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Medicinal Plants as a Source of Antimalarial Agents: A Review of Current Research

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ABSTRACT

Malaria remains a significant public health challenge, with millions affected annually and the rapid emergence of drug-resistant Plasmodium species exacerbating the issue. This review examines the historical, ethnobotanical, and contemporary scientific knowledge on the role of medicinal plants in antimalarial therapy. Many plants, such as *Artemisia annua* and *Cinchona* species, have yielded potent antimalarial compounds like artemisinin and quinine, respectively. Traditional knowledge continues to inspire modern drug discovery efforts, although much remains unexplored. Advances in in vitro and in vivo screening, bioactivity-guided fractionation, and molecular docking approaches have highlighted promising phytochemicals such as flavonoids, alkaloids, and terpenoids. Challenges in translating traditional remedies into scalable treatments include drug resistance, sustainability concerns, and gaps in interdisciplinary research. By leveraging traditional knowledge and modern science, medicinal plants offer a sustainable and innovative pathway to address the global malaria burden.

Keywords: Medicinal plants, Antimalarial agents, Drug resistance, Traditional medicine, Phytochemicals, Artemisinin.

INTRODUCTION

Malaria is one of the most dangerous tropical diseases that affect humans. There were 219 million cases of the disease and 435,000 deaths worldwide in 2017. Malaria can be treated with different types of drugs, but the appearance of strains resistant to conventional therapy poses a challenge, prompting the need for new, highly efficient drugs with different modes of action. Traditional medicine is a source of many drugs in use today, and even if the drugs and the compounds that they comprise are not always highly effective, they have been and are still an inspiration for the incipient pharmaceutical industry. Moreover, bioprospecting is very much in vogue now, and some drugs and contaminants used in medicine have a natural compound in their composition. When used in rational drug design and to locate, quantitatively assess, and interpret plant compounds' antimalarial activity, some of these compounds will likely transmute into potent antimalarial agents in the near future [1, 2, 3]. Traditional knowledge of parasite diseases such as malaria is immense and plays an important role in communities worldwide. Although recognized as a social and cultural question, traditional medicine has been criticized by some as crude and non-specific based on the philosophy that "traditional medicine" is different from other military-based medicines. Surprisingly or not, many of the antimalarial pharmaceuticals come from natural compounds, such as quinine isolated from Cinchona, artemisinin extracted from Artemisia annua, and totarol synthesized from Podocarpus nagi. However, the rate of development of new drugs, natural or otherwise, has not kept pace with the rate of appearance of drug-resistant parasites, and the search for new antimalarial compounds from medicinal plants continues. Under these circumstances, some antimalarial drugs could be found that do not have toxic effects, and quinine and artemisinin have low toxicity in antimalarial treatments. The treatment is so effective that those sensitive to artemisinin may reduce the duration of the combined artemisinin component to three days [4, 5].

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Historical Use of Medicinal Plants in Malaria Treatment

Humans have been treating malaria with medicinal plants for thousands of years, and over time this practice evolved differently in various parts of the world. Malaria has had a significant impact on human populations in both ancient cultures as well as contemporary ones, and for this reason, in nearly all of these malaria-endemic regions, traditional healing involving the use of medicinal plants has evolved. With human civilization dating back to at least the second millennium BCE, information has been recorded on the use of medicinal plants for the treatment of malaria, and this has been used as evidence in the analysis of the curative properties of particular plants. As a response to disease, knowledge of the medicinal uses of plants has developed over generations, whereby an undertaking of trial and error, astute ethnopharmacological observations, and experience led indigenous populations to the selection and curative use of medicinal plants. These archaic disease treatment practices have since been passed down through generations from parent to child [6, 7]. Knowledge of the use of medicinal plants as antimalarials has been passed down through generations in African and Indian cultures, with recent reviews including various plant species. The low incidence of malaria in certain remote communities is still due to the use of traditional medicinal practices, passed down through generations and spanning thousands of years, which can be considered a testament to the enduring efficacy of medicinal plants against malaria. However, the loss of traditional medicinal knowledge is occurring rapidly throughout the world as a result of globalization especially because indigenous people are leaving their remote villages to get an education, find work, or access modern healthcare in other areas [8, 9].

Current Antimalarial Drug Resistance and the Need for Alternative Treatments

The emergence of antimalarial drug resistance represents a serious public health issue. The development of resistance to the main drugs used in artemisinin-based combination therapies is widespread, with risks in treatment efficacy and the potential for the selection of multidrug resistance. To counter the threat to malaria control and eradication, new antimalarial therapeutics acting on different parasite targets need to be developed urgently. The search for new drugs identified anticancer therapies, and treatments for tropical diseases and bacterial infections from plants or their derivatives is one possible source for new medicines [10, 11]. Malaria, as a neglected tropical disease, affects millions of people every year, mainly in developing countries. The situation has been exacerbated by the appearance of drug-resistant parasites. The development of resistance to current antimalarial drugs by the parasite has become geographically widespread. Chloroquine was used as the most widespread first-line drug for treating for more than 30 years, but resistance has reduced its efficacy in treating illness. In addition, parasite resistance has developed to many other antimalarial drugs, including Fansidar, quinine, and mefloquine. Although artemisinin combination therapies are highly effective in treating, signs of resistance to artemisinin derivatives are present, spreading throughout the greater Mekong subregion, where delayed parasite clearance following treatment with artemisinin-based combination therapies has led to decreased efficacy. The increasing number of cases of treatment failure could facilitate the development of drug resistance and is of increasing concern as there are few alternatives available [12, 2].

Bioactive Compounds in Medicinal Plants with Antimalarial Properties

Bioactive compounds isolated from medicinal plants can possess antimalarial properties. These compounds, which can be classified into various groups such as alkaloids, flavonoids, terpenoids, etc., work through divergent pathways that are toxic to the parasites and/or toxic to the host red blood cells. The alkaloid quinine has been used for several decades against malarial parasites, primarily during the mid-20th century. Another alkaloid, artemisinin, has made an indispensable impact on worldwide antimalarial policy. Besides lowering the treatment tension between artemisinin-based combination medicine and the emergence of drug resistance, both artemisinin and its derivatives are highly threatened due to quality issues triggered by poor manufacturing practices. In this review, the antimalarial activity of phytocompounds has been documented. Two natural flavonoids, quercetin, and rutin, with IC50 values of 0.042 and 0.0466 mg/ml against Plasmodium falciparum, respectively. The antimalarial activity of flavonoids, quercetin, and its derivatives has also been reviewed. An in silico genomic approach predicted that vitexin acts on the translation system of P. falciparum. Phlomis bracteosa, Vitex negundo, and Artemisia saxatilis with significant antiprotozoal activity against P. falciparum in laboratory studies. To study the molecular basis of the action of active fractions, the major compounds possessing antiparasitic activity. Further, in silico docking studies demonstrated that flavonoids may act by interfering with intracellular signaling in parasites. Several species of the Vitex genus possess quercetin glycosides, which exhibit antimalarial activity. Perhaps these provide proven biological credibility to flavonoids, and hence

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screening from the plants can further confirm their remarkable therapeutic utility. Glycosylated C-glucosidic flavones are mainly present in Maesa species, which possess antimalarial activity. This deserves further investigation to study its antimalarial mechanism [13, 14].

Methods for Screening and Identifying Antimalarial Compounds from Medicinal Plants

In Vitro Assays Though in vitro assays that allow comparative analysis of the Plasmodium inhibitory effects of chloroquine and plant extract/protein have been developed to date, it is usually found that active extracts are less potent than pure compounds [15, 16, 17]. Therefore, in approaches where a crude extract of the medicinal plant is compared with positive drug control, it might result in a 'false negative' screening of promising plants. Results must be confirmed in in vivo assays to demonstrate that the crude drugs are not promising. In in vitro assays, a variety of parameters can be varied, and it becomes difficult to screen a library of crude extracts under different assay conditions [18, 19, 20]. In Vivo Assays In vivo assays involve treating infected laboratory animals with the plant extract under investigation and comparing their plasmodial suppressive effects with a drug-treated group and a placebo-treated group. In vivo, assays will indicate the types of compounds in the extract and quantify the level of activity. The extract is then subjected to bioactivity-guided fractionation. Compounds of interest are then located and identified using biological assays, LC-MS, and NMR [21, 22]. Bioactivity-guided fractionation involves a combination of in vitro and in vivo testing and has the advantage that it may 'terminate' the fractionation process early when bio-guided biological assays suggest that the fraction is inactive. Collection of biological and physical results, clinical observations, and metabolite analysis provides valuable information about in vivo performance, tolerability, and possible detoxification interactions. The clinical investigation of herbal remedies provides valuable information on acceptable dosage and maintenance of quality. Treatment in volunteers leads to the observation of possible side effects and dose-related harm retrospectively. Data for the assessment of dosing regimens and labels can be obtained before and after the collection of clinical trials. However, multidisciplinary research is necessary for such an approach. Ethnobotanical knowledge may help to reduce the number of responses. In some studies, DNA barcoding confirms plant identity in some fractionation steps, which significantly affects the validity of the research findings [23, 24, 25].

Case Studies of Promising Medicinal Plants with Antimalarial Activity

Focusing on a few plant species that are documented as having some literature supporting antimalarial effects is helpful. This permits the discussion to better highlight the research approaches that may be undertaken, other factors influencing study outcomes, and ultimately, how this may contribute to finding and bringing to market safe and efficacious new antimalarial treatments [26, 27]. While the focus of this paper is not to provide exhaustive coverage of all promising antimalarial plants, some examples are highlighted below to examine which plants are being researched; the evidence supporting their antimalarial activity, including studies; the methodology, including active compound identification, and assays used; and successful outcomes, which indicate the particular plant as a potential source of new antimalarial drugs that, if used appropriately, could generate income and combat malaria in low-income countries. The importance of sustainability in utilizing antimalarial plants is also highlighted [28, 29]. The decline in confirmed antimalarial plant studies suggests there is an ongoing reluctance to proceed with these types of initiatives. Likely, more species have not yet been studied. Even those that have received attention may offer more candidates of active compounds for further investigation. Since ancient times, many plants have been traditionally utilized to cure malaria, and some remain central ingredients in certain antimalarial remedies used in some regions today [30]. It is important to show scientific evidence confirming the traditional uses of these plants, but it is also important to first document such uses before embarking on studies. Without historical use of some predilection, these remain overlooked as a source of new antimalarials. Outcomes that suggest potential will, in turn, encourage investment. Although it is important at this early stage to only invest in candidate plants where sourcing and/or growing these in sufficient volume to supply a traditional treatment program is economically viable and affordable. Finally, ethical relations with source countries and communities must also be ensured [31, 32, 33].

CONCLUSION

The review underscores the vital role of medicinal plants as a reservoir for antimalarial agents, highlighting their historical significance and modern therapeutic potential. Despite the challenges posed by the emergence of drug-resistant malaria strains, the integration of traditional medicine with cutting-edge research methodologies can yield novel compounds and treatment approaches. Promising plant-

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derived compounds such as artemisinin and flavonoids demonstrate that medicinal plants are a cornerstone in combating malaria, especially in endemic regions where access to synthetic drugs is limited. However, realizing their full potential requires addressing sustainability, ethical sourcing, and rigorous scientific validation. Future research should focus on identifying and optimizing plant-derived antimalarial agents through interdisciplinary collaboration, ensuring that these natural resources contribute effectively to global malaria control efforts.

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