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The Role of Medicinal Plants in Treating Malaria: Successes and Limitations

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ABSTRACT

Malaria continues to be a global health burden, particularly in sub-Saharan Africa and parts of Asia and South America, where access to conventional antimalarial drugs is limited. The rise of drug-resistant strains of *Plasmodium falciparum* has intensified the search for alternative treatments, including those derived from traditional medicinal plants. This paper explores the historical use, pharmacological potential, clinical efficacy, and safety of plant-based antimalarials. It highlights the contributions of key medicinal species such as *Artemisia annua*, *Azadirachta indica*, and *Cryptolepis sanguinolenta*, which have shown promising antiplasmodial activity. However, limitations such as a lack of standardization, inconsistent clinical trial outcomes, toxicity risks, and regulatory challenges hinder the integration of herbal remedies into mainstream malaria treatment. The paper emphasizes the need for more rigorous scientific validation, ethnobotanical conservation, and improved public health policies to balance traditional knowledge with modern drug development frameworks.

Keywords: Malaria, Medicinal plants, *Plasmodium falciparum*, Antimalarial resistance, Phytotherapy, Herbal medicine, Traditional medicine.

INTRODUCTION

Malaria, caused by the Plasmodium falciparum parasite, remains a significant global health issue, leading to decreased productivity and increased maternal and newborn complications, which impede economic development in endemic regions. Although current antimalarials are effective, resistance, especially to chloroquine, poses challenges, prompting communities to seek natural remedies. Traditionally used plants for malaria treatment are increasingly documented, with four main factors influencing reliance on traditional medicine: limited access to orthodox options, affordability, availability, and cultural practices. In Africa, 70-80% of individuals pursue traditional healthcare, with 85% in Tanzania relying on it, and 32% of malaria patients using herbal methods exclusively. Despite the wide array of antimalarial plants available, many lack adequate testing for efficacy and safety. Mefloquine's adverse effects have reduced its use, highlighting the need for more tolerable antimalarial agents from natural sources. Studies have screened fifty-four extracts from forty-two plants against both chloroquine-sensitive and resistant strains of P. falciparum, identifying twelve with significant antiparasitic activity without harming HeLa cells. This indicates that folk medicinal plants could yield new, better-tolerated antimalarials [1, 2].

Historical Context of Malaria Treatment

Malaria is one of humanity's oldest diseases, known as 'chronic fever' in the Nile Valley of Egypt in 2650 BC. The parasite was first identified by Alphonse Laveran in 1880 from a patient in Algeria, and Sir Ronald Ross discovered the exo-erythrocytic cycle in mosquitoes in 1897. Understanding the parasite's life cycle led to effective control programs in Europe and the USA in the early 20th century, greatly reducing malaria in temperate and endemic regions. However, the lack of sustained safety measures resulted in increased malaria rates after the 1950s-1960s, the era termed the golden age of malaria control. The need for effective antimalarial drugs is urgent in areas where resistance has developed. Plant-based medicines have historically been significant in malaria treatment, potentially offering new biodynamic compounds effective against the parasite. Heme, a pentacyclic quinnoline alkaloid utilized in Africa, has derivatives for malaria treatment. Traditional healers use herbal remedies not only for physical healing but also for cultural and holistic reasons, aiming to balance individual and communal health.

Some believe these remedies can shield against witchcraft. Access to herbal medicines varies, with better infrastructure correlating with greater availability. Knowledge of herbal properties is traditionally passed down, and local herbalists are often more trusted than medical professionals due to their longstanding experience [3, 4].

Overview of Medicinal Plants

Over three thousand plants are reported to treat malaria in traditional medicine, with many sold as herbal products, especially in endemic regions where chemotherapy is difficult or costly. Preclinical studies on over six hundred plant species have identified more than two hundred extracts with bioactivity against Plasmodium parasites, showing growth inhibition in assays. This review discusses the therapeutic benefits of these plants, summarizing their antimalarial effects and the challenges of translating preclinical and clinical findings into practice. It highlights the need for both preclinical and clinical evidence, addressing concerns about the generalizability due to limited human studies and commercialization. Key topics include the sustainability, bioavailability, safety, adverse effects, and resistance issues related to therapeutic phytotherapy for malaria [5, 6].

Mechanisms of Action of Medicinal Plants against Malaria

Medicinal plants are vital in treating malaria, with many species exhibiting antimalarial effects. This review focuses on four plants demonstrating such activity and explores their mechanisms. Antimalarials disrupt Plasmodium's asexual metabolism, blocking heme detoxification or inhibiting growth processes. Due to increasing resistance to some antimalarials, investigating the mechanisms of alternative plant-based therapies is essential. Plants in traditional medicine have shown antimalarial properties. In the search for new antimalarials, experiments with crude extracts and isolated compounds were conducted. Many extracts were inactive, but a few displayed promising antimalarial effects. Further bioguided fractionation led to the identification of potent antimalarial compounds. Some function through novel mechanisms, while others act similarly to chloroquine. Tests on various parasitic strains revealed activity against chloroquine-resistant types. Traditional medicinal plants, such as Artemisia annua L., have been used for over 2000 years for fever treatment. In vitro studies indicated the active principle of this plant extract is artemisinin, a sesquiterpene lactone interacting with heme and aiding Antimalarial Tempol®'s action. Unique peroxide-bridged compounds also target heme detoxification pathways, facilitating the creation of semisynthetic artemisinin derivatives [7, 8].

Key Medicinal Plants Used in Malaria Treatment

To date, over 542 plant species have been documented as being used to treat malaria. In Africa, Asia, and South America, there are several key plant species that are widely promoted and employed for malaria chemosuppression. This list includes the following: Afzelia quanzensis (Fabaceae); Chenopodium ambrosioides (Chenopodiaceae); Croton niloticus (Euphorbiaceae); Dymondia margaretae (Asteraceae); Erythrina abyssinica (Fabaceae); Flueggea virosa (Euphorbiaceae); Hypanthus balsamical (Bignoniaceae); Magnolia kabigonensis (Magnoliaceae); Matelea subnuda (Apocynaceae); Nymphaea amoripiok (Nymphaeaceae); Phyllanthus amarus (Euphorbiaceae); Pseudobombax ellipticum (Bombacaceae); Reseda luteola (Resedaceae); Tetracera volubilis (Dilleniaceae); Wallia spp (Gentianaceae); and Zanthoxylum heitzii (Rutaceae). The most studied plants include: • Artemisia spp. (Asteraceae) • Azadirachta indica (Meliaceae) • Cassia spp. (Fabaceae) • Cryptolepis sanguinolenta (Apocynaceae) • Curcuma longa (Zingiberaceae) • Embelia ribes (Myrsinaceae) • Eucalyptus citriodora (Myrtaceae) • Eucalyptus globulus (Myrtaceae) • Euphorbia hirta (Euphorbiaceae) • Morinda citrifolia (Rubiaceae) • Momordica charantia (Cucurbitaceae) • Phyllanthus amarus (Euphorbiaceae) • Phyllanthus niruri (Euphorbiaceae) • Picralima nitida (Apocynaceae) • Poncirus trifoliata (Rutaceae) • Tacca palmata (Dioscoreaceae) • Tacca leontopetaloides (Dioscoreaceae) • Urtica dioica (Urticaceae) • Vaccinium myrtillus (Ericaceae) • Vaccinium macrocarpon (Ericaceae) • Withania somnifera (Solanaceae). Specific mixtures of these plants have been tested in vitro, in vivo, and clinically using golden hamsters, mice, or humans infected with parasites such as Plasmodium berghei, Plasmodium yoelii, Plasmodium chabaudi, or Plasmodium falciparum. Infections were followed immediately by single-dose administration or by mixed administration over several days of oral or parenteral extracts and/or individual pure compounds, and the most common mode of action being inhibition of heme crystallization by lysosomes [9, 10].

Clinical Successes of Medicinal Plants

Malaria poses a significant global health challenge, affecting over 229 million people and leading to more than 409,000 deaths annually, particularly among children under five in sub-Saharan Africa. Despite the effectiveness of current antimalarials, resistance to these drugs is rising, prompting increased interest in antimalarial plants and herbal medicines. The WHO has renewed efforts to develop effective herbal

remedies, building on a medicinal plants agenda from the mid-1990s. Many malaria deaths occur shortly after symptoms appear, spurring research into quicker symptomatic responses seen in indigenous youth. A considerable percentage of people, up to 75% in some regions, opt for herbal treatments; a survey indicated that 63% of Ugandan parents with malaria-affected children tried traditional medicine first. While several plants have been identified as "successful," evidence supporting their clinical utility is crucial for their integration into healthcare. Although hundreds of plant species have been tested for antimalarial properties, many trials show limited efficacy. Notably, no plant exceeded the effectiveness of established controls, yet some studies reported potential bioactivity consistent with effective compound ranges. Anti-inflammatory properties of some compounds may help in chronic conditions predictive of severe malaria. However, much beneficial bioactivity may be diminished during transport through rural trade networks [11, 12].

Limitations of Medicinal Plant-Based Treatments

Recurrent malaria epidemics and concerns about drug resistance have raised questions regarding the effectiveness of existing antimalarial drugs. Financial constraints hinder the creation of new synthetic drugs, prompting searches for plant-derived alternatives historically employed in folk medicine. While herbal treatments and dietary supplements show promise, their efficacy has not been rigorously confirmed through randomized trials. Although thousands of compounds have been extracted from native plants, the screening of plants from new habitats is inadequate. Herbal medicines often lack official approval, and traditional remedies may not perform consistently in clinical studies. Variances in population health may influence the treatment outcomes. Further investigation is essential to identify plant species worthy of pharmacochemical and clinical research. A review of studies involving medicinal plant preparations for acute malaria showed moderate strength of evidence, albeit with identified study limitations. Systematic reviews highlight the prevalence of herbal medicine in areas lacking modern antimalarial access. Nonetheless, the frequency of successful plant use remains poorly documented, and co-interventions often involve limited patient engagement or inadequate trials [13, 14].

Comparative Efficacy: Medicinal Plants Vs. Conventional Drugs

Over the last decades, several agencies have paid much attention to malaria and the development of conventional methods to treat and control this disease. As a result of increased research activity, biochemical mechanisms of disease and drug action are being elucidated. In parallel to this research, there are a number of reports from various groups establishing that plant extracts are able to cure malaria. Since most of these studies use acute malaria tests in mice, the extrapolation of this comparison to clinical use is questionable. There are many good well-designed studies using mice and many poorly designed cases. Congruent data provide a reliable conclusion, but at least in human studies a quarter of the data come from one centre using the same methods. Since toxicity screens and safety and quality control studies in conjunction with relative risk estimates for some plants may also be summarized carefully, a high standard of evidence is feasible for a number of medicinal plants as alternative medicines against malaria. This overview of plant extracts with reported antimalarial activity describes how traditional medicines have been sought unsuccessfully by the pharmaceutical industry. Such studies should reveal possible contacts with the pharmaceutical industry to isolate the active principle and control safety and toxicity as a precondition to clinical use, which is not yet the case. Alternatively, future studies could consider the synergism of several chemicals with unknown modes of action. In addition, it is stressed that although there are a number of plants with known efficacy, there are none that presently circulate in the market [15, 16].

Safety and Toxicity Concerns

Significant efforts to combat malaria have been bolstered by substantial funding from governments and NGOs, aimed at providing free long-lasting insecticide-treated nets, indoor residual sprays, and artemisinin-combination therapies. These interventions have helped reduce the disease burden. However, the efficacy of artemisinin derivatives is declining, with rising treatment failures raising concerns. Gametocytogenesis of P. falciparum due to ACT pressure has been cited, though issues like poor patient adherence, pharmacological challenges, and counterfeit drugs remain potential underlying causes. The emergence of resistant malaria parasites, particularly pamaquine-resistant strains, threatens radical treatment efficacy. Additionally, chloroquine-resistant P. falciparum has spread across Africa, leading to treatment failures. In response to this critical situation, the WHO has urged the development of new antimalarials to meet the 2030 eradication goal. Currently, over 90% of existing antimalarials come from natural sources, with some still in use alone or with synthesized counterparts. Growing interest in higher plants and traditional herbal products as drug sources is noted. Among various toxic plants, human

toxicity issues have been reported for S. angustifolia, C. involucrata, C. bromata, S. javacum, S. orientalis, N. oleander, A. aroids, A. musculorum, Clove, E. littorale, and E. microfila. Key factors such as delivery and dosage greatly influence the safety of these products. Phytogastric chemicals in these herbs have protective roles and may be safe at low doses while exhibiting toxicity at higher levels or when interacting with certain foods and drugs. Therefore, the safety of products from toxic plants requires thorough evaluation [17, 18].

Ethnobotanical Perspectives

A literature search on "malaria," "Ethiopia," and "medicinal plants" was conducted to compile essential data. This review summarizes malaria's causes, epidemiology, control strategies, transmission, prevention, and treatment methods, including traditional ones. Malaria is spread by female anopheles mosquitoes, distinct from other mosquito types. Its introduction to Ethiopia is unclear but likely coincided with agriculture or settlement. Ethiopia's diverse climatic regions impact disease distribution and vectors. Various ecosystems contribute to the proliferation of protozoa and animal parasites. The high prevalence of malaria is linked to human actions causing the emergence of resistant strains. Socioeconomic, political, and cultural challenges hinder prevention and treatment efforts. Unregulated anti-malarial prescriptions and inadequate health education have led to self-medication, with second-generation drugs like sulfadoxine and free drugs like chloroquine phosphate being widely accessible. Many people in semi-urban and rural areas often obtain anti-malarials from grocery shops, resulting in increased treatment failures and severe cases. This review aims to provide an overview of the drugs and key classes involved in controlling malaria in Ethiopia, along with their mechanisms, antimicrobial activities, and efforts to address resistance and other negative aspects in their use [19, 20].

Regulatory Challenges in Medicinal Plant Use

The push for tighter regulation of traditional medicine seeks to attract intellectual property investments and establish a clear patent framework at the national level. In Burkina Faso, firms are hiring consultants to assess local herbal medicines, although local interests and accountability are still concerns. Despite recognizing traditional medicine as a legitimate healthcare option, the effectiveness of proposed regulations in practice is uncertain. Funding must be directed towards strengthening Africa's civil and regulatory institutions for law implementation, enforcement, and monitoring. Improved meetings and amicable regulatory models could help address these challenges. Historically, trade with Europe and America focused on a few exports, but globalization and a growing European population of African descent have sparked interest in Africa's diverse plant assets, leading to the "Green Rush." The recognition that not all drugs should be synthetic has increased interest in Africa as a source of clinically active compounds. This diversity should be characterized through botanical, pharmacological, and chemical methods, followed by effective extraction protocols to isolate active principles. Exploitation involves incorporating standardized herbal materials into formulations, necessitating pharmacological standardization and quality control, which raises concerns about protecting intellectual property rights for traditional knowledge and new inventions arising from it [21, 22].

Future Directions in Research

Plant-derived alkaloids play a crucial role in antimalarial drugs by targeting various structures in the malaria parasite, which is essential amid growing resistance. Historically, medicinal plants have been used to combat malaria, and their inclusion in control programs, alongside experimental protocols, could enhance effectiveness. Efforts involve both indigenous and other commercially available plant extracts. Safety is vital to minimize side effects, similar to popular plant derivatives for heart diseases. Research indicates that many medicinal plants offer protective benefits against malaria, with preliminary studies showing efficacy in vitro. However, some traditional medicinal plants have been found toxic and ineffective. Recent systematic reviews highlight challenges in evaluating plant effectiveness due to cultural and language barriers, yet interdisciplinary efforts are making progress. Projects focus on additive plant combinations and interactions to optimize solutions, while others integrate natural product information with biological activities against the malaria parasite, primarily investigated in vitro [23, 24].

Integration of Traditional and Modern Medicine

From a global health perspective, traditional practices in non-Western societies are crucial for research, avoiding the imposition of non-local views on local populations. Despite this, traditional medicine's role in combating malaria has been largely overlooked. A recent review of clinical evidence on antimalarial plants sheds light on several issues. Historically, colonial powers marginalized traditional medicine by undermining folklore practices. Additionally, most traditional medicine researchers speak languages other

than English, making their knowledge inaccessible to many biomedical researchers. The field is also decentralized, lacking a unified institution like WHO to establish accepted ethical guidelines. Promoting evidence-based standards for herbal medicine could support countries heavily burdened by malaria, where such practices are already part of local life. This development could enable communities to manage their own medicine production sustainably and cost-effectively. Translating herbal medicine strategies into policy demands high-quality research that reflects traditional practices, supported by preclinical trial results. Future studies need transparent reporting and justification of dosages to enhance understanding of interventions' efficacy. The success of future research and the application of findings will require collaboration among scientists, ethnobotanists, traditional healers, and policymakers [25, 26].

Case Studies of Successful Treatments

The case studies in this section demonstrate the effectiveness of medicinal plants for malaria treatment. Each study includes background, methods, results, and limitations. A. mexicana extracts showed positive outcomes in a case-control study with minimal bias. Crude extracts were tested in children aged 1–12 years with confirmed malaria diagnoses. Infection rates dropped significantly within five days, with notable declines in parasite load on days three and seven, and only mild adverse effects occurred, typical for antimalarials. While ethical considerations were addressed, the risk of bias arose from selecting rural patients with high education levels. N. pobeguinii was evaluated in an open-label trial with positive findings and low bias risk. Six adults with fever and positive malaria tests received three forms of the extract along with standard ACT treatment. None exhibited positive tests or fever after 24 hours, with no serious adverse events. This trial is pertinent as participants regularly used herbal medicines. However, it was non-randomized, raising potential biases. Although herbal treatments accompanied antimalarials, fever was the primary measure rather than parasite load. Another study on A. mexicana faced higher bias risk due to combining herbal treatments with standard antimalarials but remained notable as a randomized trial. Sixty adults with fever and positive malaria diagnoses were randomized into three groups: 1- herbal and standard ACT, 2- standard regimen alone, or 3- standard regimen plus safe herbal treatments. Daily assessments of fever and parasite load were conducted over six days. Results indicated a reduced malaria parasite count and significant outcomes from days 1-7, with no serious adverse effects observed [27, 28].

Cultural Significance of Medicinal Plants

Meaningful relationships, notable skill and art, including knowledge of the landscape, plants, animals, food, and textiles, the regulation of survival through hunting, fishing, and gathering, all belong to the local community. Loss of one means loss of the cultural inheritance. Gathering of high-value products such as medicinal plants continues in developed countries for cultural and economic reasons. For the local community, plants and animals have religious and sentimental significance; the extinction of a species means loss of cultural belonging. Cultural identities bound to living beings could last for centuries. Medicinal plants play an important part in the mystical lore of local inhabitants and act as a medium of contact with the higher power of nature. The people pray for healing and also make vows to preserve the sanctity of sacred plants as a form of payment for favours received. Plants and animals are used for divining and initiation ceremonies. The cover of these spiritual sanctuaries must therefore be preserved, not only for the welfare of those who believe in their traditions and respect them, but also for all people, who in turn have to honour their own beliefs. Aspects of religious and cultural beliefs are passed consciously and subconsciously from one generation to the next. A community's identity is carried in its folklore, songs, sayings, dances, and festive occasions, along with a knowledge of its history, revered ancestors, and ancestral places. For that reason, there is a need to record information on biodiversity and its interaction with local culture and spirituality. Further, as attention focuses on the conservation of biodiversity, it too must include documenting and understanding the interrelations between the local plants and animals and the knowledge systems, cultural expressions, and beliefs that go with them. An understanding of these relationships will go a long way in helping to preserve the local plant and animal resources and culture. The interrelationship of plant and animal resources with culture is complex and reciprocal. Need satisfies cultural expression, and cultural expression needs a resource. The preservation of the former depends on appropriate management, and the preservation of the latter depends on the social and spiritual integrity of a community. [29-35].

CONCLUSION

Medicinal plants have played a crucial role in the historical and cultural context of malaria treatment, especially in regions where conventional healthcare systems are inaccessible or unaffordable. Numerous plant species have demonstrated antimalarial activity, and some have yielded globally recognized drugs

like artemisinin. However, despite their therapeutic promise, the effectiveness of many plant-based treatments remains unverified due to inadequate clinical trials, standardization issues, and toxicity concerns. Integrating traditional knowledge with scientific research offers a viable pathway for discovering new, effective, and affordable antimalarial agents. To fully harness the potential of medicinal plants, a multi-disciplinary approach involving ethnobotany, pharmacology, and public health policy is essential. Greater investment in research, safety evaluation, and sustainable cultivation practices will be key to ensuring these natural resources contribute meaningfully to global malaria eradication goals.

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