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Medicinal Plants: Panacea For Anti-Malarial Green Drug Discovery

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Abstract

People acknowledge the importance of medicinal herbs from ancient time. Until the discovery of modern medicine, medicinal plants have been extensively used for the treatment of some disease management like malaria, cancer, diabetes, high blood pressure, etc. throughout human evolution. Malaria is one of the earliest recognized diseases and still a threat to third world countries. Significantly, cinchona, a green herb, showed a great promise for its effectiveness in curing malaria. In this review, we venture to pursue the current trends on practices and impacts of medicinal plants on malaria.We conducted a broad search of published articles to locate original publications about potential usage of medicinal herbs against malaria till last decade using PubMed, Google Scholar, and the ancient Indian ayurvedic data. In this review, we discussed specifically the discovery of new green anti-malarial medicines starting from the ancient Ayurveda. In the beginning, we shortly introduced the current global status of malaria in terms of its casualty and treatment. We here considered the unique properties of herbal plants that show potential antimalarial effects. We also discussed several drugs extracted from medicinal plants (e.g., Irridoids, Flavonoids, Quercetin, and Hesperidin). The systematic extraction of New Green Medicinal Drugs is also addressed in the review highlighting their potential clinical manifestation based on critical targets in the prevention of malaria parasite. Nevertheless, we also mentioned the marketing strategy for these new green anti-malarial drugs. Nowadays, several anti-malarial drugs are available for the treatment of malaria in modern therapy. Overall, the review represents a complete picture of green medicines for the treatment of the disease. However, further scientific research is still required from finding the source of new medicinal plants for the

ISSN: 0971-1260
Vol-22-Issue-16-August-2019

treatment of malaria and establishes those phytomedicines in well-designed preclinical experiments and clinical trials on its anti-malarial effects and safety.

List of Abbreviation:

WHO: World Health Organization, **WRAIR**:Walter Reed Army Institution of Research,**TDR**:Training for Tropical Diseases, **NVBDCP**:National Vector-borne Disease Control Programme, **BH**:beta-Hematin, **NMCP**:National Malaria Control Programme, **NMEP**:National Malaria Eradication Programme, **DDT**:Dichlorodiphenyltrichloro acetic acid, **MPO**:Modified Plan of Operation, **EMCP**:Enhanced Malaria Control Project, **NAMP**:National Anti-malaria Programme, **NVBDCP**:National Vector Borne Disease Control Programme, **IMCP**:Intensified Malaria Control Project, **HRP**:Histidine-rich Protein

1. Introduction

Malaria secures a distinctive place in the history of human civilisation. In the last century alone, malaria claimed around ~150 to 300 million human lives whichresulted for 2 to 5 % of all deaths(Carter and Mendis, 2002). Malaria is currently killing about 1-2 million people worldwide every year (Sheet, 2016). Young below the age of 5 years is mostly affected(Gurmu et al., 2018). Malaria is a standardmodel of a disease that affects the whole society(Husin et al., 2018). People living under poverty and in the third-world countries mostly suffer from malaria (Brown, 1997). Factually, Africa is significantly affected by malaria followed by tropical areas including East Asia, China, Bangladesh, and India (Afshar et al., 2018)Notably, 40% of cases of malaria are caused by *Plasmodium falciparum*in India(Khare et al., 2018; Toghueo et al., 2018). The bark of *Cinchona* speciesbelonging to family Rubiaceaewas used as of raw materials for isolating quinine, a first anti-malarial drug, in 1820 (Saxena et al., 2003). It is the most used anti-malarial drug to date.

Moreover, another effective antimalarial drug, chloroquine, was synthesized in 1940 and until recently, this was used for the treatment of malaria (Achan et al., 2011; Mbouna et al., 2018);. Unfortunately, *P. falciparum* became resistant to chloroquine, and therefore, a drug combination including chloroquine was introduced (Attemene et al., 2018; Haidara et al., 2018; Odoh et al., 2018). However, the drug combinations were not always useful to the treatment of malaria. Hence, many research groups are currently working to develop new active compounds as an alternative to chloroquine and artemisinin (Hoopes et al., 2018; Masic et al., 2018; Matsuura et al., 2018).

People were using herbal products in medical practice in the past, and the encouragement is further increasing worldwide (Atilaw et al., 2017; Awodiran et al., 2018; Lemma et al., 2017). The promise of solving various diseases through herbal remedies has led various pharmaceutical agencies worldwide for investing in the production of cost-effective green drugs made from herbs (Alebie et al., 2017; Olanlokun et al., 2017; Shen et al., 2017). Before 1820, a suspension of finely powdered Cinchona bark in wine was used for the treatment of ague (He et al., 2017; Hoekou et al., 2017; Hussain and Green, 2017; Meshnick, 1997).Opium and Cinchona were identified as only two medicinal plants which were primarily useful for the cure of malaria (Nondo et al., 2017; Sangsopha et al., 2018;

ISSN: 0971-1260
Vol-22-Issue-16-August-2019

Singh et al., 2017a).Interestingly, the second most significant medicinal plant, Artemisia, was discovered by traditional Chinese remedy in 1979 (Abdissa et al., 2017; Jansen et al., 2017; Okokon et al., 2017; Xiao et al., 2017).

This review primarily aims to cover diverse aspects viz., malaria according to Ayurveda and its opinion in clinical manifestation,current global status of malaria properties of remedial plants for the treatment of malaria, effects of therapeutic antimalarial drug isolated from plants, new green medicinal drugs and their discovery,key-target to prevent malaria parasite and marketing of antimalarial drug. This review further provides novel perspectives in the field of green antimalarial drugs for the treatment of malaria.

2. Malaria According to Ayurveda

According to Ayurveda, malaria seemed to be a type of fever; attended with debility, trembling, headache, caught and yellowness (Mwangi et al., 2015; Razak et al., 2014).It has endemic nature and spread very quickly due to seasonal variation. The epidemic mostly occurs in the summer than the rainy season and the autumn (Boniface et al., 2015; Ngarivhume et al., 2015). However, only some part of the Indian subcontinent region including India, Munjvan, Mahavrsa, Gandhara, Anga, and Magadha observe the severity of this disease (Mammino and Bilonda, 2014; Tarkang et al., 2014). Several studies reported that patients suffering from the severe cases of malaria died and after that, the mortality rate was high (Austarheim et al., 2016; Chander et al., 2016; Komlaga et al., 2016). Ayurveda described in the following way: *"SukshmaSukshmatarasyesudosoraktadimargesusanairaplacirenayatkramoyamtenavicchhin asantapolaksyatejvaravisamovisamarabha kriya anusangavan*"(Astangasamgraha, Jvaranidana, 69) which could be translated as "vitiated dosha spreads slowly through blood and spread to all parts of body but not simultaneously in all parts This is the way in which fever is seen as interrupted or irregular onset and relief; known as visamajvara"(Soni, 2013). The patients suffering from this kind of symptoms of fever vary stage to stage-dependent manner.According to Ayurvedic theory of Atharva Veda (1500 B.C.), these stages vary due to the involvement of particular body tissues(Soni, 2013).

3. Current global status of malaria

According to the latest WHO estimates, about 214 million peoples are affected due to malaria in December 2015, and out of which 438000 were dead (Khan et al., 2017; Sheet, 2016; Tarkang et al., 2016; Zhou et al., 2016). Between 2000 and 2015, mortality rates due to malaria were decreased by 60%(Bankole et al., 2016; Irungu et al., 2015; Ma et al., 2015). However, the risk of it fell by 37% globally. In Sub-Saharan African continues to share a high proportion of global malaria (Happi et al., 2015; Toma et al., 2015). In the latest estimation, about 80% of malaria cases were reported in some countries of Sub-Saharan Africa and ~78% deaths globally(Girma et al., 2015; Kaushik et al., 2015; Lubbad et al., 2015). However, the incidence was declined by about 32% in these countries since 2000(Mohanty et al., 2015). Indian subcontinent, South America, Southeast Asia, and China

ISSN: 0971-1260
Vol-22-Issue-16-August-2019

are less affected by Falciparum malaria(Talisuna et al., 2004). Therefore, due to the low transmission rate, partial immunity does not develop as rapidly.

Plasmodium vivax is spread in both temperate and tropical regions and is relatively uncommon in tropical Africa (Mwangi et al., 2015; Razak et al., 2014). Moreover, Plasmodium ovale is found mainly in tropical Africa whereas Plasmodium malariaeis visible throughout the world (Asnake et al., 2015; Lima et al., 2015; Pala et al., 2016). However, people usually observe Plasmodium falciparum and Plasmodium vivax as the most common malaria parasites in India (Cai et al., 2015; Da et al., 2016). While Plasmodium vivax in the plains and P. falciparum predominates in forested and peripheral areas are prevalent occurs (Irungu et al., 2015; Ma et al., 2015; Oliveira et al., 2015). Recently, WHO has decided to develop the Global Technical Strategy for Malaria 2016–2030 which have an aim to eliminate malaria globally (World Health, 2015). Today, India is a member of Asia Pacific Leaders Malaria Alliance (APLMA), has decided to eradicate malaria by 2030 as per own national and global strategies on the same timelines(Dash et al., 2008; Wangdi et al., 2016; Whittaker et al., 2014).In India, central as well as state government have been spending (30-35%) share budget approximately equal in health on malaria control, except by the northeastern states (Sharma and Sharma, 1998; Sharma et al., 2015; Singh et al., 2017b; Tarkang et al., 2016).

4. Properties of Medicinal Plants in Malarial Treatments

There are several reasons like incorrect dosing, poor quality drug or drug interactions, poor diagnosis, noncompliance to the dosing regimen, etc. which might turn anti-malarial drugs to be resistance to malaria and that can cause treatment failure (Tarkang et al., 2016; Tshibangu et al., 2017; Zhou et al., 2016). In 1960, *P. falciparum* strains developed resistance to chloroquine (Gupta et al., 2018; Mukungu et al., 2016; Tariq et al., 2016; Winter et al., 2008). Extensive use of chloroquine, cost-effective treatment for malaria resulted in resistance to *P. falciparum* parasites everywhere in the world, and this was transmitted to variousmalarious areas like Central America, limitedregions of the Middle East, the island of Hispaniola, and Central Asia as well as Indian subcontinents (Afolayan et al., 2016; Bloland and World Health, 2001; Desrosiers and Weathers, 2016; Khedr et al., 2016). Mefloquine resistance is also found in some part of South-East Asia and the Amazon region of South America and sporadically in Africa (Austarheim et al., 2016; Dhawan et al., 2016; Fasinu et al., 2017; Mockenhaupt, 1995).

IndianNational Vector-borne Disease Control Programme (NVBDCP) reported that malaria was widely spread across in Indiaand recorded about 1,502,742 positive cases of malaria-infected persons, out of which 1,274 deaths in 2007 alone in India (Chander et al., 2016; Dhillon, 2008; Haidara et al., 2016).The managing of 2/3rd of the total patients by the private sector is the root for under-reporting events. Furthermore, patients' death is also not properly certificatified in urban areas as well as malaria-related diagnosis is quite raer for poor infrustucturin public health care facilities (Adia et al., 2016; Kefe et al., 2016; Tshitenge et al., 2016).*Aspidospermapyrifolium* has a significant therapeutic index because of the

ISSN: 0971-1260
Vol-22-Issue-16-August-2019

presence of alkalodic fraction at a high level of stem extract (Ceravolo et al., 2018; Jansen et al., 2017; Saxena et al., 2016). Because of that, it acts as a suitable candidate for investigation of a green drug for malaria (Berthi et al., 2018; Gupta et al., 2018; Li et al., 2017). The active isolated ingredients have no toxic activity especially concerning mutagenic as well as genotoxicity (Bapela et al., 2019; Salehi et al., 2018) (Salehi et al., 2018, Bapela et al., 2019). Bisindole alkaloid Leucoridine and a novel compound are responsible for its antimalarial activity in patients according to UPLC-HRMS analysis and their *in vitro* test (Falade et al., 2018; Shi et al., 2018).

Scrophulariaumbrosa is popularly reported as a traditional herb because of the presence of significant phytochemical occurrence in the rhizome extract (Khare et al., 2018; Mao et al., 2018; Sharma et al., 2018). The extractants were made with the help of methanol (MeOH), n-Hexane, total phenol, and total flavonoid (Attemene et al., 2018; Haidara et al., 2018).Few studies used apigenin, a commonly used dietary flavonoid as antiplasmodial agents under *in vivo* condition (Chander et al., 2016; de Souza et al., 2017; F Oga and K Singh, 2016; Hoopes et al., 2018; Li et al., 2017). Recently, scientists investigated the cytotoxicity of apigenin for the first time in the Huh7 cell line (Amiri et al., 2018; Li et al., 2017; Singh et al., 2017b).

Lately, scientists estimated *the* toxicity of apigenin *in vivo* with the help of metabolomics approaches (Lehane and Saliba, 2008; Mohanty et al., 2015; Zhao et al., 2016). Apigenin can suppress parasitemia in a significant dose-dependent manner where dosages are defined as 69.74%, 50.3% and 49.23% with the concentration of 70, 35 and 15 mg/kg/day, respectively (Abiri et al., 2018; Sharma et al., 2018; Toghueo et al., 2018). The reported IC_{50} value for apigenin after 24 hours post-transfection of Huh7 cells is 225 µg/ml (Falade et al., 2018). The toxicity of Apigenin was not noticed on the plasma membrane of red blood cells as well as on *Artemia salina*(Amiri et al., 2018; Berthi et al., 2018; Lehane and Saliba, 2008; Mohanty et al., 2015). When apigenin was administered in a clinical study with mice, scientists showed the changes in glucocorticoids and mineralocorticoids metabolism, metabolism of bile acid, metabolism of sulfur(Attemene et al., 2018; Odoh et al., 2018; Yun et al., 2018). These alterations indicate the potential role of apigenin under *in vivo*antiplasmodial activity against the malaria parasite (Atilaw et al., 2017; Haddad et al., 2017).

5. Effects of Medicinal Drugs Isolated from Plants

According to scientists, natural-products play an essential role in the development of a new drug for the handling of diseases (Asnake et al., 2015; Kiraithe et al., 2016; Lima et al., 2015; Newman et al., 2003). Indeed, a large amount of anti-malarial chemotherapeutic agents are known coming fromthe nature (Table 1 and Figue 1). Mostly these drugs isolated from the tropical plant sources (Baba et al., 2015; Kffuri et al., 2016). Therefore, chemical obtains from biological diversity is to be a vital foundation of key medicines as of anti-malarial drugs (Amoah et al., 2015; Portet et al., 2007) (Table 1).

ISSN: 0971-1260
Vol-22-Issue-16-August-2019

5.1Effect of Irridoids

Irridoidsphenylpropanoid conjugated compounds are obtained from *Morindamorindoides* (Rubiaceae) and inhibit proliferation of parasite (Sumsakul et al., 2015; Tamura et al., 2010). However, irridoidswertiamarin had been obtained from *Enicostemmalittorale* (Gentianaceae) and inhibit schizont maturation (Ma et al., 2015; Muthaura et al., 2015; Soni and Gupta, 2009).

5.2Effect of Flavonoids

Flavonoids are low molecular weight, polyphenolic and found nearly all the plant kingdom as secondary metabolites (Bankole et al., 2016; Irungu et al., 2015). Among flavonoids, flavonol quercetin and flavones luteolin have growth inhibitory properties on the protozoan parasite species likeToxoplasma, Trypanosoma and Leishmania (Chinsembu, 2015; Kirmizibekmez et al., 2004; Oliveira et al., 2015).

5.3Effect of Quercetin

Quercetin is belonging to a group of flavonoids and bioflavonoids; present in fruits and vegetables like onions, tea, apple, and berries. It has several properties like anticarcinogenic, anti-inflammatory, antioxidative, vasodilating and antiaggregatory effect (Chopra et al., 2000; Deschner et al., 1991; Ferry et al., 1996; Hayek et al., 1997; Pereira et al., 1996; Verma et al., 1988)Surprisingly, quercetin is the most abundant polyphenolic compound in diet (Ferry et al., 1996; Verma et al., 1988). Moreover, it will lead to accumulating in plasma upon its intake in dietary (Chopra et al., 2000; Deschner et al., 1991).Choi and Han (2004) reported that quercetin act as bioenhancer for calcium channel blocker agents like verapamil(Choi and Han, 2004).

5.4Effect of Hesperidin

Hesperidin is another flavonoid which is abundantly present in sweet orange and lemon as well as present up to 15% in immature fruits (Abay et al., 2015; Frausin et al., 2015). It has much medicinal importance like chronic venous insufficiency, decreasing in capillary permeability, anti-hypercholesterolemic, anti-inflammatory, analgesic activities, antifertility, antioxidant, antiallergic, anticarcinogenic, and antiulcer activities, etc. (Bisset et al., 1991; Galati et al., 1996; Iyamah and Idu, 2015; Son et al., 1991; Struckmann and Nicolaides, 1994). It causes some allergic but once it phosphorylates but no specific toxic activities are observed in both male and female human being (Bryant et al., 2015; Komlaga et al., 2015).

6. The Discovery of New Green Medicinal Drugs

Although few methodologies for finding of plants containingnovel medicinal agents are profoundly discovered by scientists, four key approaches are vital such as (a) ethnopharmacological (b) taxonomical (c) phytochemical, and (d) random (Katiyar et al., 2012). In the ethnopharmacological approach, primary information is more critical to the collection and evaluation of plants (Girma et al., 2015; Lubbad et al., 2015; Tarkang et al., 2016). In taxonomical, selection and evaluation of plants depend on either genus or family

ISSN: 0971-1260
Vol-22-Issue-16-August-2019

present in different locations. In phytochemical approaches, plants are collected and evaluated by the chemical nature of secondary metabolite present in a plant such as alkaloids (Muthaura et al., 2007; Toma et al., 2015). In the random approach, without any prior information, all the species are collected. Apart from that several new antimalarial drugs can be found in research papers (Happi et al., 2015; Kaushik et al., 2015). However, the discovery of a new compound from these scientific explorations is rarely occurring because of chemical complexity and difficulties in the screenings of compounds for identifying a new drug (Diarra et al., 2015; Haslinda et al., 2015; Houel et al., 2015; Memvanga et al., 2015; Mohanty et al., 2015). Several compounds which are present in the crude extract such as tannins and lipids may cause a problem in the pharmacological assay (Elbadawi et al., 2015; Singh et al., 2015). Therefore, the discovery of these compounds always needs preliminary chemical analysis and separation of mixtures.

7. Cause and Clinical Manifestation

Malaria is a serious, sometimes fatal, spread by an infected Anopheles mosquito (Haidara et al., 2018; Masic et al., 2018). The protozoan parasite, i.e., Plasmodium that causes the disease, requires two hosts for completing its life cycle; one is vertebrate (birds, reptiles, rodents, primates, humans) and another invertebrate (Anopheles mosquito) (Attemene et al., 2018; Gupta et al., 2018). However, sometimes contaminated blood transfusion and contaminated syringes may also transmit human malaria (Mbouna et al., 2018; Sharma et al., 2018).

Generally, four different species of Plasmodium (P) like *P. falciparum, P. vivax, P. malarae, and P. ovalae*spread the disease in the human being. Noticeably, *P. falciparum* is the most dangerous human malaria parasite (Afshar et al., 2018; Khare et al., 2018). They cause a severe problem due to asexual reproduction in the host, and it can sequester in small blood vessels (Falade et al., 2018; Hoopes et al., 2018; Winstanley, 2000). It has 14 chromosomes, encoding about 5,300 protein and almost two-thirds of which appear to be unique to the organism (Gupta et al., 2018; Mukungu et al., 2016; Tariq et al., 2016). Out of the total, 208 genes are involved in the evasion of the host immune system (Abdissa et al., 2017; Nondo et al., 2017). This information is being used in the development of new chemotherapeutic targets and antigens for potential vaccines (Chukwuocha et al., 2016; Kishore et al., 2017; Muganza et al., 2016; Tariq et al., 2016). Some promising targets are listed for the control of malaria parasite. Therefore, phytomedicine research is an emerging area which anticipates in the development of new drugs for combating and solving malaria (Ezike et al., 2016; Saxena et al., 2016; Shanker et al., 2016). Scientists have to give more efforts for newly identifying compounds which could have an off-target role in different biological disease developmental processes and establish the probable mechanistic details of their mode of actions in the human body (Cai et al., 2015; Da et al., 2016; Kiraithe et al., 2016; Koulu et al., 2016; Pala et al., 2016). However, the other three species of Plasmodium do not cause severe disease (Amoah et al., 2015; Asnake et al., 2015; Baba et al., 2015; Kffuri et al., 2016; Lima et al., 2015). Hepatic ‘hypnozoites’ created by *P. vivax* and *P. ovale*can stem relapsed situation up to 40 weeks after infection (Haslinda et al., 2015; Mohanty et al., 2015) .

ISSN: 0971-1260
Vol-22-Issue-16-August-2019

8. Key Targets to Prevent Malaria Parasite (*Plasmodium falciparum*)

Several studies discovered new drugs by targetting a mutational approach for minimising off-targets of the drug and anti-resistance for malaria parasite (Amoah et al., 2015; Ma et al., 2015; Sumsakul et al., 2015). Therefore, binding of newer compounds acting on appropriate target sites for P. falciparum is likely to be effective(Moyo et al., 2016; Saxena et al., 2016). Several biochemical compounds are known to control the invasion of malaria during infection processes (Chander et al., 2016; Haidara et al., 2018; Komlaga et al., 2016). Approximately, the drugs degrade 80% of malaria parasite after release from an infected erythrocyte in the host cell and release heme which is toxic to parasite(Combrinck et al., 2002; Ginsburg et al., 1998). Inactivation of heme depends on the formation of hemozoin formation, and inhibition of hemozoin depends on binding of the drug to the heme or inhibition of GSH dependent heme degradation (Okokon et al., 2017; Schwarzer et al., 1992; Shah and Rahim, 2017; Singh et al., 2017b). Since the action of quinoline as anti-malarial is less responsive on heme, therefore several others green drugs such as vaccines, vasicinone, and embelin are more effective treatment remembering resistance issue (Atilaw et al., 2017; Awodiran et al., 2018; Haddad et al., 2017; Masic et al., 2018).

9. Marketing of Antimalaria Drug

Malaria is a not much severe disorder if promptly diagnosed at the right time. Some medicinal drugs are commercially available today (Ali et al., 2017; Okokon et al., 2017; Shah and Rahim, 2017; Xiao et al., 2017; Zhou et al., 2016). Quinine is an alkaloid which scientists initially obtained from the bark of the Chinchona tree, and people widely use it for the treatment of malaria suffering patients(Nondo et al., 2017; Sangsopha et al., 2018; Singh et al., 2017a). Another antimalarial drug such as Mefloquine, work similar to quinine, is effective against all malarial species (Atilaw et al., 2017; Awodiran et al., 2018; Shi et al., 2018). However, it has some toxic effects like vertigo, nausea, abdominal discomfort, malaise, and insomnia (Odoh et al., 2018). However, Sulfadoxine-pyrimethamine should preferably use for malaria patients as prescribed manner; but avoid in pregnant cases(Bapela et al., 2019; Husin et al., 2018; Salehi et al., 2018). Presently, Malarone, a new anti-malaria drug generated by combinatingatovaquone and proguanil is available in market, which has high and synergistic effects as antimalarial treatment(Looareesuwan et al., 1999; Oliveira et al., 2015). It is found to be approximately 95% effective againsta a resistant malaria strain, P. falciparum; but it cost value is high and could not be readily available to ordinary people (Azebaze et al., 2015; Cai et al., 2015; Da et al., 2016; Saxena et al., 2016).

10. Conclusion

Nowadays, several antimalarial drugs are available for the treatment of malaria in modern therapy. In this review, we discussed specifically the discovery of new green anti-malarial medicines. We here considered the study of medicinal plants used for the isolation of new green drugs. We primarily aim to evaluate the use of medicinal plants; not only by ethnopharmacological investigators but also by local people. Besides, this review provides a landmark for the identification and isolating a new active green medicines through the necessary step and understanding the appropriate toxicological studies and clinical trials. In

ISSN: 0971-1260
Vol-22-Issue-16-August-2019

modern time, some medicinal plants have been identified and tested for their antiplasmodial activity at different doses. Most drugs have to show dual action and have little side effects. We highlight in the review that the ethnopharmacology is a great source of herbal plants for discovering new antimalarial therapeutic agents. This review further provides importance on developing new green drugs for malaria treatment, and there is considerable scope for future research in this field.

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Author contributions

P.K. and T.K. equally contributed to writing the manuscript.

Conflict of interest

We wish to confirm that there are no known conflicts of interest associated with this publication and there has been no significant financial support for this work that could have influenced its outcome.

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ISSN: 0971-1260
Vol-22-Issue-16-August-2019

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ISSN: 0971-1260
Vol-22-Issue-16-August-2019

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Figure 1

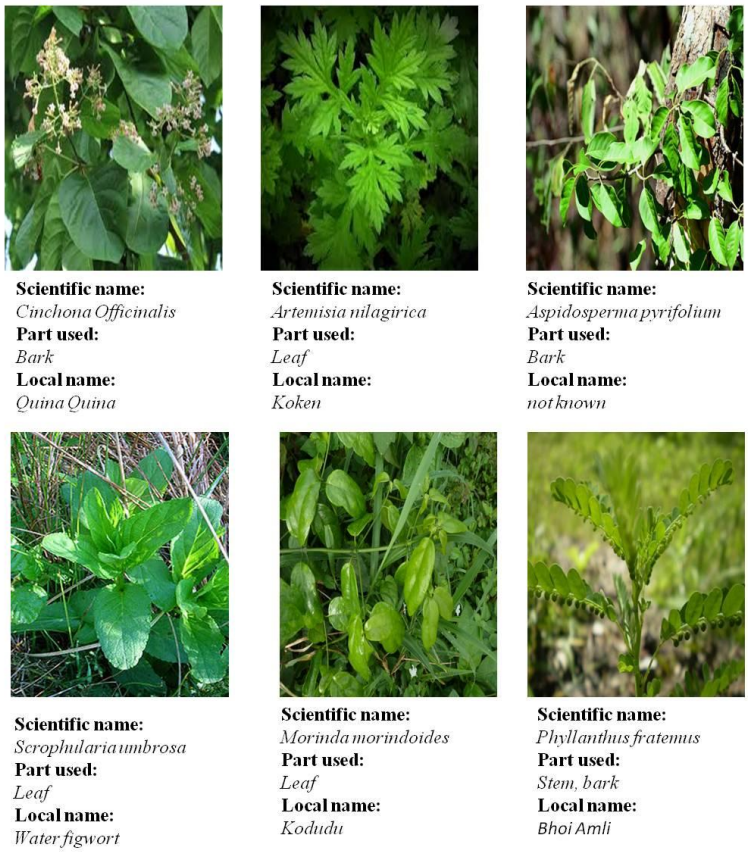

Figure 1: Few representative medicinal plants used in anti-malarial drug discovery purpose are shown here. Representative pictures are taken from google image site.

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Plants species & family	Part used	Useful extracted component	References
Ancistrocladusheyneanus (Ancistrocladaceae)	Roots	Triterpene	Bringmann et al. 1997
Triphyllumpeltatum (Oioncophyllaceae)	Leaves Twigs	Naphtyltetrahyd-roisoquinoline alkaloids	Hallock et al. 1994
Ancistrocladuskorupensis (Ancistrocladaceae)	Leaves	Naphtyltetrahyd-roisoquinoline alkaloids	Hallock et al. 1997
Artemisia indica (Asteraceae)	Roots	Steroid Sapogen in colourless oil	Chanphen et al. 1998
Brunsvigialittoralis (Amaryllidaceae)	Root bark	Alkaloids	Oketch-Rabah et al. 1997
Eurycomalongifolia (Simaroubaceae)	Bark	Acid amide	Campbell et al. 1998
Fagararhetza (Rutaceae)	Seeds & Roots	Quassinoids	Cimanga et al. 1997
Hannoachlorantha (Simaroubaceae)	Roots	Naphthaquino-nes	Kardono et al. 1991
Nepenthes thorelii (Nepenthaceae)	Whole plant	Alkamides	Shibuya et al. 1992
Phyllanthus fratemus (Euphorbiaceae)	Stem bark	Alkaloid	Francois et al. 1998

Table 1: A list of medicinal plants used for the treatment of malaria is shown here.