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# Antimalarial Activity of Lamiaceae Family Plants: Review

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## ABSTRACT

Malaria is a major infectious disease caused by *Plasmodium sp*., and it can infect human's trough females' mosquitos *Anopheles sp*. bite. Plasmodium resistance to malarial drugs used today occurs mostly in endemic areas, so it is necessary to look for alternative medicines for malaria, especially medicines derived from plants

**Objective**: The objective of writing this literature review is to see the ability of the Lamiaceae family plant as a source of new malaria medicines.

**Methods:** Scientific evidence of traditional use, antiplasmodial activity, and active antimalarial compounds from plants belong to Lamiaceae family used to support this article are carried out by searching online for articles related to the title of this article.

**Results:** Lamiaceae family plants used for malaria treatment traditionally in many countries, and many of them have been examined for their antimalarial activity *in vitro* against *P. falciparum* or *in vivo* against *P. berghei* in mice, and they have antimalarial effect with various potency. There are forty active antimalarial compounds isolated from plants of Lamiaceae family, and these could be candidates for new antimalarial medicines.

**Conclusion:** Lamiaceae family is proven to be a source of plants that have antimalarial activity, this can be seen from their traditional use as malarial drugs in various countries, the number of plant extracts with antimalarial activity and many active antimalarial substances isolated from Lamiaceae family plants, but they still need to be further examined to become antimalarial drugs.

**Keywords:** Diabetes patient, Mobile application, Primary health care.

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## INTRODUCTION

Malaria is a tropical disease caused by parasite *Plasmodium sp*., and it can infect human's trough females' mosquitos *Anopheles sp*. bite. According to WHO, in 2017, there are still around 219 million cases of malaria globally, with a mortality rate of 435,000. The rate of mortality and morbidity is still high, especially in developing countries[1]. Malaria is highly lethal unless diagnosed. The types of Plasmodium that initiate malaria in humans are *P. falciparum, P. vivax, P. ovale, P. malariae,* and *P. knowlesi*. The fatal *Plasmodium* type of malaria is *P. falciparum*.[2,3,4] .

*Plasmodium falciparum* resistance to some malarial drugs could be a problem, particularly in the endemic zones[5]. Antimalarial drug resistance can increase morbidity and mortality due to malaria. Resistance occurs mainly because of mutations in the gene from Plasmodium[6]. This has highlighted the imperative have to be compelled to develop new antiprotozoal agents, ideally cheap medicine that area unit reasonable for developing countries, wherever protozoal infection is prevailing.

The Lamiaceae or earlier called Labiatae may be a family of flowering plants, large shrubs, and herbs, with a cosmopolitan distribution containing 236 genera and has been explicit about containing 6900–7200 species. Salvia was al largest genus in the Lamiaceae family; it contained 900 plant species. Some large genus of plants that belong to the family Lamiaceae are Scutellaria, Stachys, Plectranthus (300 species), Teucrium, Vitex, Thymus, and Nepeta (200 species)[7]. Plants belonging to the Lamiaceae are taken into consideration a splendid supply for locating new herbal medication with capability bioactivities[7].

## METHODS AND MATERIAL

Scientific evidence of traditional use, antiplasmodial activity, and active antimalarial compounds from plants belonging to the Lamiaceae family used to support this article are taken from the online journal literature.

## LITERATURE FINDING

The systematic literature review was carried out by searching online for articles related to the title of this article. The article search began on April 28, 2020, with keywords; "Lamiaceae antimalaria", "Lamiaceae antiplasmodial". The following searching database is: "Pubmed" and "Google scholar", The articles for this review are articles published after 2000, not in the form of review article or opinion.

## RESULTS AND DISCUSSIONS

In several countries in Africa and Asia, the the Lamiaceae family plants are widely used as a traditional antimalarial herbal medicine (Table 1).

**Table 1**. Traditional use of Lamiaceae plants as antimalarial medicine

| Plant species | Part used | Geographical region | Reference |
|---|---|---|---|
| *Ajuga bracteosa* | Leaves | West Himalaya, India<br>Yemen<br>Saudi Arabia | 9,10 |
| *Ajuga integrifolia* Buch. Ham. | Aerial parts | Lesser Himalayas–Pakistan | 11,12,13 |
| | Leaves | Maradori Valley, Pakistan | 13 |
| *Ajuga parviflora* Benth | Leaves | Lesser Himalayas, Pakistan | 12 |
| *Clerodendrum johnstonii* Oliv. | Rootbark, Leaves | East sub-County, Kenya | 11 |
| *Fuerstia africana* T.C.E.Fr. | Aerial parts | East sub-County, Kenya | 11 |
| *Gmelina arborea* Roxb. | Leaves | south-eastern Nigeria | 14 |
| *Hoslundia oposita* | Root bark | Tanzania | 15 |
| *Leonotis leonurus (L.) R. Br.* | Leaves | South African | 16 |
| *Leonotis leonurus ex Hort (yellow)* | Leaves | South African | 16 |
| *Leucas aspera* (Willd.) Link | Whole plants | Lesser Himalayas, Pakistan | 12 |
| *Leucas calostachys* Oliv. | Aerial parts | East sub-County, Kenya | 11 |
| *Leucas cephalotes* | Whole plants | West Himalaya, India | 9 |
| *Mentha piperita* | Leaves | West Himalaya, India | 9 |
| *Mentha spicata* L. | Aerial part | Somali Region, Ethiopia | 17 |
| Nepeta hindostana | Leaves | West Himalaya, India | 9 |
| *Ocimum basilicum* L. | Leaves | Lesser Himalayas, Pakistan | 12 |
| *Ocimum gratissimum* L. | Whole plants | Democratic Republic of Congo | 18 |
| | Leaves | south-eastern Nigeria<br>Middle Belt Nigerian | 14<br>19<br>20 |
| *Ocimum lamiifloium* Hochst. ex Benth | Leaves | Ethiopia | 21 |
| *Ocimum spicatum* Deflers | Leaves | Somali Region, Ethiopia | 17 |
| *Ocimum suave* Willd. | Leaves | Kwale county of Kenya | 22 |
| *Ocimum tenuiflorum* L. | Root | Lesser Himalayas, Pakistan | 12 |
| *Ocimun kilimandscharicum* Gürke | Aerial parts | East sub-County, Kenya | 11 |
| *Origanum majorana* L. | Aerial Part | Faisalabad, Pakistan | 13 |
| *Origanum vulgare* L. | Aerial Part | Faisalabad, Pakistan | 13 |
| *Plectranthus barbatus* Andrews. | Leaves, Stem | Yemen<br>Saudi Arabia<br>Kwale county of Kenya | 23<br>22 |
| | Leaves | East sub-County, Kenya | 11 |
| *Rotheca myricoides* (Hochst.) Steane & Mabb. | Aerial parts | East sub-County, Kenya | 11 |
| *Roylea cinerea* | Leaves | West Himalaya, India | 9 |
| *Roylea cinerea* (D.Don) Baillon | Leaves | Kedarnath, Garhwal, Uttarakhand, India,<br>NorthWestern Himalaya, India | 24 |
| *Solenostemon monostachyus* (P. Beauv.) Briq. | Leaves | Southeast Nigeria | 19<br>24 |
| *Thymus linearis* Benth. | Whole plants | Lesser Himalayas, Pakistan | 12 |

The most utilized plants of the 31 species of family Lamiaceae come from the genus Ocimum (7 plants) followed by the genus Ajuga (3 plants) and Leucas (3 plants), Leonotis (2), Mentha (2), Origanum (2), Rovlea (2), Clerodendrum, Fuerstia, Gmelina, Hoslundia, Nepeta, Plectranthus, Rotheca, Solenostemon, Thymus, and Vitex each with one plant. The most widely used part of herbal malarial management is the leaves and roots, while of all the libraries reviewed, the way to make the most preparations of medicine is by boiling plant parts in water (decocted). It can be concluded, that traditionally, plants from the Lamiaceae family have long been consumed to treat malaria, the research into antiplasmodial activity and its active compounds from this family plant are interesting to do.

Several plants commonly used as malaria drugs and several other plants from the Lamiaceae family have been investigated for their antimalarial efficacy both *in vitro* against *Plasmodium falciparum* or *in vivo* against *Plasmodium berghei* in animal mice, as shown in Table 2.

**Table 2**. Antiplasmodial activity of plants of Lamiaceae family

| Plant species | Antiplasmodial activity against *P. falciparum*. $IC_{50}$ and strains used | Antiplasmodial activity against *P. berghei* in mice | References |
|---|---|---|---|
| *Ajuga laxmannii* | The aerial parts methanolic extract, *n*-hexane fractions, and ethyl acetate fractions, $IC_{50}$ >50 µg/mL, 7.5 µg/mL, and 3.2 µg/mL (K1) respectively | | 25 |
| *Ajuga remota* / *Ajuga bracteosa* Wall ex Benth. | the leaves ethanolic extract gave $IC_{50}$ of 55 µg/ml (FCA/20GHA); and $IC_{50}$ of 57 µg/mL (W2) | Crude ethanolic extract of Leaves, at the daily dose of 250, 500 and 750 mg/kg/day, caused inhibition of growth of 32.7, 60.5 and 68.8% respectively | 27, 16 |
| *Fuerstia africana* T. C. E. Fries | The whole plants chloroform extract, $IC_{50}$ was 3.76 µg/mL (D6) | After oral administration of stems and leaves extract dose of 300 mg/kg/day, the parasitemia reduction on $4^{th}$ day post-infection was 44 %.<br><br>After intraperitoneal administration of stems and leaves extract, the parasitemia reduction on $4^{th}$ days was 74% respectively. | 28, 29 |
| *Gomphostemma niveum* | | The leaves aqueous extract 300, 400 and 500 mg/kg/day gave reduction of parasitemia of 11.43, 23.28, and 52.43% respectively<br><br>The leaves aqueous extract at 300, 400, and 500 mg/kg/day, the level of parasitemia reduction was 29.76, 55.45, and 79.98%, respectively. | 30 |
| *Hoslundia opposita* Vahl. | The root bark *n*-hexane extract, of $IC_{50}$ was 5.6 µg/mL (K1) | The root bark *n*-hexane extract at 190 mg/kg body weight daily caused 26% inhibition of growth. | 15 |
| *Leonotis leonurus ex Hort (yellow)* | The $IC_{50}$ of leaves ethanolic extract was 12.8 µg/mL – at the early stages; 13.9 µg/mL – at the late stages (K1) | | 16 |
| *Leucas cephalotes* | The whole plants petroleum ether, Chloroform and methanol extract, $IC_{50}$ >5 µg/mL; 3.96 µg/mL and >5 µg/mL respectively (K1) | | 9 |
| *Marrubium astracanicum subsp. macrodon* | The methanolic extract, n-hexane extract and chloroform extract of aerial parts, $IC_{50}$ was 6.39 µg/mL. 4.64, µg/mL, 3.36 µg/mL respectively | | 31 |
| *Mentha piperita* | The whole plants petroleum ether, Chloroform and methanol extract gave $IC_{50}$>5 µg/mL (K1) | | 9 |
| *Nepeta hindostana* | The leaves petroleum ether, Chloroform and | | 9 |

| | | | |
|---|---|---|---|
| | methanol extract, $IC_{50}$ was 1.71 µg/mL: 1.52 µg/mL and >5 µg/mL respectively (K1) | | |
| *Nepeta nuda subsp. nuda* | The aerial parts methanol extract, n-hexane extract and chloroform extract gave $IC_{50}$ = 11.31 µg/mL. 3.37 µg/mL, 2.95 µg/mL respectively | | 31 |
| *Ocimum basilicum* L. | The ethanolic extract of leaves, $IC_{50}$ = 43.81 µg/mL | | 32 |
| | Essential oil $IC_{50}$= 21 µg/mL (FcB1) | | 33 |
| *Ocimum canum* Sims | Essential oil, $IC_{50}$= 20.6 µg/mL (FcB1) | | 33 |
| *Ocimum gratissimum L* | | Essential oil at 200, 300 and 500 mg/kg body weight, the level of parasitemia reduction were 55.0, 75.2 and 77.8% respectively | 34 |
| *Ocimum lamiifloium* Hochst. ex Benth | | The leaves aqueous crude extract at 600 mg/kg body weight caused 35.53% inhibition of parasite growth. | 35 |
| *Ocimum sanctum* | The ethanolic leaves extract, $IC_{50}$ = 35.58 µg/mL | | 32 |
| *Ocotea usambarensis* Engl. | Stem bark MeOH; 0.98 µg/mL (D6), 2.40 µg/mL (W2) | | 36 |
| *Origanum compactum* Benth. | The essential oil gave $IC_{50}$ of 34 µg/mL<br>Ethyl acetate extract: $IC_{50}$ 33 µg/mL | | 37 |
| *Otostegia integrifolia* Benth | | The leaves methanolic extract of leaves at 25, 50 and 100mg/kg/day, the level of parasitemia reduction were 42.37, 75.28 and 80.52% respectively | 38 |
| *Plectranthus Amboinicus* (Lour) Spreng | | The aqueous extract at 250 mg/kg and 500 mg/kg gave the level of parasitemia reduction after 96 hours of 67.9% and 76.2%, respectively. | 39 |
| *Plectranthus barbatus* Andr. | The ethanolic extract of leaves, $IC_{50}$= 6.5 µg/mL (K1) | The aqueous and organic (chloroform-methanol = 1:1) root extract at doses 100 mg/kg/day, the level of parasitemia reduction were 55.23% and 54.78%, respectively. | 10 |
| *Roylea cinerea* | The leaves petroleum ether, Chloroform and methanol extract gave $IC_{50}$= 4.39 µg/mL: 1.84 µg/mL and >5 µg/mL respectively (K1) | | 9 |
| *Salvia sclarea* | The $IC_{50}$ of methanolic extract, *n*-hexane extract and chloroform extract of aerial parts, $IC_{50}$ = 6.60 µg/mL. 3.78 µg/mL, 2.54 µg/mL respectively | | 31 |
| *Salvia dichroantha* | The $IC_{50}$ of methanolic extract, *n*-hexane extract and chloroform extract of aerial parts, $IC_{50}$ = 8.85 | | 31 |

| | | | |
|---|---|---|---|
| | µg/mL. 4.17 µg/mL, 3.72 µg/mL respectively | | |
| *Salvia tomentosa* | The methanolic extract, *n*-hexane extract and chloroform extract of aerial parts gave $IC_{50}$ of 9.94 µg/mL. 3.47 µg/mL, 3.14 µg/mL respectively | | 31 |
| *Satureja thymbra* | Essential oil, $IC_{50}$= 17-26 µg/mL (D10); $IC_{50}$= 9-11 µg/mL (W2) | | 40 |
| *Scutellaria havanensis* Jacq. | The fresh aerial parts methanolic and chloroform extracts gave $IC_{50}$ values of 32.2 and 7.7 µg/mL, respectively. | | 41 |
| *Solenostemon monostachyus* P. Beauv | | The herbs extract (75–225mg/kg) and fractions (chloroform and aqueous; 150 mg/kg) decreased parasitaemia level in mice: prophylactic (28.48–71.72%), suppressive (12.52–72.47%), and curative (22.4–82.34%) | 42 |
| Thymus herba-barona | Essential oil $IC_{50}$= 29,1 - >50 µg/mL (D10); 24,.2 µg/mL (W2) | | 40 |
| *Zhumeria majdae* Rech.f. & Wendelbo | The *n*-hexane extract of roots, $IC_{50}$ = 2.1 µg/mL. | | 44 |

The results of this review showed that that 31 plants of Lamiaceae family had been evaluated for their antimalarial activity, 25 plants were examined for their antimalarial effect by *in vitro* against *P. falciparum*, and ten plants were assessed for their antimalarial effect by *in vivo* against *P. berghei* in mice. Based on Jonville guidelines, antiplasmodial activities are grouped as follows: high ($IC_{50}$ <5 µg/mL), promising (5-15 µg/mL), low (15-50 µg/mL) and inactive ($IC_{50}$> 50 µg/mL) ) (Jonville, 2008). From Table 2, plants extract that has high antiplasmodial purpose against *P. falciparum,* without seeing the strain type, is the chloroform extract from the whole plant of *Fuerstia africana T. C. E. Fries.* With an $IC_{50}$ value of 3.76 µg/mL; chloroform extract of whole plants of *Leucas cephalotes* with $IC_{50}$ of 3.96 µg/mL; *n*-hexane extract of aerial parts of *Marrubium astracanicum* subsp. Macrodon with $IC_{50}$ value 4.64, µg/mL; extracts of petroleum ether and chloroform from the leaves of the *Nepeta hindostane* plant with $IC_{50,}$ respectively 1.71 µg/mL and 1.52 µg/mL; methanolic extract, *n*-hexane, and chloroform of *Nepeta nuda* subsp. Nuda with $IC_{50}$ values of 11.31 µg/mL, 3.37 µg/mL, and 2.95 µg/mL, respectively; methanolic extract of stem bark of *Ocotea usambarensis* Engl. With $IC_{50}$ values of 0.98 µg/mL; extracts of petroleum ether and chloroform from the aerial parts of *Roylea cinereal* with $IC_{50}$ values 4.39 µg/mL and 1.84 µg/mL respectively; *n*-hexane and chloroform extracts of the aerial parts of *Salvia sclarea* with $IC_{50}$ 3.78 µg/mL, and 2.54 µg/mL respectively; *n*-hexane and chloroform extracts of the aerial parts of *Salvia dichroantha* with $IC_{50}$ respectively 4.17 µg/mL and 2.54 µg/mL; *n*-hexane and chloroform extracts of the aerial parts of *Salvia tomentosa* with $IC_{50}$ 3.47 µg/mL and 3.14 µg/mL respectively; chloroform extracts from stembark of *Vitex madiensis* Oliv with $IC_{50}$ 2.36 µg/mL; *n*-hexane extract of *Zhumeria majdae* roots Rech.f. & Wendelbo with $IC_{50}$ 2.1 µg / mL. Plants extract of Lamiaceae family that has the best antimalarial effect by *in vivo* test against *P. berghei* in mice, was methanol leaves extract of *Otostegia integrifolia* Benth with 100 mg/kg/day gave a reduction in parasitemia of 80.52%. These Lamiaceae plants with high antiplasmodial activity are very prospective to be further investigated and developed as candidates for antimalarial herbal medicines.

In this review, there are 17 plants of Lamiaceae family had been investigated for their active antimalarial compounds, as shown in Table 3.

**Table 3.** Antiplasmodial compounds isolated from Lamiaceae family

| Plants species | Isolated compound | [a]antiplasmodia[l] activity *in vitro* against *P. falciparum*, $IC_{50}$ and strains used<br>[b]antimalarial activity in vivo against *P. berghei* in mice | References |
|---|---|---|---|
| *Ajuga laxmannii* | Isoorientin | 9.7 µg/mL (K1) [a] | 25 |
| *Ajuga remota* Benth | Ajugarin-1 | 23.0 µg/mL (FCA20/GHA) [a] | 45 |
| | Ergosterol-5,8-endoperoxide | 8.2 µg/mL (FCA20/GHA) [a] | |
| *Fuerstia africana* T. C. E. Fries | Ferruginol | 1.95 mg/ml (D6) [a] | 29 |
| *Gomphostemma niveum* | Gomphostenin | at 50, 100, 150 and 200 mg/kg/day gave suppression values 28.31, 54.63, 74.63 and 80.60% respectively against *P. berghei* (ANKA) in mice [b] | 30 |
| | Acetyl Gomphostenin | at 50, 100, 150 and 200 mg/kg/day gave percent suppression values 45.09, 82.92, 87.51 and 92.65 respectively against *P. berghei* (ANKA) in mice [b] | |
| *Hoslundia opposita* Vahl. | 3-O-benzoylhosloppone | 0,4 µg/mL (K1) [a]<br>0,22 µg/mL (NF 54) [a] | 46 |
| *Leucas mollissima* Wall. | Anisofolin A | 4.39 µM [a] | 47 |
| | apigenin 7-O-β-D (– 6′′-p-E-coumaroyl)-glucoside | 35% inhibition at ten µM [a] | 47 |
| *Otostegia integrifolia* Benth | Otostegindiol | At 25, 50 and 100mg/kg/day gave suppression values of 50.13, 65.58 and 73.16% respectively against *P. berghei* (ANKA) in mice [b] | 38 |
| *Perovskia abrotanoides* | Cryptotanshinone | 12.5 µM (3D7) [a] | 48 |
| | 1β-hydroxycryptotanshinone | 26.9 µM (3D7) [a] | 48 |
| | 1-oxocryptotanshinone | 17.6 µM (3D7) [a] | 48 |
| | 1-oxomiltirone | 13.0 µM (3D7) [a] | 48 |
| *Phlomis brunneogaleata* | Luteolin 7- O-beta- D-glucopyranoside | 2.4 µg/mL [a] | 49 |
| | Chrysoeriol 7- O-beta- D-glucopyranoside | 5.9 µg/mL [a] | 49 |
| *Plectranthus barbatus* Andr. | dehydroabietane | - | 50 |
| | 5.6-Didehydro-7-hydroxy-taxodone | 9.2 µM [a] | 50 |
| | Taxodione | 8.5 µM [a] | 50 |
| | 20-deoxocarnosol | 11.1 µM [a] | 50 |
| | 6α,11,12, -trihydroxy-7β,20-epoxy-8,11,13-abietatriene | 31.6 µM [a] | 50 |
| *Salvia hydrangea* DC. ex Benth. | Hydrangenone | 1.4 µM (K1) [a] | 51 |
| *Salvia leriifolia* Benth. | Leriifoliol | 0.4 µM (NF54) [a] | 52 |
| | Leriifolione | 3.6 µM (NF54) [a] | 52 |
| *Salvia sahendica* | 12-Deoxy-salvipisone | 8.8 µM (K1) [a] | 53 |
| | Sahandinone | 5.1 µM (K1) [a] | 53 |
| | 12-Deoxy-6,7-dehydroroyleanone | 17.8 µM (K1) [a] | 53 |
| | $\Delta^9$-Ferruginol | 0.9 µM (K1) [a] | 53 |
| | Ferruginol | 0.9 µM (K1) [a] | 53 |
| | 7α-Acetoxyroyleanone | 1.3 µM (K1) [a] | 53 |
| | Sahandol | 4.7 µM (K1) [a] | 53 |
| | Sahandone | 17.2 µM (K1) [a] | 53 |
| *Satureja parvifolia* (Philippi) Epling | Ursolic acid | 4.9 µg/mL (K1) [a] | 54 |

| | | | |
|---|---|---|---|
| | Oleanolic acid | 9.3 µg/mL (K1) [a] | 54 |
| | Eriodictyol | 17.2 µg/mL (K1) [a] | 54 |
| *Scutellaria havanensis* Jacq. | Wogonin | 4.3 µg/mL (*P. berghei* ANKA) [b] | 41 |
| *Teucrium ramosissimum* | Homalomenol C | 1.2 µg/mL (FcB1) [a] | 55 |
| | 4b- hydroxy-11,12,13-trinor-5-eudesmen-1,7-dione | 3.3 µg/mL (FcB1) [a] | 55 |
| | Oxo-T-cadinol | 4.4 µg/mL (FcB1) [a] | 55 |
| *Zhumeria majdae* Rech.f. & Wendelbo | 11,14-dihydroxy-8,11,13-abietatrien-7-one | 8.65 µM (NF 54) [a] | 44 |
| | Lanugon Q | 15.6 µM (NF 54) [a] | 44 |

From this literature reviewed, there are 40 active antimalarial compounds isolated from the Lamiaceae family, as shown in Table 3. The isolated antimalarial active compounds from the Lamiaceae family mostly was abietane diterpene and the other compounds are diterpenoids, triterpenoids, and flavonoids. Several active antimalarial compounds have been successfully isolated from some plants of the Lamiaceae family; it means that more plants of this tribe need to be investigated for their antimalarial activity to obtain new antimalarial drugs. Abietanes are a group of natural diterpenoids isolated from various plants. The biological activities of abietanes compounds are very diverse, so it becomes a fascinating material to be studied in the field of medicine or pharmacological community. Besides being contained in resins or plant extracts from the Araucariaceae, Cupressaceae, Phyllocladaceae, Pinaceae, and Podocarpaceae families, abietanes compounds are also found in many families of angiosperms such as Asteraceae, Celastraceae, Hydrocharitaceae, and Lamiaceae)[55].

Isoorientin is a flavone-C-glycoside compound that isolated from methanolic extract of aerial parts of *Ajuga laxmannii,* and It was one of the significant constituents of *A. laxmannii*. Isoorientin has a promising antiplasmodial action against *P. falciparum* with $IC_{50}$ value of 9.7 µg/mL[25].

*Ajuga remota* is the most commonly exploited medicinal herbs for malarial management in Kenya. Ajugarin-1 (diterpene) and ergosterol-5,8-endoperoxide (triterpene) were isolated from chloroform extract of *Ajuga remota* aerial parts. The two isolates were assessed for their in vitro antiplasmodial activity against *P. falciparum* (FCA 20/GHA). Ajugarin-1 has moderate antiplasmodial effect with $IC_{50}$ value of 23.0 µg/mL and ergosterol- 5,8-endoperoxide has a promising antiplasmodial activity with $IC_{50}$ amount of 8.2 µg/mL[44].

Ferruginol is an abietane diterpenoid isolated from the methanolic extract of aerial parts of *F. africana*. The existence of ferruginol in *F. africana* is first known in the genus Fuerstia, and previously ferruginol was also found in the genus Coleus (syn: Plectranthus) dan Salvia[56]. Antimalarial activity of ferruginol was determined using the D6 (chloroquine-sensitive) strains of *P. falciparum*, and the result, ferruginol, has strong antimalarial activity with $IC_{50}$ value of 1.95 mg/mL (control, chloroquine has $IC_{50}$ values of 1.94 ng/mL) [29].

Two novel clerodane diterpenes compounds, Gomphostenin and acetyl Gomphostenin, was isolated from aqueous and the *Gomphostemma niveum* leaves chloroform extract. In vivo antimalarial evaluation against *P. berghei* in mice of extracts aqueous extract, *Gomphostemma niveum* leave chloroform extract, Gomphostenin, and acetyl Gomphostenin showed that acetyl Gomphostenin has the best antiplasmodial activity with 92.65% of chemosuppression at a dose level of 200 mg/kg per day. In comparison, gomphostenin gave 80.60% chemosuppression at a dose level of 200 mg/kg per day. The studies have revealed that clerodane class of diterpenes Gomphostenin and acetyl Gomphostenin certainlyis a promising compound for malaria management and a valuable antimalarial chemotherapy[30].

*Hoslundia opposita* Vahl. is a little bush and broadly disseminated in East and West[58]? The 3-O-benzoylhosloppone, 3-O-cinnamoylhosloppone, 3-0-benzoylhinokiol, and 3-0-benzoylhosloquinone are abietane-type esters, secluded from the root bark of Hoslundia opposita Vahl. Only 3-O-benzoylhosloppone can repress the development of P. falciparum (the multidrug resistant strain K) in vitro with an $IC_{50}$ estimation of 0,4 µg/mL. This compound must be analyzed further to get one of the possibilities for malarial drugs[46].

Anisofolin A and apigenin 7-O-β-D (− 6′′-p-E-coumaroyl)-glucoside are flavonoids isolated from methanolic extract of *Leucas mollissima* Wall. roots. These compounds were assessed for their antiplasmodial effect against *P. falciparum* (3D7). Anisofolin A has an antimalarial effect with $IC_{50}$ values of 4.39 µM and apigenin 7-O-β-D (− 6′′-p-E-coumaroyl)-glucoside can inhibit *P. falciparum* development (35 % inhibition at 10 µM) [47].

The genus Otostegia of Lamiaceae family consists of 15 species. The plants of the families are endemic plants of the northern part of tropical Africa to the south-western and Central Asia. Otostegindiol is the labdane diterpenoids that separated from an active ethyl acetate fraction, and this compound produced chemosuppressive effect at 100 mg/kg/day gave 73.16% suppression values. The antiplasmodial activity of the leaves extracts of *O. integrifolia* makes this plant extract potential as the antimalarial herbal medicine candidate [38].

Cryptotanshinone;1β-hydroxycryptotanshinone; 1-oxocryptotanshinone; and 1-oxomiltirone were tanshinones that separated from *Perovskia abrotanoides* roots. Tanshinones are 20-norditerpenenes with an abietane-type skeleton containing a quinone moiety in the C-ring. The four tanshinone compounds were evaluated for their antiplasmodial effect against *P. falciparum* (3D7) and the $IC_{50}$ values in the ranging 5-45 µM [48].

The *Phlomis brunneogaleata* (Lamiaceae) extract was fractionated by anti-plasmodium activity-guided and led to the isolation of two flavone glycosides: Luteolin 7- O-beta- D-glucopyranoside and chrysoeriol 7- O-beta- D-glucopyranoside. The Luteolin 7- O-beta- D-glucopyranoside has a strong antiplasmodial activity against. *falciparum* with $IC_{50}$ values of 2.4, while chrysoeriol 7- O-beta- D-glucopyranoside has a promising antiplasmodial activity with $IC_{50}$ values of 5.9 µg/mL[49].

The genus Plectranthus of Lamiaceae family is an assortment of plants that have various organic exercises and use in conventional recuperating rehearses. The genus contains around 300 species and dispersed in tropical and subtropical zones of Africa, Asia, and Australia[59]. Five abietane-type diterpenes were secluded from the aerial parts of *Plectranthus barbatus*. The 5,6-didehydro-7-hydroxy taxodone has moderate effectt against *P. falciparum*. Taxodione; 20-deoxocarnosol, and 6α,11,12, -trihydroxy-7β,20-epoxy-8,11,13-abietatriene indicated a high antiprotozoal impact yet this was because of high cytotoxicity, while dehydroabietane showed up no antiprotozoal potential[50].

The genus Salvia is a rich origin of structurally differing terpenoids. The capacity to synthesize isoprenoids with unusual scaffolds is is one of the most distinctive highlights of Salvia specie[57]. Hydrangenone (was a colorless needle separated from the roots of *Salvia hydrangea* DC. Ex Benth *n*-hexane extract. This compound has antiplasmodial action against *P. falciparum* with an $IC_{50}$ value of 1.4 μM[51]. Phytochemical investigation of the lipophilic extract of *Salvia leriifolia* roots led to the newly rearranged abietane diterpenoids leriifoliol and leriifolione. The genus is described by the presence of a broad range of isoprenoids, including sesterterpenoids and di- and triterpenoids, with unique carbon framework. The stilbene-like abietane diterpenoid leriifoliol and leriifolione, a unique five-membered C-ring abietane diterpenoid from the roots, are examined. Leriifoliol exhibited an $IC_{50}$ of 0.4 μM against *P. falciparum*[52].

Bioassay-guided isolation of a *Satureja parvifolia* methanolic extract prompted to the separation of flavonoid eriodictyol, and two triterpenoic acids: ursolic and oleanolic acids as its active compounds against *P. falciparum* K1. These compounds are reported as constituents of *S. parvifolia* for the first time in this research. Ursolic acid showed an $IC_{50}$ of 4.9 μg/ml, luteolin 6.4 μg/ml, oleanolic acid 9.3 μg/ml, and eriodictyol 17.2 μg/ml against *P. falciparum* K1. Antiplasmodial effect of eriodictyol and luteolin is described in the journal. Ursolic acid gave a strong antiplasmodial activity, while luteolin, oleanolic acid, and erodictyol gave a promising antiplasmodial activity[54].

The leaves and stems of *S. havanensis* are characterized by a large deposit of flavonoids. The methanol and chloroform extracts of *S. havanensis* possess antiplasmodial activities. Wogonin was identified as a significant antiplasmodial active compound of leaves chloroform extract against *P. berghei* protozoa[41].

Tuecrium is a genus from the Lamiaceae family that consists of more than 300 plant species. The previous research reveals that the plants from this teucrium genus contain essential oils, monoterpenoids and sesquiterpenoids and oxygenated sesquiterpenoids. Teucrium genus is also one of the vital sources of diterpenoids with neoclerodane skeleton. Triterpenoids, sesquiterpenoids, and steroids, flavonoids, also had been isolated from plants of this genus. Triterpenoids, steroids, sesquiterpenoids, and flavonoids were also separated from these plants[61]. Sesquiterpenes compound, homalomenol C, 4b- hydroxy-11,12,13-trinor-5-eudesmen-1,7-dione, and oxo-T-cadinol, were separated from the ethyl acetate extract of the aerial parts of *Teucrium ramosissimum* bio guided by the antiplasmodial activity [55].

Salvia is the most prominent genus of the Lamiaceae family. It has over 900 species found all through the world. A few of these species have been appplied as therapeutic, fragrant, and ornamental plants [7]. Salvia species are especially abundant in diverse diterpenoids[62]. Prior phytochemical study of the aerial parts of *S. sahendica* guided to discovery of sesterterpenes, nor-sesterterpenes, and nor-diterpenes, while rearranged abietane diterpenoids have been listed from the roots[63]. There are eight abietane-type diterpenoids separated from aerial parts of *S. sahendica,* and they were assessed for their in vitro antiplasmodial effect. The $IC_{50}$ values of the compounds extended from 0.8 μM to over 8.8 μM against *P. falciparum* (K1), Ferruginol; Δ9-ferruginol; and 7-acetoxy royleanone were the foremost dynamic antiplasmodial compounds, followed by sahandol; sahandinone; 12-deoxy-salvipisone; and sahandone [53]. Some active antimalarial compounds from this plant have a potential to become new antimalarial drugs so that further research is needed.

The hexane extract from *Zhumeria majdae* Rech.f. and Wendelbo roots indicated predominant movement against *P. falciparum* with $IC_{50}$ estimations of 2.1 μg/ml. From eight abietane-type diterpenoids that disengaged and recognized in roots, only 11,14-dihydroxy-8,11,13-abietatrien-7-one displayed promising natural movement against P. falciparum ($IC_{50}$ 8.65 μM), and lanugon Q demonstrated an $IC_{50}$ estimation of 15.6 μM. All in all, 11,14-dihydroxy-8,11,13-abietatrien-7-one and Lanugon Q could be potential for antiplasmodial agent[44].

In this reviewed article, the most antimalarial active compounds isolated from the Lamiaceae family are diterpenoids (28 compounds), especially abietane type diterpenoids (18 compounds). Other groups of active antimalarial compounds from this plant family are flavonoids (6 compounds), triterpenoids (2 compounds), isoprenoid heptacyclic (1 compound) and sesquiterpene (3 compounds)

## CONCLUSION

Lamiaceae family is proven to be a source of plants that have antimalarial activity. This can be seen from the traditional use of Lamiaceae tribal plants as malaria drugs in various countries, the number of plant extracts that have high antimalarial activity and also many active antimalarial substances isolated from plants of Lamiaceae family, but they still need to be further examined to become new antimalarial drugs.

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