants consuming one to two bowls daily. Eligible subjects with type 2 diabetes aged 30 to 70 had their fasting blood glucose (FBG), postprandial blood glucose (2 hPPBG), anthropometric parameters, and adverse effects evaluated before and after a 40-day intervention. An 80% reduction in FBG levels was noted in those continuing with the leaves, with 97% reporting no side effects. This provided strong evidence for the anti-diabetic effects of Nirjharini leaves. In a Bangladesh study on Shafala, 70 diabetic patients aged 30 to 65 were examined, with evaluations including FBG levels and various health parameters over one month. A significant reduction in FBG was reported in the Shafala juice group, while the control groups had insignificant improvements and experienced side effects, unlike the Shafala group. Clinical studies on Sita Ashok, used in managing diabetes in Nepal, evaluated the effects of either a placebo or capsules in adults with vitiligo and type 2 diabetes. Participants maintained dietary control, with a drop-out rate under 25%. Nearly 75% experienced hypoglycemia, possibly indicating the indirect anti-diabetic effects of the treatment [19, 20].

Challenges in Research and Application

Despite the great potential of plants in lowering blood glucose levels in diabetic or prediabetic patients, some obstacles need to be discussed and addressed in future research, especially regarding malaria patients. Most of the plants still require further scientific investigation before being widely accepted as cheats to help lower blood glucose levels in malaria patients, while their names and proposed medicinal values were collected based on these plants' usage as folk medicine by local communities. As such, an evidence-based examination of the effectiveness and safety of the plants and their phytochemicals is warranted as an urgent endeavor. There is an increasing gulf of knowledge around these plants, as many of them still need to be thoroughly studied either bio- or pharmacologically, while some draw massive attention from researchers around the world in the cases of identifying their bioactive compounds' structure, mode of action, in silico screening, and docking studies. Some plants have received extensive exploration on their effectiveness in lowering blood glucose levels, and their bioactive compounds have often moved from the bench to the bedside. As such, bio- and pharmacological research on candidate plants, especially on the plants less studied to date, should also receive more attention, given recent epidemiological knowledge on the 7th specificity. It is a well-acknowledged fact that malaria control is a major barrier to diabetes management, especially in tropical developing countries, where health

authorities typically prioritize malaria prevention, with scarce human resources spent on non-plasmodial diseases, such as diabetes. There is no record of these plants as approved traditional treatment for diabetes in the national health agency's database. While some native plants have gained recognition nationally, publicly, and internationally, other plants are often used as 'secret remedies' passed from generation to generation and sometimes are merely small-scale traditional medicine [21, 22].

Future Directions in Research

In low-income African countries, diabetes is more prevalent than in high-income nations, leading to increased public health concerns and higher morbidity and mortality associated with malaria. Untreated diabetic patients face aggravated malaria symptoms. It is crucial to evaluate economic, psychological, and social impacts after anti-malarial treatment and diabetes glycemic control. Self-management of diabetes and establishing screening and management programs are essential to reduce morbidity and mortality related to malaria. Clear explanations of prevention and management methods can enhance patient compliance. Point-of-care tests for diabetes should occur based on immunological or clinical criteria shortly after starting anti-retroviral therapy. Epidemiological studies are needed to allocate resources effectively and combat diabetes complications in resource-poor settings. Health facilities must be equipped with glucometers for diabetes diagnosis. Developing a diabetes management textbook in indigenous languages is also recommended. Patients with diabetes should be educated about the current treatment landscape concerning malaria. Public health initiatives should explore local medicinal plants with antiplasmodial properties, and strategies must integrate prevention and education on co-existing diabetes and malaria infections in tropical countries. Future studies should investigate the pharmacological efficacy and safety of traditional medicinal plants used against diabetes to promote sustainable remedies for managing the condition and its complications [23, 24].

CONCLUSION

The co-occurrence of diabetes and malaria presents a formidable challenge to public health systems, especially in resource-limited settings. Conventional treatments are often inadequate in managing the multifactorial complications arising from this comorbidity. Medicinal plants offer a promising alternative due to their natural bioactive compounds, historical usage, and relative safety. Their dual role in managing blood glucose levels and combating malaria parasites makes them invaluable in the context of integrative disease management. However, while ethnobotanical evidence is compelling, there is an urgent need for scientific validation through pharmacological studies and clinical trials. Strengthening research in this area can lead to the development of effective, accessible, and culturally acceptable therapies. Furthermore, conserving medicinal plant biodiversity and promoting community education on sustainable use will ensure long-term benefits for healthcare systems and biodiversity alike. Leveraging these natural resources responsibly may pave the way for novel therapeutic strategies that are both effective and holistic in managing diabetes-related complications in malaria-endemic regions.

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