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The potency of plant antimalarial

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Abstract

Malaria has remained a major cause of morbidity and mortality in all parts of the world. It is associated with high economic burden on the nation, high prevalence of mortality in children, pregnant women and non-immune individuals, thus malaria is a global public health problem. This protozoan infection is mainly characterized by fever, pains, loss of appetite and anaemia, researchers had discovered potent antimalarial drugs mainly from plant sources in order to overcome resistance of antimalarials, vectors, inability to develop malarial vaccines and also toxic effects of conventional antimalarial drugs. Antimalarials obtained from plants have significant roles in drug discovery and development for the treatment of fever, pains, inflammation as well as *Plasmodium falciparum* infection, therefore this review focuses on the analgesics, antipyretics and anti-inflammatory activities as well as antiplasmodial activities of plants.

Keywords: Malaria; Potency; Plant antimalarials; Analgesics; Antipyretics; Anti-inflammatories

1. Introduction

Malaria is a protozoan infection which causes the highest burden in Africa because the deadliest species (*Plasmodium falciparum*) is most common in Africa. It is one of the public health disease associated with high mortality rate (of about 600,000 deaths yearly) as well as morbidity [1].

This deliberating disease affects mostly children under the age of five years as well as pregnant women, one death every 30 seconds is recorded because malaria causes about 400-900 million cases of fever and approximately 1-3 million deaths every year [2].

A heavy malaria burden in some countries is marked by economic impact which includes costs of health care, working days lost due to sickness, days lost in education, reduced productivity due to cerebral malaria brain damage, and loss of investment and tourism. The infection is responsible for 40% of public health expenditure, 30-50% of inpatient admissions and up to 50% of outpatient visits [3].

The reemergence of *P.falciparum* parasite to all conventional drugs is a major problem because the high prevalence of multi-resistant strain of this parasite continues to reduce the potency of antimalarial drugs [4,5]. This problem is also compounded by non-availability of malaria vaccine, therefore drugs from natural sources (plants) play important functions in the prevention and treatment of fever, pain, inflammation and *P.falciparum* infections.

Plants from different botanical sources have been used by various Traditional Medicinal Practitioners (TMP) for the prevention and treatment of pains, fever, inflammation and *P. falciparum* infection (Malaria) [6,7]. Numerous claims on

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the potency and use of various plant species for prophylaxis and cure of malaria have been cited by the TMP, some of these claims have been validated scientifically [8].

Medicinal Antimalarial drugs may be collected from wild or cultivated plants, many factors including time of the year, time of the day, stage of maturity and age, these may vary during the course of plant growth and may affect quality of the active substances [9]. Secondary plant materials can be used as fresh or dried plant materials, the drying of the crude drugs may be by natural, artificial method or Lyophilization (Freeze-drying). Several research indicated that the assessment of antimalarial activities of many plants were conducted in lyophilized forms [9].

Different parts of plant such as leaf, bark, stem, root, fruit etc. are used for prevention and treatment of malaria. Decoction (boiled teas) may be used to prepare some of these plant antimalarial drugs in order to replicate the methods used by the TMP, other methods of preparations are infusions (hot teas), tinctures (alcohol and water extracts), paste, powder and macerations (cold-soaking) [5,9].

The bark of Cinchona tree was the first plant antimalarial drug used by the natives of Peru for the prevention and treatment of malaria, quinine was synthesized from this and served as a lead structure for the synthesis of several antimalarial drugs such as quinidine, cinchonine, and cinchonidine followed by chloroquine, mefloquine, pyrimethamine, proguanil, atovaquone (sold together with proguanil as "Malarone"), or primaquine. Quinine (alone or in combination with doxocycline, tetracycline or clindamycin) is still used today to treat acute cases of severe *P. falciparum* infections [10].

Artemisinin was the second Plant antimalarial drug isolated and synthesized from *Artemisia annua* in China in the seventies. As a result of recrudescence associated with Artemisinin, Artemisinin-combined therapies (ACT) were formally adopted as first-line treatment of uncomplicated malaria in Nigeria from 2005 onwards and atovaquone (Malarone®) [11], which is a synthetic compound (2-alkyl-3-hydroxynaphthoquinone) analogue of lapachol from the Tabebuia species (Bignoniaceae). There is need to reduce unnecessary treatment and delay the emergency of resistance to ACT while ensuring the effective treatment of malaria by ACT [12].

About 1,200 plant species are used traditionally all over the world for the prevention and treatment of pains, fever, inflammatory conditions and *P.falciparum* infections, thus Plant kingdom has proven an effective source of antimalarial drugs in the past.

Plant antimalarials are accessible and inexpensive, therefore have fitted the immediate personal need and commonly used in medicine from time immemorial [8].

The most commonly used antimalarial drugs are produced traditionally from natural plants, with the achievements of synthetic chemistry specifically Structure Activity Relationship (SAR) and the advancement of rational antimalarial drug design, plant antimalarials play important roles in the provision of traditional antimalarial drugs and these serve as stepping points for the development of synthetic antimalarial drugs [3, 5]. This review highlights plants from various natural sources used traditionally for the prophylaxis and treatment of pains, fever, inflammation and *P.falciparum* infections.

Analgesics are the most commonly used drugs for alleviating pains and curing fever as well as inflammatory conditions. Pain is an unpleasant emotional condition which affects quality of life and general function of the body [13, 14] this condition is managed by analgesics. Analgesics also known as pain relievers are categorized into non-narcotic (non-opioid) which include acetaminophen, aspirin, non-steroidal anti-inflammatory drugs (NSAIDs) and narcotic analgesics [13, 14].

Acetaminophen (paracetamol) is used for mild pain, fever, as an alternative for aspirin and lacks anti-inflammatory activity. Therapeutically, acetaminophen is used for pain relief in the symptomatic treatment of various musculoskeletal and joint disorders. Acetaminophen is devoid of gastrointestinal side effects like the NSAIDs. At a chronic use, paracetamol saturates the hepatic pathway normally involved in its metabolism, hence it is being metabolized by an alternative pathway to N-acetyl-p-benzoquinone imine(NABQI), a toxic metabolite, which is deactivated by glutathione. Excess NABQI causes necrosis of the liver and renal tubules since glutathione may be easily depleted [14, 15].

Aspirin (acetyl salicylic acid) has analgesic, anti-inflammatory and antipyretic properties which many analgesics do not have. Aspirin is used for pains related to headache, myalgia, rheumatoid arthritis and rheumatic fever, neuralgia, dysmenorrhea and arthralgia. The adverse effects are gastrointestinal effects, blood dysfunction, auditory and vestibular disturbances and skin reactions [14, 15].

Non-steroidal anti-inflammatory drugs (NSAIDs) possess analgesic, anti-inflammatory and antipyretic activities. They are ibuprofen, piroxicam, diclofenac, and naproxen and have been used successfully to relieve biliary pain, acute pain of renal colic, postoperative pain, mild pain of sickle cell crisis, and ectopic bone formation pain and dysmenorrhea. They are mostly associated with gastrointestinal side effects [14, 15].

Table 1 Natural plants used for the treatment of malaria

S/no	Plants	Common names	Parts	Countries	References
1	*Agelathus dodoneifolius*	African mistletoe	Twigs, leaves, stem bark, whole plant	Nigeria, Ghana, Senegal, Mali	8, 16
2	*Allium sativum*	Garlic	Bulbs	Cameroon, Nigeria, Uganda	5
3	*Anarcadium occidentale*		Leaves, Stembark	Nigeria, Ghana, Cameroon	
4	*Artemisia annua*	Sweet wormwood	Leaves, seeds	Burundi, Nigeria	5,8
5	*Azadirachta indica*	Dogoyanro, neem	Barks, leaves	Nigeria	5
6	*Carica papaya*	Paw paw	Leaves, fruits, roots, Barks	Cameroon, Nigeria, Uganda Burkina Faso, Ghana,	5, 8
7	*Cymbopogon citratus*	Lemon grass	Whole plant, root	Cameroon, Nigeria	5
8	*Euphorbia hirta*	Hairy spurge	Barks, leaves	Ivory coast, Cameroon, Togo	5
9	*Garnicia kola*	Bitter kola	Stem barks	Nigeria	5
10	*Khaya senegalensis*	African mahogany	Barks, leaves	Cameroon, Nigeria	5
11	*Mangifera indica*	Mango	Barks, Leaves	Cameroon, Nigeria, Uganda, Ghana	5
12	*Moringa oleifera*	Moringa	Leaves	Ghana, Uganda , Nigeria	5
13	*Musa sapientum*	Ayaba	Leaves, Fruits	Nigeria	8
14	*Nauclea latifolia*	African peach	Leaves	Nigeria, Ghana	5
15	*Ocimum gratissimum*	Tea bush	Leaves, stem barks,	Nigeria, Ghana, Togo, Cameroun	5,8
16	*Parkia biglobosa*	African locust bean	Stem bark, Leaves, root, seeds, whole plant	Nigeria, Ghana, Uganda, Ethiopia	5
17	*Psidium guajava*	Guava	Barks, Leaves, Stem, Root	Nigeria, Ghana	5,8
18	*Sida acuta*	Broom weed	Leaves	Kenya, Ivory coast, Nigeria	5, 8
19	*Vernonia ambigua*	Orungo	Whole plant	Nigeria	5
20	*Vernonia amygdalina*	Bitter leaf	Leaves	Nigeria, Ghana	5,8
21	*Zingiber officinale*	Ginger	Rhizome	Cameroon , Nigeria	5

Narcotic analgesics (opioid analgesics). They are classified into strong opioids and they are full agonists such as morphine, diamorphine, hydromorine, methadone, pethidine, oxycodone, levorpharmol, fentanyl and alfetanil. Partial agonists such as etazocine, butorphanol, halbuphine and dezocine. They are mostly effective in severe pain and chronic or terminal pain. Morphine or related drugs are associated with drug dependence and withdrawal syndrome [14, 15].

Codeine is a mild opioid analgesic, analogues include dextropropoxyphene and dihydrocodeine. They are usually combined with non–opioid analgesics for the treatment of moderate to severe pain. The adverse effects include constipation, respiratory depression and allergic reactions [14, 15] with the set back of creating efficient vaccines, in addition to severe adverse effects of the conventional antimalarial drugs, this article showcases the analgesics, antipyretic, anti-inflammatory activities and antiplasmodial activities of indigenous plants. Numerous variety of plants possessing antimalarial activities is illustrated in Table 1.

2. Antimalarial activities of natural plants

2.1. *Agelathus dodoneifolius*

The analgesic, antipyretic and anti-inflammatory activities of methanolic extract of African mistletoe had been validated. The extract indicated a significant ($p < 0.01$) and dose-dependent inhibition of the acetic acid-induced abdominal constriction in mice, increased threshold for pain perception dose-dependently in the hot plate test in mice and decreased acute and delayed phases of formalin-induced pain dose dependently ($p < 0.01$) [16].

The extract also exhibited a significant ($p < 0.01$) dose-dependent anti-inflammatory effect in carrageenan-induced oedema in rats. Significantly reduced dose -dependent rectal temperature in rats was also showed by the extract. The anti-inflammatory effect of *A. dodoneifolius* and its potential use for the treatment of neutrophil-dependent inflammatory diseases, dose-dependent inhibitory activities on the oxidant activities of neutrophils were observed by all the tested extracts [16].

The African mistletoe (*A.dodoneifolius*) methanolic extract was investigated for *in vivo* and *in vitro* antiplasmodial activities against *Plasmodium berghei* and clinical isolates of *Plasmodium falciparum* respectively. *A. dodoneifolius* exhibited maximum inhibition (78.7±1.6, 80.1±1.0 and 69.8±1.2%) of parasitaemia and moderate antiplasmodial activity *in vitro* (21.54μg/ml > IC50 > 50μg/ml) among *Parkia biglobosa* (host plant) and *Vernonia ambigua* [1,16].

The water extract of A.*dodoneifolius* showed a dose-dependent inhibition of parasitaemia in the *in vivo* antiplasmodial tests likewise, the *in vitro* screening demonstrated a strong and concentration-dependent activity (21.54 μg/ml < IC50< 50 μg/ml) of the extract against the clinical isolates of *Plasmodium falciparum.* The methanol whole plant extract of African mistletoe and its methanolic fraction exhibited significant ($p< 0.01$) and dose -dependent chemo -suppressive effect and these correlated with in the survival times of the infected mice [1,16].

2.2. *Allium sativum*

The *in vivo* evaluation of analgesic activities of *A.sativum* displayed reduced number of acetic acid writhing (abdominal constriction) (37-48.1%)in mice at different doses while the *in vitro* evaluation demonstrated potent inhibitory activity against *P. falciparum* with IC_{50} of 0.5 ± 0.42μg/ml [5, 17].

2.3. *Anacardium occidentale*

Anacardium occidentalis extract significantly reduced acetic acid induced writhing in mice and the number and time of paw licking induced by formalin ($P < 0.05$) in a dose related manner. It also displayed the neurogenic and inflammatory phases of formalin ($P < 0.05$). Analgesia was exihibited in the inhibition of nociception induced by tail immersion in 55°C hot water. The extract increased the latencies of tail withdrawal to a similar degree as pentazocine. The extract caused significant reduction of carrageenan induced paw oedema in rats ($P < 0.05$) in a dose dependent manner. These results show that the leaf extracts of *Anacardium occidentalis possess* highly potent analgesic and anti-inflammatory activities [18].

Evaluation of ethanolic extract of *A.occidentalis* indicated moderate *in vivo* inhibition of parasitaemia against *P.berghei berghei* and the extract also displayed potent *in vitro* antiplasmodial activities (IC_{50} 0.577 ug/ml) against *P.falciparum* [19].

2.4. *Artemisia annua*

Various species of Artemisia have been reported to display potent analgesic, antipyretic and anti-inflammatory in accordance with numerous studies [20]. Research had shown that *A. annua* exhibited weak to strong *in vitro* inhibition (3.27-4-95 Ug/ml) of *P.Falciparum* parasitaemia and *in vivo* inhibition of 52.8-95.3% against *P.berghei berghei* [5].

2.5. *Azadirachta indica*

The potency of Analgesic, antipyretic and anti-inflammatory activities of the extract of *Azadirachta indica* indicated significant analgesic activities, at the doses of 250mg and 500mg/kg per body weight. It also exhibited significant anti-inflammatory and antipyretic activities at doses of 125mg, 250mg and 500mg/kg per body weight in dose related manner [8].

The antiplasmodial activities of *A. indica* have been associated with the vast bioactive components of the plant in relation to their potent antioxidant activities reported by several researchers [5].

2.6. *Carica papaya*

Research had indicated that the extract *C.papaya* leaves at different doses of 100, 300, and 600 mg/kg BW exihibited similar analgesic potency with paracetamol as control group ($P<0.05$) [21]. The antiplasmodial evaluation of *C.papaya* indicated 100% inhibition against *in vivo P.berghei berghei* and IC 50 of 15.2-16.8 (µg/ml) *in vitro* reduction against *P.falciparum* [5].

2.7. *Cymbopogon citratus*

A dose-dependent analgesia of *C.citratus* for the hyperalgesia induced by subplantar injections of either carrageenin or prostaglandin E_2 was investigated. The potency of this plant was further confirmed by the isolation of Myrcene which exhibited higher analgesic activities [22]. The *in vivo* antiplasmodial activities and *in vitro* antiplasmodial activities of *C.citratus* were reported to be 87.2% and 9.1-12.1ug/ml according to a research [5].

2.8. *Euphorbia hirta*

Research showed that the extract of *E.hirta* potently inhibited acetic acid induced writhing in mice, yeast induced hyperpyrexia in rats and dextran-induced rat paw edema [23]. *E.hirta* was investigated to cause 59.1% *in vivo* inhibition of *P.berghei berghei* and *in vitro* inhibition of IC_{50} of 4.33-10.7(µg/ml) against *P.falciparum* [5].

2.9. *Garnicia kola*

Research indicated that GB1, a hydroxybiflavanonol isolated from Garcinia *kola* displayed potent analgesic, anti-inflammatory and antipyretic activities [24]. The *in vitro* antiplasmodial activities of *G.Kola* against *P.falciparum* was evaluated to be 1.6-2.9 µg/ml [5].

2.10. *Khaya senegalensis*

The stembark extract of *K. senegalensis* displayed potent dose-dependent analgesic, antipyretic and anti-inflammatory activities in acetic acid induced writhing response in mice, rat tail-flick test and yeast induced hyperthermia [25]. The ethanolic extract of *K. senegalensis* exhibited potent inhibition of *P.berghei berghei in vivo (< 80%)* and inhibition of *P.falciparum in vitro* (IC_{50} of <5.00 (µg/ml) [5].

2.11. *Mangifera indica*

Aqueous extract of *Mangifera indica* exhibited potent dose-dependent inhibition of acetic acid-induced abdominal constriction and formalin-induced licking in mice (maximal inhibition: 94.4% and 99.5% respectively). It also displayed potent inhibition of both carrageenan- and formalin-induced oedema in rat, guinea-pigs and mice (maximal inhibitions: 39.5, 45.0 and 48.6, respectively) [26]. Evaluation of both *in vivo* and *in vitro* antiplasmodial activities of extracts of *M.indica* against P.*berghei berghei* and P.*falciparum* indicated 67.7-100% and IC_{50} of 14.0 -24.3 µg/ml [5].

2.12. *Moringa oleifera*

Ethanolic extract of *M.oleifera* exhibited potent analgesic activities in both hotplate and tail immersion model at the dose of 25mg/kg/body weight. The extract also displayed potent anti-inflammatory activities in both indomethacine induced oedema and carrageenan induced oedema at the dose of 750mg/kg/body weight [27]. *M.oleifera* ethanolic

extract also indicated potent inhibition of *P.berghei berghei in vivo* (100%) and *in vitro* inhibition of *P.falciparum* at the IC $_{50}$ of 15.1 µg/ml [5].

2.13. *Musa sapientum*

The water extract of *M.sapientum* exhibited potent anti-inflammatory activities in Nitric Oxide inhibition model according to research. The decoction of leaves of species (*M.paradidisaca*) similar to *M.sapientum* displayed potent antiplasmodial activities against chloroquine-resistant strain of *P.falciparum in vitro* [28].

2.14. *Nauclea latifolia*

The aqueous extract of the root bark of *N. latifolia* showed potent analgesic, antipyretic and anti-inflammatory activities in both acetic acid-induced abdominal constriction and hot-plate tests in mice and formalin-induced pain test in rats, as models of nociception. The extract also displayed potent anti- inflammatory activities in egg-albumin induced inflammation and pyrexia induced by yeast in rats at the dose of 50-200mg/kg/body weight [29]. The extracts of *N. latifolia* also exhibited remarkable inhibition of parasitaemia against *P.berghei berghei in vivo* at 63.8% and potent *in vitro* inhibition of *P.falciparum* of IC_{50} of 0.60 ug/ml [5].

2.15. *Ocimum gratissimum*

Evaluation of *O.gratissimum* essential oil in classic pain models (hot plate test and formalin test) indicated potent analgesic activities and potent anti-inflammatory activities in murine pain models at a dose of 40 mg/kg/body weight [30]. *In vivo* antiplasmodial activities of *O.gratissimum* extract against *P.berghei berghei* were reported to be 88% inhibition and *in vitro* antiplasmodial activities against *P.falciparum* were investigated to 1.84 ug/ml IC_{50} [5].

2.16. *Parkia biglobosa*

The extract from the bark of *P. biglobosa exhibited* dose-dependent analgesic, antipyretic and anti-inflammatory activities in acetic acid induced nociception test in mice and yeast induced pyrexia test in rats. The extract also displayed potent anti-inflammatory activities in croton oil ear inflammation in test animals and carrageenin-induced rat paw oedema at the dose of 25-100mg/kg/body weight [31]. The antiplasmodial activities of the stem bark extract of *P.biglobosa* were evaluated against malaria model *Plasmodium berghei berghei* and clinical isolates of *Plasmodium falciparum*. The extract exhibited potent dose –dependent reduction of parasitaemia *in vivo* (55.6%-100%) and *in vitro* (IC_{50} of 12.9-56.2 ug/ml) clinically [1, 5, 8, 23].

2.17. *Psidium guajava*

Psidium guajava ethanolic extract was evaluated for analgesic and antipyretic activities in rats using yeast induced hyperpyrexia, hot plate latency assay and formalin induced paw licking test in rats. The research confirmed the potency of analgesic and antipyretic activities of *P.guajava* [32].

The ethanolic extract of *P.guajava* was investigated for antiplasmodial activities against *in vivo P.bergehei berghei* and *in vitro* against *P.falciparum*. The extract exhibited potent inhibition of parasitaemia (<80%) and remarkable inhibition of parasitaemia (IC_{50} of 6.00ug/ml) [5].

2.18. *Sida acuta*

The extract of *s. acuta* was evaluated for analgesic activities in hot plate and tail immersion models at the three dose levels in mice. The extract indicated potent analgesic activities at a dose of 500mg/kg/body weight. The antipyretic activities of the extract were also reported to be potent according to research. Evaluation of anti-inflammatory activities of the extract in tail immersion and mouse ear oedema model showed potent dose –dependent reduction of oedema [33].

S. acuta extract was investigated for antiplasmodial activities against *P.falciparum in vitro.* The extract indicated potent inhibition of *P.falciparum* chloroquine resistant strain with IC_{50} of 0.92-3.90 ug/ml [5].

2.19. *Vernonia ambigua*

A species (Vernonia *hymenolepis**)*** similar to *V.ambigua* was investigated for analgesic activities using both formalin test and sensorimotor Activity Testing in mice. Potent dose-dependent analgesic activities were reported [34]. The whole plant extract of *V.ambigua* was evaluated for both *in vivo* and *in vitro* antiplasmodial activities. The extract exhibited moderate inhibition against *P.berghei berghei* in suppressive, curative and prophylactic antiplasmodial test (56.9%,

56.7% and 63.0% respectively). The extract also displayed remarkable inhibition of *P.falciparum in vitro* with IC_{50} of 31.6 ug/ml [34].

2.20. *Vernonia amydalina*

Evaluation of the analgesic, antipyretic and anti- inflammatory activities of ethanolic extract of *V.Amydalina* was conducted in tail withdrawal, formalin-induced nociception test and yeast induced pyrexia test in mice and rats. The findings indicated potent dose-dependent analgesic, antipyretic and anti-inflammatory activities at the dose of 25-200mg/kg/body weight [35].

In vivo antiplasmodial activities and *in vitro* antiplasmodial activities of *V.Amydalina* showed potent inhibition (97.8%) of parasitaemia in *P.berghei berghei* antiplasmodial model and moderate IC_{50} of 4.10 ug/ml against *P.falciparum in vitro* [5].

2.21. *Zingiber officinale*

Investigation of the analgesic activities of *Z. officinale* indicated potent anti-nociceptive activities according to research. Potent anti-inflammatory activities were also exhibited in cyclooxygenase-1, cyclooxygenase-2 inhibition model and 5-lipoxygenase inhibition model [36].

Z. officinale extract exhibited moderate inhibition of parasitaemia against *P.bergehei berghei* model *in vivo* and also demonstrated moderate inhibitory antiplasmodial activities against *P.falciparum in vitro* with IC_{50} of 15.9 ug/ml [5].

2.22. Phytochemicals

Traditional products act at different stages in malaria treatment, thus they are useful in combination therapy. Evaluation of plant extracts has resulted in production of various secondary metabolites (Phytochemicals) with potent antimalarial activities [5]. Phytochemicals isolated from these plants are indicated in Table 2.

Table 2 Phytochemicals isolated from plant antimalarials

S/no	Plants	Phytochemicals	References
1	*Agelathus dodoneifolius*	Alkaloids , Tannins , Saponins ,Sterols ,Terpenes ,Glycosides , Phenols ,Anthraquinones , Reducing sugars, Resins ,Volatile oils	16
2	*Allium sativum*	Volatile oil, Flavonoids, Saponins, Steroids, Alkaloids, Tannins, Cadenolide, Reducing sugar, Cardiac glycosides, Anthraquinone , Cyanogenic glycosides	5, 17
3	*Anarcadium occidentale*	Flavonoids, Triterpenes, Steroids, Xanthones, Alkaloids, Tannins, Saponins, Cardenolides, Alkyl-phenols, Glycosides, Essential oil, Terpenoids	18, 19
4	*Artemisia annua*	Sesquiterpenes lactone, Flavonoids, Steroids, Cardiac glycosides, Reducing sugar, Phenolic acids, Coumarins, Essential oil	37
5	*Azadirachta indica*	Flavonoids, tannins, phenols, coumarin, terpene	8, 23, 38
	Carica papaya	Alkaloid, Flavonoid, Saponin, Tannin, Cardiac glycosides, Phenols, Cyanogenic glycosides	21
	Cymbopogon citratus	Essential oil, Flavonoids, Phytosterol, Phenols, Coumarin, Anthocyanin,	30
	Euphorbia hirta	Saponins, Alkaloids, Flavonoids, Steroids, Tannins, Terpenoids, Glycosides	23
	Garnicia kola	Tannins, Saponins, Alkaloids, Cardiac glycosides, Flavonoids,	24
	Khaya senegalensis	Resin, Reducing sugar, Saponins, Phenols, Terpenes, Carotenoids, Coumarins, Steroids, Steroidal glycosides, Tannins, Anthocyanins	25
	Mangifera indica	Carotenoids, Polyphenols, Tannins, Flavonoids, Triterpenes,	26

	Moringa oleifera	Tannin, Phenolic compounds, Flavonoids, Steroids, Terpenoids, Alkaloids, Glycosides	27
	Musa sapientum	Alkaloids, Anthraquinones, Cardiac glycosides, Flavonoids, Reducing sugars, Saponins, Steroids, Tannins, Terpenoids	28
	Nauclea latifolia	Tannins, Flavonoids, Alkaloids,Saponins, Cardiac glycosides, Terpenoids, Steroids, Reducing sugar, anthraquinones, , Resins, Polyphenols, Carotenoids, Limonoids, Xanthonoids, Balsam, Cyanogenic glycosides , Reducing sugar	29
	Ocimum gratissimum	Essential oil, Terpenes, Sesquiterpenes, Phenols, Flavonoids,	30
	Parkia biglobosa	Flavonoids, Tannins, Terpenes, Saponins, Steroids, Phenols, Reducing sugars., Cardiac glycosides, Alkaloids, Tannins	31
	Psidium guajava	Tannins, Flavonoids, Saponins, Triterpenoids, Glycosides, Phenols, Triterpenoid acids, Essential oils , Sesquiterpene alcohols.	32
	Sida acuta	Tannins, Terpenoids, Alkaloids, Glycosides, Phenols, Saponins, Flavonoids,	33
	Vernonia ambigua	Saponins, Glycosides, Tannins, Flavonoids, Steroids, Terpenes, Anthraquinones, Reducing sugars, Phenols, Alkalods	34
	Vernonia amygdalina	Tannins, Saponins, Phenols, Flavonoids, Steroids, Alkaloids, Terpenes, Steroidal glycosides, Terpenoids, Sesquiterpenes lactone	35
	Zingiber officinale	Essential oils, Phenolic compounds, Flavonoids, Reducing sugars, Alkaloids, Glycosides, Saponins, Steroids, Terpenoids, Tannins	36

3. Mechanisms of pharmacological activities of plant antimalarials

Several studies have attributed the potency of anticonceptive, antipyretic, and anti-inflammatory activities of plant products to be related to the inhibition of pathways of some enzymes namely lipo-oxygynase , cyclooxygenase and nitric oxide synthase (NOS) . Some of these plants also exert their pharmacological effects through the inhibition of tumor necrosis factor (TNF)- α-induced neutrophil adherence as well as production of vasoconstrictor nitric oxide production (NO) [30]. The suppression of both peripherally non-opioid mediated and centrally opioid mediated nociceptive and inflammatory activities also play roles in these activities [27]. The cyclic monophosphate guanosin/triphosphate adenosine (NO/cGMP/ATP)-sensitive- K(+) channel pathway and/or facilitation of the GABAergic transmission were also implicated in these actions [29]. The inhibition of some other pathways including (opioidergic, ATP sensitive K+ channels, nitric oxide, muscarinic, adrenergic and voltage-gated calcium channel) were not left out [35, 36].

The antiplasmodial activities of these natural plants may be explained by their phytochemical composition due to the presence of bioactive components which are also regarded as the antioxidants. These antioxidants are also represented in the remaining antimalarial activities including analgesics, suppression of hyperpyrexia and reduction of inflammatory activities in accordance with numerous research [5, 8, 23, 31].

4. Conclusion

The plant kingdom comprises phytochemicals which are secondary metabolites found in plants, the pharmacological activities including the analgesics, antipyretics, anti-inflammatory activities as well as antiplasmadial activities also known as antimalarial activities have been related to various documentation of potent phytocomponents which are antioxidants. The antimalarial activities of several active compounds isolated from natural plants are remarkable which suffer limited investigation, there is need to establish the efficacy and safety of plant antimalarials due to their potency, with the hope that they will serve as alternatives to the currently used analgesics and less effective ACT which may be monotherapy or in combination therapy.

Compliance with ethical standards

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