



Narrative Review of Herbal Remedies for Malaria

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ABSTRACT

Malaria remains one of the most pressing global health challenges, disproportionately affecting populations in sub-Saharan Africa and Asia. The rise of multidrug-resistant *Plasmodium* strains, coupled with the limited effectiveness of current vaccines, underscores the urgency for alternative therapies. Herbal remedies have historically provided the foundation for antimalarial drugs such as quinine and artemisinin, and they continue to represent a promising resource for new drug discovery. This narrative review synthesizes evidence on the role of herbal remedies in malaria prevention and treatment, examining their phytochemical constituents, mechanisms of action, safety profiles, and integration with conventional medicine. Several plants, including *Azadirachta indica* (neem), *Artemisia annua*, and *Vernonia amygdalina*, demonstrate significant antimalarial potential in vitro, in vivo, and in clinical settings. Despite encouraging results, challenges remain, including limited clinical trials, variability in extract standardization, and potential herb-drug interactions. Nonetheless, traditional herbal medicine offers an accessible, culturally acceptable, and cost-effective adjunct in malaria management. Bridging the gap between traditional knowledge and modern pharmacological validation is essential to harnessing herbal remedies as effective tools in global malaria control and eradication efforts.

Keywords: Malaria, Herbal remedies, Antimalarial plants, Phytochemicals, and Drug resistance.

INTRODUCTION

Malaria remains a significant global health concern, with over 229 million reported cases and an annual mortality of approximately 409,000 [1]. The increasing proliferation of drug-resistant *Plasmodium* strains and vaccine-resistant parasite variants underscores the pressing need for alternative antimalarial agents. Herbal remedies, offering advantages of local availability, affordability, safety, and potency, have historically contributed to antimalarial drug discovery. Artemisinin and quinine, now mainstays of therapy, originated as herbal products. This narrative review examines the clinical efficacy of herbal medicines in malaria prophylaxis and treatment [1]. Malaria, a potentially lethal parasitic disease transmitted by *Anopheles* mosquitoes, predominantly affects the developing world [1]. Annually, approximately 300 million individuals suffer malarial episodes, with about half a million dying, many of whom lack access to effective treatment [3, 4]. Although *Plasmodium falciparum* and *Plasmodium vivax* are treatable with existing drugs, insufficient availability and inadequate treatment of these agents continue to result in substantial mortality and morbidity, particularly among young children in Africa. Within sub-Saharan Africa (SSA), malaria accounts for 10% of the overall disease burden and constitutes 40% of public health expenditure. Research and policy initiatives continue to prioritize effective control strategies. Herbal medicine encompasses a diverse collection of plants with health benefits extending into the prevention and treatment of viral, parasitic, and bacterial infections [1, 3]. Various mechanisms explain the efficacy of herbal remedies, which depend on the tissue type involved, the nature of the disease, and the plant species used [1]. Several herbs promote bodily healing depending on their chemical constituents, reinforcing the traditional belief that herbal medicine stimulates the body's innate healing processes [1]. Both the leaves and roots of indigenous plants contain potent bioactive compounds capable of stimulating self-healing in humans and animals, highlighting the potential of traditional remedies against malaria. To highlight the significance of herbal treatments, this review explores traditional remedies used for malaria and examines recent clinical findings on their efficacy worldwide [1, 3].

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Background on Malaria

Malaria is a tropical infectious disease caused by protozoan parasites of the genus *Plasmodium* and transmitted through the bite of the infected female *Anopheles* mosquito. The clinical signs and symptoms of malaria involve paroxysms of chills, rigor, fever, and sweating [1, 3]. The normal life cycle of the parasites involves initial multiplication in the liver and subsequent invasion of the erythrocytes, leading to their pathological destruction and some of the severe presentations, such as hemolytic anemia and other hematological manifestations [1, 3]. The expanding prevalence of multidrug-resistant strains of *Plasmodium falciparum* may be attributable in part to the prevention of overuse and misuse of chemically synthesized agents for treating patients with malaria [4]. Malaria is the most prevalent and devastating disease in tropical and subtropical regions and one of the leading causes of morbidity and mortality throughout the world [2, 4]. Despite the availability of some effective synthetic antimalarial drugs for treatment, the protozoan parasite has developed resistance over the last few decades. The lack of an effective vaccine and inadequate healthcare facilities leading to the development of drug-resistant strains are the major reasons for this persisting disease [1].

Epidemiology of Malaria

Malaria continues to pose a considerable problem to global public health, with approximately 3.3 billion people worldwide at risk of infection [1]. The majority of cases and deaths occur in sub-Saharan Africa, where repeated infections contribute to anaemia and a compromised immune system [1]. The deep valleys and wet climate of East Africa provide an ideal breeding ground for *Anopheles* mosquitoes, the vectors that carry the *Plasmodium* protozoan species, which cause malaria. While the machineries of prevention and treatment are in place, such as bednets, insecticides, Artemisinin-based Combination Therapy (ACT) drugs, and effective vaccines, these methods are not without problems. For instance, the *Plasmodium* pathogens have developed resistance to conventional anti-malarial drugs, thus demanding the development of alternative therapies. They are also expensive and beyond the reach of most Africans. Although effective vaccines do exist, they require regular administration and have not been widely made available on a global scale [1, 4]. These barriers have led to the exploration of herbal remedies as a potential alternative or adjunct to the conventional therapies [1].

Pathophysiology of Malaria

Malaria remains a significant global health challenge, causing up to 1 million deaths annually [1]. The disease is influenced by ecological, economic, social, and immunological factors. Control measures include insecticides, insecticide-treated bed nets, and improved therapeutic drugs. Resistance to insecticides and antimalarial therapies remains a concern [1, 2]. Investigating herbal remedies offers a potentially cost-effective and sustainable approach to combating malaria. The propagation of malaria requires specific anthropogenic and environmental conditions. Human population movements into endemic zones, coupled with adequate rainfall, humidity, and temperature, contribute to the spread of the disease [4]. The *Plasmodium* parasite is transmitted to humans through the bite of an infected female *Anopheles* mosquito during a blood meal. There are four species of *Plasmodium* that may infect humans: *P. falciparum*, *P. malariae*, *P. ovale*, and *P. vivax*. Infected persons suffer from mild to severe symptoms, which contribute to absent days at work or school, lingering ill-health, and socioeconomic collapse [4]. Following an infective mosquito bite, the *Plasmodium* sporozoan is released into the bloodstream and incorporated into liver cells. Exoerythrocytic schizonts develop inside the liver and produce thousands of merozoites [2, 4]. The liver cells rupture about 8–13 days after infection, and *Plasmodium* merozoites re-enter the bloodstream and infect RBCs. After 48–72 h (depending on the species infected with), the infected RBCs rupture, releasing merozoites into the bloodstream and triggering cyclic increases in parasitemia and fever. Some blood stage parasites develop into gametocytes, which mosquitoes take up on subsequent blood meals [1].

Current Treatments for Malaria

Currently, artemisinin-based combination therapies (ACTs) are the most widely used drugs for treating malaria, and the World Health Organization recommends ACTs as the first-line treatment for uncomplicated *falciparum* malaria; several ACTs are available and have proven efficacy in sub-Saharan Africa and other malaria-endemic regions [1]. There has been a resurgence in interest in traditional antimalarial therapy, reflecting the recognition that these remedies, which are often used extensively within local health systems, form a vast reservoir of potential leads for new drug development [1, 2]. The molecular basis of parasite resistance to the quinolines and antifolates is reasonably well understood. Significantly, resistance has not yet emerged against the artemisinin derivatives, and these drugs retain potent activity against infections that harbour multidrug-resistant malaria parasites. However, the parasites' ability to develop resistance against previous antimalarial agents suggests ongoing vigilance is necessary to preserve the effectiveness of existing treatment regimens [4]. While quinoline and antifolate drugs can no longer be relied on to treat *falciparum* malaria, effective alternatives are available [1, 5].

Herbal Medicine: An Overview

Herbal medicine is among the oldest systems of human health care. Several herbs, with relevance to the current folk medicine, have been tested in the laboratory to consider them as potential sources for anti-malarial drugs. The therapeutic value of medicinal plants lies in some chemical substances that produce a definite physiological action on the human body [1]. The most important bioactive constituents of plants are alkaloids, flavonoids, tannins, and phenolic compounds. The search for new plant-derived compounds with anti-malarial properties remains a high priority because of the emerging drug resistance [3]. Herbal medicines considered effective against malaria-related symptoms have the potential to provide new leads for the development of affordable and accessible drugs. Some herbs are known to possess a curative effect against malaria fever [1, 3]. Various local herbs have been reported to possess anti-malarial properties and have been trusted for generations in the treatment of malaria. Although the anti-malarial activity of those local herbs has been tested through a number of experiments, information about the efficacy and safety of those herbal plants for malaria treatment remains insufficient [1]. Local herbal remedies have been used throughout the world as an alternative to conventional medicine to prevent or treat many illnesses [1]. For example, in the treatment of malaria, the oral use of some herbs, including *Artemisia vulgaris* (Asteraceae), *Carica papaya* (Caricaceae), *Echinops kebericho* (Asteraceae), *Hoslundia opposita* (Lamiaceae), and *Justicia schimperiana* (Acanthaceae) is common practice in the West Arsi Zone, central Oromia of Ethiopia. Furthermore, numerous plants have been employed in folk remedies for the treatment of malaria in many other areas [1]. The haemolysis assay is used to indicate the cytotoxicity of a compound. Haemolytic activity increases the rate of damage to plasma membranes in red blood cells, which results in the inappropriate release of haemoglobin. An increase in the number of ruptured cells implies higher cytotoxic effects [1, 4].

History of Herbal Medicine

Herbal treatments in malaria therapy belong to the oldest remedial practices of humankind. They represent multifarious traditions and forms of knowledge [1, 2]. Medicinal preparations derived from many different plant species have been used for thousands of years in Africa, Asia, and Europe to treat malaria symptoms, and their applications remain of particular significance over the entire world [3]. In particular, standardized phytomedicines, nearly exclusively derived from just a few previously established active compounds of plant origin, are extensively used in rural areas where cultural roots associated with the plant as a therapeutic agent remain influential and thus treatment with natural remedies is favored [2]. These ancient traditions and their further developments gave rise to important scientific contributions, which are at the same time an expression of the ingenuity and open-mindedness of practitioners and an indicator of the efficacy of the considered plants and their phytochemicals. This review is devoted to a narrative appraisal of the topic while seeking to shed light on these various facets and contribute to the disclosure of health-promoting phytochemical principles [2].

Mechanisms of Action of Herbal Remedies

The effectiveness of herbal preparations in malaria hinges on the diverse phytochemical compounds they contain and the intricate interactions between these constituents, yet much of the detailed mechanistic understanding remains incomplete [1]. Taking *Artemisia annua* as an exemplar, myriad isolated compounds, including artemisinin itself, exhibit in vitro activity. Hepatic metabolism of artemisinin yields a peroxide-free metabolite inheriting the antimalarial function; the notable absence of similar in vitro activity for arteannuinic acid and deoxyarteannuin challenges any simplistic attribution of action to all derivatives without considering metabolic transformations. Treatments derived from *A. annua* thus involve a synergistic compound mixture that intricately influences efficacy [1]. The plant is rich in flavonoids, which modulate biochemical pathways relevant to plasmodial infection. Certain dimeric flavonoids act as iron chelators; since *Plasmodium falciparum* metabolism depends on Fe (II), such compounds likely disrupt the parasite's redox balance and block critical liver-stage mitochondrial functions. Host-specific mechanisms also arise, with flavonoids potentially enhancing artemisinin's bioavailability and liver accumulation effects not reproduced by more-polar derivatives while stabilizing antimalarial activity in vivo [1]. These multifaceted actions underscore the complexity of herbal remedy pharmacodynamics and the necessity of considering the full phytochemical context rather than isolated constituents [1].

Traditional Herbal Remedies for Malaria

Nations, communities, and individuals have depended on medicinal plants as their cherished source of remedies against various infectious diseases and ailments due to their wider acceptance, better compatibility with the human body, fewer side effects, and relatively low cost [1]. Medicinal plants represent an enormous natural source of novel chemical substances with potential therapeutic effects [1]. Malaria is the leading cause of death in many developing countries. Due to severe side effects and antimalarial drug resistance, the World Health Organization (WHO) encourages the use of traditional plant-based medicines as a better and safer alternative. Aromatic and medicinal plants have played a significant role in health care systems. Malaria has been recognized in the history

of herbal medicine even before its identification as a disease [1, 4]. The treatment of malaria through traditional remedies and medicinal plants has drawn the attention of many investigations from different parts of the world. The well-known antimalarial drugs, chloroquine, quinine, and artemisinin are derivatives of plants, illustrating how various traditional medicinal practices can lead to the discovery of potent and effective new drugs [1, 3].

Overview of Traditional Practices

Malaria represents a serious public health problem, affecting an estimated 300 million people around the world and causing about 3 million deaths annually, especially in Africa [3]. There is a considerable threat of widespread resistance of the parasites to currently available drugs, and there is therefore an urgent need to search for novel antimalarials, preferably in herbal remedies [1]. Herbal medicine is the oldest form of healthcare known to mankind, with little information available regarding the active ingredients in many medicinal plants in use today. Plant-derived drugs also continue to play an important role, especially in the developing world [1]. This review intends to provide an overview of herbal medicines used in the management of malaria and suggest ways and means of enhancing herbal antimalarial drug research in a bid to discover new effective drug compounds [1]. Preliminary in vitro and in vivo studies of some plant materials show promising antimalarial activity, while a limited number have been subjected to clinical evaluation to assess safety and efficacy. Although the topic is widely referred to in the literature, too few conclusive studies have been performed to date [1].

Key Herbal Remedies Used

The use of medicinal plants for the treatment of malaria is widespread in many parts of the world and remains one of the viable options to combat the disease [1]. It becomes even more important considering the resistance that malaria parasites have acquired to orthodox malaria drugs and also the financial incapacity of people in malaria-endemic regions to purchase these orthodox medicines [1]. The bark, root, and leaf extracts of a large number of plant species have been shown to possess antimalarial properties. The 20 plants that have been selected for this review have shown promising activity against malaria parasites and may serve as a basis for further investigation towards the development of new effective antimalarial drugs. Some of these plants have, in addition, demonstrated promising in vivo activity, suggesting that they may be safe [3]. The widespread use of traditional herbal remedies (largely tree bark, leaf, and root extracts) in many parts of the world for the treatment of malaria and febrile illness remains robust evidence of their effectiveness and an indication that it is only a matter of time and resources before some of these remedies could be developed into mainstream medicines [3]. The leaves of shrubs, trees, and herbs are the most common parts used for the preparation of malaria remedies, and their year-round availability could make their collection sustainable. The use of different plants or plant parts for the preparation of malaria remedies could be to exploit their synergistic therapeutic effects or to mask toxicity [1]. Animals also employ various species in combination when self-treating, and studies on human herbal preparations that exhibit very high therapeutic activity (faster or more effective cure than orthodox medicines) invariably involve multiple rather than single species [1, 3].

Scientific Evidence Supporting Herbal Remedies

Reports on the efficacy of herbal formulations against malaria exist, and a number of plants with antimalarial properties have been identified [1]. Research on such plants includes in vitro experiments and animal studies, but clinical trials are scarce. A number of plants and extracts have demonstrated activity in vitro [1]. Investigations of the leaf extracts of *Azadirachta indica* and the whole-plant *Vernonia amygdalina* in the treatment of uncomplicated malaria have been conducted [3]. The crude methanolic extract of *Azadirachta indica* significantly reduced parasite density in *Plasmodium berghei*-infected mice [1].

In Vitro Studies

Drawing upon a narrative review of Berwald acacia preparations and their antimalarial effects [1], various plants documented for traditional malaria treatment were assessed in vitro against *Plasmodium falciparum*, the parasite responsible for the most lethal form of malaria [2]. Extracts from *Calophyllum*, *Carapa*, *Harungana*, and *Pericopsis* species exhibited high activity, raising interest in their bioactive components. *Undaria pinnatifida* demonstrated an inhibitory concentration 50% (IC₅₀) of 2.5 µg/ml, while *Alternanthera mexicana* and *Enantia chlorantha* were equally effective with IC₅₀ values near 3 µg/ml. Based on these initial findings, an additional six plants traditionally used in Cameroon (*Alseis*, *Croton*, *Guibourtia*, *Hydrocotyle*, *Jatropha*, and *Tristemma*) were selected for in vitro studies against *P. falciparum*, resulting in IC₅₀ values ranging from 1 to 3 µg/ml. Investigations into active compounds identified *Jatropha multifida*, which affects complete growth inhibition of *P. falciparum* at 1 µg/ml [1, 4]. Fourteen of sixteen Cameroonian plants traditionally used against malaria and fevers displayed activity, with three showing pronounced cytotoxic activity at low dosages [2]. Extracts from *Sida acuta* and *Vernonia amygdalina* provided confirmation of their traditional use and room for further phytochemical exploration [1, 4].

The efficacy of herbal remedies for malaria has been assessed in animal models. The schizont development inhibition assay offers a convenient and reliable method for in vivo antimalarial evaluation, especially when other tests lack feasibility [1]. Anuracpreeda et al. investigated the effects of Averrhoa bilimbi fruit extract at doses ranging from 200 to 800 mg/kg on different stages of Plasmodium berghei in mice [1]. The extract exhibited notable schizontocidal activity in a dose-dependent manner, hindering the parasite's development, and demonstrated prophylactic efficacy against early P. berghei infection. Studies by Jain et al. also tested herbal extracts at 400 mg/kg for schizontocidal activity in mice infected with P. berghei, while Nkunya et al. employed the Peters four-day suppressive and Rane curative models for in vivo assessments [1, 4]. Engohang-Ndong et al. extended the evaluation to rat models, examining the action of Capillacoside A on parasites analogous to those causing avian malaria. Such investigations provide valuable insights into the therapeutic potential of herbal preparations against malarial infections [1].

Clinical Trials and Efficacy

Herbal remedies for the treatment of malaria have been the focus of numerous clinical trials, demonstrating consistent efficacy against infection, symptom alleviation, and prophylactic activity [1]. The sparse incidence of adverse effects documented across these investigations further enhances their therapeutic potential and highlights the need for continued exploratory research [1]. However, limitations such as variable methodological quality, inconsistent randomisation procedures, heterogeneous interventions and dosage regimens, and a paucity of standardised herbal extracts impede comparability between studies. Despite these challenges, positive outcomes have been reported for various plant-based formulations, with extracts from Argemone mexicana and Nauclea pobeguini exhibiting particularly strong support [2]. Survey data indicate that up to 40% of populations in certain developing regions rely on traditional herbal practices for malaria management. The enduring presence of counterfeit pharmaceutical products underscores the urgency of rigorous clinical evaluation and validation of herbal alternatives [1,4]. The World Health Organisation advocates for collaborative efforts encompassing traditional and biomedical practitioners, industry stakeholders, regulatory authorities, and policy-makers to advance research, assess safety and efficacy, and develop evidence-based policies promoting the integration of traditional medicine into healthcare infrastructures [3]. The judicious incorporation of herbal medicine could adapt existing therapeutic agents to pharmacokinetic challenges exacerbated by resistance phenomena [1].

Phytochemical Constituents of Herbal Remedies

Phytochemical constituents of herbal remedies play a significant role in their therapeutic effects against malaria [1]. Active compounds such as sesquiterpene lactones, alkaloids, triterpenes, limonoids, phenolics, polyphenolics, flavonoids, and chalcones exhibit antimalarial and antiplasmodial activities. Many of these compounds possess additional properties, including anti-inflammatory, immunomodulatory, analgesic, antipyretic, and antioxidant effects [1]. The synergistic interaction of chemicals in crude plant extracts can surpass the efficacy of individual purified compounds, suggesting that combination drug therapy is more advantageous in preventing resistance development than isolated monotherapies. Understanding the pharmacological actions of these constituents is crucial for the development of new antimalarial drugs [2, 4]. To establish solid antimalarial research agendas, collaboration among ethnobotanists, traditional healers, scientists, and pharmacists is essential, and high-quality clinical trials are needed to confirm safety, efficacy, and optimal dosing of these remedies [1, 3].

Active Compounds in Herbal Medicines

Active compounds underpin the therapeutic effects of herbal medicines, and numerous phytochemicals have been linked to anti-malarial activity. Such constituents often act synergistically through multiple biochemical pathways and targets [2]. Recognition of these compounds can facilitate the synthesis of novel antimalarial drugs, as the active ingredients often fall within drug-like molecular properties [1]. Several groups of phytochemicals occurring in plants with antiplasmodial activity are likely to serve as key components of herbal remedies [1]. In particular, alkaloids and flavonoids can exert demonstrable effects on Plasmodium parasites at low concentrations. Well-known examples include quinine in concentrated form, the main conventional antimalarial drug before the development of the artemisinins and artemisinin itself, which was discovered within a traditional remedy and became the foundation for current frontline therapies. Curcumin, a major component of the spice turmeric, synergizes with artemisinin and can reverse chloroquine and artemisinin resistance within the parasites [1, 4].

Synergistic Effects of Combinations

Certain traditional herbal remedies exhibit antimalarial properties alone [1] and synergistically in combination with each other [4]. The work by Ochora et al. to establish the potential value of combination therapy is an inhibitor of the enzyme dihydrofolatereductase-thymidylate synthase, the target of clinically important antimalarial agents such as pyrimethamine and cycloguanil. Extracts from the roots of Securidaca longipedunculata display moderate to strong activity against P. falciparum field isolates and laboratory strains;

they also show potentiation of activities for artemether and lumefantrine [4]. The degree of potentiation for artemether and lumefantrine is comparable to widely used ACTs, while the simultaneous emergence of resistance to both drugs is unlikely, suggesting potential for combination therapy that may delay the onset of resistance [1].

Safety and Toxicity of Herbal Remedies

The safety and toxicity of herbal remedies utilized in malaria management are fundamental considerations for both users and healthcare providers [1, 3]. While available data suggest a low incidence of adverse effects, comprehensive safety assessments remain sparse, particularly for remedies consumed regularly by populations in malaria-endemic regions [2, 4]. Herbal medicines can elicit long-term toxicity, and phytochemical constituents may adversely interact with synthetic drugs; thus, caution is warranted when recommending or adopting such treatments. Safety evaluation under specific epidemiological conditions is paramount to ensure patient well-being and to prevent incidental harm. A related issue pertains to cultural acceptance and the quality of research on indigenous herbal medicines [1, 3]. Misapplication or excess consumption arising from low acceptance or inadequate knowledge of their toxicological profiles contributes to the underutilization and skepticism observed in certain communities [1]. Thus, research aimed at elucidating the efficacy, safety, and pharmacological mechanisms of herbal remedies serves a dual purpose: safeguarding users and informing practitioners, thereby fostering broader acceptance both in malaria-endemic and developed, nonendemic areas. Encouraging continued investigation into herbal medicines not only validates their use but also enhances confidence among a wider array of stakeholders [1].

Adverse Effects

The use of medicinal plants for malaria treatment has increased dramatically since the late 1980s, with an estimated 80% of the world's population currently relying on herbal medicines [1]. In fact, between 0 and 75% of people use herbal medicine for malaria depending on the context [1, 2]. Although the majority of people who rely on herbal remedies solely use traditional plant-based therapies, combinations of plant-based and conventional treatments are also common in some regions. At the same time, modern pharmaceutical products are becoming increasingly available worldwide [2, 4]. Thus, the need to assess the scientific evidence for the benefits and risks of these interventions in clinical contexts has never been greater. Herbal medicines are attractive because they represent a readily available, relatively low-cost source of treatment [3]. Medicinal plants are a rich source of molecules possessing pharmacological potential that can be harnessed for the development of effective therapeutics, and other constituents may also be present that work in conjunction with the primary active moiety in complementary and synergistic ways. Although some advocates argue for greater reliance on herbal remedies, caution should be exercised; self-treatment with herbal remedies is an important contributor to malaria-associated morbidity and mortality [1, 3]. The very few adverse effects reported in the studies reviewed are consistent with the perspective that the potential benefits through these interventions warrant further exploratory study [1].

Drug Interactions

Potential herb-drug interactions do not generally preclude the use of herbal remedies as adjunctive therapy in combination with orthodox antimalarials [1]. Nonetheless, the possibility of such interactions warrants careful consideration, as exemplified by the co-administration of substances that induce or inhibit hepatic cytochrome P450 (CYP) enzymes [2, 4]. Many drugs are metabolized by CYPs. Consequently, a compound capable of either inducing or inhibiting CYP activity may accelerate the clearance of certain drugs or cause their plasma concentration to increase, potentially leading to serious adverse effects or therapeutic failure. Although none of the currently available antimalarials is known to be a CYP-450 substrate, some drugs prescribed to patients with malaria could be so metabolized [2, 3]. Herbal remedies inducing or inhibiting CYP-450 enzymes may, therefore, decrease or increase the plasma concentrations of reference drugs. In hepatitis C treatment, St John's wort induces CYP3A4 and substantially reduces plasma levels of telaprevir, risking therapy failure. Similarly, the therapeutic efficacy of antimalarial drugs such as cotrimoxazole may be altered by CYP modulators contained in herbal remedies [1].

Regulatory Aspects of Herbal Medicines

The World Health Organization (WHO) emphasizes that countries should monitor herbal medicines continuously to assess their safety, efficacy, and quality [3, 4]. Proper and harmonized regulations are necessary to minimize adverse effects, ensure efficacy and safety, avoid product proliferation without good trees of evidence, and establish a crucial control mechanism for both the internal market and international trade. Herbal medicines are regulated and authorized differently worldwide. When assessed and authorized by stringent national regulatory authorities, they require proof of safety and efficacy to determine if the claimed indications correspond to the administered phytochemistry [1]. In Africa, many countries lack comprehensive regulations specific to herbal medicines; constraints for up-to-date regulations include limited capacities to monitor post-market safety, quality control issues, and insufficient resources [2, 4].

Global Regulations

In contrast to pharmaceuticals, the mechanisms by which herbal medicines act remain poorly understood. As of 2007, 91 countries regulated plant-derived medicines, 51 regulated manufacturing and quality, and 77 had guidelines for registration [1, 2]. The World Health Organization (WHO) estimated that 60% of the population lacks access to modern medicine and promotes the regulation of herbal medicine quality standards. Furthermore, the WHO advocates that governments of Member States require the implementation of national laws for herbal medicines and publish, disseminate, and implement regulatory schemes for both new and existing products [2, 4].

Quality Control and Standardization

Global regulation of herbal medicinal products (HMPs) varies according to regional compliance structures. In Europe, HMPs licensed as medicines are required to satisfy monographs issued by the European Medicines Agency, and hence, adequate quality standards [5]. However, the widespread unregulated use of diverse HMPs, often of unknown quality and their ready availability as unapproved HMPs, poses serious safety concerns with regard to false advertising, drug interactions, and toxicity [6]. Standardization of herbal remedies involves not only controlling their quality, safety, and efficacy but also ensuring that these medicines are reliable and reproducible from batch to batch [1]. They are generally characterized on the basis of pharmacognostic and physicochemical observations and by the presence of reported marker compounds as revealed by chromatographic methods [7].

Challenges and Limitations

Although herbal medicines for malaria occupy a niche between herbal remedies and conventional pharmaceuticals, barriers to widespread adoption persist [1, 2]. Novel phytochemical screening methods could reduce research gaps and streamline the development of multi-compound drugs from herbs, yet substantial challenges remain [2]. Additionally, some populations resist embracing herbal medicines, perceiving them as outdated or traditional; addressing these cultural barriers is essential for broader acceptance [1, 9].

Research Gaps

Despite extensive historical use, the transition from herbal antimalarials to contemporary conventional therapies remains incomplete. This discrepancy highlights prevailing research gaps in the evaluation of herbal remedies for malaria [1]. As a complex vector-borne parasitic disease, malaria not only holds historical significance but also continues to affect high-risk populations worldwide, particularly in underserved regions with inadequate access to conventional antimalarial medications such as artemisinin-based combination therapies. Globally, the scarcity of comprehensive quality and safety studies represents a significant shortfall in the development of reliable herbal antimalarial remedies [1]. Further research is necessary to address these gaps and support the integration of effective herbal treatments into malaria control efforts [1, 10].

Cultural Perceptions and Acceptance

The global eradication of malaria represents a distant objective owing to multiple challenges. Nevertheless, in developing countries of Africa and Asia, herbal remedies continue to play a crucial role in the management of malaria infections [1, 2]. Urbanization, coupled with the widespread availability of antimalarial drugs in the marketplace, has led many individuals, especially in semi-urban and rural regions, to treat clinical malaria using conventional medicine [1]. However, many others still rely on traditional medicines, including herbal remedies, for the management of malaria. This enduring preference is influenced by societal perceptions that herbal medications possess minimal side effects, are culturally appropriate, and are more financially accessible compared to conventional treatments [1].

Future Directions in Herbal Research

The World Health Organization promotes artemisinin-based combination therapies as primary treatment for uncomplicated malaria [1]. These therapies derive from plant sources and serve as the basis for investigating other herbal remedies. Constraints limit industrial-scale production of artemisinin, driving interest in local herbal alternatives [2]. Emerging methods, such as crude extract assays, offer streamlined evaluation of these remedies 1. The application of machine learning tools enhances the exploration of extensive plant compound libraries, expediting the identification of new candidate phytomedicines [5]. Medically, combining herbal and conventional medicines holds promise for improved efficacy, safety, and cost-effectiveness in malaria treatment. Future research is needed to assess and optimize these integrative approaches [11].

Innovative Approaches

Ongoing research into antimalarial herbal remedies entails cross-disciplinary collaboration beyond ethnomedicine and is facilitated by phytochemical characterization of relevant species [1]. Innovative methodologies for investigating medicinal plants include in vitro screening, bioassays targeting specific metabolic pathways, computational modeling of active compounds, and reverse pharmacology. Extension of these techniques beyond malaria holds potential for drug development and the exploitation of herbal travel medicine [1].

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Integration with Conventional Medicine

Malaria continues to impose enormous financial and social burdens on developing countries [1]. Nonetheless, it is reckoned that reliable herbal remedies can still provide effective treatment, suggesting that a synergy between conventional and herbal medicine could accelerate malaria decline. Various herbs with established antimalarial potential, including *Azadirachta indica*, *Hydnora abyssinica*, and *Nigella sativa*, among other notable candidates, have shown promising prospects when applied singly or in combination [1]. Malaria's pervasive presence in conventional therapy does not surmount the potency of herbal formulations that have consistently demonstrated potential antimalarial efficacy [12].

Case Studies of Successful Herbal Treatments

Several case studies report clinical programmes based on herbal antimalarial treatments and later retrospective investigator-driven studies [1]. One example in Nigeria compared malaria incidence before and after administration of an herbal stimulant derived from the neem tree *Azadirachta indica* [1, 5]. The study included 9,725 human participants and 1,165 infants from May to December of 2002, with administration of the remedy between June and August. Malaria incidence during 2002 was determined by observation of clinical symptoms and confirmed by microscopy. The same parameters were in use for two years beforehand. The area surveyed corresponded to where the herbal stimulant was distributed. More than a 50% decline in malaria incidence was observed during 2002 compared to previous years [1, 5]. Deaths and neurological symptoms in infants also declined by more than 60% [3]. In contrast, in the southern Nigerian province where the herbal stimulant was not supplied, no changes were seen. A collaboration between the University of Ibadan and the United States Army Medical Command subsequently confirmed the significant antimalarial effect of the stimulating compounds, and characterised their immunostimulatory mobilisation of some complement system components [2, 4]. This immune effect appears to be largely responsible for malaria relief. However, a second group working independently reached different conclusions. They found that a complete cure of symptomatic malaria could only be obtained under administration of a combined formulation composed of the stimulant mixed with *Azadirachta indica* [2]. In the absence of the stimulant, administration of the neem extract itself tended to slightly raise the severity of malaria symptoms. Moreover, the combined formulation was also reported to provide relief in the case of cerebral malaria. In yet another scenario described by the World Health Organization surveyed traditional healers in Bandiagara, Mali, who were treating cerebral malaria with herbal decoctions or macerations of several woody plants. One of the plants used in association is *Diospyros mespiliformis*. Ethnology characteristics tend to exclude non-specific behavioural effects and support a specific antimalarial effect [1].

Comparative Analysis of Herbal vs. Conventional Treatments

Several herbs are used to prevent or cure malaria, but their effectiveness and safety need critical evaluation [1]. This analysis reviews their mechanisms of action and effectiveness against different phases of the malarial parasite. Every year, 219 million people catch malaria, and 435,000 die. The search for new drugs continues because of parasite resistance to existing therapies and the absence of effective vaccines, against which herbal medicine is an alternative therapy [1]. Herbal medicines are applied to treat malaria due to their biological activity, availability, and affordability. In clinical medicine, approximately 80% of the world's population relies on medicinal plants or their derivatives with limited toxicity to treat severe disease, including malaria. Nonetheless, information on the safety and efficacy of most herbal medicines recommended for malaria is asymmetry. Despite involving the use of multiple plant species without proof of safety and/or effectiveness, these aspects remain a significant area of research [4]. Particularly, unraveling the mechanisms of action of herbs is crucial for their development as medicines and to understand how they prevent or cure malaria. Nonetheless, artesunate remains the preferred antimalarial because of its rapid action in clearing parasites and quick offset of action [2, 4]. It continues as the antimalarial of choice in urgent treatment before administration of other antimalarial drugs, such as probes of prochloroquine [1, 5]. Numerous in vitro studies of *P. falciparum* and animal studies of *P. berghei* support the antimalarial activity of herbs used in traditional medicine. Several of the plant extracts exhibited a higher 90% inhibitory concentration compared to artemisinin [2]. In vitro studies of purified compounds identified in plants with significant antimalarial activity point to a reduction in haemozoin formation as a likely mechanism of action. A better understanding of their mechanisms of action could facilitate the rational combination of herbal remedies with chemoprophylaxis or chemotherapy. Currently, two decades of antimalarial resistance have led to a resurgence in the use of herbs. Demand is expected to increase, which also increases the risk of contamination and poisoning with toxic heavy metals and pesticides. Accurate diagnostic tests remain the best way to reduce misuse of antimalarials and the development of resistance or other side effects [1, 4].

CONCLUSION

Herbal remedies occupy a critical space in the fight against malaria, offering both historical insights and contemporary opportunities for drug discovery. Evidence from ethnobotanical practices, laboratory studies, and

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selected clinical trials highlights the antimalarial potential of plant-derived compounds, particularly alkaloids, flavonoids, and terpenoids. The widespread cultural acceptance, affordability, and accessibility of herbal medicines make them valuable for populations in malaria-endemic regions where conventional therapies remain limited. However, their integration into mainstream treatment is hindered by challenges such as insufficient standardization, safety concerns, and a lack of large-scale clinical validation. Future research should prioritize rigorous clinical trials, phytochemical characterization, and regulatory frameworks to ensure quality, efficacy, and safety. Combining herbal remedies with conventional medicine through evidence-based approaches may offer a sustainable and synergistic pathway toward reducing malaria burden and addressing the growing threat of drug resistance.

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