Kwaghe International
Journal of Sciences and Technology

ISSN: 1595-7977

Index: Harvard, Boston, Sydney University, Dimensions, Lens, ResearchGet Scilit, Semantic, Google Scholar, Base etc

https://doi.org/10.58578/KIJST.v3i1.9359

A Review on Antiplasmodial Activities of *Hyptis suaveolens* Plant

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Article Info:

Submitted:	Revised:	Accepted:	Published:
Feb 6, 2025	Mar 6, 2026	Mar 18, 2026	Mar 23, 2026

Abstract

Hyptis suaveolens (L.), a member of the Lamiaceae family, has long been used in traditional medicine and has recently attracted increasing attention for its antimalarial potential. This review synthesizes existing evidence on the antimalarial properties of *H. suaveolens*, with particular emphasis on its bioactive constituents, including flavonoids, terpenoids, and essential oils, which have demonstrated notable activity against malaria parasites. Evidence from both *in vitro* and *in vivo* studies indicates that extracts of *H. suaveolens* can inhibit *Plasmodium* species, particularly *Plasmodium falciparum*, the major causative agent of human malaria. The review further examines the proposed mechanisms underlying these effects, including inhibition of parasite growth, cytotoxic activity, and immunomodulatory responses. In addition, it highlights key challenges that must be addressed for therapeutic development, notably the standardization of plant extracts, clarification of toxicity profiles, and the need for rigorous clinical trials. Overall, the review underscores the promise of *H. suaveolens* as a potential source of novel antimalarial agents and contributes to ongoing efforts to identify plant-based alternatives for malaria treatment.

Keywords: *Hyptis suaveolens*; Antimalarial Activity; Phytochemicals; *Plasmodium falciparum*; Medicinal Plants

Introduction

In recent years *Hyptis suaveolens*, generally known as bush mint has gained significant attention as a result of its diverse pharmacological properties, particularly its antimalarial activities [9]. This plant, being native to tropical regions is a member of the *Lamiaceae* family, possessing aromatic leaves and a rich phytochemical profile, which includes essential oils, flavonoids, tannins, saponins, and alkaloids [29]. These compounds have been proven to carry out various biological activities, including antimicrobial, anti-inflammatory, and antioxidant effects [25]. This contributes to the plant's traditional use in folk medicine for treating a range of ailments, including malaria.

The exploration of the antimalarial potential of *Hyptis suaveolens* through various experimental studies, has demonstrated its efficacy against *Plasmodium* species, most notably against *Plasmodium berghei*. Research The ethanolic extracts of the leaves have been shown to exhibit significant suppressive effects on malaria parasites through extensive research, suggesting an interference with the life cycle of the parasites or enhancement of the host's immune response by the bioactive compounds present in the plant [5,11]. Hence, the traditional knowledge of utilizing *Hyptis suaveolens* in the treatment of malaria is supported by scientific evidence, underscoring the importance of integrating ethnopharmacological insights with modern pharmacological research to validate and potentially enhance the therapeutic applications of this plant [25,33].

Hyptis suaveolens also plays a role in integrated pest management, particularly its insecticidal and repellent properties against mosquito vectors such as *Anopheles gambiae* [2,3]. Its essential oils have demonstrated larvicidal and adulticidal activities, making it a promising candidate for natural mosquito control strategies [2,3,37]. The action of *Hyptis suaveolens* both as a therapeutic agent against malaria and as a biopesticide proves its potential utility in public health and agricultural practices, especially in regions where malaria is endemic and chemical insecticides may pose risks to human health and the environment [3].

Hyptis suaveolens has been shown to have antioxidant qualities in addition to its antimalarial ones, which may help explain some of its medicinal benefits. The plant's flavonoids and phenolic compounds are linked to the scavenging of free radicals, which lowers inflammation and oxidative stress two important factors in the pathophysiology of many diseases, including malaria [16]. *Hyptis suaveolens's* diverse pharmacological profile makes it an invaluable tool for creating new therapeutic medicines and highlights the need for thorough evaluations that summarize the body of knowledge regarding its antimalarial properties and other health advantages [31].

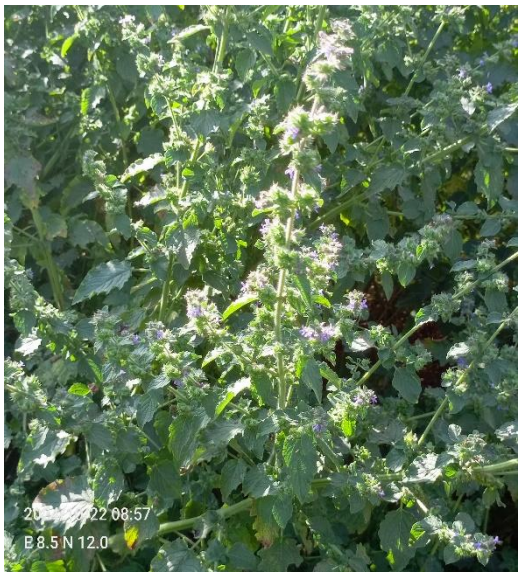

Fig. 1 *Hyptis Suaveolens* Plant

Traditional Uses and Ethnobotanical Significance

The native tropical regions of the plant accommodate various cultures which constitute the roots of the currently known traditional uses and ethnobotanical significance of Hyptis suaveolens. For centuries, it has been utilized in traditional medicine systems, primarily for its antimalarial properties, among other therapeutic applications. The ethnobotanical knowledge surrounding Hyptis suaveolens reflects the rich cultural heritage and the reliance of local communities on natural resources for healthcare [32,40].

Hyptis suaveolens is recognized for its efficacy in treating malaria by many African communities, a disease that poses a significant health threat in these regions. Traditional healers often leverage the plant's purported antimalarial properties by prescribing the leaves of this plant as a remedy for malaria. Its utilization in traditional medicine is supported by

ethnopharmacological studies that document its application in various medicinal preparations, including teas, decoctions, and infusions [40]. The Kwale community in Kenya, for example, has been noted for its use of local plants, including *Hyptis suaveolens*, in traditional antimalarial phytotherapy, highlighting the plant's importance in local healthcare practices [32,42].

The ethnobotanical importance of *Hyptis suaveolens* surpasses its antimalarial uses. Traditionally, the plant has been employed in the treatment of numerous ailments, such as respiratory infections, gastrointestinal disorders, and skin conditions, extending beyond its antimalarial applications. Its leaves are often crushed and applied topically to wounds or used in poultices for their anti-inflammatory properties. This multifaceted use underscores the plant's role as a vital [26] component of traditional medicine, where it serves as a general health tonic not only as a remedy for malaria [34].

The knowledge of Hyptis suaveolens and its medicinal properties has been transmitted through generations, often via oral traditions. This ancestral wisdom is vital for preserving cultural identity and practices, especially in rural areas where modern healthcare access may be scarce.

Hyptis suaveolens and its medicinal properties has been passed down through generations, often through oral traditions [31]. The reliance on local flora for medicinal purposes is common in many cultures, and the documentation of such practices aids the conservation of biodiversity and the sustainable use of plant resources [23,45]. Ethnobotanical studies have shown that communities often possess extensive knowledge about the plants in their environment, including their uses, preparation methods, and potential side effects.

The fusion of traditional knowledge with contemporary scientific research holds the promise of deepening the understanding of *Hyptis suaveolens* pharmacological properties. Ethnopharmacological approaches have been substantiated by studies showcasing the effectiveness of traditional remedies in treating malaria and other ailments. For instance, the discovery of bioactive compounds in *Hyptis suaveolens* that demonstrate antimalarial activity corroborates the plant's traditional uses, offering a scientific foundation for its application in herbal medicine [7,8]. This synergy between traditional knowledge and scientific validation is crucial for the development of new therapeutic agents derived from natural products.

Additionally, the growing global interest in herbal medicine has led to more research into the traditional importance of plants like *Hyptis suaveolens*. The World Health Organization (WHO) has highlighted the important role of traditional medicine in primary healthcare, especially in developing countries where many people rely on herbal remedies[30]. The recognition of traditional knowledge as a valuable resource for drug discovery has prompted researchers to explore the potential of plants used in traditional medicine for the development of new antimalarial drugs [4,47].

Phytochemical Composition

The phytochemical makeup of *Hyptis suaveolens*, also known as bush mint, has been extensively studied due to its variety of bioactive compounds that contribute to its medicinal properties[6]. This plant, part of the *Lamiaceae* family, boasts a rich assortment of secondary metabolites, including flavonoids, alkaloids, saponins, tannins, terpenoids, and phenolic compounds, which underpin its various pharmacological activities [6,16,29].

Flavonoids, a significant class of phytochemicals in *Hyptis suaveolens*, are renowned for their antioxidant properties, which are essential in neutralizing free radicals and mitigating oxidative stress in biological systems. Compounds like quercetin and kaempferol are associated with anti-inflammatory, anti-carcinogenic, and hepatoprotective effects, thereby enhancing the plant's therapeutic potential [16,9,44]. The presence of flavonoids in the plant's extracts has been consistently reported across various studies, highlighting their significance in traditional medicine practices [16,9,44].

Alkaloids, another significant group of phytochemicals found in *Hyptis suaveolens*, are renowned for their varied biological activities, such as analgesic and antimalarial effects. The presence of alkaloids in this plant has been linked to its traditional use in treating various ailments, including malaria, where it has demonstrated promising results against Plasmodium species [6,11]. Additionally, the significant quantities of saponins in the plant contribute to its insecticidal properties, positioning it as a potential candidate for biopesticide applications [5,6,37].

Tannins and phenolic compounds are also notable constituents of *Hyptis suaveolens*. Tannins are known for their astringent properties and potential health benefits, including antimicrobial and antiviral activities. Phenolic compounds, like rosmarinic acid, exhibit strong antioxidant activity, further enhancing the plant's therapeutic profile [16,36,44]. The

synergistic effects of these phytochemicals contribute to the overall pharmacological efficacy of *Hyptis suaveolens*, making it a valuable resource in herbal medicine [36].

The essential oils extracted from *Hyptis suaveolens* contain a variety of terpenoids, responsible for the plant's distinctive aroma and linked to various biological activities, such as antimicrobial and insect repellent properties. Studies have identified key components of the essential oil, like thymol and sabinene, which exhibit significant insecticidal and repellent effects against mosquito vectors [2,12]. This underscores the potential of *Hyptis suaveolens* not only as a medicinal plant but also as a natural alternative for pest control.

Antimalarial Activity

The antimalarial activity of *Hyptis suaveolens*, a member of the *Lamiaceae* family, has acquired study interest owing to its potential as a natural treatment for malaria, a disease induced by Plasmodium parasites. The effectiveness of this plant in treating malaria is mostly due to its abundant phytochemical makeup, which encompasses several bioactive chemicals recognised for their therapeutic qualities. Flavonoids, alkaloids, and terpenoids have been recognised as significant contributors to the antimalarial effects reported in multiple investigations [11,29].

Research have shown that ethanolic extracts of *Hyptis suaveolens* has considerable antimalarial activity against *Plasmodium berghei* in experimental models [11]. Conducted a trial in which ethanolic leaf extract was inserted to infected mice, which result to a decrease in parasitemia levels relative to the control group [11]. The research shows that the extract's antimalarial activity was dose-dependent, with increased concentrations resulting in greater inhibition of the parasite's proliferation. This discovery corresponds with the conventional uses of the plant in herbal therapy, where it has been used to treat malaria and other fever conditions [17,11,29].

The antimalarial mechanism of *Hyptis suaveolens* is thought to entail the suppression of essential metabolic pathways in the malaria parasite. Flavonoids, including quercetin and kaempferol, have been associated with the disruption of the parasite's life cycle by slowing its replication and survival within the host [29]. Also, alkaloids seen in the plant may demonstrate cytotoxic effects on malaria parasites, hence enhancing the noted antimalarial efficacy [29]. The combined effects of these phytochemicals lead the overall effectiveness of the plant, making it as a suitable subject for further study as a natural antimalarial agent.

Additionally, the essential oils gotten from *Hyptis suaveolens* have been investigated for their efficacy in malaria vector control. The essential oils contain several terpenoids that shows insecticidal and repellant effects against mosquito species, especially Anopheles gambiae, the principal malaria vector [5,37]. The larvicidal effectiveness of these essential oils has been recorded, showing their capability to reduce mosquito populations, and reducing the danger of malaria transmission [5,37]. The dual function of *Hyptis suaveolens*, serving as both a therapeutic agent against the malaria parasite and a biopesticide against its vectors, underscores its versatile potential in malaria management efforts.

Besides its direct antimalarial benefits, *Hyptis suaveolens* may cause the overall health of persons afflicted with malaria due to its antioxidant capabilities. The plant contains abundant phenolic compounds that scavenge free radicals and mitigate oxidative stress, a frequent outcome of malaria infection [9,16]. By reducing oxidative damage, these chemicals may boost the host's immunological response and promote recovery results in malaria patients.

Notwithstanding the encouraging results of the antimalarial efficacy of *Hyptis suaveolens*, additional investigation is required to comprehensively clarify the precise mechanisms of action, ideal dosages, and possible adverse effects linked to its application. Clinical trials and pharmacological study will be crucial in confirming the effectiveness and safety of this plant as an adjunctive treatment for malaria. Furthermore, investigating the possibility of synergistic interactions with traditional antimalarial medications may result in more effective treatment protocols and assist in addressing the escalating problem of drug resistance in malaria management.

Mechanisms of Action

The mechanisms of action of antimalarial chemicals from *Hyptis suaveolens* are increasingly significant, especially due to the rising prevalence of drug-resistant strains of *Plasmodium falciparum* [46]. Comprehending these pathways is important for making successful treatments and potentially adding traditional herbal remedies into contemporary pharmacology. The antimalarial effectiveness of *Hyptis suaveolens* is related to its intricate phytochemical profile, encompassing flavonoids, alkaloids, and terpenoids, each playing a role in its therapeutic effects via diverse biochemical pathways [19,39,46].

Antimalarial drugs primarily exert their effects by targeting the heme detoxification pathway in the malaria parasite. The malaria parasite destroys haemoglobin from the host's red blood cells during its lifecycle, producing free heme, which is harmful to the parasite. To reduce this toxicity, the parasite changes free heme into a less harmful form called hemozoin. Compounds like chloroquine and other quinoline derivatives obstruct this polymerisation process, resulting in the buildup of harmful free heme within the parasite [19,41]. Flavonoids in Hyptis suaveolens may contribute to this mechanism, as research indicates that specific flavonoids can prevent hemozoin production, thus increasing toxic heme buildup and facilitating parasite mortality [19].

The interaction of antimalarial drugs with the mitochondrial effectiveness of the parasite is another essential mechanism of action. The mitochondria of *Plasmodium* species are important for energy production and metabolic functions. Certain research shows that chemicals from *Hyptis suaveolens* may interfere with mitochondrial effectiveness, resulting in diminished ATP generation and heightened oxidative stress in the parasite [14,28]. This disturbance may trigger apoptotic pathways, ultimately leading in cell death. The production of reactive oxygen species (ROS) resulting from mitochondrial dysfunction might intensify oxidative damage, hence increasing the overall toxicity of antimalarial agents [24,38].

Furthermore, the regulation of calcium homeostasis inside the parasite is an additional hypothesized way by which *Hyptis suaveolens* may shows its antimalarial properties. Calcium ions are important in numerous biological activities, particularly in signaling pathways that govern cell development and death. Certain antimalarial agents have been used to disrupt calcium signaling, causing dysregulation of these mechanisms and ultimately culminating in cellular apoptosis [20,45]. The potential capacity of *Hyptis suaveolens* extracts to affect calcium transport and signaling in *Plasmodium falciparum* may give a new dimension of antimalarial efficacy.

The addition of particular enzymes included in the parasite's metabolic pathways is a crucial mechanism of action for antimalarial agents. The addition of dihydroorotate dehydrogenase (DHODH), an enzyme essential for pyrimidine production, has been seen as a target for many antimalarial drugs [38]. These compounds can effectively trigger the growth and replication of the malaria parasite by affecting the synthesis of nucleotides essential for DNA and RNA formation. The possible existence of enzyme inhibitors in the

phytochemical composition of *Hyptis suaveolens* shows that this plant may function through analogous enzymatic pathways.

The immunomodulatory properties of *Hyptis suaveolens* must not be disregarded. Research suggests that some phytochemicals may augment the host's immunological response, hence making the body's ability to fight malaria infections [17]. These chemicals may offer a supplementary mechanism of action by influencing cytokine synthesis and augmenting immune cell activity, in addition to their direct effects on the parasite.

Toxicity and Safety Profile

The toxicity and safety profile of *Hyptis suaveolens*, a plant noted for its antimalarial effects, is a important element of its prospective medicinal use. Comprehending the safety profile of herbal treatments is important, especially considering the growing dependence on natural products in contemporary medicine. The grading of toxicity includes multiple elements, including as the plant's chemical makeup, the extraction method, and the dosage employed in medicinal applications [43].

The phytochemicals found in *Hyptis suaveolens*, including flavonoids, alkaloids, and terpenoids, enhance its pharmacological properties but may potentially bring toxicity hazards. The toxicity of these chemicals can fluctuate considerably depending on their quantity and distinct chemical structure. Some flavonoids possess antioxidant characteristics, whilst others may show lethal effects at elevated quantities [10]. Consequently, it is essential to delineate the dose-response connection of the diverse phytochemicals in *Hyptis suaveolens* to guarantee safe therapeutic application.

Acute toxicity studies frequently represent the initial phase in evaluating the safety of herbal extracts. These researches often entail the administration of a singular high dose of the extract to animal models and monitoring for any unwanted effects. Preliminary investigations on *Hyptis suaveolens* show that the plant has a low acute toxicity profile, with no notable mortality or serious side effects at dosages up to 2000 mg/kg body weight [18]. These data show that the plant may be safe for modest use; however, additional research is required to validate these results across various populations and settings.

Subacute toxicity studies, characterized by repeated administration over an extended duration, yield further insights into the safety profile of *Hyptis suaveolens*. These

studies evaluate the potential for cumulative toxicity and the long-term consequences on organ systems. Studies show that extended exposure to specific phytochemicals may result in organ-specific toxicity, especially in the liver and kidneys, which are essential for the metabolism and excretion of these substances [22]. Consequently, it is imperative to perform thorough subacute toxicity evaluations to assess any potential long-term health hazards linked to the utilization of *Hyptis suaveolens*.

An additional significant element of the toxicity profile is the possibility of herb-drug interactions. The phytochemicals in *Hyptis suaveolens* may affect the metabolism of conventional medications, leading in modified pharmacokinetics and possible toxicity [35]. Certain flavonoids can inhibit cytochrome P450 enzymes, which metabolize numerous medicinal drugs. This combination may elevate plasma levels of concomitant medications, hence heightening the risk of undesirable consequences. Consequently, it is imperative for healthcare practitioners to recognize the potential interactions when endorsing *Hyptis suaveolens* as an adjunctive therapy.

The preparation and extraction process of *Hyptis suaveolens* significantly influences its toxicity profile. Several extraction techniques can produce differing quantities of phytochemicals, potentially affecting both effectiveness and safety. For example, extracts derived from organic solvents may concentrate specific harmful chemicals, whereas aqueous extracts may be safer for ingestion [27]. Standardising extraction techniques and implementing quality control are critical measures in the development of safe herbal products.

Alongside acute and subacute toxicity investigations, genotoxicity evaluations are essential for assessing the safety of *Hyptis suaveolens*. Genotoxic agents can inflict harm on DNA, potentially resulting in mutations and cancer. Initial research suggests that particular extracts of *Hyptis suaveolens* may exhibit genotoxic effects, warranting additional examination to identify the relevant chemicals and their modes of action [15]. Comprehending the genotoxic potential of the plant is essential for guaranteeing its safe application, especially in populations susceptible to cancer.

Moreover, the safety profile of *Hyptis suaveolens* must be evaluated within the framework of its typical application. Numerous societies have relied on this plant for therapeutic applications for generations, frequently without rigorous evaluations of its safety. Although traditional knowledge gives significant insights about the plant's

effectiveness and safety, scientific validation is crucial to confirm that these practices are based on reliable data [49].

Conclusion

Hyptis suaveolens demonstrates noteworthy antimalarial activity, attributed to its diverse bioactive compounds such as flavonoids, terpenoids, and essential oils. Both in vitro and in vivo studies have highlighted the plant potential to inhibit *Plasmodium* species, particularly *Plasmodium falciparum*, positioning it as a valuable candidate for the development of antimalarial therapies. However, challenges persist, including the need for standardization of plant extracts, further exploration of its toxicity, and clinical trials to confirm its therapeutic efficacy. Nevertheless, the promising pharmacological properties of *H. suaveolens* indicate that ongoing research could lead to the discovery of novel and effective treatments for malaria.

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