



The Potential of Herbal Antidiabetic Agents in Treating Malaria-Related Complications

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ABSTRACT

Malaria and diabetes are both significant global health concerns that, when co-occurring, exacerbate the risk of severe complications and increased mortality. Malaria, primarily caused by *Plasmodium falciparum* and *P. vivax*, remains a major cause of morbidity and mortality, particularly in malaria-endemic regions in Africa and Asia. Concurrently, the global rise in diabetes prevalence, particularly Type 2 diabetes, adds another layer of complexity to managing infections like malaria, especially due to the altered glucose metabolism in diabetic patients. Malaria typically induces hypoglycemia, while diabetes is characterized by hyperglycemia, creating a dangerous overlap for patients suffering from both. Traditional herbal remedies, often used for managing diabetes, have shown promise in managing not only the metabolic dysregulation seen in diabetes but also in mitigating malaria-related complications. This paper examines the role of herbal antidiabetic agents in treating malaria-related complications by examining mechanisms of action, preclinical and clinical evidence, and the potential for integrating these remedies into modern therapeutic practices. Special emphasis is given to the use of synergistic herbal formulations that could provide multi-faceted benefits in the treatment of malaria and diabetes.

Keywords: Herbal medicine, antidiabetic agents, malaria-related complications, diabetes, hypoglycemia, hyperglycemia.

INTRODUCTION

The increasing prevalence and resistant strains of malaria to conventional drugs, daily management of diabetes as well as profound overlap of malaria and diabetes result in the shift of current malaria management and demand discovery and a well-thought optimized innovative treatment approaches through traditional knowledge of medicine. Malaria is a global public health challenge and its prevalence in developing regions of Africa and Asia is much more substantial and increasing. Every year more than 200 million people worldwide get infected with malaria and about 770,000 die from the associated acute symptoms [1]. Currently, quinones, artemisinins and duo artemisinin-based combined therapies are used worldwide to treat malaria however artemisinin resistance strains are also discovered in five countries and emerging. In this context the emergence and spread of multidrug-resistant strains of *Plasmodium falciparum* and *P. vivax* strains has rekindled scientists' and practitioners' interest in innovative treatment options with a special emphasis on the role of traditional pharmacopoeias. The daily management of diabetes necessitates careful and constant blood glucose monitoring. One corner stone of managing diabetes is caring that the food choices are the good food ones and keeping track of blood glucose daily. The ever-increasing prevalence of diabetes along with the current management cost is also an alarming situation not only for poor people but also developing and under-developed countries with budget-limitations in health sector [2, 3, 4]. Every poverty-stricken country tries to get out of the situation with some means. Malaria and Diabetes are profound overlap to one another. Diabetes highly dopes

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hyperglycemia, which is an elevated blood sugar concentration and on the other malaria highly dopes hypoglycemia or low blood sugar level that is the major complication of severe malaria. The blood glucose should be actively monitoring with capillary blood sampling to avoid further complications and the effect of this kind of monitoring, and managing the diabetics on the top of poverty is totally unbearable. On top of that, the malaria, a killer disease, with ever emerging resistant strains of plasmodium highly complicates the poor diabetic patient's situation. Because of this reality the ancient time herbologists, herbalists and some local medicinal practitioner know that, these diseases can be managed with something they extracted from the plants. There are a number of plant preparations are being used by local people of developing nations of tropical and subtropical regions for the treatment of complicated or co-morbid malaria disease/diabetes, known as A/H for long time. There is a historical usage of plants in medicine by every major culture; approximately 80% of the world populations still rely on traditional herbal medicine to treat diseases. In this scenario, effort shall be given to discuss co-morbid used plant species for treatment of malaria and diabetes as a new outlook as well as the existing use of these plants shall be highlighted. In the end, further discussion will be given on the critical issue of integrating traditional herbal medicine into mainstream medical practice, and the possibilities that smart drugs, derived from traditional herbal medicine, might be discovered through modern scientific research methods. There is an urgent need for good quality research to determine the safety, quality, effectiveness and the required dose of herbal remedies for the treatment of diseases. Clinical studies might be guided by preclinical studies that can provide information on safety, active constituents, and mechanism of action; they could help to build on traditional knowledge, congested industrial interests pursuing the development of pharmaceutical versions of the most promising ethnomedical treatments. Several ethnomedical practices showed the possibility of combination therapy, a result possibly obtained due to the synergistic activity of different chemicals and/or phytochemicals of different plants. This is already accepted in the case of Ayurveda and Traditional Chinese Medicine, which postulate the use of different herbs together to obtain therapeutic benefits. This has long been an important part of these medical traditions and it is known from more recent scientific work. For example, WHO green lighted channelled access to quite complicated ingestion of infusions derived from five different plants to treat HIV in a country with a high preponderance of this pathology. Restricting this ingestion with more practical advice, such as information about extracts in capsules, was responsible for an increase of the pathology that was subsequently reverted. It was then determined that only the full extract provided benefits, as it contained eight phytochemicals that inhibited the growth of the HIV while in any smaller quantities, they actually favored the viral proliferation. An increasing number of non-specialized Biology magazines have been making the general public, with increasing awareness, of the scientific research behind some ethnomedicines and botanicals used in U.S.A. and Europe. There has been a tendency of the public of these countries to use phytotherapies more and more frequently, although it is known that many of the plants commonly available in pharmacists and parapharmacies might not have some possible beneficial pharmacological actions [5, 6, 7].

Understanding The Link Between Diabetes and Malaria

Diabetes and malaria are both conditions of global health concern. While diabetes is a metabolic disorder characterized by chronic hyperglycemia, malaria is an infectious disease caused by Plasmodium parasites. Both hyperglycemia in diabetes and hypoglycemia during malaria stress the importance of maintaining glucose homeostasis. There are other ways in which these diseases can interact. Metabolic dysregulation in diabetes may increase susceptibility to malaria through direct physiological mechanisms. The liver and adipose tissue work in concert to control whole-body glucose metabolism by particular molecules; research from murine models indicates that the broad metabolic dysregulation observed in diabetes leads to increased liver RBC hosteering and the subsequent proliferation of the parasite. There is potential for increased disease severity or complications. The immune response of the host to Plasmodium parasites is complex and not yet fully understood; however, it is clear that a robust immune response is required to combat infection. Type 2 diabetes results in low-level inflammation; therefore, mild or asymptomatic malaria infections may be more prevalent and severe cases more difficult to clear in diabetics. It is recognized that ancient biochemical pathways for glucose metabolism regulated immunity, and recent work underscores the importance of glucose metabolism in the function of immune cells [8, 9, 10]. Indeed, four recent multicounty analysis revealed that diabetes, a metabolic disorder characterized by chronic hyperglycemia, is associated with an increased risk for malaria infection and severe cases of

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malarial disease. On a cellular level, proposed mechanisms include the promotion of Plasmodium RBC invasion by increased availability of particular amino acids in the diabetic host, deregulation of glucose homeostasis in the host cell leading to increased intracellular glucose levels, and infection with resistant Plasmodium strains. In addition, multiscale agent-based modeling predicts that broad metabolic dysregulation in diabetes, or conditions mimicking diabetic-like conditions, can further increase susceptibility to the parasite. On the epidemiological level, data suggest that these diseases co-occur broadly; one analysis of two cohorts with a combined total of over 100,000 participants indicated that after controlling for confounders, diabetics had an adjusted hazard ratio of malaria infection of 1.9 compared to the general population. Individually, diabetes and malaria give rise to substantial mortality and morbidity; taken together, there is even greater potential for patient complications [11, 12, 13].

Herbal Antidiabetic Agents: Mechanisms of Action

Medicinal plants with antidiabetic properties have come to be the focus of attention in the development of new, efficient, and affordable antidiabetic drugs. In a recently published study, 75 Brazilian medicinal plants, belonging to 75 species and 40 families, were evaluated for their effects on glucose metabolism or the control of diabetes. There are 12 species which could significantly lower the plasma glucose concentration in treated animals or inhibited the increase of plasma glucose concentration in glucose-loaded animals. More than half of the active species could be used traditionally for treating diabetes in Brazil, other countries, or regions. The biochemical components considered responsible for the antidiabetic properties can be divided into flavonoids, alkaloids, terpenoids and derived compounds, as well as polyphenols. These distinct components possess a variety of properties, acting on the glucose metabolism, as insulin mimetics or sensitizers, or displaying potential antioxidant activity. Details about the glucose metabolism, insulin sensitivity, and insulinotropic and antioxidant activities for these components are provided to interpret the effects on glucose homeostasis of the herbs studied, which could contribute to their contro hyperglycemic properties. With millions of malaria cases and hundreds of thousands of deaths worldwide, primarily in children under 5 years of age, malaria remains a major cause of morbidity and mortality. Increasing concerns are addressed to the severe complications that often accompany episodes of disease related to Plasmodium falciparum or P. vivax. The present review critically discusses the effects of plant-derived or herbal remedies on infectious diseases that represent an important socio-economic and medical issue, focusing on those used in the treatment or prevention of acute or chronic diseases caused by protozoa, bacteria and viruses. Enough preclinical data have been collected on the treatment of uncomplicated human malaria with Artemisia annua tea and artesunate, tincture of Mitragyna ciliata stem bark, and extracts of Cryptolepis sanguinolenta and Alstonia boonei, to warrant small clinical trials. The reduction of P. falciparum parasitaemia of vitamins role in the resistance process and the development of vaccines of P. falciparum is also considered. Potentially, the presence of quercetin and myricetin in the traditional therapy for severe malaria could also reduce the strong cytokinemia observed in patients [14, 15, 16].

Evidence of Antidiabetic Agents in Treating Malaria-Related Complications

Malaria is one of the leading global public health problems and deadliest parasitic infectious diseases. The emergence of drug resistance by malaria parasites and concerns of the adverse effects of some antimalarial drugs in clinical use make the development of new drug compounds to treat malaria more urgent. The potential of herbal anti-diabetic agents to treat and/or manage conditions identified in pregnancy-associated malaria (PAM) was analyzed and clinical and preclinical evidence was reviewed. The clinical evidence was based on shared outcomes observed during routine screening tests conducted on diabetes mellitus (Type 2) patients coincidentally infected with malaria. The preclinical evidence was based on effects similar to conditions seen in PAM and Type 2 diabetes obtained from an experimental study on the effect of co-infection on glycemia in pregnant diabetic mice infected with Plasmodium berghei NK-65 [17, 18, 19]. Malaria is linked to anemia, hypoglycemia, hyperinsulinemia, and hypoinsulinemia due to pancreatic injury by oxidative stress and leads to high morbidity and mortality. The study suggests that the use of herbal antidiabetic agents with hypoglycemic properties may be a new intervention to manage the risk factors associated with mortality in malaria or diabetes mellitus infected individuals. Despite the existing studies evidencing the antidiabetic agents' overall efficacy in reducing mortality rates in malaria, HIV/AIDS, and TB 1, this is the first study to identify the potential of antidiabetic agents in treating and/or managing malaria infection [20, 21, 22].

Challenges and Future Directions

Guided by the global health policy agenda, building on traditional knowledge and the increase in evidence-based ethnomedical research, particularly for complex diseases, many of which are referred to as infectious and parasitic diseases, demands for integration of medicinal plants into healthcare systems are growing. Since the 1980s, reports of the health effects of parasites on non-communicable diseases have appeared. Malaria-related complications, like other infections, play an important role in Diabetes Mellitus (DM) pathogenesis and activities. In both murine models of malaria and severe malaria patients, researchers have found obese, insulin-resistant or type 1 diabetes-prone animals that were unexpectedly protected from cerebral malaria and exhibited other disease-specific protective phenotypes. Patients with type 1 diabetes and cerebral malaria were protected from reactive hypoglycemia and deep ketosis during bacterial sepsis [23, 24, 25]. The pattern of liver-stage malaria infections without blood stages of *Plasmodium yoelii* or a subpatent blood parasitemia containing human malaria parasites, protected animals from severe disease and death. These findings emphasize metabolic and immunologic homeostasis in CM. Collectively, these types of promising benefits of malaria on the course and complications of DM suggest that progress in understanding these points may lead to the discovery of potentially effective methods for treatment. Herbal antidiabetic agents offer important possibilities in this regard and would be an attractive medicine for treating DM based on malaria protection. Efforts toward integrating malaria metabolomics and transcriptomics as well as analysis of whole glutathione-related molecule dynamics have been made as the first attempt to explore underlying biological mechanisms, especially for the association between malaria infections and DM in vivo. Further efforts to prolong treatment and observation time for diabetes and malaria co-infected mice, as well as those exploring comprehensive further research, are essential and urgently needed potentials of herbal antidiabetic agents in treating or preventing malaria-related complications [26, 27, 28, 29, 30, 31, 32, 33].

Challenges and Future Directions

The use of plants in the treatment of malaria-related complications in DM has a centuries-old tradition. Components of the crude extract of the Cinchona plant used to prepare Jesuits bark reduced fever in two Peruvian viceroys. Since then, the use of artemisinin, based on artemisinin and other metabolites by the AP29 *Artemisia annua* L. plant has become an internationally recognized basis for the comprehensive treatment strategy. It is worth noting that formulations based on seed oil from *Tectona grandis* L. and enjoe root were successfully used in clinical studies in Western Kenya for immuno-defective diseases caused by babesiosis and marked by pancytopenia [34, 35, 36, 37, 38]. The results obtained due to the demonstrated immunostimulatory potential of the decoction. Serious clinical conditions strongly limit the possibility of using well-known natural preparations. A number of people healed by herbalists despite negative results and quarrels with family members leave children debilitated by chronic diseases. These were the origins of long-term considerations on the use of one species, rather than a complex of species, considering the cosmological, topographic, social and health context in which the disease occurred. Current studies were carried out to flip possible singular herbal formulations from the perspective of Rajasthani Vyas, but a form of sanitary-legal analysis has been adopted. This is the first report on the inadvisability of entering the significant group of plants under state protection in international means, which reveals a wide range of ideological problems regarding plants. The comprehensive view of medicinal plants in the presented research comprehensively embraces the Rajasthani knowledge of health and disease, in the case of a certain class of morbid events, drives the researchers away. Settlement of small claims, but with time, the losses suffered due to the invocation of many classified subjects against natural barcover compensated by other harvests. In the documents, therefore, not a single remedy can be found to treat similar diseases. Considering this, common use for species, cultivated trees are considered, including in similar usages. While the above is general for most of Rajasthan and also experienced in North Cameroon, Malaria is considered through an ecological climate with an emphasis on the differentiations of the groups considered [34, 35, 36, 37, 38]. The comparative-historical method, foremost among which are those of a medical nature, help determine the Socio-environmental traits of using medical knowledge and the understanding of health and disease of the broader community work. It is hoped that this review, on the one hand, will not lead to the deduction of the medicinal components of knowledge in the contexts where the treatment does not have a clearly established pathogenesis, but also indicate the need for a broader approach to the application of the results of anthropological studies. Regular cooperation of existing professionals and those who undergo field studies is needed, as a nodal,

therapist, or phytomedicine, considered in the fields of biological anthropology, ethnobotany and tradition. The conclusions cannot be considered for individual species, only an ethno-broadened interpretation of the broader context helps dispel doubts and resistance toward the usage of critical knowledge-display population health [25, 26, 27].

CONCLUSION

Herbal antidiabetic agents represent a promising frontier in addressing the complex interplay between malaria and diabetes. The mechanisms of action of these plants, particularly in regulating glucose metabolism and mitigating inflammation, align with the challenges posed by the co-morbidity of these diseases. While substantial preclinical and some clinical evidence support the efficacy of certain herbal remedies, there remains an urgent need for more rigorous clinical trials to validate their safety, effectiveness, and optimal dosage. The integration of these traditional remedies into mainstream healthcare systems, particularly in malaria-endemic regions, could provide cost-effective, accessible treatment options for vulnerable populations. Further research into the synergistic effects of combining herbal treatments, along with modern pharmaceutical therapies, could enhance therapeutic outcomes. Ultimately, the growing body of evidence supports the potential of herbal antidiabetic agents in treating malaria-related complications and underscores the importance of preserving and leveraging traditional knowledge in combating global health challenges.

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