



## PLANTS AND PHYTOCHEMICALS AS POTENTIAL SOURCE OF ANTIMALARIAL DRUGS

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### ABSTRACT

A large number of bioactive compounds exist in various medicinal plants. Different part of plants and different types of extracts has been screened for their antimalarial activity in in- vitro and in – vivo test models. At present many plant derived antimalarial drugs like quinine from *Cinchona officinalis*, artemisinin, artesunate derived from *Artemisa annua* etc. are in clinical use for treatment of malaria. Resistance to artemisinin based drugs is now being observed. There is an urgent need of effective and safe antimalarial drugs. Novel antimalarial agents are being sought from traditional compounds. This review describes a number of plants and their extracts possessing antimalarial activity.

**KEYWORDS:** Malaria, Medicinal Plants, Extracts, Alkaloids, *Plasmodium falciparum*.

### INTRODUCTION

Malaria is one of the major health problems worldwide. It affects about a quarter of a billion people and leads to almost 900000 death annually (WHO 2009).<sup>[1]</sup> The disease is caused by infection with protozoan parasite of the genus *Plasmodium*. Four *Plasmodium* species are known to infect humans: *P.falciparum*, *P.vivax*, *P.ovale* and *P.malariae*. Out of these *P. falciparum* and *P.vivax* causes most of the malarial infection worldwide. Malaria due to *P.ovale* and *P.malariae* is relatively uncommon. *P.falciparum* is associated with the most severe disease.<sup>[2]</sup>

For the year 2010, the National vector borne disease control programme (NVBDCP) has reported 1.49 million slide proven malaria cases in India, out of which 0.78 million (52%) were falciparum malaria with 767 recorded death.<sup>[3]</sup> The WHO estimates that the actual number of malaria cases in India is much higher, and an expert committee has estimated that about 40,000 malaria deaths occurs annually.<sup>[4]</sup>

There are some problems related to prevention and treatment of malaria First- it is not truly possible to prevent infection because no antimalarial drug kills sporozite. Drugs can only prevent the development of symptomatic malaria caused by asexual erythrocytic

forms. Second – no single antimalarial drug is effective against all liver and intra erythrocytic stages. Pharmacological prevention of malaria poses a difficult challenge because *P.falciparum* which causes nearly all the deaths from malaria has become progressively resistant to available antimalarial drugs. Chloroquine and multidrug resistant *P.falciparum* is especially prevalent and severe in South East Asia and oecania and existing antimalarial drugs are toxic. Therefore, effective and safe antimalarial drugs are urgently required.

Recent studies on antimalarial compounds of plant origin have shown promising results. Novel antimalarial agents are being sought from traditional / herbal medicines. *Artemisa annua* (Qinghaosu) have a long history of use in the traditional Chinese medicine for the treatment of fever. Discovery of artemisinin by Chinese scientists in 1971 provided an exciting new natural product lead compound.<sup>[5]</sup>

Artemisinin analogs such as artesunate are now used for the treatment of malaria in many countries and many other analogs of artemisinin have been prepared to improve its activity and utility.<sup>[6]</sup> Resistance to artemisinin based drugs is now being observed.<sup>[7]</sup> In order to counter resistance , currently combination of artemisinin and other antimalarials are used worldwide

such as dihydro artemisinin + piperazine phosphate, artemether + lumefantrine, artesunate + mefloquine, artesunate, sulphamethoxy pyrazine + pyrimethamine and one fixed dose combination Pyronaridine + artesunate is in Phase III clinical trial.<sup>[8]</sup> Febrifugine and isofebrifugine have been isolated as the active antimalarial compounds from the Chinese herb Chang Shan (*Dichro febrifuga* Lour.). This review describes a number of plants and their extracts possessing antimalarial activity.

## MATERIAL AND METHODS

Data collection-The data for present review was collected from internet, online Journals and from various Ayurvedic texts like Database on Medicinal plants used in Ayurveda Central Council for Research in Ayurveda & Siddha. Dept. of ISM & H, Ministry of Health & Family welfare, Govt, of India, New Delhi Volumes 1-8; Reviews on Indian Medicinal Plants, Volumes 1-9 and The Wealth of India, Council of Scientific and Industrial Research New Delhi Volumes –IA, 2B, iii – XI. Most of the papers reviewed herein pertinent to herbal medicine research were published in internationally recognized peer-reviewed journals. Some of the medicinal plants/extracts and isolated compounds reported to be useful for the treatment of malaria are.

### **Aegle marmelos - correa (Rutacea), English name- Bael Tree, Hindi- Bael**

A moderate sized slender tree, growing wild throughout the deciduous forests of India upto an altitude of 1200m in the western Himalayas and in Andaman islands. Alcoholic extracts of the seeds and leaves were screened in vivo and in vitro for antimalarial activity against the NK65 strain of *Plasmodium berghei*. Seeds were found to possess schizontocidal activity (about 50%) in vivo as well as in vitro, while the leaves showed 46.10 ± 3.72% inhibition in vitro only when tested at a dose of 1g/kg for 4 days (in vivo) and 100µg/ml (in vitro).<sup>[10]</sup>

### **Alstonia scholaris Linn. (Apocynaceae) Eng- Devil's tree, Hindi – Chatium**

A large evergreen tree found almost throughout India upto an altitude of 600m. Echitamine chloride obtained from the bark showed antimalarial activity in a rodent test infected with *plasmodium berghei* at both 320µg and 1.6mg/kg levels.<sup>[11]</sup> A dose dependent improvement of condition and delayed mortality amongst animals receiving methanol extract (40g/kg bark crude extract) of the plant was seen.<sup>[12]</sup>

### **Andrographis paniculata burm F. (Acanthaceae), Eng.- The creat, Hindi- Kalmegh**

An erect annual herb, found in the plains throughout India. Alcoholic extract of the plant was found to possess schizonticidal activity 39.26% in vivo as well as 46.23% in vitro at a dose of 1g/kg for 4 days and 100µg/ml respectively against the NK65 strain of *plasmodium berghei* in *Mastomys natalensis*.<sup>[10]</sup> Studies with the crude alcoholic extract (2g/kg for 4 days) and its

fractions (n-butanol, hexane, aqueous and chloroform) showed reduction in the level of parasitaemia in a dose dependent manner. N- butanol fraction exhibited better activity.

Extract yielded neoandrographolide, deoxyandrographolide, andrographolide and andrographiside which were tested in vivo at 1.25, 2.5, 5 and 10mg/kg for 4 days. Out of all compounds, neoandrographolide and desoxyandrographolide were the most active and produced more than 80% inhibition at 2.5mg/kg. Andrographolide at 5mg/kg also produced significant inhibition (72.7± 6.9%), while andrographiside was least active (57.5 ± 5%) at a dose of 10mg/kg. Chloroquine (positive control) produced 100% inhibition at the dose of 10mg/kg. The 4 diterpenes were also tested in vitro against *plasmodium berghei* (25µg/ml). All the 4 compounds showed 40-54% inhibition whereas chloroquine at this concentration produced 61.3 ± 6.7% inhibition. Chemoprophylactic activity of neoandrographolide was tested using different protocols. 15 days of therapy with neoandrographolide before infection suppressed the parasitaemia.

### **Artemisia absinthium Linn (Asteraceae) Eng- absinthe, Hindi- vilayathi afsanthin.**

An aromatic and bitter shrub found in Kashmir, up to an altitude, 2100m. The aqueous and alcoholic leaf extracts (po,sc,ip) were shown to possess definite schizonticidal activity in a 4 day test against chloroquine sensitive strain of *P. berghei* in mice. The highest suppression of parasitaemia was observed with the alcoholic extracts given orally at 74mg/kg dose. Aqueous extract was less active. Antimalarial activity of various constituents (artemisinin, artemether, arteether etc.) was reviewed by vasanth et al 1990.<sup>[11]</sup>

**A. annua Linn** – A plant native to China and was later introduced in India for cultivation. Plant got prominence worldwide after its constituent artemisinin, exhibited pronounced antimalarial activity. Artemisinin and arteether (α,β,30:70 epimer mixture) were prepared by the Central Institute of medicinal and aromatic plants and CDRI, Lucknow. Antimalarial activity of artemisinin and arteether against blood induced *P. berghei* infection was evaluated in swiss mice. Artemisinin was given as suspension in groundnut oil (100mg/kg for 7 days) was fully curative. Higher doses (316 and 1000mg/kg,im) for 7 days were highly toxic. Arteether, a new potential antimalarial drug for cerebral malaria showed 80% curative action when 2 doses of 5mg/kg were given intramuscularly. Three doses (5mg/kg) were fully curative against sensitive strains of *P. berghei*. Other derivatives of artemisinin were comparable to arteether when tested against *P.berghei* in K-173 infected mice. They were also found to be active against chloroquine resistant NS strain infection in mice.<sup>[14]</sup> Administration of artemisinin (5mg/kg) resulted in complete loss of mosquito infectivity within 24 hrs. Artemisinin had no sporonticidal action, gametocytocidal/sporonticidal

activity of sesquiterpene lactone  $\alpha$   $\beta$  arteether (2.5-5 mg/kg, im) was reported against *P. cynomolgi* B<sup>15</sup>. as shown by complete absence of mosquito infectivity. Blood schizontocidal activity of  $\alpha$  and  $\beta$  arteether (5mg/kg for 3 days against *P. Cynomolgi* B infection) were comparable and curative in rhesus monkey.<sup>[16]</sup> Artemisinin and  $\alpha$   $\beta$  arteether showed no casual prophylaxis or radical cure at 20mg/kg dose. Blood schizonticidal activity of enantiomers of arteether ( $\alpha$  arteether and  $\alpha$   $\beta$  arteether) were evaluated against a multiresistant strain of *p. yoelii nigeriensis* in rats.  $\alpha$   $\beta$  arteether (2.5mg/kg, im x 3 days) showed curative action while  $\alpha$  arteether was curative at doses 5 mg/kg for 3 doses. A multiple drug resistant strain of *P. yoelii nigeriensis* resistant to mefloquine (128mg/Kg for 6 days), quinine (300mg/kg for 7 days) and chloroquine (64mg/kg for 8 days) was found to be completely susceptible to arteether. A dose of 5 mg/kg im for 3 days was curative in swiss mice. Artemisinin 50 mg/kg for 7 days however had only suppressive action against this strain. Current status of artemisinin and its derivatives, in malaria has been reviewed by valecha and Tripathi 1997.<sup>[17]</sup>

**A. capillaris Thunb** -The plant occurs wild in some districts of western Rajasthan and is an aromatic, annual, growing upto 2.5m high. Alcoholic extract of the plant was found to possess schizonticidal activity in vivo ( $70.28 \pm 0.71\%$ ) as well as in vitro ( $62.38 \pm 0.41\%$ ) at a dose of 1g/kg for 4 days and 100 $\mu$ g/ml respectively against the NK 65 strain of *P. Berghei*.<sup>[10]</sup>

**A. japonica Thunb**-The plant occurs at high altitude of western Himalayas in Ladakh and Lahaul. Ethanolic extract from aerial parts against chloroquine sensitive (FAN-5, FMN-13, FMN-17) and resistant (MP-11, S0) strains showed some antimalarial activity. Ethanolic extract also inhibited schizont maturation in concentration dependent manner (2.5 $\mu$ g to 40 $\mu$ g/10ml blood) against chloroquine sensitive FDL- RI strain of *P. falciparum* in vitro.<sup>[18]</sup>

**A. maritima Linn**-The plant is common in several areas of north western India such as Kashmir and Himachal Pradesh. Ethanolic extract prolonged the survival time of mice for a period of 60 days against *P. berghei* (320 and 640 mg/kg, sc). In vitro study of the extract inhibited the schizont maturation against the isolates of *P. falciparum*.<sup>[18]</sup>

**A. nilagirica (Clarke)**-This plant occurs in several parts of India. Ethanolic extract of root (640 & 320 mg/kg, sc) prolonged the survival time of mice for a period of 60 days against *P. berghei* infection. The extract inhibited schizont maturation in in- vitro studies against FDL- RI strain of *P. falciparum*.<sup>[18]</sup>

**Atalantia monophylla Roxb. (Rutaceae), Eng- wild lime, Hindi- Jungli Nimbu**

A large thorny shrub or small tree found in peninsular India, Orissa, Assam, Meghalaya, and Andamans.

Ethanollic extracts of the aerial parts showed antimalarial activity against chloroquine sensitive (FAN-5, FMN-13 and FMN-17) and resistant (MP-11 and 50) culture strains of *P. falciparum* in vitro.<sup>[19]</sup>

**Azadirachta indica A.juss (Meliaceae) Eng- Margosa tree, Hindi- Neem**

A large evergreen tree commonly found throughout India and often cultivated. Ethanolic extracts of leaves and seeds showed in vitro antimalarial activity against chloroquine sensitive and resistant strains of *P. falciparum*. Four limonoids meldenin, isomeldenin, nimocinol and nimbadiol isolated from ethanolic leaf extract showed antimalarial activity against chloroquine resistant *P. falciparum* strain K<sub>1</sub> at IC<sub>50</sub> 5.23, 50, 50 and 50  $\mu$ g/ml, respectively. Out of 4 fractions of the leaves one fraction (C) showed antimalarial activity at IC<sub>50</sub> 200  $\mu$ g/ml, while other 3 fractions (A,B,D) were found to be reactive. Meldenin was most active.<sup>[20]</sup> Neem seed extracts showed in vitro antiplasmodium activity against *P. falciparum*. Extract inhibited growth and development of asexual and sexual stages of drug sensitive and drug resistant strains (chloroquine and pyrimethamine) of malarial parasite. Maturation stages of gametocytes were also killed by various neem fractions. Neem seed fractions were active against parasite stages that cause clinical infection as well as stages responsible for malaria transmission.<sup>[21]</sup>

**Bidens pilosa Linn. (Asteraceae), Eng-Begger lice, Spanish Needle**

An erect much branched annual found throughout India. Study of antimalarial activity of leaf extracts of *B. pilosa* using combination of phytochemistry and bioassay showed that compound showed activity against malarial parasite (*P. Falciparum* NF54 strain) with an Ic 50 value of 6.0 $\mu$ g/ml also inhibited growth of *P. falciparum* FCR-3 strain with an Ic value of 0.35  $\mu$ g/ml.<sup>[22]</sup> In vivo effect in mice infected with *P. Berghei* NK-65 strain showed that there was decrease in parasitemia in RBC by 20.7 from 32.8% of that of control to 12% after an iv injection 0.8mg/kg/day x 4 days.<sup>[23]</sup>

**Bougainvillea spectabilis willd. (Nyctaginaceae), Eng-great Bougainvillea, Hindi - Bouganvel**

A scandent shrub grown throughout India as ornamental. Alcoholic extract of the leaves showed antimalarial activity against erythrocytic stages of *P. berghei* (NK65 strain) in vitro but no activity was observed in vivo studies.<sup>[10]</sup>

**Brucea javanica Linn (Simaroubaceae), Eng-Macassar Kernels**

A somewhat foetid shrub distributed in North Bengal, Assam and southwards to Kerela and in the Andaman islands. Chloroform extract from fruits were shown to possess most potent in vitro antimalarial activity. Three compounds (bruceine A, bruceine B hydrate and brucine C) were isolated from chloroquine extract of fruit. When tested in vitro against multi resistant strain of *P.*

falciparum, bruceine A and B were similar in activity ( $ID_{50}$  of 8.66 and 8.15ng/ml) where as bruceine C had an  $ID_{50}$  of 1.05 ng/ml. These compounds had comparable in vitro activity to the mefloquine.<sup>[23]</sup>

**Caesalpinia bonduc Linn (Caesalpiniaceae), Eng-Bonduc nut, Hindi- Latakaranj**

An armed liana, found throughout plains of India especially western, eastern and southern India.  $\beta$ -caesalpine isolated from the plant was effective at higher (1.6 mg/kg sc) dose against *P.berghei*. Ethanolic extract of the defatted seed kernels also showed antimalarial activity on *P.berghei* mouse model. The bark extract showed antiplasmodial activity in vitro against *P.falciparum*.<sup>[24]</sup> In a clinical trial conducted at Government Ayurveda college Balangir (Orissa), 20 patients with malaria (*P.vivax*) were treated with dry seed powder 3g daily for 10 days. Out of 20, 13 patients were cured, 3 showed partial response and 4 did not show any response.<sup>[25]</sup>

**C. pluriosa-** Ethanol extract from stem bark was effective against 2 main strains of malarial parasite. It was effective in –vitro as well as in-vivo tests. Chemical analysis revealed it to be most active compound against malaria. In vitro tests 2 fractions were significantly effective. Ethanol extract was synergistic with artemisinin based drugs artesunate. The plant extract was around 50%,artesunate around 60% and combination was around 80% effective.<sup>[27]</sup>

**Calotropis procera (Asclepiadaceae) Eng- Madar tree, Hindi- Arka**

A small, erect and compact shrub found wild throughout India. Alcoholic extract of plant (excluding root) exhibited antimalarial activity ( $35.57 \pm 9.49\%$  inhibition) against erythrocytic stages of *P.berghei* in vitro but not in vivo.<sup>[10]</sup> Ethyl acetate, acetone and methanol extracts of flower, bud, root ( $62-125\mu\text{g/ml}$ ) showed inhibition against chloroquine resistant strains of *P.falciparum* (MRC 20 and MRC 76 in vitro). Ethanolic extracts of the leaves, stem buds, root and flowers were effective against chloroquine resistant and sensitive strains of *P. falciparum*. Flower and bud extracts are most active.<sup>[25]</sup> Schizonticidal activity of ethyl alcohol of flower and leaves and chloroform extract of root were reported against *P.falciparum*.<sup>[28]</sup>

**Carica papaya Linn (Caricaceae), Eng – Papaya, Hindi – Papita.**

Papaya was introduced into India in the 16<sup>th</sup> century and was naturalised quickly. Now it is widely cultivated throughout India. The extracts of rind and pulp of raw fruit showed antimalarial activity against *P.falciparum* FCK2 in vitro, with  $IC_{50}$  15.19 and 18.09  $\mu\text{g/ml}$ , respectively.<sup>[29]</sup>

**Casearia tomentosa Roxb. (Flacourtiaceae), Hindi – Chilla**

A tomentoes shrub or tree found throughout India upto an altitude of 900m in hills and Andaman Islands. Leaf

and stem extracts showed antiplasmodial activity against *P.falciparum*.  $IC_{50}$  of 2 extracts were 9 and 33 $\mu\text{g/ml}$ , respectively and percentage inhibition was 99 and 98 at 100 $\mu\text{g/ml}$ , 99 and 85 at 50 $\mu\text{g/ml}$ , 99 and 30 at 25 $\mu\text{g/ml}$ . The leaf extract produced 84% inhibition at 12-15 $\mu\text{g/ml}$ .<sup>[25]</sup>

**Cassia absus Linn (Caesalpiniaceae) Hindi – Banar**

An erect annual herb distributed throughout India ascending upto 1500m in the hills. Alcoholic extract of the seed showed antimalarial activity against NK 65 strain of *P.berghei* in vivo (22% inhibition).<sup>[10]</sup>

**Cassia tora Linn. (Caesalpiniaceae), Eng- Ringworm plant, Hindi – parand**

An annual herb found as a weed throughout India. Ethanolic extract of stem (25, 50 and 100  $\mu\text{g/ml}$ ) showed 18, 23 and 53% in vitro inhibition against chloroquine sensitive strain of *P.falciparum*. The  $IC_{50}$  of the extract was reported as 110 $\mu\text{g/ml}$ .<sup>[25]</sup>

**Chenopodium ambrosiodes Linn (Chenopodiaceae) Eng – Indian worm seed, Hindi – khatua**

A branched shrub or herb, native to the West Indies and Central and South America introduced in to Jammu and Kashmir at 270-900m and Dehradun. Ethanolic extract of plant (50%) showed  $52.70 \pm 2.95$  and  $40.66 \pm 0.51\%$  schizonticidal activity against NK 65 strain of *P. berghei* in vivo and in vitro respectively at a dose of 100mg/kg for 4 days and 100 $\mu\text{g/ml}$  respectively.<sup>[10]</sup>

**Cichorium intybus Linn (Asteraceae) Eng- cichory, Hindi – Hinduba**

An erect perennial herb native to temperate parts of the world and is found in Punjab and Andhra. It is cultivated in Bihar, Himachal, Assam, Maharashtra, Gujarat, Tamil Nadu, Orissa and Kerala. The 50% ethanolic extract of seeds showed  $29.70 \pm 1.02$  and  $60.52 \pm 1.60\%$  in vivo and in vitro antimalarial activities against NK65 strain of *P.berghei*.<sup>[10]</sup>

**Cinchona Linn (Rubiaceae) Eng- yellow bark, cinchona bark, Hindi- Kunain**

A tree with a stout, straight bore trunk grown in plantations in West Bengal and Nilgiris, upto an altitude of 1500m. Quinine has been isolated from cinchona alkaloids and many synthetic derivatives were prepared. Nandi has reviewed use of cinchona and its alkaloids, their production and marketing in India.

**Cinnamomum tamala (Buch.han) (Lauraceae) Hindi – Dalchini**

The 50% ethanolic extract of leaves showed schizonticidal activity against *P.berghei* NK65 strain in vivo and in vitro at a dose of 1g/kg for 4 days and 100 $\mu\text{g/ml}$ , respectively.<sup>[10]</sup>

**Citrus simensis Linn (Rutaceae) Eng – Malta, Hindi- Musambi**

Petroleum, ether and methanol extracts of rind of ripe fruit showed in vitro antimalarial activity against

*P.falciparum* FCK2 strain with  $IC_{50}$  51.06 and 53.61  $\mu\text{g/ml}$ , respectively. The  $IC_{50}$  of aqueous extract was  $> 1000\mu\text{g/ml}$ .<sup>[29]</sup>

**Chlorodendrum pylonidis Linn (Verbenaceae) Hindi-Arni**

A large shrub, occurring in warmer regions in India. The 99% ethanolic extract of the leaves of 2 different specimens of the plant showed antimalarial activity against *P.falciparum*.  $IC_{50}$  values were found to be 48 and 25  $\mu\text{g/ml}$  with 2 specimens tested.<sup>[25]</sup>

**Clerodendrum viscosum vent. (Verbenaceae) Hindi – Titabhamt**

A gregarious shrub, common throughout India. The 95% ethanolic extract of the defatted powder of the leaves showed *in vivo* antimalarial activity in mice at 150 to 1000  $\text{mg/kg}$ .<sup>[30]</sup>

**Cocculus pendulus J.R. & Forst (Menispermaceae)**

A scandent shrub, distributed in waste drier parts of India, upto 700m altitude. Ethanolic extract of leaves at concentrations of 12.5, 25, 50 and 100  $\mu\text{g/ml}$  showed 85, 87, 94 and 98% inhibition respectively against chloroquine sensitive strain of *P.falciparum*.<sup>[25]</sup>

**Commiphora wightii Arn. (Burseraceae) Eng – Gum gulgul, Hindi – Gugul**

A small tree or shrub with spinescent branches, occurring in arid rocky tracts of Rajasthan, Gujarat, Madhya Pradesh and Karnataka. *In vitro* schizonticidal activity of ethanol extract of oleo gum resin and hexane fraction against *P.falciparum* was reported as 0.585 and 0.0068  $\text{mg/ml}$ , respectively.<sup>[28]</sup>

**Coptis teeta wall (Ranunculaceae) Eng – Gold Thread, Hindi – Mamira**

A perennial herb, occurring in Arunachal Pradesh. Crude water extract of rhizome exhibited *in vitro* antimalarial activity against *P.falciparum* at concentrations of 66, 132, 660 and 1320  $\mu\text{g/ml}$  and the percentage of schizonts inhibited was 94.83, 98.28, 100 and 100%, respectively.<sup>[31]</sup>

**Corchorus depressus Linn (Tiliacea) Hindi – Baphuli**

A prostrate deep rooted much branched perennial herb found in the drier parts of north India. Ethanolic extract of pulverized aerial parts showed 12, 34, and 84% inhibition of *P.falciparum* at 25, 50, and 100  $\mu\text{g/ml}$ , respectively.<sup>[25]</sup>

**Couroupita guianensis Aubl. (Lecythidaceae) Eng – Cannol ball tree**

An evergreen shrub found in the Himalayas from Nepal eastwards and in Khasi hills, altitude of 1200-2400m. Petroleum, ether and methanol extracts of flower, leaves, bark and fruits showed antimalarial activity in mice against *P.berghei* at a dose of 40, 80 and 160  $\text{mg/kg}$ , sc.<sup>[32]</sup>

**Derris indica Lank. (Fabaceae), Eng- Pongam oil tree, Hindi – Karanj**

A medium sized glabrous tree found throughout India upto an altitude of 1200m. Alcoholic extract of seeds possess schizonticidal activity *in vivo* and *in vitro* at a dose of 1  $\text{g/kg}$  for 4 days and 100  $\mu\text{g/ml}$ , respectively. Ethanolic extract of bark and leaves showed significant *in vitro* antiplasmodial activity against *P.falciparum* (100  $\mu\text{g/ml}$ ).<sup>[25]</sup>

**Dichria febrifuga Lour (Hydrangeaceae) Hindi-Basak**

An evergreen shrub found in the Himalayas from Nepal eastwards and in Khasi Hills, altitude 1200-2400m. Aqueous extract of the plant (2.5  $\text{mg/kg}$ ) showed antimalarial activity against *P.berghei*. Extract inhibited the infecting rate by the parasite upto 10 days.<sup>[33]</sup>

**Icacina senegalensis-** The plant is used to treat malaria. Crude extract and various fractions proved antiplasmodial with no toxicity<sup>34</sup>. Antiplasmodial activity of *I. senegalensis* leaf extracts in a study *in vitro* assay based on plasma LDH detection has been scientifically demonstrated.<sup>[34]</sup>

**Juniperus communis Linn (Cupressaceae), Eng-Juniper, Hindi- Hapusha.**

An evergreen shrub or a bush 60-150 cm high with upright branches, found in Himalayas & Himachal Pradesh. Distributed in temperate and subarctic Europe, Asia, North Africa, North America. Essential oils from the plant have been shown to possess antimalarial activity.<sup>[35]</sup>

**Leonotis nepetiifolia Linn (Lamiaceae) Eng-Knodgrass, Hindi- Gathivan.**

Erect, woody herb up to 2 m tall, naturalized almost throughout the hotter parts of India. Uma Reddy<sup>36</sup> reported antimalarial activity from the seed oil of this plant.

**Momordica charantia Linn (Cucurbitaceae), Eng-Bitter gourd, Hindi- Karela.**

It is an annual, much branched, stem tendrillar, climber. It is found throughout India, often cultivated. Preliminary pharmacological studies demonstrated antimalarial activity from the plant extracts.<sup>[37]</sup>

**Nyctanthes abortifitidis Linn (Oleaceae) Eng- Night Jasmine, Hindi- Harsingar.**

It is a native of India, occurring wild in Sub Himalayan region, Chota Nagpur, Rajasthan, MP and Southwards to Godavari. Pharmacological studies demonstrated antimalarial activity from the plant.<sup>[38]</sup>

**Remijia ferruginea (Rubiaceae) -** Origin from Brazil. Quinine like alkaloids was detected in the bark of *Remijia* species.

**Strychnos psuedoquina (Rubiaceae)**- Origin from Brazil. Bark of this plant has been shown to possess antimalarial activity in vivo.<sup>[39]</sup>

**Miscellaneous plants – Various other medicinal plants and their products** have been shown to possess antimalarial activity eg. *Allium cepa*, *Allium sativum*, *Inula racemosa*, *Piper nigrum*, *Swertia chirtia*, *Enicostemma axillare* and *Tinospora cordifolia*<sup>[40]</sup> etc

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