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Studies on Bionomics of *Anopheles fluviatilis* and its Sibling Species in Nainital District, U.P.

R.P. SHUKLA, NUTAN NANDA[a], A.C. PANDEY[b], V.K. KOHLI, HEMA JOSHI[a] and S.K. SUBBARAO[a]

A study on the bionomics of *Anopheles fluviatilis sensu lato* was carried out in two physiographic regions, viz. Bhabar and Terai of District Nainital, Uttar Pradesh. In both areas, *An. fluviatilis* was found resting indoors predominantly in cattlesheds. Cytological examination of *An. fluviatilis* revealed that species T and U were sympatric in Bhabar and Terai villages with predominance of species T. These two sibling species appear to be poor vectors of malaria.

Keywords: *An. fluviatilis*, Bionomics, Malaria vector, Sibling species

INTRODUCTION

An. fluviatilis James is widely distributed in India, and variations in the feeding preference and infection rates have been reported i.e. low densities with high anthropophagy and high infection rate in hills and foothills; and high densities, high zoophagy and low infection rates in plains[1]. In Nainital district, which was hyperendemic for malaria[2,3], *An. culicifacies sensu lato* and *An. fluviatilis sensu lato* were the only vectors of malaria[4] and *An. fluviatilis* was repeatedly found as an efficient vector[5,6]. Cytotaxonomic studies have shown that the above mentioned vectors are species complexes. *An. culicifacies* is a complex of four sibling species[7] and *An. fluviatilis* is a complex of three sibling species provisionally designated as species S, T and U[8]. These sibling species vary in their biological characteristics[9-11]. This paper reports the results of the study

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carried out during 1991-94 on the bionomics of *An. fluviatilis s.l.* and its sibling species composition in Bhabar and Terai villages of District Nainital.

MATERIALS AND METHODS

Study area

In District Nainital, there are two long narrow belts of land with markedly different physical features in the foothills of the Himalayas. Immediately skirting the foothills is a waterless belt of porous and sandy soil with a width ranging from 10-15 km, known as the Bhabar area. Adjoining to Bhabar belt towards south is a wet belt of loamy, clay like soil about 13-16 km wide, known as the Terai. In Bhabar, two villages, viz. Pachaunia and Nai Avadi with a human population of 286 and 225 respectively were selected. These villages are located near a forest where the main source of water for irrigation is a perennial stream. In Terai, the selected villages, viz. Matkota and Tilpuri comprising of a population of 314 and 525 respectively, are located near a forest and the Haripura reservoir. The main source of water for irrigation and drinking in these villages are artesian wells and reservoir.

In the selected villages of both regions, larval surveys in peri-domestic and intra-domestic breeding habitats were carried out at fortnightly intervals using standard dipper. Larval samples from various breeding habitats were brought to laboratory and reared up to emergence of adults for species identification. Adult indoor resting densities were monitored by hand catch using suction tube method in the morning between 0600 to 0800 hrs from human dwellings and cattlesheds, and per man hour densities were calculated. All night biting collections were made in study villages of Terai from 1800 to 0600 hrs on man and cattle in human dwellings and cattlesheds respectively.

Head and thorax of *An. fluviatilis s.l.* specimens and of those which were cytologically identified as sibling species (n = 489)[9] were stored dry and processed for the detection of *Plasmodium* infection using two-site immunoradiometric assay (IRMA)[12]. Identification of sibling species was done by using diagnostic paracentric inversions on the ovarian polytene chromosomes[7].

Fortnightly surveys were carried out for fever in the study villages and the blood smears collected were stained with JSB stain and examined for malaria parasite. Radical treatment to the malaria positive cases was given as per National Malaria Eradication Programme (NMEP) drug policy.

RESULTS AND DISCUSSION

An. fluviatilis breeding was mainly observed in artesian (irrigation) drains, and streams in Terai (larval density per dip ranging from 0.11-0.78) and small ponds in Bhabar (up to 0.82/dip); whereas very few larvae were recorded from cemented tanks and shallow wells of Bhabar and Terai areas respectively with larval density per dip ranging 0 to 0.16.

During the study period a total of eight anopheline species, viz. *An. culicifacies, An. fluviatilis, An. annularis, An. subpictus, An. splendidus, An. stephensi, An. vagus* and *An. barbirostris* were recorded from selected villages in Bhabar whereas in Terai villages, in addition to the above mentioned anophelines, *An. nigerrimus, An. varuna* and *An. aconitus* were also found.

Per man hour densities (MHD) of vector anophelines (*An. fluviatilis* and *An. culicifacies*) and total anophelines for two calendar years in Terai and Bhabar villages are shown in Figs. 1 and 2. Adult *An. fluviatilis* densities were low from May to August in Terai (range 0 to 10.5) and Bhabar (range 0.5 to 9.5). The densities started building up after monsoon and high densities of *An. fluviatilis* were observed from September to April, the peak in February (229.0) and October (52.0) in Terai and Bhabar areas respectively. Prevalence ratio of *An. fluviatilis* in cattlesheds and human dwellings was 9:1 in Bhabar and 21:1 in Terai showing high preference for resting in cattlesheds. Indoor collections of *An. fluviatilis* females showed 326 unfed, 1470 full-fed, 1580 semigravid and 747 gravid in Terai villages whereas examination of abdominal conditions in Bhabar collections revealed 78 unfed, 239 full-fed, 258 semigravid and 132 gravid. These data suggest that *An. fluviatilis* is an indoor resting species and spends most of the period of gonotrophic cycle indoors in both Bhabar and Terai regions.

Results of whole night biting of *An. fluviatilis*

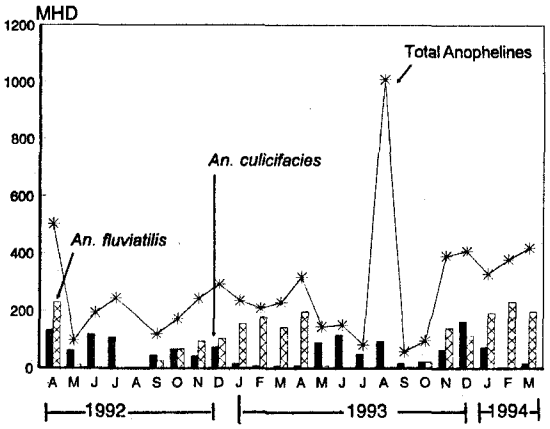

Fig. 1: Man hour densities of vectors and total anopheline in Terai villages

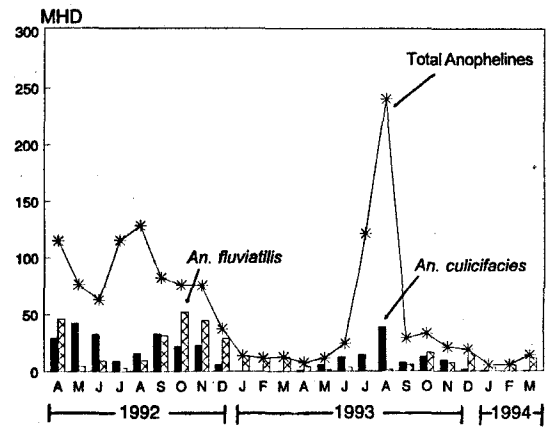

Fig. 2: Man hour densities of vectors and total anophelines in Bhabar villages

on cattle and human baits during summer and post-monsoon months in Terai area are given in Tables 1 and 2. Biting of *An. fluviatilis* on cattle baits was observed throughout the night, the peak biting occurred during second quarter of night in both the seasons. Biting on human baits was very low ranging from 0.08 to 0.33 bites/bait/night, which suggests that *An. fluviatilis* in

Terai area has very little preference for human blood and is almost zoophagic. Our earlier report[9] on feeding preferences of sibling species of *An. fluviatilis* complex revealed that species T and U were found sympatric in Bhabar and Terai areas. Out of 138 specimens cytologically identified from Bhabar area, 132 (95.7%) were species T and only 6 (4.3%) were species U. In Terai out of 599 samples, 435 (72.6%) were species T and 164 (27.4%) were species U. In both the areas species U were exclusively zoophagic and species T were occasionally found feeding on human blood with an HBI of 0.01.

An. fluviatilis specimens collected from study villages in Bhabar and Terai areas during October 1991 and February 1992 when it was a predominant species, were examined for the presence of *P. vivax* and *P. falciparum* sporozoite antigens by two-site immuno-radiometric assay using species specific monoclonal antibodies. None out of 248 *An. fluviatilis s.l.* and 241 cytologically identified specimens (163 species T and 78 spe-

Table 1. Results of all night biting collections of *An. fluviatilis s.l.* on cattle and human baits in Terai during summer

Time (hrs)	Numbers biting on			
	Cattle*		Human**	
	Nos.	Biting nos./bait/night	Nos.	Biting nos./bait/night
1800-1900	0	0	0	0
1900-2000	28	3.50	0	0
2000-2100	117	14.62	0	0
2100-2200	184	23.00	0	0
2200-2300	215	26.87	1	0.16
2300-2400	139	17.37	2	0.33
0000-0100	123	15.37	0	0
0100-0200	116	14.50	0	0
0200-0300	120	15.00	1	0.16
0300-0400	64	8.00	0	0
0400-0500	52	6.50	0	0
0500-0600	65	8.12	0	0
Total	1223	152.87	4	0.66

*Total of eight night collections of April 1993; **Total of six night collections of April 1993.

Table 2. Results of all night biting collections of *An. fluviatilis s.l.* on cattle and human baits in Terai during winter

Time (hrs)	Number biting on			
	Cattle*		Human**	
	Nos.	Biting nos./bait/night	Nos.	Biting nos./bait/night
1800-1900	4	1.00	0	0
1900-2000	7	1.75	1	0.08
2000-2100	6	1.50	0	0
2100-2200	8	2.00	1	0.08
2200-2300	5	1.25	1	0.08
2300-2400	6	1.50	0	0
0000-0100	3	0.75	0	0
0100-0200	4	1.00	0	0
0200-0300	2	0.50	0	0
0300-0400	7	1.75	4	0.33
0400-0500	2	0.50	0	0
0500-0600	0	0.0	1	0.08
Total	54	13.50	8	0.67

*Total of four night collections of November 1993; **Total of twelve night collections between September and October 1993.

cies U) had sporozoite antigens of above mentioned species of human malaria parasites. These observations suggest poor vectorial potential of *An. fluviatilis* sibling species prevalent in the study villages. Results from night biting collections and blood meal analysis data[9] suggest that the preference of species T and U to feed on cattle could be one of the major factors for their poor vectorial potential.

Malaria incidence in Bhabar and Terai villages was also monitored for two calendar years (Table 3). The slide positivity rate (SPR) in 1992 and 1993 was 29.7 and 12.5 per cent in Terai and 5.2 and 1.3 per cent in Bhabar villages respectively. Majority of cases in Terai were recorded from May to September (21 of the total 32 malaria positive cases during 1992-93) when *An. fluviatilis* densities were low (MHD ranging from 0-24.5) and *An. culicifacies* were encountered in high numbers (MHD ranging from 13.5-117.5, Fig. 1). Similar situation existed in Bhabar where *An. culicifacies* adult prevalence was recorded high from May to September and *An. fluviatilis* from October to April (no malaria case was found during

Table 3. Malaria cases in the study villages for two calendar years

Year	Area	No. (+ve)												Total	Total B.S. exam.	*Pv*	*Pf*	SPR
		Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec					
1992	Bhabar	–	–	–	0	0	0	1	0	1	0	0	0	2	38	2	0	5.2
	Terai	–	–	–	2	1	7	2	4	2	4	0	0	22	74	20	2	29.7
1993	Bhabar	0	0	0	0	0	0	0	1	0	0	0	0	1	74	1	0	1.3
	Terai	0	1	0	2	0	2	0	1	2	2	0	0	10	80	6	4	12.5
1994	Bhabar	0	0	0	–	–	–	–	–	–	–	–	–	0	6	0	0	0.0
	Terai	0	0	0	–	–	–	–	–	–	–	–	–	0	10	0	0	0.0

(–) Fever survey not done; Bhabar population (511); Terai population (839).

these months). Since majority of malaria cases found were of *P. vivax* which caused relapses, therefore, it needs to be ascertained whether these cases were due to active transmission by *An. culicifacies*. Studies are indicated on the bionomics of *An. culicifacies* sibling species in these areas in order to establish their role in malaria transmission.

Earlier workers have reported preference of *An. fluviatilis* to rest predominantly in human dwellings[1,6] with high human blood index[1,13]. In Terai this species was reported to have high anthropophilic index (47%) and sporozoite rate (11.1%)[6,14] but subsequently due to its low preference for human blood and resting behaviour, *An. fluviatilis* was reported as a secondary vector[9]. Results of the present investigation also revealed that *An. fluviatilis* sibling species T and U prevalent in the study villages prefer to rest in cattlesheds and are almost zoophagic thereby playing a minor role in malaria transmission. These results are further supported by the similar observations recorded in Districts Dehradun and Hardwar (Uttar Pradesh) where species T and U are prevalent[15].

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A Longitudinal Study of Sero-reactivity to *Plasmodium falciparum* Antigen in Children and Adult Living in an Endemic Area of U.P.

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Antibody levels to *Pf* RESA derived peptide R1 (EENVEHDA-C) from individuals living in malaria endemic areas correlated well with levels of endemicity. Serological and parasitological investigations were done in 32 adults (>20 yrs) and 35 children (2-5 yrs) for three years; i.e. from 1992-95 periodically in village Piyawoli, U.P. Antibody levels against R1 peptide was estimated by ELISA, and blood smear for *P. falciparum* and *P. vivax* were screened using Jaswant Singh-Bhattacharya (JSB) staining. It appeared from our investigations that anti-R1 antibodies had a short span of life, i.e. 6-9 months. The longevity of these antibodies do not differ much in adults and children. The studies do not indicate any protective role for these antibodies. However, the levels of anti-R1 antibodies in a population living under malariogenic condition are related to *Pf* malaria endemicity.

Keywords: Longitudinal study, Malaria endemic area, Octapeptide of *Pf*155/RESA, Peptide ELISA, Serology, Slide positivity rate

INTRODUCTION

Due to poor malaria surveillance[1] resurgence of malaria took place in late 1960's. Tedious and inadequate analysis of blood slide examination needed an efficient surveillance system. As peptide ELISA gives period prevalence it has been considered as a method for malaria epidemiology.

The *Pf* antigen (*Pf*155/RESA)[2] has been considered as one of the malaria vaccine candi-

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date antigens[3,4]. The C-terminal repeat region of *Pf*155/RESA which is conserved in different *Pf* strains[4] consists of repeats of 4-amino acids (EENV) and 8-amino acids (EENVEHDA). Humoral immune responses against these peptides related only anti-EENV antibodies in protection against *Pf*malaria[5]. However, studies on antibody responses to EENVEHDA-Cys[6-8] in population residing under malariogenic conditions suggested an association between the levels of anti-R1 antibodies and degrees of malaria priming. Lack of information on the longevity of anti-R1 antibody limits the possibilities of determining *Pf*malaria endemicity by estimating anti-R1 antibodies.

Therefore, we have made an attempt to investigate the life span and protective role of anti-R1 antibody in a longitudinal study in a *Pf* malaria endemic village, in U.P. Both serological (estimation of anti-R1-antibodies) and parasitological examinations were carried out periodically in subjects (adults and children) for three consecutive years.

MATERIALS AND METHODS

Antigen: A synthetic nonapeptide, EENVEHDA-C was purchased from Cambridge Research Biochemicals, U.K.

Negative control: Nonendemic Srinagar population were taken as negative control, Mean+2SD (0.35 O.D.) was taken as cut off value for determining seropositivity in healthy control of Piyawoli village.

Study area: The study area covered Piyawoli village of Dadri PHC, District Ghaziabad (U.P.). The village is surrounded by ponds, *kuccha* drain and many water bodies. Malaria is high and seasonal. Main vector is *An. culicifacies*, anthropophilic index (A.I.) was found to be 10.4 and a human cattle ratio was 5:2 in 1989 indicating a high malariogenic area[9]. The malaria transmission in this area occurs in July to November. During the rainy season, first *Pv*-cycle appears which followed by *Pf*-cycle. From our own study in 1988, 18 deaths were reported due to malaria (Table 1).

Study population: The entire populaton of the study village was 3000; most of the inhabitants were farmers but a sizable segment of the population consisted of migrant labourers. Survey was started in the month of September 1992, when malaria positive fever cases (32 adults and 35 children) were enrolled in the study population as active groups. A parallel group residing in the same area but with no symptom of fever and no history of malaria in recent past was taken as positive control.

Parasitological examination: Finger prick blood from malaria patients and healthy individuals were collected monthly from September 1992 and then from 1993 onwards periodically. Blood samples were collected in the months as shown in Figs. 1 and 2.

Each and every sample of finger prick blood cllected during the longitudinal study period

Table 1. Epidemiological data of malaria in Piyawoli village during the year 1988

Time of sample collection	Mode of operation	Total slide exam.	Total (+ve)	*Pv*	*Pf*	Mix	SPR	SfR
28 Jul to 24 Nov	Reported death (18)	71	27	3	24	–	42.2	38
Dec	Mass survey	500	112	12	100	–	22.4	20
Jan to Oct	Slide examination	1761	904	211	691	2	51.3	39.2
2 Dec	Only NTPC employee residing in Piyawoli	35	8	0	8	–	22.8	22.8
Dec	Slide examination	196	55	6	48	1	28	25
Dec	Spleen examination 196		Spleen rate 33.6		Av. spleen enlargement 1.57		Av. spleen 0.52	

Pv—Plasmodium vivax; Pf—Plasmodium falciparum; SPR—Slide positivity rate; SfR—Slide falciparum rate.

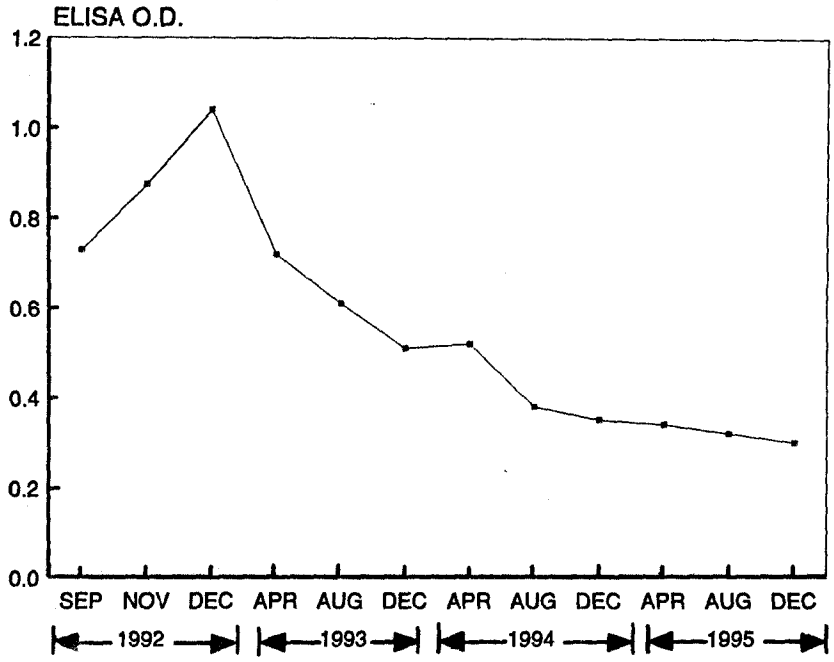


Fig.1: R1 ELISA OD with standard deviation in 35 malaria positive children during the years 1992-1995. Longitudinal study, vertical lines represent standard deviation

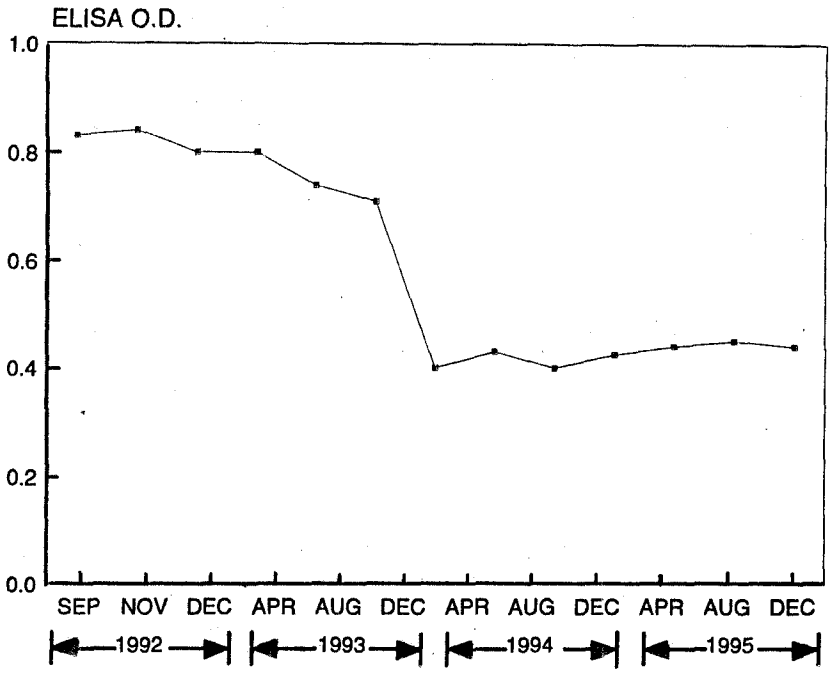


Fig.2: R1 ELISA OD of 32 malaria positive adults from 1992-1995. Vertical lines represent standard deviation

was examined for malaria parasite identification. All blood films thick and thin smears were stained with JSB and examined microscopically.

Serological examination: 50 µl finger prick blood samples were collected in 3 mm Whatman paper and kept at –20°C until used. Filter paper elution of blood sample was done at 1:100 dilution and was used for ELISA.

ELISA: Synthetic peptide at a conc. of 1 µg/ml was used for coating of ELISA plate. The procedure has been described in detail elsewhere[7]. Briefly, 96 well costar (USA) ELISA plates were coated with the peptide and kept at 4°C overnight and then at 37°C for 1 h. Bovine serum albumin blocking and antibody incubation were done as described earlier. Bound antibodies were detected by rabbit antihuman horse radish peroxidase conjugated polyvalent Ig with orthophenylenediamine (OPD) as substrate. OD was taken at 490 nm in Sanofi, Pasteur (France) ELISA reader.

Statistical analysis: Statistical evaluation was done by student's *t*-test.

RESULTS

Table 1 describes malaria status of Piyawoli

village in 1988, four years before the present longitudinal study was undertaken. The village was highly endemic in malaria and 18 deaths were reported during August and November 1988 from our previous study. Slide positivity rate (SPR) was high (30.1) throughout the year. High endemicity was probably due to presence of numerous water bodies and migrant labourers as reservoir of malaria infection. Both *Pv* and *Pf* infections occurred in this area.

A total of 1843 blood samples from 1992 to 1995 were collected from all fever cases during the longitudinal study to assess the malaria situation. In the beginning all malaria smear positive cases were followed up. Subsequently there were a number of drop outs. At the end of the study, only 35 children and 32 adults remained in the completion list. We could complete serological investigations for the desired period only in these two groups.

There was a high incidence of malaria in 1992 (Table 2). Slide positivity for malaria parasite (MP) was higher in children than in the adults. However, this data may not reflect the true malaria situation since the slides were collected from those individuals who had fever. The sample size was not large enough to look for significant differences between these groups. However, it appears that the malaria infectivity is more in children which is due to less protective immune responses against malaria in children.

Antibody to R1 peptide from the two groups were compared (Figs. 1 and 2). In the year 1992 following the transmission season the R1 antibody level remained high (ELISA OD values; Figs.1 and 2) in both the groups showed a falling tendency in the later years. Parasitological examination (Table 3) showed that there was transmission of malaria in the village in the subsequent years. Though the longevity of the R1 antibody does not vary remarkably in both the groups there was more inconsistency in antibody levels in children groups. At the beginning of malaria infection in September and October 1992, the ELISA OD observed with R1 antigen was higher in children than in adult population compared to those in the latter part of the

Table 2. Study of malaria positive follow-up cases (Sep-Oct 1992)

Age group (yrs)	Mean age (yrs)	Total slides exam.	No. of active female patient		No. of active male patient		No. (+)'ve	SPR
			Pv	*Pf*	*Pv*	*Pf*		
2-5	3.1±1.4	104	8	7	10	11	30	34.6
>20	34.8±16.4	178	1	12	6	13	32	20.2

Pv—Plasmodium vivax; Pf—Plasmodium falciparum; SPR—Slide positivity rate.

Table 3. Parasitological information during study period

Year	Blood slide exam.	*Pv*	*Pf*	SPR	SfR	PI/1000 cases
1992	604	19	83	16.88	13.74	34
1993	383	22	8	7.8	2.0	10
1994	479	111	10	25.26	2.0	40
1995	377	19	3	5.3	0.7	7

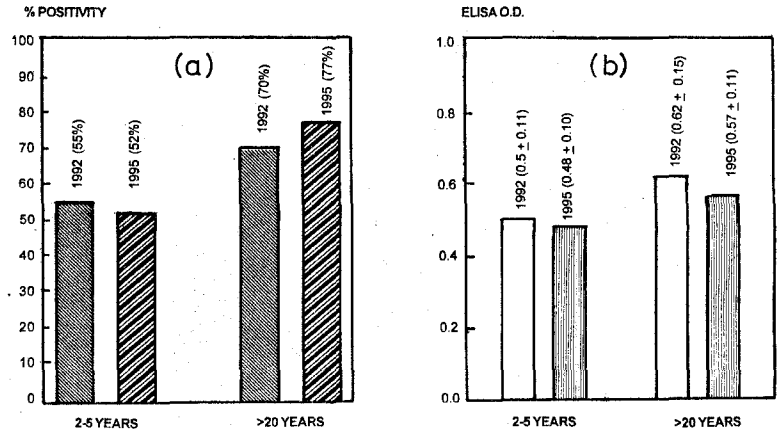
SPR—Slide positivity rate; SfR— Slide falciparum rate; PI/1000—Parasite incidence per thousand cases.

longitudinal study (*t*-test, children $p<0.001$, the difference is highly significant, for adult $p < 0.05$ difference is significant).

The results with a control group of normal children (0-5 yrs) and normal adults is given in Figs. 3a and b. In 1992, 150 children showed moderate ELISA OD and moderate per cent positivity where as in 81 adults, the ELISA OD and per cent positivity was higher. In December1995 a different group of 42 normal children showed similar results as in 1992 where a control group of 41 adults showed little elevated values as seen in 1992. In a high endemic area like Piyawoli, control population also had high antibody titre whereas our previous study with nonendemic Srinagar population had low (Mean+2S.D.) 0.35 ELISA OD as cut off value.

DISCUSSION

Variation in the levels of anti-R1 antibody at different periods may reflect the intensity of



Figs. 3a and *b*: ELISA OD and percentage positivity of children and adult from control group in the years 1992 and 1995

transmission. The decline of R1 antibody levels in both the age groups in later part of the study period suggest that the intensity of malaria transmission is declining. It is shown that immune response gets boosted by repeated natural infection[10].

It has also been shown in our previous studies that anti-R1 antibody levels are correlated well with levels of endemicity[11,12]. However, the longevity of anti-R1 antibody has to be taken into consideration in such studies.

It appeared from our longitudinal study that anti-R1 antibody had a short life span (6-9 months). Antibodies to other *Pf* antigens like CSP and MSA-1 were also reported to be short-lived[13,14]. There were no remarkable differences between the adults and children in the life span of anti-R1 antibody. Variability in antibody level indicated that children did not face many repeated exposure compared to the adults, since antibody increased with number of exposures and high level of antibodies were the cumulative effect of repeated infections.

At the beginning of the survey (1992) there was positive correlation between antibody and parasitological status in both the groups. Whereas, in 1994 such association was seen between these two parameters in both the groups which may probably reflect the immune status of individuals. However, an association was seen between anti-R1 antibody level and parasite positivity rate (SPR) in 1995 in individual analysis, raising a question whether anti-R1 antibody contribute to protection against *Pf* malaria.

The protective value of anti-RESA antibodies have been described in detail[15-19]. It appears from our studies that anti-R1 antibodies do not confer protection against *Pf* malaria. Similar observations were found from earlier studies[19]. It has been established that parasites evade host-immune defense by immunomodulation, antigenic variation and parasite immuno suppressive factors[20,21]. It is evident from the previous and the present study, that anti-R1 antibodies are produced in individuals living in malaria endemic areas and the protective capacity of these antibodies is marginal. The antibodies have a short life span (6-9 months) and relate to the degree of exposure. Thus, measuring anti-R1 antibody levels may function as one of the parameters in estimating the levels of malaria endemicity.

Longitudinal analysis of seroreactivity to *Pf* antigen in small children living in a holoendemic area of Liberia was studied and found to be not a reliable parameter for protective immunity[22,23]. Our results with R1 confirms this observation.

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Plants Showing Antiplasmodial Activity — From Crude Extracts to Isolated Compounds

POONAM SHARMA and JAYASHRI DEVI SHARMA

The derivation of important antimalarial compounds started with the discovery of *Cinchona* bark powder with wine. Subsequently, post World War-I was a period of intensive work in maintaining such ethnobotanical records, in which the use of quinine has remained the drug of choice in malaria. After World War-II new chemical techniques were used to fractionate and isolate, and also for structure determinations, which led to an ever increasing number of potential antiplasmodial compounds. Recently experimental studies in animals and in clinical trials, showed the emergence of CQ-sensitive and CQ-resistant strains of *Plasmodium*. This paper is an attempt to update a historical list of antimalarial plants and their natural products as studied by pharmacognostic extraction methods of crude drug research of those times. Further an attempt has been undertaken to list the compounds as classified into three major groups, namely alkaloids, terpenes and quassinoids and aromatic and miscellaneous compounds. The most promising is a quassinoid, artemisinin derived from *Artemisia annua* which has caused a resurgence for the quest of newer antimalarial compounds.

Keywords: Alkaloids, Antimalarial, Chloroquine resistance, Crude extracts, Ethnobotany, Natural products, *Plasmodium*, Quassinoids and aromatic compounds

INTRODUCTION

Natural products are important source of biologically active compounds and have potential for the development of novel antimalarial drugs[1]. First time a natural product gained wide acceptance as a treatment for malaria was in the 16th century when the therapeutic action of the bark of *Cinchona* tree was disclosed by the natives of Peru to Jesuit missionaries[2], who, in turn brought its utility to Europe in the 17th century[3]. Prior to 1820,

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ague was treated with suspension of finely powdered *Cinchona* bark in wine[4]. In the beginning of the nineteenth century, new chemical techniques were developed that made possible the isolation of vegetable alkaloids. Among the first to be studied were Opium and *Cinchona* because of their medicinal value[5]. Isolation of the major alkaloids of *Cinchona* bark, including quinine itself, was achieved by Pelletier and Caventou in Paris in 1820[6]. The second most important plant from ethnobotanical origin, emerged 150 years later, when the plant *Artemisia annua* was recovered as a Chinese traditional remedy, along with its chemical characterizations, studied to isolate Quinghaosu[7]. Ethnobotanical records afforded the discovery of a succession of synthetic drugs that exhibited potent antimalarial activity in a 30-year period between 1925 and 1955[8].

The prevalence of multidrug-resistant strains and the cases of adverse reactions of available antimalarial drug have necessitated a search for newer and more efficient antimalarial drugs[9,10]. The first recorded instance of drug-resistant malaria occurred in Brazil early in this century with the discovery of quinine-resistant *Plasmodium falciparum*[11]. While *Plasmodium falciparum* resistant to chloroquine was first reported in the late 1950's in South America and Thailand[12]. Quinghaosu (Artemisinin, QHS) is a novel antimalarial drug developed from the traditional Chinese remedy whose plasmodicidal effects have been confirmed in experimental studies in animals and in clinical trials against both CQ-sensitive and CQ-resistant strains of *P. falciparum*[13,14].

Malaria still remains one of the greatest causes of illness and death in the world[15]. Each year this disease infects up to half a billion people and exacts a toll of roughly two million deaths[16]. The eradication of the disease has been hampered by the emergence and spread of multidrug resistant malarial parasites, especially *P. falciparum* strains resistant to many antimalarial drugs[17]. WHO experts say that the numebr of people worldwide infected with malaria is still increasing at the rate of about five per cent annually[18] despite the extensive programme by the drug control and eradication by the WHO. The prevalence of multidrug-resistant strains and the cases of adverse reactions of available antimalarial drugs have necessitated a search for newer and more efficient antimalarials from plants.

This paper is an attempt, both to update a list of plants found to combat malaria and to summarize published data regarding the active fractions/extracts by bringing together the scattered information of innumerable studies (Table 1). Further the isolated compouds have been classified into three major groups — alkaloids (Table 2); terpenes and quassinoids (Table 3); and aromatic and micellaneous compounds (Table 4).

DISCUSSION

The results of above studies indicate that these taxonomically different plants possess

Table 1. A composite table of different crude extracts derived from various parts of plants showing their *in vitro* and *in vivo* antiplasmodial activities against different species and strains of *Plasmodia*

Plant species	Family	Part used	Extract/ Fraction	Toxicity	Dose efficiency	*Plasmodium* sp and strain
Abutilon grandiflorum	Malvaceae	Roots[19]	Ethylacetate	IC_{50} (µg/ml)	10.0	*P. berghei* Anka
Abutilon grandiflorum	Malvaceae	Leaves[20]	Ethanol Petroleum ether Ethylacetate Water	IC_{50} (µg/ml)	180 105 230 27	*P. falciparum* KI
		Roots	Ethanol Petroleum ether Ethylacetate Water		27 10 >500 >500	
Acacia clavigera	Leguminosae	Stem bark[21]	Petroleum ether Dichloromethane Methanol	IC_{50} (µg/ml)	100-499 100-499 >499	*P. falciparum* KI
Acacia polyacantha	Mimosaceae	Root bark[20]	Ethanol Petroleum ether Ethylacetate Water	IC_{50} (µg/ml)	93 27 13 >500	*P. falciparum* KI
Acampe pachyglossa	Orchidaceae	Leaves[20]	Ethanol Petroleum ether Ethylacetate Water	IC_{50} (µg/ml)	68 160 11 50	*P. falciparum* KI
Achyranthesa spera	Amaranthaceae	Root bark[19]	Ethylacetate	IC_{50} (µg/ml)	3.0	*P. berghei* Anka
Achyranthesa spera	Amaranthaceae	Root bark[20]	Ethanol Petroleum ether Ethylacetate Water	IC_{50} (µg/ml)	78 72 3.0 >500	*P. falciparum* KI
Adansonia digitata	Bombacaceae	Stem bark[20]	Ethanol Petroleum ether Ethylacetate Water	IC_{50} (µg/ml)	42 38 8.2 280	*P. falciparum* KI
*Aegle marmelos**	Rutaceae	Seed[22]	Ethanol	% inhibition	60.45 & 54.06	*P. berghei* NK65 *in vivo* and *in vitro*
Aerva lannata	Amaranthaceae	Whole plant[20]	Ethanol Petroleum ether Ethylacetate Water	IC_{50} (µg/ml)	48 86 8.6 >500	*P. falciparum* KI

contd...

Table 1. (*contd.*)

Plant species	Family	Part used	Extract/ Fraction	Toxicity	Dose efficiency	*Plasmodium* sp and strain
Alacia madagascari-ensis	Celastraceae	Roots[20]	Ethanol Petroleum ether Ethylacetate Water	IC_{50} (µg/ml)	1.9 0.8 1.6 36	*P. falciparum* K1
Albizia anthelmintica	Leguminosae	Stem bark[21]	Petroleum ether Dichloromethane Methanol	IC_{50} (µg/ml)	>499 >499 >499	*P. falciparum* K1
Albizia chinensis	Fabaceae	Bark[23]	Aqueous ethanol	IC_{50} (µg/ml)	>20000 & 9600	*P. falciparum* D6 and W2
Albizia gummifera	Mimosaceae	Stem bark[20]	Ethanol Petroleum ether Ethylacetate Water	IC_{50} (ng/ml)	90 24 15 150	*P. falciparum* K1
Alnus incana	Betulaceae	Stipes[24]	Ethylacetate	ED_{50} (µg/ml)	8.7&7.3	*P. falciparum* D6 and W2
Ampelocissus africana	Ampelideaceae	Leaves[20]	Ethanol Petroleum ether Ethylacetate Water	IC_{50} (µg/ml)	32 80 9.0 42	*P. falciparum* K1
Ancistrocladus barteri	Ancistrocladaceae	Root[25]	Ethanol	IC_{50} (µg/ml)	4.933 & N.T.	*P. falciparum* NF 54 and *P. berghei* Anka
		Leaf	Petroleum ether Dichloroethane Ethanol		>50 N.T. 12.293 & N.T. 0.658 & 7.344	
Ancistrocladus heyneamus	Ancistrocladaceae	Root[25]	Dichloro-methane/M Ethanol (1:1) Aqueous Petroleum ether	IC_{50} (µg/ml)	3.11 & N.T. 41.92 & N.T. >50 & N.T. 12.36 & N.T.	*P. falciparum* NF 54 and *P. berghei* Anka
Ancistrocladus robertroniorumi	Ancistrocladaceae	Leaf	Ethylalcohol	IC_{50} (µg/ml)	>50 & N.T.	*P. falciparum* NF 54 and *P. berghei* Anka
		Bark	Ethylalcohol		>50 & N.T.	
		Branch	Dichloromethane/ ammonia		>50 & N.T.	

contd...

Table 1. (*contd.*)

Plant species	Family	Part used	Extract/ Fraction	Toxicity	Dose efficiency	*Plasmodium* sp and strain
Ancistrocladus tectorius	Ancistrocladaceae	Leaf[25]	Dichloromethane	IC_{50} (µg/ml)	0.709 & 9.616	*P. falciparum* NF 54 *P. berghei* Anka
		Bark	Dichloromethane/ ammonia		0.798 & 0.648	
*Andrographis paniculata**	Acanthaceae	Whole plant[22]	Ethanol	% inhibition	39.26 & 46.23	*P. berghei* NK 65 *in vivo* and *in vitro*
Annona muricata	Annonaceae	Leaves[26]	Ethanol	IC_{50} (ng/ml)	39.9	*P. falciparum*
Ansellia africana	Orchidaceae	Leaves[20]	Ethanol Petroleum ether Ethylacetate Water	IC_{50} (µg/ml)	55 80 10 380	*P. falciparum* K1
*Artemisia absinthium**	Asteraceae	Leaves[27]	Ethanol Water	Parasitaemia suppression	96% at 74 mg/kg 66% at 25 mg/kg	*P. berghei*
Artemisia afra	Asteraceae	Root bark[21]	Petroleum ether Dichloromethane Methanol	IC_{50} (µg/ml)	50-99 10-49 10-49	*P. falciparum* K1
		Aerial	Petroleum ether Dichloromethane Methanol		10-49 100-499 100-499	
*Artemisia japonica**	Asteraceae	Aerial parts of roots[28]	Petroleum ether, ethanol	Complete cure	Petroleum ether produced at 320 mg/kg	*P. falciparum* FDL-R1
*Artemisia maritima**	Asteraceae	Aerial parts of roots[28]	Ethanol	% schizont maturation inhibition	100% at 40 (µg/ml)	*P. falciparum* FDL-R1
*Artemisia nilegarica**	Asteraceae	Roots[28]	Ethanol	% schizont maturation inhibition	100% at 40 (µg/ml)	*P. falciparum* FDL-R1
*Artemisia parviflora**	Asteraceae	Aerial parts[29]	Ethanol	MED_{50} (µg/ml)	250, 100, 200, 150 & 200	*P. falciparum* FAN-5, FMN-13, FMN-17, MP-11 and S0
*Artemisia scoporia**	Asteraceae	Whole plant excluding root[22]	Ethanol	% inhibition	70.28 & 62.38	*P. berghei* NK 65 *in vivo* and *in vitro*
Aspidosperma oblongum	N.a.	N.a.[30]	Ethanol	IC_{50} (ng/ml)	4742.5 & 847.4	*P. falciparum* W2 and D6

contd...

Table 1. (*contd.*)

Plant species	Family	Part used	Extract/ Fraction	Toxicity	Dose efficiency	*Plasmodium* sp and strain
Aspilia mossambicensis	Asteraceae	Leaves[31]	Aqueous	IC_{50} (µg/ml)	406, 730 & 720	*P. falciparum* M24, K67 and ENT-7
*Atlantia monophyla**	Rutaceae	Aerial parts[29]	Ethanol	MED_{50} (µg/ml)	50, 50 50, 50 & 50	*P. falciparum* FAN-5 FMN-13, FMN-17, MP-11 and SO
*Azadirachta indica**	Meliaceae	Leaves[32]	Ethanol Ether acetone	MED_{50} (µg/ml)	25-75 750-1000	*P. falciparum* FAN-5, FCK-2 FCK-3,
		Seeds	Ethanol Water		200 700	FMN-33 and MP-11
*Azadirachta indica**	Meliaceae	Leaves[33]	Water	Significant activity	at 125-500 mg/kg	*P. berghei*
*Azadirachta indica**	Meliaceae	Leaves[34]	Water	% parasitaemia suppression	41.2%	*P. berghei*
*Azadirachta indica**	Meliaceae	Stem bark[21]	Petroleum ether Dichloromethane Methanol	IC_{50} (µg/ml)	N.T. 100-499 N.T.	*P. falciparum* K1
		Leaves	Petroleum ether Dichloromethane Methanol		50-99 >499 >499	
Balanites aegyptica	Zygophylaceae	Stem bark[21]	Petroleum ether Dichloromethane Methanol	IC_{50} (µg/ml)	>499 10-49 50-99	*P. facliparum* K1
Bidens pilosa	Asteraceae	Whole plant[35]	Ethanol Butanol	% inhibition	90 N.T.	*P. falciparum* BH26/86
		Stem	Chloroform Butanol Ethanol		47 N.T. 90	
		Leaves	Chloroform Butanol Ethanol		94 79 90	
		Roots	Chloroform Butanol		86 68	
Bombax rhodognapho-lon	Bombaceae	Root bark[20]	Ethanol Petroleum ether Ethylacetate Water	IC_{50} (µg/ml)	80 26 34 230	*P. falciparum* K1

contd...

Table 1. (*contd.*)

Plant species	Family	Part used	Extract/ Fraction	Toxicity	Dose efficiency	*Plasmodium* sp and strain
Bougainvillea spectabilis[*]	Nyctaginaceae	Leaf[22]	Ethanol	% inhibition	Nil & 59.17	*P. berghei* NK 65 *in vivo* and *in vitro*
Bridelia cathartica	**Euphorbiaceae**	**Root[36]**	**Ethanol** **Water**	**ID_{50} (µg/ml)**	**0.05** **0.05**	***P. falciparum* FCK-3**
		Stem	**Ethanol**		**0.05**	
Bridelia cathartica	Euphorbiaceae	Root bark[21]	Petroleum ether Dichloromethane Methanol	IC_{50} (µg/ml)	100-499 50-99 >499	*P. falciparum* K1
Brucea javanica	**Simaroubaceae**	**Fruits[37]**	Aqueous infusion **Chloroform**	IC_{50} (µg/ml)	0.43 & **0.006**	***P. falciparum***
			Aqueous influsion Chloroform	ED_{50} (mg/kg/day)	5000 & 7.4	*P. berghei*
Caesalpinea bonducella	Caesalpineaceae	Whole plant[21]	Petroleum ether Dichloromethane Metanol	IC_{50} (µg/ml)	N.T. N.T. >499	*P. falciparum* K1
Calotropis procera[*]	Asclepiadaceae	Whole plant excluding root[22]	Ethanol	% inhibition	Nil & 35.57	*P. berghei* NK 65 *in vivo* and *in vitro*
Canthium phyllanthoideum	Rubiaceae	Stem bark[31]	Aqueous	IC_{50} (µg/ml)	208, 360 & 540	*P. falciparum* M24, K67 and ENT-7
Carapa guianensis	N.a.	N.a.[30]	Ethanol	IC_{50} (µg/ml)	32037.0 & 11640.0	*P. falciparum* W2 and D6
Cassia abbreviata	Caesalpineaceae	Roots[38]	Methanol	IC_{50} (µg/ml)	7.07	*P. falciparum*
Cassia abbreviata	Caesalpineaceae	Root bark[21]	Petroleum ether Dichloromethane Methanol	IC_{50} (µg/ml)	50-99 100-499 100-499	*P. falciparum* K1
Cassia abuscus[*]	Leguminosae	Seed[22]	Ethanol	% inhibition	22.03 & Nil	*P. berghei* NK 65 *in vivo* and *in vitro*
Cassia aff. abbreviata	Caesalpineaceae	Roots[20]	Ethanol Petroleum ether Ethylacetate Water	IC_{50} (µg/ml)	85 160 39 400	*P. falciparum* K1
Cassia occidentalis	Caesalpineaceae	Leaves[39]	Water	IC_{50} (µg/ml)	0.66 & 0.5	*P. falciparum* FCC-2 and FZR

contd..

Table 1. (*contd.*)

Plant species	Family	Part used	Extract/ Fraction	Toxicity	Dose efficiency	*Plasmodium* sp and strain
Cassia occidentalis	Caesalpineaceae	Whole plant[21]	Petroleum ether Dichloromethane Methanol	IC_{50} (µg/ml)	>499 >499 >499	*P. falciparum* K1
Cassia siamea	Caesalpineaceae	Leaves[40]	Water	IC_{50} (µg/ml)	>7.5	*P. falciparum*
Catha edulis	Celastraceae	Aerial[21]	Petroleum ether Dichloromethane Methanol	IC_{50} (µg/ml)	N.T. N.T. >499	*P. falciparum* K1
*Chenopodium ambrosioides**	Chenopodiaceae	Whole plant excluding root[22]	Ethanol	% inhibition	52.70 & 40.66	*P. berghei* NK 65 *in vivo* and *in vitro*
*Cichorium intybus**	Asteraceae	Seed[22]	Ethanol	% inhibition	29.70 & 60.52	*P. berghei* NK 65 *in vivo* and *in vitro*
*Cinnamomum tamala**	Lauraceae	Leaf[22]	Ethanol	% inhibition	62.69 & 67.82	*P. berghei* NK 65 *in vivo* and *in vitro*
Cissampelos mucronata	Menispermaceae	Roots[19]	Ethylacetate	IC_{50} (µg/ml)	0.38	*P. berghei* Anka
Cissampelos mucronata	Menispermaceae	Roots[20]	Ethanol Petroleum ether Ethylacetate Water	IC_{50} (µg/ml)	1.3 8.0 0.38 1.2	*P. falciparum* K1
Clausena anisata	Rutaceae	Root bark[21]	Petroleum ether Dichloromethane Methanol	IC_{50} (µg/ml)	>499 >499 100-499	*P. falciparum* K1
		Stem bark	Petroleum ether Dichloromethane Methanol		100-499 50-99 50-99	
		Leaves	Petroleum ether Dichloromethane Methanol		>499 100-499 100-499	
*Cleome icosandra**	Capparidaceae	Whole plant excluding root[22]	Ethanol	% inhibition	Nil & 5.76	*P. berghei* NK 65 *in vivo* and *in vitro*
Clerodendrum myricoides	Verbanaceae	Root bark[20]	Ethanol Petroleum ether Ethylacetate Water	IC_{50} (µg/ml)	300 47 11 300	*P. falciparum* K1

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Table 1. (*contd.*)

Plant species	Family	Part used	Extract/ Fraction	Toxicity	Dose efficiency	*Plasmodium* sp and strain
Clerodendrum pleiosciadium	Verbanaceae	Leaves[20]	Ethanol Petroleum ether Ethylacetate Water	IC_{50} (µg/ml)	59 40 40 49	*P. falciparum* K1
Clutia robusta	Euphorbiaceae	Root bark[21]	Petroleum ether Dichloromethane Methanol	IC_{50} (µg/ml)	>499 >499 >499	*P. falciparum* K1
Cochlospermum angolense	Cochlospermaceae	Roots[41]	Ethanol	IC_{50} (µg/ml)	10	*P. falciparum*
Cochlospermum tinctorim	Cochlospermaceae	Tubercle[42]	Infusion in water Docoction in water	IC_{50} (ng/ml)	0.93 & 1.31 1.35 & 0.92	*P. falciparum* F32 and FCB1
Combertum aff. psidioides sub sp *psilophylum*	Combretaceae	Root bark[20]	Ethanol Petroleum ether Ethylacetate Water	IC_{50} (µg/ml)	31 39 6.5 30	*P. falciparum* K1
Conyza pyrrhopappa	Asteraceae	Leaves[21]	Petroleum ether Dichloromethane Methanol	IC_{50} (µg/ml)	100-499 10-49 50-99	*P. falciparum* K1
*Coptis teeta**	Ranunculaceae	Rhizome[43]	Water	IC_{50} (µg/ml)	8.8 & N.A.	*P. falciparum* and *P. berghei*
Coutarea latifolia	Rubiaceae	Stem bark[44]	Aq. Ethanol Diethyl ether Ethylacetate Hydrolysed ethylacetate	IC_{50} (µg/ml)	69.5 31.3 9.2 7.3	*P. falciparum* FCM-5
Crassocephalum bojeri	Asteraceae	Aerial[21]	Petroleum ether Dichloromethane Methanol	IC_{50} (µg/ml)	100-499 10-49 50-99	*P. falciparum* K1
Crinium portifolium	Amaryllidaceae	Whole plant[21]	Petroleum ether Dichloromethane Methanol	IC_{50} (µg/ml)	N.T. N.T. >499	*P. falciparum* K1
Crinium stuhlmanni	Amaryllidaceae	Whole plant[21]	Petroleum ether Dichloromethane Methol	IC_{50} (µg/ml)	N.T. N.T. 50-99	*P. falciparum* K1
Crinium papilosum	Amaryllidaceae	Whole plant[21]	Petroleum ether Dichloromethane Methol	IC_{50} (µg/ml)	N.T. N.T. 10-49	*P. falciparum* K1
Crossopterix febrifuga	Rubiaceae	Stem bark[21]	Petroleum ether Dichloromethane Methanol	IC_{50} (µg/ml)	100-499 100-499 100-499	*P. falciaprum* K1

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Table 1. (*contd.*)

Plant species	Family	Part used	Extract/ Fraction	Toxicity	Dose efficiency	*Plasmodium* sp and strain
Croton guatemalensis	Euphorbiaceae	Cortex[45]	Dichloromethane	IC_{50}	27.8 & 23.1	*P. falciaprum* NF 54 and K1
		Leaves	Dichloromethane	(µg/ml)	19.8 & 22.1	
Cuccumis aculeatus	Cucurbitaceae	Whole fruit[31]	Aqueous	IC_{50} (µg/ml)	60,30 & 30	*P. falciparum* M24, K67 and ENT-7
Cussonia arborea	Araliaceae	Root bark[21]	Petroleum ether Dichloromethane Methanol	IC_{50} (µg/ml)	10-49 10-49 >499	*P. falciparum* K1
Cussonia zimmermanni	Araliaceae	Root bark[20]	Ethanol Petroleum ether Ethylacetate Water	IC_{50} (µg/ml)	90 3.3 20 400	*P. falciparum* K1
Cussonia zimmermanni	Araliaceae	Root bark[19]	Petroleum ether	IC_{50} (µg/ml)	3.3	*P. berghei* Anka
*Cyperus rotundus**	Cyperaceae	Whole plant excluding root[22]	Ethanol	% inhibition	49.65 & Nil	*P. berghei* NK 65 *in vivo* and *in vitro*
Cyperus rotundus	Cyperaceae	Tubers[21]	Petroleum ether Dichloromethane Methanol	IC_{50} (µg/ml)	10-49 N.T. 5-9	*P. falciparum* K1
		Aerial	Petroleum ether Dichloromethane Methanol		100-499 10-49 N.T.	
*Cyperus scariosus**	Cyperaceae	Whole plant excluding root[22]	Ethanol	% inhibition	Nil & 54.34	*P. berghei* NK 65 *in vivo* and *in vitro*
Dialium guineense	Caesalpineaceae	Twigs and leaves[40]	Water	IC_{50} (equiv. µg)	15 $<IC_{50}$ <22.5	*P. falciparum*
Dichapetalum guineense	Chailletiaceae	All parts[40]	Water	IC_{50} (equiv. µg)	15 $<IC_{50}<22.5$	*P. falciparum*
Diospyros zembensis	Ebenaceae	Leaves[20]	Ethanol Petroleum ether Ethylacetate Water	IC_{50} (µg/ml)	110 190 35 300	*P. falciparum* K1
Dissotis brazzae	Melastomataceae	Roots[46]	Aqueous	IC_{50} (µg/ml)	218.1 & 131.7	*P. falciparum* ENT-36 and K 67
		Roots	Methanol		40.8 & 42.9	

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Table 1. (*contd.*)

Plant species	Family	Part used	Extract/ Fraction	Toxicity	Dose efficiency	*Plasmodium* sp and strain
		Leaves	Aqueous		14.7 & 28.2	
		Stem	Aqueous		6.1 & > 468.4	
		Stem	Methanol		14.5* & >377.9	
		Aerial	Aqueous		38.0 & 393.0	
		Aerial	Methanol		25.0 & 432.2	
Doliocarpus dentatum	N.a.	N.a.[30]	Ethanol	IC_{50} (ng/ml)	11641 & 15,2273	*P. falciparum* W2 and D6
Dombeya shupangae	Sterculiaceae	Leaves[20]	Ethanol	IC_{50} (µg/ml)	290	*P. falciparum* K1
			Petroleum ether		85	
			Ethylacetate		110	
			Water		8.2	
		Root bark	Ethanol		22	
			Petroleum ether		7.5	
			Ethylacetate		290	
			Water		230	
*Echinops echinatus**	Asteraceae	Aerial parts[29]	Ethanol	MED_{50} (µg/ml)	>2000	*P. falciaprum* FAN-5
					>2000	FMN-13,
					>2000	FMN-17,
					N.A. & N.A.	MP-11 and SO
Enantia chlorantha	Annonaceae	Bark[47]	Aqueous	ED_{50} (mg/ml)	6.9	*P. yoelii nigeriensis*
			Ethanol		0.32	
*Enicostema hyssopifolium**	Gentianaceae	Root[22]	Ethanol	% inhibition	58.23 & 60.13	*P. berghei* NK 65 *in vivo* and *in vitro*
Entandrophr-agma bussei	Meliaceae	Stem bark[21]	Petroleum ether	IC_{50} (µg/ml)	10-49	*P. falciaprum* K1
			Dichloromethane		10-49	
			Methanol		100-499	
Erythirina sacleuxii	Fabaceae	Root bark[19]	Ethylacetate	IC_{50} (µg/ml)	3.3	*P. berghei* Anka
Erythirina sacleuxii	Fabaceae	Leaves[20]	Ethanol	IC_{50} (µg/ml)	140	*P. falciparum* K1
			Petroleum ether		10	
			Ethylacetate		120	
			Water		3.6	
		Root bark	Ethanol		20	
			Petroleum ether		3.0	
			Ethylacetate		200	
			Water		80	
Etilingera eliator	Zingiberaceae	Fruit[23]	Aqueous	IC_{50} (ng/ml)	>20000 & 9610	*P. falciparum* D6 and W2
		Stalk	Ethanol		>20000 & 8820	

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Table 1. (*contd.*)

Plant species	Family	Part used	Extract/ Fraction	Toxicity	Dose efficiency	*Plasmodium* sp and strain
Etlingera sp	Zingiberaceae	Stalk[23]	Aqueous ethanol	IC_{50} (ng/ml)	>20000 & 15890	*P. falciparum* D6 and W2
*Eucalyptus globulus**	Myrtaceae	Aerial parts[29]	Ethanol	MED_{50} (µg/ml)	150, 75, 100, 100 & 100	*P. falciparum* FAN-5, MN-13, FMN-17, MP-11 and SO
*Euphorbia thymifolia**	Euphorbiaceae	Whole plant excluding root[22]	Ethanol	% inhibition	41.14 & 65.70	*P. berghei* NK 65 *in vivo* and *in vitro*
Evodia fatraina	Rutaceae	Stem bark[48]	Ethylacetate	IC_{50} (µg/ml)	8.5	*P. falciparum* FCM-29
			Butanol		16	FCM-29C1
			Ethanol		16	FCM-29C1
			Ethanol		20	FCM-29C3
			Ethanol		12.5	FCM-22
Ficus polita	Moraceae	Leaves[26]	Ethanol	IC_{50} (µg/ml)	20.8	*P. falciparum*
Garcinia gummigulta	N.a.	N.a.[49]	N.a.	% inhibition	97.5	*P. falciparum* K1
Gardenia-jovis tonantis	Rubiaceae	Root bark[31]	Aqueous	IC_{50} (µg/ml)	820, 880 & 1750	*P. falciparum* M24, K67 and ENT-7
Gardenia-jovis tontantis	Rubiaceae	Stem bark[21]	Petroleum ether	IC_{50} (µg/ml)	N.T.	*P. falciparum* K1
			Dichloromethane		N.T.	
Geiisosperm-um serıceum	N.a.	N.a.[30]	Ethanol	IC_{50} (ng/ml)	5632.6 & 2156.2	*P. falciparum* W2 and D6
*Glycirrhiza glabra**	Leguminosae	Root[22]	Ethanol	% inhibition	Nil & 63.54	*P. berghei* NK 65 *in vivo* and *in vitro*
Gompherena celosioides	Amaranthaceae	Leaves[20]	Ethanol	IC_{50} (µg/ml)	230	*P. falciparum* K1
			Petroleum ether		45	
			Ethylacetate		15	
			Water		>500	
Gompherena celesioides	Amaranthaceae	All parts[40]	Water	IC_{50} (equiv. µg)	7.5<IC_{50} <15 µg	*P. falciparum*
Grewia egglingii	Tiliaceae	Stem bark[21]	Petroleum ether	IC_{50} (µg/ml)	50-99	*P. falciparum* K1
			Dichloromethane		N.T.	
			Methanol		N.T.	
Grewia forbesii	Tiliaceae	Leaves[21]	Petroleum ether	IC_{50} (µg/ml)	>499	*P. falciparum* K1
			Dichloromethane		100-499	
			Methanol		100-499	

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Table 1. (*contd.*)

Plant species	Family	Part used	Extract/ Fraction	Toxicity	Dose efficiency	*Plasmodium* sp and strain
Gynandropsis gynandra	Capparidaceae	Roots[21]	Ethanol Petroleum ether Ethylacetate Water	IC_{50} (µg/ml)	300 87 14 >500	*P. falciparum* K1
Harungana madagascariensis	Guttiferae	Roots[19]	Ethylacetate Petroleum ether	IC_{50} (µg/ml)	4.0 6.0	*P. berghei* Anka
		Stem bark	Ethylacetate Petroleum ether		10.0 10.0	
Harungana madagascariensis	Guttiferae	Leaves[20] Stem bark Roots	Ethanol	IC_{50} (µg/ml)	65 29 34	*P. falciparum* K1
		Leaves Stem bark Roots	Petroleum ether		11 10 6.0	
		Leaves Stem bark Roots	Ethylacetate		21 10 4.0	
		Leaves Stem bark Roots	Water		150 88 150	
*Hedychium spicatum**	Zingiberaceae	Root[22]	Ethanol	% inhibition	Nil & 64.76	*P. berghei* NK65 *in vivo* and *in vitro*
Henisia crinita sub sp *parviflora*	Rubiaceae	Leaves[20] Stem bark Roots	Ethanol Petroleum ether Ethylacetate Water	IC_{50} (µg/ml)	95 30 29 >300	*P. falciparum* K1
Hernandia voyronii	Hernandiaceae	Stem[50] bark	Ethanol	IC_{50} (µg/ml)	3.53	*P. falciparum* FCM-29C1
Heteromorpha trifolia	Apiaceae	Stem bark	Aqueous	IC_{50} (µg/ml)	475,370 & 580	*P. falciparum* M24, K67 and ENT-7
Hoslundia opposita	Lamiaceae	Root bark[21]	Petroleum ether Dichloromethane Methanol	IC_{50} (µg/ml)	5-9 10-49 100-499	*P. falciparum* K1
		Stem bark	Petroleum ether Dichloromethane Methanol		50-99 >499 >499	

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Table 1. (*contd.*)

Plant species	Family	Part used	Extract/ Fraction	Toxicity	Dose efficiency	*Plasmodium* sp and strain
Hoslundia opposita	Lamiaceae	Roots[20]	Ethanol Petroleum ether Ethylacetate Water	IC_{50} (µg/ml)	33 10 18 >100	*P. falciparum* K1
Jacaranda copaia	N.a.	N.a.[30]	Ethanol	IC_{50} (ng/ml)	11641 & 15273	*P. falciparum* W2 and D6
Jatropa gossypiifolia	Euphorbiaceae	Leaves[40]	Water	IC_{50} (equiv. µg)	15 $<IC_{50}<22.5$	*P. falciparum*
*Jurinea macrocephala**	Asteraceae	Root[22]	Ethanol	% inhibition	49.27 & 65.39	*P. berghei* NK 65 *in vivo* and *in vitro*
Keetia zangibarica	Rubiaceae	Leaves[20]	Ethanol Petroleum ether Ethylacetate Water	IC_{50} (µg/ml)	92 140 32 190	*P. falciparum* K1
		Stem bark	Ethanol Petroleum ether Ethylacetate Water		>250 90 35 >310	
		Root	Ethanol Petroleum ether Ethylacetate Water		98 12 4.0 >450	
Keetia zangibarica	Rubiaceae	Roots[19]	Ethylacetate	IC_{50} (µg/ml)	4.0	*P. berghei* Anka
Kigelia africana	Bignoniaceae	Stem bark[20]	Petroleum ether Dichloromethane	IC_{50} (µg/ml)	>499 >499	*P. falciparum* K1
		Leaves	Methanol Petroleum ether Dichloromethane Methanol		10-49 >499 >499 100-499	
Lagenaria sphaerica	Cucurbitaceae	Leaves[20]	Ethanol Petroleum ether Ethylacetate Water	IC_{50} (µg/ml)	220 120 40 450	*P. falciparum* K1
Lannea edulis	Anacardeaceae	Roots[20]	Ethanol Petroleum ether Ethylacetate Water	IC_{50} (µg/ml)	40 18 17 400	*P. falciparum* K1

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Table 1. (*contd.*)

Plant species	Family	Part used	Extract/ Fraction	Toxicity	Dose efficiency	*Plasmodium* sp and strain
Lanisium domesticum	Meliaceae	Bark[23]	Aqueous ethanol	IC_{50} (ng/ml)	9364 & 3105	*P. falciparum*
Lantana camara	Verbanaceae	Root bark[21]	Petroleum ether Dichloromethane Methanol	IC_{50} (µg/ml)	5-9 10-49 100-499	*P. falciparum* K1
*Launaca nudicaulis**	Asteraceae	Whole plant excluding root[22]	Ethanol	% inhibition	49.26 & Nil	*P. berghei* NK 65 *in vivo* and *in vitro*
Leonotis mollissima	Lamiaceae	Leaves[20]	Ethanol	IC_{50} (µg/ml)	30	*P. falciparum* K1
		Roots	Petroleum ether Ethylacetate Water		190 26 80	
		Roots	Ethanol Petroleum ether Ethylacetate Water		9.0 28 95 >500	
Lippia cheralieri	Verbanaceae	Leaves[39]	Water	IC_{50} (mg/ml)	0.30 & 0.38	*P. falciparum* FCC-2 and FZR
Luffa aegyptiaca	Cucurbitaceae	Leaves[26]	Ethanol	IC_{50} (µg/ml)	30.0	*P. falciparum* K1
Luffa cylindrica	Cucurbitaceae	Leaves[20]	Ethanol Petroleum ether Ethylacetate Water	IC_{50} (µg/ml)	100 300 30 >500	*P. falciparum* K1
Mammea longifolia	N.a.	N.a.[49]	N.A.	% inhibition	86	*P. falciparum* FCM-29 C1
Margaritaria discoidea	Euphorbia-ceae	Root bark[21]	Petroleum ether Dichloromethane Methanol	IC_{50} (µg/ml)	10-49 10-49 100-499	*P. falciparum* K1
Maytenus senegalensis	Celastraceae	Stem bark[19]	Ethylacetate	IC_{50} (µg/ml)	0.16	*P. berghei* Anka
Maytenus senegalensis (Morogor region)	Celastraceae	Stem bark[20]	Ethanol Petroleum ether Ethylacetate Water	IC_{50} (µg/ml)	1.9 4.5 12 7.5	*P. falciparum* K1
		Root bark	Ethanol Petroleum ether		2.0 8.0	
			Ethylacetate Water		0.16 0.62	

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Table 1. (*contd.*)

Plant species	Family	Part used	Extract/ Fraction	Toxicity	Dose efficiency	*Plasmodium* sp and strain
Maytenus senegalensis (Kagera) region)		Stem bark	Ethanol Petroleum ether Ethylacetate Water	IC_{50} (µg/ml)	3.0 80 85 205	*P. falciparum* K1
Mikania cordata	Asteraceae	Leaves[21]	Ethanol Petroleum ether Ethylacetate Water	IC_{50} (µg/ml)	130 160 14 240	*P. falciparum* K1
Momordica charantia	Cucurbitaceae	Leaves[26]	Ethanol	IC_{50} (µg/ml)	68.4	*P. falciparum*
*Momordica dioica**	Cucurbitaceae	Whole plant[22]	Ethanol	% inhibition	87.65 & Toxic	*P. berghei* NK65 *in vivo* and *in vitro*
Momordica foetida	Cucubitaceae	Leaves[20]	Ethanol Petroleum ehter Ethylacetate Water	IC_{50} (µg/ml)	80 50 29 170	*P. falciparum* K1
Morinda lucida	Rubiacae	Leaves[51]	Petroleum ether	% suppression	51.6% at 600 mg/kg &	*P. berghei*
		Stem bark	Chloroform (Fraction B)		96.4% at 900 mg/kg	
Morinda lucida	Rubiaceae	Leaves[52]	Petrol	% chemosuppression	16-68% at 6.25-50 mg/kg/day	*P. berghei*
Moringa pterygosperma	Moringaceae	Twigs and leaves[26]	Ethanol	IC_{50} (µg/ml)	60.0	*P. falciparum*
Nauclea latifolia	Rubiaceae	Roots[40]	Water	IC_{50} (~µg)	15µg < IC_{50} <22.5 µg	*P. falciparum*
Neurolaena lobata	Asteraceae	Leaves[45]	Dichloromethane	IC_{50} (µg/ml)	8.6 & 10.6	*P. falciparum* NF54 and K1
Newbouldia laevis	Bignoniaceae	Leaves[26]	Ethanol	IC_{50} (µg/ml)	12.6	*P. falciparum*
*Nyctanthes arbortristis**	Oleaceae	Stem bark[22]	Ethanol	% inhibition	Nil & 21.33	*P. berghei* NK 65 *in vivo* and *in vitro*
		Leaf			64.70 & 69.47	
		Root			21.46 & 55.38	
		Seed			Nil & 45.08	
		Flower			Nil & 20.54	

contd...

Table 1. (*contd.*)

Plant species	Family	Part used	Extract/ Fraction	Toxicity	Dose efficiency	*Plasmodium* sp and strain
Nyctanthes arbortristris	Nyctaginaceae	Aerial parts[29]	Ethanol	MED_{50} (µg/ml)	1000, 1200, 1000, N.A. & N.A.	*P. falciparum* FAN-5 FMN-17, MP-11 and SO
Ocimum sanctum[*]	Labiatae	Root[22]	Ethanol	% inhibition	24.11 & 11.62	*P. berghei* NK65
		Whole plant excluding root			Nil & 29.65	
Oscimum sanctum[*]	Lamiaceae	Aerial parts[29]	Ethanol	MED_{50} (µg/ml)	>2000, >2000, >2000, N.A. & N.A.	*P. falciparum* FAN-5, FMN-13, FMN-17, MP-11 and SO
Ocotea usambarensis	Lauraceae	Root bark[21]	Petroleum ether Dichloromethane Methanol	IC_{50} (µg/ml)	10-49 10-49 100-499	*P. falciparum* K1
Olinia usambarensis	Oliniaceae	Stem bark[31]	Aqueous	IC_{50} (µg/ml)	204, 130 & 380	*P. falciparum* M24, K67 and ENT-7
Oxyanthus pyriformis sub sp *tangan yikensis*	Rubiaceae	Leaves[20]	Ethanol Petroleum ether Ethylacetate Water	IC_{50} (µg/ml)	130 100 90 40	*P. falciparum* K1
		Roots	Ethanol Petroleum ether Ethylacetate Water		30 40 260 300	
Ozoroa insignis	Anacardiaceae	Root bark[21]	Petroleum ether Dichloromethane Methanol	IC_{50} (µg/ml)	10-49 10-49 >499	*P. falciparum* K1
Pallinia pinnata	Sapindaceae	Leaves[20]	Ethanol Petroleum ether Ethylacetate Water	IC_{50} (µg/ml)	40 36 25 50	*P. falciparum* K1
Parinari excelsa	Chrysobalan-caceae	Stem bark[20]	Ethanol Petroleum ether Ethylacetate Water	IC_{50} (µg/ml)	41 12 10 92	*P. falciparum* K1
Parinari excelsasabin	Rosaceae	Stem bark[21]	Petroleum ether Dichloromethane Methanol	IC_{50} (µg/ml)	10-49 10-49 >499	*P. falciparum* K1

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Table 1. (*contd.*)

Plant species	Family	Part used	Extract/ Fraction	Toxicity	Dose efficiency	*Plasmodium* sp and strain
Parkia filicoidea	Mimosaceae	Root bark[20]	Ethanol Petroleum ether Ethylacetate Water	IC_{50} (µg/ml)	140 39 48 130	*P. falciparum* K1
Paullinia pinnata	Sapindaceae	All parts[40]	Water	IC_{50} (equiv. µg)	15 $<IC_{50}<22.5$	*P. falciparum*
Pavetta crassipes	Rubiaceae	All parts[40]	Water	IC_{50} (µg/ml)	<7.5	*P. falciparum*
Pavetta crassipes	Rubiaceae	Leaves[20]	Ethanol Petroleum ether Ethylacetate Water	IC_{50} (µg/ml)	170 95 33 >500	*P. falciparum* K1
*Pedalium murex**	Pedaliaceae	Fruit[22]	Ethanol	% inhibition	Nil& 5.23	*P. berghei* NK 65 *in vivo* and *in vitro*
Phyllanthus reticulatus	Euphorbiaceae	Roots[46]	Aqueous	IC_{50} (µg/ml)	159.8 & 165.1	*P. falciparum* ENT-36 and K 67
		Leaves	Aqueous		10.0 & 1.7	
		Stem	Aqueous		23.9 & 7.7	
		Stem	Methanol		21.5 & 52.2	
*Physalis minima**	Solanaceae	Whole plant excluding root[22]	Ethanol	% inhibition	Nil& 57.5	*P. berghei* NK 65 *in vivo* and *in vitro*
Picralima nitida	Apocyanaceae	Seeds[53]	Dichloromethane Methanol Water Petroleum ether	IC_{50} (µg/ml)	5.15 & 5.03 7.35 & 12.99 17.40 & 12.15 20.81 & 25.87	*P. falciparum* W2 and D6
		Fruit rind	Dichloromethane Methanol		1.61 & 2.41 20.79 & 32.16	
		Stem bark	Dichloromethane Methanol		6.46 & 14.86 2.00 & 1.23	
Picralima nitida	Apocyanaceae	Root[54]	Dichloromethane Methanol Water	IC_{50} (µg/ml)	0.188 1.629 10.914	*P. falciparum* NF 54
		Stem bark	Dichloromethane Methanol Water		0.545 1.792 >50	

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Table 1. (*contd.*)

Plant species	Family	Part used	Extract/ Fraction	Toxicity	Dose efficiency	*Plasmodium* sp and strain
		Fruit rind	Dichloromethane Methanol Water Petroleum ether		17.660 41.342 1.581 >50	
		Leaves	Dichloromethane Methanol Water Petroleum ether		>50 7.361 >50 >50	
		Seeds	Dichloromethane Methanol Water		12.435 >50 >50	
Piliostigma thonningii	Leguminosae	Stem bark[21]	Petroleum ether Dichloromethane Methanol	IC_{50} (µg/ml)	100-499 100-499 100-499	*P. falciparum* K1
		Leaves	Petroleum ether Dichloromethane Methanol		100-499 10-49 10-49	
Pisum sativum•	Fabaceae	Leaves[33]	Methanol	Significant activity	At 50 mg/kg	*P. berghei*
Pithecelobium acemosum	N.A.	N.A.[30]	Ethanol	IC_{50} (ng/ml)	185040.0 & inactive	*P. falciparum* W2 and D6
Pittosporum vividiflorum	Pittosporaceae	Stem bark[31]	Aqueous	IC_{50} (µg/ml)	80.30 & 170	*P. falciparum* M24, K67 and ENT-7
Plantago major	Plantaginaceae	Whole plant[21]	Petroleum ether Dichloromethane Methanol	IC_{50} (µg/ml)	100-499 10-49 >499	*P. falciparum* K1
Pongamia pinnata•	Leguminosae	Seed[22]	Ethanol	% inhibition	38.91 & 39.92	*P. berghei* NK 65 *in vivo* and *in vitro*
Potomorphe peltata	N.a.	N.a.[30]	Ethanol	IC_{50} (µg/ml)	9078.8 & partially active	*P. falciparum* W2 and D6
Potomorphe umbellata	Piperaceae	Leaves[55]	Ethanol	Reduction in parasitaemia	60% at 500 mg/kg	*P. berghei*
Prunella amygdalus•	Labiate	Fruit[22]	Ethanol	% inhibition	Nil & 10.27	*P. berghei* NK 65 *in vivo* and *in vitro*

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Table 1. (*contd.*)

Plant species	Family	Part used	Extract/ Fraction	Toxicity	Dose efficiency	*Plasmodium* sp and strain
*Prunus persica**	Rosaceae	Seed[22]	Ethanol	% inhibition	62.23 & 70.90	*P. berghei* NK65
		Leaf			Toxic & 3.06	
Psidium guajava	Myrtaceae	Leaves[21]	Petroleum ether Dichloromethane Methanol	IC_{50} (µg/ml)	10-49 100-499 50-99	*P. falciparum* K1
Psidium guajava	Myrtaceae	Leaves[20]	Ethanol Petroleum ether Ethylacetate Water	IC_{50} (µg/ml)	36 13 10 80	*P. falciparum* K1
Rauwolfia mombasiana	Apocyanaceae	Root bark[21]	Petroleum ether Dichloromethane Methanol	IC_{50} (µg/ml)	100-499 N.T. 100-499	*P. falciparum* K1
		Stem bark	Petroleum ether Dichloromethane Methanol		N.T. 10-49 >499	
Rhamnus staddo	Rhamnaceae	Root bark[31]	Aqueous	IC_{50} (µg/ml)	520,490 & 740	*P. falciparum* M24, K67 and ENT-7
Rhiocissus tridentata	Vitaceae	Whole tuber[31]	Aqueous	IC_{50} (µg/ml)	100,40 & 70	*P. falciparum* M24, K67 and ENT-7
Salacia madagascari-ensis	Celastraceae	Roots[19]	Petroleum ether	IC_{50} (µg/ml)	0.80	*P. berghei* Anka
Sansevieria guineensis	Agavaceae	Roots[45]	Dichloromethane	IC_{50} (µg/ml)	17.0 & 15.8	*P. falciparum* NF54 and K1
		Leaves	Dichloromethane		38.5 & 39.5	
Scadoxus multiflorus	Amaryllidaceae	Whole plant[21]	Petroleum ether Dichloromethane Methanol	IC_{50} (µg/ml)	N.T. N.T. 50-99	*P. falciparum* K1
Sclerocarya cafra	Anacardiaceae	Stem bark[21]	Petroleum ether Dichloromethane Methanol	IC_{50} (µg/ml)	> 499 >499 > 499	*P. falciparum* K1
Scutia myrtina	Rhamnaceae	Root bark[31]	Aqueous	IC_{50} (µg/ml)	40,240 & 320	*P. falciparum* M24, K67 and ENT-7
Senna petersiana	Caesalpinea-ceae	Root[38]	Methanol Water Dichloromethane	IC_{50} (µg/ml)	>30 >100 13.26	*P. falciparum* VI/S

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Table 1. (*contd.*)

Plant species	Family	Part used	Extract/ Fraction	Toxicity	Dose efficiency	*Plasmodium* sp and strain
		Leaves	Methanol		2.67	
			Water		3.97	
			Dichloromethane		6.94	
Shrebera alata	Oleaceae	Stem bark[31]	Aqueous	IC_{50} (µg/ml)	627,160 & 380	*P. falciparum* M24, K67 and ENT-7
*Sida rambifolia**	Malvaceae	Fruit[22]	Ethanol	% inhibition	Nil & 8.11	*P. berghei* NK 65 *in vivo* and *in vitro*
		Root			Nil & 56.05	
Simarouba amara	Simarouba-ceae	Cortex[45]	Dichloromethane	IC_{50} (µg/ml)	0.195 & 0.184	*P. falciparum* NF 54 and K1
*Solanum nigrum**	Solanaceae	Whole plant excluding root[22]	Ethanol	% inhibition	Nil & 51.95	*P. berghei* NK 65 *in vivo* and *in vitro*
Sorindeia madagascariensis	Anacardiaceae	Root bark[21]	Petroleum ether	IC_{50} (µg/ml)	100-499	*P. falciparum* K1
			Dichloromethane		100-499	
			Methanol		>499	
Spathodea campanulata	Bignoniaceae	Leaves[56]	Hexane	ED_{50} (mg/kg/day)	Infective	*P. berghei*
			Water		100-400	
Spilanthes oleraceae	Asteraceae	Flowers[39]	Water	IC_{50} (mg/ml)	0.18 & 0.20	*P. falciparum* FCC2 and FZR
*Spinacia oleraceae**	Chenopodi-ceae	Seed[22]	Ethanol	% inhibition	28.67 & 59.43	*P. berghei* NK 65 *in vivo* and *in vitro*
Spirostachys africana	Euphorbiaceae	Root[36]	Ethanol	ID_{50} (µg/ml)	5	*P. falciparum* FUP
			Water		5	
		Leaves	Petroleum ether		5	
Stryphnoden-dron guyanensae		N.a.[30]	Ethanol	IC_{50} (ng/ml)	38903 & partially active	*P. falciparum* W2 and D6
Suregada zanzibariensis	Euphorbiaceae	Roots[46]	Aqueous	IC_{50} (µg/ml)	291.4 & 378.8	*P. falciparum* ENT-36 and K67
		Leaves	Aqueous		1.5 & 1.5	
		Stem	Aqueous		95.5 & >412.8	
Tamarandus indica	Caesalpinea-ceae	Fruits[21]	Petroleum ether	IC_{50} (µg/ml)	N.T.	*P. falciparum* K1
			Dichloromethane		N.T.	
			Methanol		>499	

contd...

Table 1. (*contd.*)

Plant species	Family	Part used	Extract/ Fraction	Toxicity	Dose efficiency	*Plasmodium* sp and strain
Tamarandus indica	Caesalpineaceae	Leaves[20]	Ethanol Petroleum ether Ethylacetate Water	IC_{50} (µg/ml)	100 90 70 270	*P. falciparum* K1
Tamarix gallice[*]	Tamariaceae	Whole plant excluding root[22]	Ethanol	% inhibition	Nil & 28.03	*P. berghei* NK 65 *in vivo* and *in vitro*
Terminalia spinosa	Combretaceae	Stem bark[46]	Aqueous	IC_{50} (µg/ml)	29.5 & 9.9	*P. falciparum* ENT-36 and K67
		Stem wood	Aqueous		49.2 & 35.9	
Thylachium africanum	Capparidaceae	Leaves[20]	Ethanol Petroleum ether Ethylacetate Water	IC_{50} (µg/ml)	290 88 30 >500	*P. falciparum* K1
Tinospora cordifolia[*]	Menispermaceae	Whole plant[22]	Ethanol	% inhibition	40.58 & 65.29	*P. berghei* NK 65 *in vivo* and *in vitro*
Todalia asiatica	Rutaceae	Root bark[21]	Petroleum ether Dichloromethane Methanol	IC_{50} (µg/ml)	50-99 10-49 >499	*P. falciparum* K1
		Stem bark	Petroleum ether Dichloromethane Methanol		100-499 10-49 50-99	
Tribulus terrestris[*]	Zygophyllaceae	Fruit[22]	Ethanol	% inhibition	6.66 & 15.68	*P. berghei* NK 65 *in vivo* and *in vitro*
Tridax procumbans	Asteraceae	Whole plant[21]	Petroleum ether Dichloromethane Methanol	IC_{50} (µg/ml)	100-499 100-499 >499	*P. falciparum* K1
Triphophyllum peltatum	Dioncophyllaceae	Leaf[25]	Petroleum ether Dichloromethane Dichloromethane/ ammonia Ethylalcohol	IC_{50} (µg/ml)	35.433 & N.T. 0.815 & 3.313 2.925 & N.T. 10.692 & N.T.	*P. falciparum* NF 54 and *P. berghei* Anka
		Bark	Dichloromethane/ ammonia		0.014 & 0.081	
Turraea mombassana	Meliaceae	Whole root[31]	Aqueous	IC_{50} (µg/ml)	150, 90 & 100	*P. falciparum* M24, K67 and ENT-7

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Table 1. (*contd.*)

Plant species	Family	Part used	Extract/ Fraction	Toxicity	Dose efficiency	*Plasmodium* sp and strain
Tynanthus elegans	N.a.	N.a.[30]	Ethanol	IC_{50} (ng/ml)	807030.0 & inactive	*P. falciparum* W2 and D6
Uapaca nitida	**Euphorbiaceae**	**Root bark[57]**	Ethanol **Hexane** Acetone Chloroform	**IC_{50}**	45 ng/ml **1.3 ng/ml** 91 µg/ml 25 µg/ml	***P. falciparum*** **K1**
		Leaves	Methanol Hexane		18 µg/ml 1.84 ng/ml	
Urtica dioica	Urticaceae	Rhizome[24]	Ethylacetate	ED_{50} (µg/ml)	3.9 & 3.8	*P. falciparum* D6 and W2
Vangueria infausta	Rubiaceae	Root bark[21]	Petroleum ether Dichloromethane Methanol	IC_{50} (µg/ml)	>499 N.T. 10-49	*P. falciparum* K1
		Stem bark	Petroleum ether Dichloromethane Methanol		N.T. 10-49 100-499	
Vepris lanceolata	Rutaceae	Root bark[19]	Ethylacetate Water	IC_{50} (µg/ml)	7.0 9.5	*P. berghei* Anka
Vepris lanceolata	Rutaceae	Leaves[20]	Ethanol Petroleum ether Ethylacetate Water	IC_{50} (µg/ml)	10 15 26 12	*P. falciparum* K1
		Root bark	Ethanol Petroleum ether Ethylacetate Water		11 7.0 9.5 60	
Vernonia amygdalina	Asteraceae	Leaves[21]	Petroleum ether Dichloromethane Methanol	IC_{50} (µg/ml)	N.T. N.T. >499	*P falciparum* K1
Vernonia colorata	Asteraceae	Root bark[21]	Petroleum ether Dichloromethane Methanol	IC_{50} (µg/ml)	100-499 >499 >499	*P. falciparum* K1
		Stem bark	Petroleum ether Dichloromethane Methanol		50-99 50-99 50-99	
		Leaves	Petroleum ether Dichloromethane Methanol		100-499 >499 >499	
Viburnum opulus	Caprifoliaceae	Stipes[24]	Ethylacetate	ED_{50} (µg/ml)	7.4 & 9.8	*P. falciparum* D6 and W2
Vismia orientale	Guttiferae	Stem bark[21]	Petroleum ether Dichloromethane	IC_{50} (µg/ml)	N.T. N.T.	*P. falciparum* K1

contd..

Table 1. (*contd.*)

Plant species	Family	Part used	Extract/ Fraction	Toxicity	Dose efficiency	*Plasmodium* sp and strain
			Methanol		N.T.	
		Leaves	Petroleum ether	IC_{50}	N.T.	
			Dichloromethane	(μg/ml)	>499	
			Methanol		>499	
Withania somnifera	Solanaceae	Seed[22]	Ethanol	% inhibition	Nil & 47.76	*P. berghei* NK 65 *in vivo* and *in vitro*
Xanthium strumarium	Asteraceae	Arial parts[29]	Ethanol	MED_{50} (μg/ml)	25, 25, 25, 50 & 50	*P. falciparum* FAN-5, FMN-13, FMN-17, MP-11 and SO
Ximenia cafra	Olacaceae	Leaves[21]	Petroleum ether	IC_{50}	>499	*P. falciparum*
			Dichloromethane	(μg/ml)	100-499	K1
			Methanol		100-499	
Zanthoxylum chalybeum (Dares Salaam region)	Rutaceae	Stem bark[20]	Ethanol	IC_{50}	31	*P. falciparum*
			Petroleum ether	(μg/ml)	2.2	K1
			Ethylacetate		7.0	
			Water		0.7	
		Root bark	Ethanol		42	
			Petroleum ether		10	
			Ethylacetate		20	
			Water		10	
Zanthoxylum chalybeum (Kagra region)		Stem bark	Ethanol		13	
			Petroleum ether		4.2	
			Ethylacetate		12	
			Water		6.9	
		Root bark	Ethanol		23	
			Petroleum ether		1.2	
			Ethylacetate		7.0	
			Water		0.43	
Zanthoxylum chalybeum	Rutaceae	Root bark[19]	Water	IC_{50} (μg/ml)	0.43	*P. berghei* Anka
Zanthoxylum gilleti	Rutaceae	Root bark[21]	Petroleum ether	IC_{50}	10-49	*P. falciparum*
			Dichloromethane	(μg/ml)	50-99	K1
			Methanol		10-49	
		Stem bark	Petroleum ether		50-99	
			Dichloromethane		50-99	
			Methanol		10-49	
Zanthoxylum xylubeum	Rutaceae	Stem bark[21]	Petroleum ether	IC_{50}	100-499	*P. falciparum*
			Dichloromethane	(μg/ml)	100-499	K1
			Methanol		100-499	

N.A. — Tested but found to be not active; N.T. — Not tested; N.a. — Not available; Plants which have significantly high efficacies are in bold words; Plants frequently found in Indian subcontinent which have been scientifically studied are highlighted by(*).

Table 2. A composite table of alkaloids derived from plants showing their dose related effects *in vivo* for *P. berghei* and *in vitro* for *P. falciparum*. Alkaloids from *Stychnos* and *Alstonia* species are reported to be many more times effective than those derived from *Cinchona*

Plant species	Family	Part used	Type of alkaloid	Compound	Toxicity	Dose efficiency	*Plasmodium* sp and strain
N.a.	Ancistroclad-aceae	N.a.	**Napthyliso-quinoline alkaloids**[58]	Ancistrocladine	IC_{50} (μg/ml)	18.353 & N.A.	*P. falciparum*
				Hamatine		3.338 & N.A.	NF 54 and
				Ancistrobarterine A		10.326 & N.A.	*P. berghei*
				Ancistrobrevine A		19.33 & N.A.	(Anka)
	Dioncophyll-aceae			**Dioncophylline C**		**0.014 & 0.015**	respectively
				Dioncolactone A		1.337 & 0.598	
				Dioncophyllacine A		17.571 & N.A.	
				Dioncophylline A		1.443 & 0.961	
				7-epi-Dioncophylline A		0.190 & 2.946	
				N-Methyldioncophylline A		17.411 & 0.067	
				Dioncophylline A/4'-0-Demethyldioncophylline A		0.411 & 0.438	
				5'-O-Demethyl-8-O-methyl-7-epidioncophylline A		1.584 & 4.580	
N.a.	Menisperm-aceae	N.a.	Bisbenzyliso-quinoline alkaloid[59]	Funiferine	IC_{50} (μM)	0.63	*P. falciparum* K1
				Tiliageine		6.32	
				Daphnoline		0.96	
				Aromoline		1.36	
				Homoaromoline		3.46	
				Oxyacanthine HCl		1.06	
				Thalisopidine		0.09	
				Phaeanthine		1.46	
				Tetrandrine		0.57	
				Isotetrandrine		0.16	
				Tetrandrine methioidide		>65.4	
				Pycnamine		0.83	
				Fangchinoline		1.43	
				Berbamine		0.45	
				Obamegine		0.74	
				Dinklacorine		3.92	
				Isochondodendrine		22.0	
				Trigillentimine		42.1	

contd...

Table 2. (*contd.*)

Plant species	Family	Part used	Type of alkaloid	Compound	Toxicity	Dose efficiency	*Plasmodium* sp and strain
				Cochsoline		1.16	
				Cocsuline		~88.9	
				Isotrilobine		2.06	
				Coculine methioidide		>17.8	
				Gilletine		1.81	
				Insularine picrate		2.07	
N.a.	Rutaceae	N.a.	Acridone alkaloids[60]	Normelicopidine	IC_{50} (µg/ml)	>100 & >100	*P. falciparum* HB3 and W2 respectively
				Meliocopidine		14.1 & 5.54	
				Melicopicine		37.2 & 30.2	
				1,3-Dihydroxy-N-methyl acridone		>100 & >100	
			Pyranoacridone alkaloids	Noracronycine		>100 & >100	
				N-Desmethyl acromycine		10.4 & 2.35	
				Acromycine		7.03 & 1.44	
				2-Nitroacronycine		2.78 & 1.93	
				1,2-Dihydroxy-1,2-dihydroacronycine		10.9 & 9.14	
				1,2-Dihydroxy-1,2-dihydro-N-desmethyl-acronycine		7.92 & 6.05	
				2-Hydroxy-1,2-dehydro-acronycine		13.7&3.26	
				2(-)1,2-Dihydroacronycine-2yl (3-amino)-2,3,6-trideoxy-α-l-arabino hexapyranose		4.86 & 0.60	
				2(S)(-)1,2 Dihydroacronycine-2-yl(4-O-acetyl-3-bromo)-2,3,6-trideoxy-α-l-arabino hexapyranose		6.94 & 1.46	
				1-Methoxy-3-(2-methyl-2-propanaloxy)-9-acridanone-4-carbeldehyde		16.8 & 10.8	
				Dimer AB-2		>100 & >100	
				Trimer AB-3		>100 & >100	
				Dimer Diels-Alder adduct		>100 & >100	

contd..

Table 2. (*contd.*)

Plant species	Family	Part used	Type of alkaloid	Compound	Toxicity	Dose efficiency	*Plasmodium* sp and strain
				2(R)(-)1,2, Dihydroacronycine-2-yl(4-O-acetyl-3-bromo)-2,3,6-trideoxy-α-l-arabinohexyopyranose		3.45 & 1.78	
			Furoquionoline alkaloids	Haplopine		8.90 & 8.34	
				Skimmiamine		15.7 & 14.1	
				Kokusaginine		23.1 & 7.70	
				Acronycidine		19.9 & 5.72	
				Acronydine		12.1 &2.18	
Alstonia angustifolia	Apocyanaceae	Roots	Alkaloids[61]	Alstonerine	ED_{50} (μM)	46.3	*P. falciparum* K1
				Alstophylline		82.5	
				Macralstonine acetate		3.43	
				Macrocarpamine		9.36	
				11-methoxyakuammicine		41.3	
				Norffluorocuraine		129	
				Pleiocarpamine		20.5	
				Villastonine		2.92	
				Vincamajine		138	
Alstonia coriacea	Apocyanaceae	Bark	Quinine type[62]	Corialstonine	IC_{50} (μM)	5.71	*P. falciparum* K1
				Corialstonidine		5.45	
Alstonia scholaris	Apocyanaceae	N.a.	Indole alkaloid[63]	Echitamine chloride	ED_{50} (μg/kg)	320 to 1.6	*P. berghei*
Ancistrocladus abbreviatus	Ancistrocladaceae	Stem bark	Napthyliso-quinoline alkaloids[64]	Dioncophylline A	IC_{50} (ng/ml)	961 & 1443	*P. berghei* (Anka) and *P. falciparum* NF-54 respect-ively
				N-methyldioncophylline A		9207 & 13637	
Ancistrocladus barteri		Root	Napthyliso-quinoline alkaloids	Ancistrobrevine D		6069 & 12222	
				Ancistrocladine		>50000 & 18353	
Ancistrocladus heyneanus	Ancistrocladaceae	Root	Napthyliso-quinoline alkaloids[65]	Ancistroheynine	IC_{50} (μg/ml)	2.1	*P. falciparum*

contd...

Table 2. (*contd.*)

Plant species	Family	Part used	Type of alkaloid	Compound	Toxicity	Dose efficiency	*Plasmodium* sp and strain
Anisocycla cymosa	Menispermaceae	N.a.	Bisbenzyliso-quinoline alkaloid[66]	Coscoline	IC_{50} (µg/ml)	<0.2	*P. falciparum*
Beilschmiedia madang	Lauraceae	Wood	Bisbenzyliso-quinoline alkaloid[67]	Dehatrine	IC_{50} (µM)	0.17	*P. falciparum* K1
Cinchona sp	Rubiaceae	Bark	*Cinchona* alkaloid[68]	Quinine Dihydroquinine Quinidine	IC_{50} (nM)	29.3 & 103.2 21.3 & 151.7 13.4 & 43.7	*P. falciparum* D6 and W2 respectively
Cinchona sp	Rubiaceae	Bark	*Cinchona* alkaloid[69]	Dihydroquinidine 9-Epiquinine Quinine Quinidine Cinchonine	EC_{50} (ng/ml)	10.4 & 74.1 3471 & 1179 52.1 & 252.2 21.8 & 67.7 28.2 & 67.5	*P. falciparum* Quinine suceptible and Quinine resistant lines respectively
N.a.	Rutaceae (*Citrus* glycosmis severinia*)	Root bark	Acridone alkoloids[70]	Glandisine-II Glandisine-I Citpressine-I Citpressine-II O-Methylglycocitrine-II Glycocitrine-I Grandisinine Citrussinine-I N-Methylatalaphilline Glyfoline 1,3-O-Methyl-N-methylacridone 1,3,5,6-O-Methyl-N-methylacridone Des-N-Methylnoracronycine Atalaphillidine Noracronycine 5-Hydroxynoracronycine Citracridone-I Atalaphilinine	% inhibition at 10 (µg/ml)	78 60 23 27 26 96 26 30 91 0 80 0 95 90 12 88 15 94	*P. yoelli* sub sp *nigeriensis*

contd...

Table 2. (*contd.*)

Plant species	Family	Part used	Type of alkaloid	Compound	Toxicity	Dose efficiency	*Plasmodium* sp and strain
				N-Methylseverifoline		25	
				5-Hydroxy-N-methylseverifoline		92	
				Acronycine		85	
				5-Methoxyacronycine		75	
				Dimethoxyacronycine		31	
				Honyumine		0	
				Glycobismine-A		96	
Crematosperma sp	Annonaceae	N.a.	Bisbenzyliso-quinoline alkaloid[71]	Monterine Cordobimine	IC_{50} (μM)	1.59 0.58	*P. falciparum* FcB1
Crinium amabile	Amaryllid-aceae	Bulb	Alkaloid[72]	(-) Amabiline (-) Buphanisine (-) Augustine (-) Crinamine (-) Lycorine	ED_{50} (ng/ml)	>10000 & >10000 3500 & 5340 140 & 180 2180 & 2520 320 & 300	*P. falciparum* D6 and W2 respectively
Cryptolepis sanguinolenta	Asclepiadaceae	Root bark	Indolequinoline alkaloid[73]	Crytolepine	IC_{50} (μg/ml)	0.031	*P. falciparum* K1
Cryptolepis sanguinolenta	Asclepiadaceae	Root	Indolequinoline alkaloid[74]	Cryptolepine hydrochloride	IC_{50} (μM) chemo-suppression	0.114 80.5% at 50 mg/kg/day	*P. falciparum* K1 *P. berghei*
Cryptolepis sanguinolenta	Asclepidaceae	Root	Indolequinoline alkaloid[75]	Cryptolepine hydrochloride Cryptolepine Isocryptolepine	IC_{50} (μM)	0.3, 0.43 & 0.44 0.19, 0.56 & N.T. N.T., 0.3 & N.T.	*P. falciparum* F32, FcB1 and FcR3 respectively
Cyclea barbata	Menispermaceae	Root	Bisbenzyliso-quinoline alkaloid[76]	Tetrandrine Limacine Thalrugosine Homoaromoline Cycleapeltine	ED_{50} (ng/ml)	179 & 160 52.7 & 164 65.1 & 78.0 232 & 451 29.0 & 40.6	*P. falciparum* D6 and W2 respectively
Enatia chlorantha	N.a.	Stem bark	Protoberberine alkaloids[77]	Berberine Palmatine Jatrohizine	IC_{50} (ng/ml)	141 & 148 281 & 163 422 & 1607	*P. falciparum* D6 and W2 respectively

contd...

Table 2. (*contd.*)

Plant species	Family	Part used	Type of alkaloid	Compound	Toxicity	Dose efficiency	*Plasmodium* sp and strain
Galipea longiflia	Rutaceae	Stem bark	Quinoline alkaloids[78]	2-n-propylquinoline Chimanine B Chimanine D 2-n-pentylquinoline 4 methoxy-2-phenyl-quinoline 2(3,4-methylenedioxy-phenylethyl) quinoline	% mice survival at 0.31 mMol/kg after 14 days post infection	60 40 60 100 60 40	*P. vinckei petteri*
Hernandia voyronii jumelle	Hernandiaceae	Whole plant	Isoquinoline alkaloid[79]	Harveline A Harveline B Harveline C	IC_{50} (nM)	3282 1687 3168	*P. falciparum* FCM-29
Isopyrum thalictroides	Ranunculaceae	Roots	Bisbenzyliso-quinoline alkaloid[80]	Penduline Tetrandrine	IC_{50} (ng/ml)	17, 19.5, 12.2, 19.5 N.T. 81.5, 84.6, 69.6	*P. falciparum* Nigerian, F32, FcB1 and W2 respectively
Nectandra salicifolia	Lauraceae	Trunk bark, Root, Leaf/Twig	Bisbenzyliso-quinoline alkaloid[81]	(+)-Costaricine (+)-isoboldine (+)-laurolitsine {(+)-norboldine} (+)-norpurpureine (+)-boldine (+)-norisocorydine (+)-isocorydine (+)-laurotetanine (1S)-N-methylcoclaurine (1S)-norjuziphine (1S)-juziphine (1S)-reticuline (+)N-methyl Laurotetanine (9S)-sesbiferine-(9S)-O-methyl-flavinantine	IC_{50} (µg/ml)	50 & 294 668 & 904 1240 & 1750 1510 & 1750 2130 & 1470 1990 & 1900 1900 & 2830 3900 & 2530 2710 & 3810 4100 & 3100 4090 & 4480 5800 & 3650 7150 & 2700 7100 & 9020	*P. falciparum* D6 and W2 respectively
Nauclea diderrichii	Rubiaceae	Bark	Alkaloid[82]	Alkaloid hydrochlorides	IC_{50} (µg/ml)	5	*P. falciparum* W2

contd....

Table 2. (*contd.*)

Plant species	Family	Part used	Type of alkaloid	Compound	Toxicity	Dose efficiency	*Plasmodium* sp and strain
Pachygone dasycarpa	Menispermaceae	Stem bark	Bisbenzyliso-quinoline alkaloids[83]	(+)-Angchibangkine (+)-O-Methylangchibangkine (+)-12-O-Methyltricordatine	IC_{50} (ng/ml)	306 & 265 326 & 204 17.1 & 63.0	*P. falciparum* D6 and W2
Picralima nitida	Apocyanaceae	Seeds	Indolemono-terpene alkaloids[84]	Akuammine	ED_{50} (ng/ml)	530 & 1.110	*P. falciparum* D6 and W2 respectively
Picrasma javanica	Simaroubaceae	Bark	Alkaloids[85]	4-methoxy-1-vinyl-β-carboline 6-hydroxy-4-methoxy-1-vinyl-β-carboline	ID_{50} (ng/ml)	2432 3280	*P. falciparum*
Pogonopus tubulosus	Rubiaceae	Stem bark	Alkaloids[86]	Tubulosine Pssychotrine Cephaeline	IC_{50} (μg/ml)	0.006 & 0.011 0.14 & 0.39 0.027 & 0.011	*P. falciparum* 2087 and INDO
				Tubulosine Pssychotrine Cephaeline	IC_{50} (mg/kg/day)	0.45 >2 6	*P. berghei* NK 65
Polyalthia nitidissima	Annonaceae	N.a.	Bisbenzyliso-quinoline alkaloids[71]	Lindoldhamine	IC_{50} (μM)	4.29	*P. falciparum* FcBl
Popowia pisocarpa	Annonaceae	N.a.	Bisbenzyliso-quinoline alkaloids[71]	O-methyl dauricine Dauricoline Popisonine	IC_{50} (μM)	1.96 2.09 1.11	*P. falciparum* FcBl
Psychotria camponutans	Rubiaceae	Stem and roots	Indole alkaloids[87]	1-Hydroxybenzoiso-chromanquinone 1-Acetyl-benzoiso-chromanquinone Benz(G)isoquinoline 5, 10 dione	IC_{50} (μg/ml)	2.66 6.02 0.84	*P. falciparum* K1
Strychnopsis thouarsii	Menispermaceae	Leaves	Bisbenzyliso-quinoline alkaloids[88]	7-O-dimethyl-tetrandrine	IC_{50} (nM)	740	*P. falciparum* FCM-29/Cameroon
Spirospermum penduliflorum		Stem and roots		Limacine		789	

Table 2. (*contd.*)

Plant species	Family	Part used	Type of alkaloid	Compound	Toxicity	Dose efficiency	*Plasmodium* sp and strain
Spirospermum penduliflorum	Menispermaceae	N.a.	Bisbenzyliso-quinoline alkaloids[71]	Limacine	IC_{50} (μM)	1.27	*P. falciparum* FcBl
Stephania erecta	Menispermaceae	Tubers	Bisbenzyliso-quinoline alkaloids[89]	(+)-N-Methyltelobine	ED_{50} (ng/ml)	97.4 & 255.7	*P. falciparum* D6 and W2 respectively
				(+)-1,2-Dehydrotelobione		306.7 & 256.4	
				(+)-2-Norisotetrandrine		66.1 & 45.3	
				(+)-Isotetrandrine		165.1 & 54.6	
				(+)-2-Northalrugosine		68.5 & 125.1	
				(+)-Thalrugosine		120.6 & 229.7	
				(+)-Homoaromoline		104.6 & 288.3	
				(+)-Stephibaberine		130.0 & 310.0	
				(+)-Daphnandrine		63.0 & 223.2	
				(+)-2-Norcepharanthine		46.6 & 129.4	
				(+)-Cepharanthine		140.4 & 294.8	
				(+)-2-Norobaberine		45.9 & 93.7	
				(+)-Obaberine		231.0 & 216.0	
Stephania pierrei	Menispermaceae	Tubers	Isoquinoline alkaloids[90]	(-)-Asimilobine	ED_{50} (ng/ml)	950 & 470	*P. falciparum* D6 and W2 respectively
				(-)-Isolameline		2560 & 1610	
				(-)-Xylopine		440 & 2270	
				(-)-Dicentrine		1260 & 2550	
				(-)-Nordicentrine		470 & 1030	
				(-)-Phanostenine		2010 & 2880	
				(-)-Cassythicine		2290 & 2260	
				(-)-Tetrahydropalmatine		>10000 & 5020	
				(-)-Capurine		4340 & 1910	
				(-)-Thaicanine		1610 & 550	
				(-)-Corydalmine		2840 & 840	
				(-)-Xylopinine		>10000 & >10000	
				(-)-Tetrahydrostephabine		2230 & 1940	
				(+)-Reticuline		4050 & 4470	
				(+)-Codamine		5800 & 4010	
				(-)-Delavaine		>10000 & 10000	
				(-)-Salutaridine		>10000 & 10000	
				(-)-Asimilobine-2-O-D-glucoside		>10000 & >10000	
				(-)-Anonaine		1290 & 1900	

contd...

Table 2. (*contd.*)

Plant species	Family	Part used	Type of alkaloid	Compound	Toxicity	Dose efficiency	*Plasmodium* sp and strain
				(-)-Roemeroline		3150 & 1780	
				(+)-Magnoflorine		>10000 & >10000	
				(-)-N-Methyltetrahydro-palmatine		>10000 & >10000	
				(+)-Oblongogine		>10000 & >10000	
Strychnopsis thousarsii	Menispermaceae	N.a.	Bisbenzyliso-quinoline alkaloids[71]	Fangchinoline	IC_{50} (μM)	0.93	*P. falciparum* FcBl
Strychnos henningsii	Loganeaceae	Stem bark	Indole alkaloids[91]	Holstiline	IC_{50} (μM)	31.5	*P. falciparum* K1
				Holstiine		32.7	
Stryhnos myrtoides	Loganiaceae	Stem bark	Indole alkaloids[92]	Strychnobrasiline	IC_{50} (μM)	73.08	*P. falciparum* FCM-29
				Malagashanine		69.12	
Strychnos usambarensis	Loganeaceae	Leaves	Indole alkaloids[91]	Isostrychnopentamine	IC_{50} (μM)	0.765	*P. falciparum* K1
				Strchnofoline		13.8	
				Strychnopantamine		0.164	
				Strychnopantamine methane		0.140	
				Sulphonaya		4.11	
				Usambarine		1.98	
				18,19-Dihydrousambartine oxalate		3.02	
		Root bark		5,6-dihydroflavopereirine		0.88	
				Usambarensine		0.023	
				3',4'-Dihydrousambarensine		5.345	
				Nb-methylusambarensine; Chloride		0.156	
Strychnos usambarensis	Loganeaceae	Leaves	Bisindole monoterpene alkaloids[93]	Usambarensine	IC_{50} (μg/ml)	0.38	*P. falciparum* K1
				3',4'-Dihydrousambarensine		0.01	
				Nb-methylusambarensine; Chloride		2.39	
				Usambarine		1.85	
				18,19-Dihydrousambarine oxalate		1.07	

contd...

Table 2. (*contd.*)

Plant species	Family	Part used	Type of alkaloid	Compound	Toxicity	Dose efficiency	*Plasmodium* sp and strain
				Strychnopentamine		0.09	
				Strychnopentamine methanesulphonate		0.09	
				Isostrychnopentamine base		N.T.	
				Akagerine		6.98	
				Tubulosine		0.020	
Strychnos variabilis	Loganiaceae	Leaf	Indole alkaloids[91]	O-Acetylisoretuline	IC_{50} (μM)	22.1	*P. falciparum* K1
		Leaf + Root bark		Isoretuline		~92	
				Retuline		~92	
				Retulinal/isoretulinal		36	
		Root bark		Isostrychnobaline		2.07	
				Diedehydro isostrychnoboline monomethane sulphonate		1.67	
				12'-Hydroxyisostrychnobiline monomethane sulphonate		1.58	
				Strychnobiline		1.03	
Toddalia asiatica	Rutaceae	Root bark	Alkaloid[31]	Nitidine	IC_{50} (μg/ml)	0.045	*P. falciparum* K39
				Dihydronitidine		1.03	
Triclisia patens	Menisperm-aceae	Wood	Bisbenzyliso-quinoline alkaloid[94]	Phaenthine	IC_{50} (nM)	704.87 365.85	*P. falciparum* T9-96 and K1
Triphyophyllum peltatum	Dioncophylle-aceae	Stem bark	Napthyliso-quinoline alkaloids[95]	Dioncophylline C	IC_{50} (μg/ml)	0.014 & 0.015	*P. falciparum* and *P. berghei*
				Dioncophylline B		< 1	
				Dioncopeltine A		< 1	
Triphyophyllum peltatum	Dioncophylle-aceae	Root	Napthyliso-quinoline alkaloids[64]	Dioncophylline B	IC_{50} (ng/ml)	228 & 224	*P. berghei* (Anka)
				Dioncophylline A		38 & 21	*P. falciparum* NF 54 respectively

N.A. — Tested but found to be not active; N.T. — Not tested; N.a. — Not available; Plants having significantly high efficacies are in bold words; Plants, frequently found in Indian subcontinent and have been scientifically studied are highlighted by (*); Acridone alkaloids from Rutaceae have been collectively derived from *Citrus, Glycosmis* and *Severinia*.

Table 3. A composite table of terpenes and quassinoids derived from plants showing their dose related effects *in vivo* for *P. berghei* and *in vitro* for *P. falciparum*. Quassinoids from *Ailanthus*, *Brucea* and *Eurycoma* species are quiet effective than those of others

Plant species	Family	Part used	Type of terpene	Compound	Toxicity	Dose efficiency	*Plasmodium* sp and strain
N.a.	**Simaroubaceae**	**N.a.**	**Quassinoid**[96]	Chapparin	IC_{50} (μg/ml)	0.180	***P. falciparum* K1**
				Glaucarubol		0.410	
				Glaucarubin		0.055	
				Ailanthinone		**0.009**	
				Holacanthone		0.007	
				Glaucarubinone		0.004	
				Undulatone		0.006	
				6-α-Sencioyloxy-Chaparrinone		0.008	
				Brusatol		0.003	
				Bruceantin		0.008	
				Bruceantinol		0.002	
				Isobruceine A		0.002	
				Simalikalactone D		0.0009	
				Samaderine		0.015	
N.a.	Meliaceae (*Azadirachta indica** and *Melia azedarach**)	Bark	Tetratriter-penoid[97]	Gedunin	IC_{50} (μM)	1	*P. falciparum*
Ailanthus altissima	Simaroubaceae	Woody parts	Quassinoids[98]	Ailanthinone	IC_{50} (μM)	0.084 & 0.090	*P. falciparum* K1 and T9-96 respectively
Ambrosia maritima	Asteraceae	N.a.	Sesquiterpene lactone[99]	Ambrosin	IC_{50} (μg/ml)	0.72	*P. falciparum* NF 54
Achillea millefolium L.	Asteraceae	N.a.	Natural peroxides[100]	α-peroxyachifolid	EC_{50} (μg/ml)	1	*P. falciparum* FCH-5
Anthemis nobilis L.	Asteraceae	N.a.		α-peroxyachifolid		5	
Aretemisia annua L.	Asteraceae	N.a.		Quinghaosu		0.01	

contd...

Table 3. (*contd.*)

Plant species	Family	Part used	Type of terpene	Compound	Toxicity	Dose efficiency	*Plasmodium* sp and strain
Artemisia abrotanum L.	Asteraceae	N.a.		Arteinculton		5-10	
Artemisia arbotanum	Asteraceae	Aerial parts	Sesqui-terpenes[101]	1(S*)-hydroxy-α-bisboloxide A acetate	IC_{50} (μM)	3.75	*P. falciparum* K1
				1(R*),(2R*)-dihydroxy-3,(15)-dehydro-2,3-dihydro-α-bisaboloxide A acetate		Not active at 50	
Artemisia maritima L.	Asteraceae	N.a.	Natural peroxide[100]	Arteinculton	EC_{50} (μg/ml)	5-10	*P. falciparum* FCH-5
*Andrographis paniculata**	N.a.	Whole plant	Diterpene[102]	Neoandrographolide Deoxyandrographolide Andrographolide Andrographisside	% inhibition at 10 mg/kg x 4 days	34.1 29.1 60.5 57.5	*P. berghei* NK 65
Bruceae javanica	Simaroubaceae	Fruits	Quassinoids[98]	Bruceantin	IC_{50} (μM)	0.013 & 0.008	*P. falciparum* K1 and T9-96 respectively
Bruceae javanica	Simaroubaceae	Fruits	Quassinoid[103]	Bruceantin	IC_{50} (μg/ml)	0.006 0.011 0.006	*P. falciparum* Wellcone, RFCR 3 and PKIG 6 respectively
Bruceae javanica	Simaroubaceae	Fruits	Quassinoid[104]	Bruceine A Bruceine B hydrate Bruceine C	ID_{50} (ng/ml)	13.94 18.95 6.95	*P. falciparum*
Bruceae javanica L.	**Simaroubaceae**	**Fruits**	**Quassinoids[105]**	**Bruceantin** Bruceantinol Bruceine A Bruceine B Bruceine C Dehydrobruceine A Brusatol	**IC_{50}** (μg/ml)	**0.0008** 0.002 0.011 0.003 0.005 0.011 0.046	***P. falciparum* K1**

contd...

Table 3. *(contd.)*

Plant species	Family	Part used	Type of terpene	Compound	Toxicity	Dose efficiency	*Plasmodium* sp and strain
				Bruceine D		0.015	
				Yadanzioside A		0.031	
				Yadanzioside C		N.T.	
				Yadanzioside F		5.00	
				Yadanzioside I		22.04	
*Caesalpinia bonducella**	Caesalpineaceae	N.a.	Diterpene[63]	β-caesalpin	Effective dose	1.6 mg/kg	*P. berghei*
Castela nicholsoni	Simaroubaceae	Woody parts	Quassinoid[98]	Chaparrin	IC_{50} (μM)	0.084 & 0.090	*P. falciparum* K1 and T9-96 respectively
Cephalotaxus harringtonia	Cephalotaxaceae	Seeds	Quasinoid[98]	Cephalotoxine	IC_{50} (μM)	0.004 & 0.004	*P. falciparum* K1 and T9-96 respectively
Cyperus rotundu	Cyperaceae	Tubers	Sesquit-erpenes[106]	α-cyperone	IC_{50} (μg/ml)	5.50	*P. falciparum* K1
				α-selinene		>50	
				β-selinene		>50	
				β-cyperene		5.56	
				humulene		>50	
Cyperus rotundus	Cyperaceae	Tubers	Sesquit-erpenes[107]	Patchoulenone	EC_{50}(M)	1.08×10^{-4}	*P. falciparum* K1
			Sesquiterpene peroxide	Caryophyllene-Oxide		3.45×10^{-4}	
				10,12-peroxycalamenene		2.33×10^{-6}	
				4,7-dimethyl-1-tetralone		8.62×10^{-5}	
Eupatorium rufescens	Asteraceae	Leaves	Bisabolane type sesquiterpene[108]	Zingiberene-3, 6-α-endoperoxide	EC_{50} (μg/ml)	10	*P. falciparum*
				Zingiberene-3, 6-β-endoperoxide		10	
Eurycoma longifolia	Simaroubaceae	Roots	Quassinoids[109]	Eurycomanol	IC_{50} (μg/ml)	3.81	*P. falciparum* Gombak A,
						3.53	Gombak C,
						2.48	ST9,
						4.89	ST12,

contd...

Table 3. (*contd.*)

Plant species	Family	Pa.. used	Type of terpene	Compound	Toxicity	Dose efficiency	*Plasmodium* sp and strain
						2.38 1.59 2.14 1.23 2.42	ST85, ST 148, ST 168, ST 179 and ST 197 respectively
				Eurycomanol2-o-β-d-glucopyranoside		2.25 0.389 0.99 3.49 0.68 1.15 1.187 1.37 1.20	
				13,18-dihydroeurycomanol		2.34 0.504 1.190 2.34 0.733 1.03 1.16 1.63 0.985	
Eurycoma longifolia	Simaroubaceae	Roots	Quassinoid glycoside[110] Aglycone	Eurycomanol-2-o-β-D-lycopyranoside Eurycomanol	IC_{50} (μg/ml)	1.590 1.544	*P. falciparum* Gombak A
Eurycoma longifolia Jack	Simaroubaceae	Roots	Quassinoid[111]	Eurycomalactone Eurycomanone Eurycomanone 6-hydroxy-5,6-dehydro-eurycomalactone	IC_{50} (μg/ml)	0.21 0.11 0.28 1.15	*P. falciparum* K1

contd...

Table 3. (*contd.*)

Plant species	Family	Part used	Type of terpene	Compound	Toxicity	Dose efficiency	*Plasmodium* sp and strain
Margaritaria discoidea	Euphorbiaceae	Root bark	Sesquit-erpene[106]	Securinine	IC_{50} (μg/ml)	5.35	*P. falciparum* K1
Nardostachys chinensis Batalin	Valerianaceae	N.a.	Narural peroxide[100]	Narducinon	EC_{50} (μg/ml)	1.4	*P. falciparum* FCH-5
Neurolaena lobata	Asteraceae	Leaves	Sesquiterpene lactones[112]	Neurolenin A Neurolenin B Neurolenin C/D (1:3) Neurolenin C/D (3:2)	IC_{50} (μg/ml)	0.336 0.263 2.794 0.236	*P. falciparum* NF54
Parthenium hysterophous	Asteraceae	N.a.	Sesquiterpene pseudoguian-olide[113]	Parthenin	IC_{50} (μg/ml)	1.289	*P. falciparum* K1
Picrolemma pseudocoffea	Simaroubaceae	Roots	Quassinoid[114]	Sergeolide	50% inhibition	0.002 to 0.006	*P. falciparum* FUP
					ED_{50} (mg/kg/day)	0.2	*P. berghei* NK 65
Rosa rugurosa Then.	N.a.	N.a.	Natural peroxide[100]	Rugasol A	EC_{50} (μg/ml)	1	*P. falciparum* FCH-5
Senecio selloi	Asteraceae	Leaves	Bisabolane type sesquiterpene[108]	Zingiberene 3,6-α-endoperoxide	ED_{50} (μg/ml)	10	*P. falciparum*
Simaba cedron	Simaroubaceae	Stem bark	Quassinoid[115]	Cedronin	IC_{50} (μg/ml) ED_{50} (mg/kg/day)	0.23 0.25 1.8	*P. falciparum* FCC-2 and FZR-8 respectively *P. vinkei petteri*, 279
Simaba guianensis	Simaroubaceae	Bark	Quassinoid[30]	Simalilactone D Gutolactone	IC_{50} (ng/ml)	1.6 & 1.5 4.0 & 4.1	*P. falciparum* W2 and D6 respectively
Simarouba amara	Simaroubaceae	Fruits	Quassinoid[116]	Ailanthione 2'-Acetylglaucarubinone	IC_{50} (μg/ml) &	9 & 1.25 8 & 2.19	*P. falciparum* K1 *P. berghei*, N

contd...

Table 3. (*contd.*)

Plant species	Family	Part used	Type of terpene	Compound	Toxicity	Dose efficiency	*Plasmodium* sp and strain
				Holacanthine	ED_{50}	7 & 1.70	
				Glaucarubinone	(mg/kg/day)	4 & 0.86	
U. lucida sp *lucida* Benth.	Annonaceae	Root bark Stem bark Leaves	Benzopyranyl sesquiterpene[117]	Lucidene	IC_{50} (μg/ml)	50	*P. falciparum* K1
U. pandensis Verdc.	Annonaceae	Root bark Stem bark Leaves	Indolese squit-erpenoids[117]	3-Farnesylindole	IC_{50} (μg/ml)	16.7	*P. falciparum* K1
				(6',7'-Dihydro-8,9'-dihydroxy)-3-farnesylindole		50.0	
				(8,9'-dihydroxy)-3-farnesylindole		2.86	
U. tanzaniane Verdc.	Annonaceae	Root bark Stem bark Leaves	Benzopyranyl sesquiterpene[117]	Tanzanene	IC_{50} (μg/ml)	50	*P. falciparum* K1
Vernonia brasiliana	*Asteraceae*	Leaves	Triterpene[118]	Lupeol	Reduction in parasitaemia	45% at 25 μg/ml & 0% at 15 mg/kg	*P. falciparum* BHz 26/86 and *P. berghei*
				β-amyrin		1% at 25 μg/ml & N.T.	
				Germanicol		15% at 25 μg/ml & N.T.	
Xanthium strumanium	Asteraceae	N.a.	Sesquiterpene lactone[119]	Tomentosin	IC_{50} (μg/ml)	7.8	*P. falciparum* K1
				8-epi-xanthatin-1β-5β,epoxide		7.8	
				8-epi-xanthatin		125	
				Xanthumin		31	
Zanthoxylum gelletii	Rutaceae	Root bark	Sesquit-erpene[106]	N-isobutyldeca-2, 4-dienamide	IC_{50} (μg/ml)	5.37	*P. falciparum* K1
				Fagarmide		12.34	
				Lupeol		>50	
				Sesamin		>50	
				4,7,8-trimethoxyfuro [2,3-b]-quinoline		>50	

N.A. — Tested, but found to be not active; N.T. — Not tested; N.a. — Not available; Plants having significantly high efficacies are in bold words; Plants, frequently found in Indian subcontinent and have been scientifically studied are highlighted by (*) ; Tetratriterpenoids from Meliaceae have been collectively derived from *Azadirachta indica* and *Melia azaderarch.*

Table 4. A composite table of aromatic and miscellaneous compounds derived randomly from plants showing their dose related effects *in vivo* for *P. berghei* and *in vitro* for *P. falciparum. Diosma* and *Melia* are much effective than others

Plant species	Family	Part used	Type of compounds	Compound	Toxicity	Dose efficiency	*Plasmodium* sp and strain
N.a.	Meliaceae		Limnoids[120]	Khayanthone	IC_{50}	50	*P. falciparum* K1
	(Azadirachta indica)*			Meldenin	(μg/ml)	inactive at 50	
	Cedrela odorata	Leaves		Nimbinin		0.77	
		Leaves		Vilasinin 1,3, diacetate		50	
		Stem bark		1, 1-β-acatoxykhivorin		50	
				3-desacetylkhivorin		50	
	Guarea multiflora	Leaves		Gedunin		0.72	
		Stem bark		1 1-β-acetoxygedunin		3.11	
		Stem wood		Dihydrogedunin		2.63	
		Fruits		Nimbin		50	
		Leaves		Salannin		1.74	
	Melia azaderarch)*	Stem bark		Carapolide A		inactive at 50	
				Carapolide E		inactive at 50	
				Rohituka mixture		inactive at 50	
				Guarea B		50	
				Evodulone		18.27	
				Desacetyldehydronomilin		inactive at 50	
				Limonin		inactive at 50	
				Prieurianin		14.08	
				Rohittukin		inactive at 50	
				Bussein mixture		50	
				Chukrassin mixture		50	
				Entandrophragmin		50	
				6-hydroxycarapin		inactive at 50	
				Dehydrocarapin		inactive at 50	
				Mexicanolide		inactive at 50	
*Citrus auranthium**	Rutaceae	N.a.	Limnoid[121]	Nomilin	IC_{50}	84.1	*P. falciparum* FCM
				Limonin	(μM)	>100	SU_1
Daphnai	Ranunculaceae	Bark	Coumarin[122]	Daphnetin	IC_{50} (μM)	25-40	*P. falciparum* FCR-3
Diosma pilosa	N.a.	N.a.	Coumarin	5,6,7-trimethoxycoumarin	IC_{50}	1.0	*P. falciparum*
			Flavone[121]	Quercetin	(μM)	6.4	FCM SU_1

contd...

Table 4. (*contd.*)

Plant species	Family	Part used	Type of compounds	Compound	Toxicity	Dose efficiency	*Plasmodium* sp and strain
Diospyros montana	Ebenaceae	Stem bark	Bisnaphth-oquinoid[123]	Diospyrin	IC_{50} (μM)	626	*P. falciparum* K1
Exostema caribaeum	Rubiaceae	Stem bark	Coumarin[44]	4',5'-dihydroxy-7-methoxy-4-phenyl-5,2'-oxidocoumarin	IC_{50} (μg/ml)	16.5	*P. falciparum* FCH-5/ Tansania
Fagaropsis angolensis	N.a.	N.a.	Limnoid[121]	Rutaevin	IC_{50} (μM)	82.2	*P. falciparum* FCM SU_1
Glycirrhiza glabra	Fabaceae	Roots	Chalcone[124]	Licochalcone A	IC_{50} (μg/ml)	0.6 & 0.6	*P. falciparum* 3D7 Dd_2
Haplophyllum tuberculatum	N.a.	N.A.	Lignan[121]	Justicidin A	IC_{50} (μM)	1.9	*P. falciparum* FCM SU_1
Hypericum calycinum	Guttiferae	Aerial parts	Phloroglucinol derivatives[125]	The compound is related to a number of phloroglucinol derivatives isolated from spp of Asteraceae	IC_{50} (μg/ml)	0.88	*P. falciparum* K1
Lippia multiflora	Verbanaceae	Dried plant material	Essential oil[126]	N.a.	ID_{50} (μg/ml)	1/12000	*P. falciparum* FcBl and F32
Melia azaderarch*	**Meliaceae**	**N.a.**	**Limnoid**[121]	Rutin **Gedunin**	IC_{50} (μM)	>100 **0.08**	***P. falciparum* FCM SU_1**
Milettia thonningii	Papillionaceae	N.a.	Flavonoids[121]	Robustic acid Alpinumisoflavone	IC_{50} (μM)	49.0 24.6	*P. falciparum* FCM SU_1
Morinda lucida	Rubiaceae	Stem bark	Anthra-quinones[127]	Digitolutein Rubiadin 1-methyl ether Damnacanthal	IC_5 (μg/ml)	12.92 8.10 9.20	*P. falciparum*

contd...

Table 4. (*contd.*)

Plant species	Family	Part used	Type of compounds	Compound	Toxicity	Dose efficiency	*Plasmodium* sp and strain
Peucedanum astruthium	Apiaceae	N.a.	Coumarin[121]	Ostruthin Osthol	IC_{50} (μM)	2.4 25.1	*P. falciparum* FCMSU_1
Spathodea campanulata	Bignoneaceae	Stem bark	N.a.[128]	Ursolic acid Tomentosolic acid 20-β-hydroxyursolic acid	% suppression	97 81 42	*P. berghei berghei*
Swertia chirata	Gentianaceae	N.a.	Xanthone[63]	Swerchirin	Effective dose	320 gm/kg to 1.6 mg/kg	*P. berghei*
Tabebuia ochracea spp *neochrysantha*	Bignoniaceae	Stem bark	Furanonaphtho-quinones[129]	5,8-dihydroxy-2-(1'-hydroxyl) derivative	IC_{50} (M)	8.40×10^{-7}	*P. berghei*
				2-acetyl-7-methoxy-8-hydroxy derivative		1.31×10^{-5}	
				5-and 8-hydroxy-2-(1'-hydroxyl)-ethylnaphtho-(2,3-b)-furan-4,9-dione		1.67×10^{-7} & 6.77×10^{-7}	*P. berghei* and *P. falciparum* FcB2
Tephrosia apollinea	Papillionaceae	N.a.	Flavonoids[121]	Tephroglabrin (-) Semiglabrin Semiglabrin (+) Glabratephrin	IC_{50} (μM)	31.4 30.7 32.9 9.0	*P. falciparum* FCMSU_1
Tetradenia riparia	Lamiaceae	Leaves and stem	Essential oil[130]	N.a.	IC_{50} (μg/ml)	27.5 & 50.3	*P. falciparum* D10 and FAC8 respectively
Uvaria faulknerae Verdc.	Annonaceae	Root bark Stem bark Leaves	Benzylated dihydrochal-cones[117]	Uvaretin Chamuaretin	IC_{50} (μg/ml)	3.49 45.52	*P. falciparum* K1
U. kirkii Hook and *U.* sp (Pande)	Annonaceae	Root bark Stem bark	Benzylated dihydrochal-cones	Uvaretin Diuvaretin		3.49 4.20	

contd...

Table 4. (*contd.*)

Plant species	Family	Part used	Type of compounds	Compound	Toxicity	Dose efficiency	*Plasmodium* sp and strain
U. leptocladon Oliv	Annonaceae	Root bark Stem bark	Benzylated dihydrochal-cones[117]	Uvaretin Triuvaretin	IC_{50} (μg/ml)	3.49 46.02	*P. falciparum* K1
		Leaves		Isotriuvaretin Chamuaretin		20.85 5.32	
U. lucida sp *lucida* Benth.	Annonaceae	Root bark Stem bark	Benzylated dihydrochal-cones	Uvaretin Diuvaretin		3.49 4.20	
		Leaves		Chamuvaretin		5.32	
U. pandensis Verdc.	Annonaceae	Root bark Stem bark Leaves	Cyclohexene epoxides	(+)-pandoxide (+)-Senepoxide (-)-Pipoxide 7-Hydroxy-4',5,6, 8-tetramethoxy-flavanone		>25 25 8.35 50	
Uvaria scheffleri Diels	Annonaceae	Root bark Stem bark Leaves	Chalcone	Glutenol		>50	
Uvaria sp (Pande)	Annonaceae	Root bark Stem bark	Benzylated dihydrochal-cones	Uvaretin Diuvaretin		3.49 4.20	
		Leaves		Guaiol		>50	
U. tanzaniane Verdc.	Annonaceae	Root bark Stem bark	Benzylated dihydrochal-cones	Uvaretin Isotriuvaretin Chamuvaretin		3.49 20.85 5.32	

N.A. — Tested, but found to be not active; N.T. — Not tested; N.a. — Not available; Plants having significantly high efficacies are in bold words; Plants, frequently found in Indian subcontinent and have been scientifically studied are highlighted by (*); Limnoids from Meliaceae have been collectively derived from *Azadirachta indica*, *Cedrela odorata*, *Guarea multiflora* and *Melia azaderarch*.

significant antiplasmodial activity as recorded in terms of IC_{50}, EC_{50}, MED_{50}, per cent inhibition ED_{50} etc. Reviews of antimalarial agents from plants in the early 1990's do not show any significant presence of antimalarial active principles among the top 30 extensively investigated medicinal plants[131]. However, a compilation of 87 plants which are found effective against *P. falciparum* and *P. yoelli* have only one plant, namely *Azadirachta indica* common with the earlier mentioned top 30 plants[132]. In most reviews of plants used as antimalarials, ethnobotanical listings have no scientific support[133]. Some studies have been conducted against *P. berghei* and cannot be applied to *P. falciaprum* in individual studies[134]. Of these numerous plants that have been forwarded to be candidates for antimalarial activity, only few have served the rigors of complete scientific and accountable evaluation. Crude extracts were the simplest of available medications and are still promoted by WHO policies as emerging alternate systems of medicine to reach the large populations not covered by formal medical care in remote areas. The Indian systems of Ayurveda and Siddha, Unani and Homeopathic have also extensively listed such plants and requires greater scientific support.

The extensive compilation of antimalarial plants brings out the more effective crude extracts in this review as shown in Table 1. Table 1 shows the best three dose efficacies of *Uapaca nitida* (IC_{50} 0.00130 μg/ml), *Brucea javanica* (IC_{50} 0.006 μg/ml) and *Bridelia catharctica* (ID_{50} 0.005 μg/ml). Of these *Brucea javanica* has been studied most extensively and its quassinoids were found to be effective at IC_{50} of 0.0009 μg/ml against *P. falciparum* K1. The plants of the family Simaroubaceae were also found to be the most effective at IC_{50} of 0.0009 μg/ml (Table 3). Alkaloids from Rutaceae, Ancistrocladaceae, Menispermaceae and Apocyanaceae show the most effective IC_{50}. The family Dioncophyllaceae shows the most effective IC_{50} at 0.014 and 0.015 μg/ml against *P. falciparum* NF 54 and *P. berghei* Anka respectively, while *Alstonia angustifolia* shows ED_{50} of 2.92 μg/ml (Table 2). Ursolic acid from *Spathodea campanulata* (Bignoniaceae) produced the highest suppression *in vivo* of 97% at 60 mg/kg/day. The other effective plants are *Melia azaderarch* from Meliaceae at ID_{50} of 0.08 μg/ml and *Glycirrhiza glabra* at IC_{50} of 0.6 μg/ml (Table 4).

While these plants are comparable to *Artemisia annua* at IC_{50} of 0.01 μg/ml from which artemisinin is commercially exploited the most extensively studied plants are of the family Simaroubaceae, namely *Brucea javanica* which appears frequently in research studies. *Eurycoma longifolia* also seems to be popular for research purposes with IC_{50} of 0.11 μg/ml. *Alstonia, brucea, Simarouba, Eurycoma* etc. are examples of some plants which have been studied frequently against different *Plasmodium* strains by different methods and without conclusive evidences even after two decades of scientific evaluation. Deriving cytotoxic/antiplasmodial activity ratios in these extracts is a desirable

parameter for showing selective antiplasmodial activity and can be attempted for these promising plants[115]

The isolation and elucidation of the chemical strucutre of different active components in the medicinal plants is of major value because it identifies a new lead compound. Such lead compounds can be developed further for chemical synthesis of candidate antimalarial drugs. Tables 2, 3 and 4 have listed the class of compounds which need to be further characterised pari-pasu along with its antiplasmodial activity which requires team work drawn from various disciplines ranging from Ethnobotany, Phytochemistry, Pure chemistry, Biological testing and their use in alternate system of medicine and eventually scientific and clinical evaluations. In the present competitive world, the pursuit of products specially aimed at tropical diseases is still not considered to be sufficiently profitable to feature among the research priorities of the pharmaceutical industry.

The century that started by relying on the bark of a tree to treat malaira is still in the search of newer natural products. After such extensive chemical characterization the only successful lead compound was a quinoline alkaloid from *Cinchona*. The newest structural characterization of the sesquiterpene peroxides belonging to a whole new family of compounds derived from the Chinese herbal remedy artemisinin is currently under investigation. Some of its derivatives, such as artemether, artesunate, and dihydroartemisin, are already in use in various commercial formulations. Further advances of research methodologies in direct screening for bioactive molecules from plant extract would avoid the tedious and slow methods of these earlier studies and also keep pace against multidrug resistant falciparum malaria.

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Changing Scenario of Malaria : A Study at Calcutta

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Sixty cases of *P. falciparum* and 165 cases of *P. vivax* were studied clinically along with species identification of parasite after examination of the blood slide by experts at Calcutta. It was observed that malaria had been changing its clinical profile. The classic paroxysm is evident only in 40% cases of *P. falciparum* and 47.27% of *P. vivax* malaria, but the difference between the two groups is not statistically significant. On the other hand continuous or remittent type of fever has been observed in 40% and 27.27% cases of *P. falciparum* and *P. vivax* respectively, while absence of classic paroxysms of fever, in association with splenomegaly when present, poses a diagnostic difficulty with enteric fever. Association of jaundice in 40% and 9.09% cases with *P. falciparum* and *P. vivax* respectively along with hepatomegaly in 80% and 63.63% in them in conjunction with nausea and/or vomiting leads to clinical mimicry with infective hepatitis. Splenomegaly which has been described as cardinal feature of malaria was observed in 40% cases with *P. falciparum* and only in 18.18% cases of *P. vivax* malaria and this is a clear deviation from earlier description and this difference between the two groups is highly significant at 99% level of confidence. Co-existent enteric fever was observed in 3.33% of falciparum and 2.6% of vivax malaria, though this difference is not statistically significant. Acute respiratory distress was observed in 6.6% of *P. falciparum* malaria only. Oliguria with impaired renal function was noted in 5% cases of *P. falciparum* malaria. The present study has also noted convulsion or coma in 8.33%, purpura with disseminated intravascular coagulation in 3.33% and black water fever in 3.33% cases in falciparum malaria which were not observed in cases with vivax malaria and these differences are statistically significant. However, stupor with bilateral extensor planter response was observed in two cases (1.3%) of vivax malaria.

Keywords: Calcutta, *P. falciparum, P. vivax*, Urban malaria

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INTRODUCTION

Malaria is the commonest vector-borne parasitic disease in the world, being endemic in 103 countries around the globe with population at risk of more than 2.5 billion and causing 1 to 3 million deaths annually[1-3]. There has been a major resurgence of malaria in India associated with developing resistance of anopheline mosquito to insecticides and increasing prevalence of chloroquine resistance in *Plasmodium falciparum* malaria[4]. In spite of phenomenal progress in medical science, malaria still continues to be one of the major killers in tropical countries[5]. Along with changing character of the vector, malaria specially falciparum has also shown a changing profile of clinical presentation and the accompanying acute and chronic complications and its response to treatment[6]. With this idea in background, we have analysed the changing clinical profile of malaria as observed in Calcutta.

MATERIALS AND METHODS

Sixty cases of *P. falciparum* malaria and 165 cases of *P. vivax* malaria diagnosed from O.P.D. and indoor admissions of Medical College and School of Tropical Medicine, Calcutta, were randomly selected during the period from June 1994 to May 1997, for the present study. A thorough history mentioning the age, sex, fever with its type, range, chill, rigor, sweating, headache, nausea and/or vomiting, dizziness, arthralgia, myalgia, cough and cold, acute respiratory distress, oliguria with impairment of renal function, delirium, convulsion, coma and history of passing red or black urine were meticulously noted and recorded. The presence of anaemia, jaundice, skin rashes including haemorrhagic manifestations, splenomegaly, hepatomegaly and other positive findings in respiratory, cardiovascular or nervous system were also recorded. The cases were diagnosed for malaria by demonstration of malaria parasite by thick and thin film after proper staining along with other necessary investigation. Cases clinically thought to be malaria positive but without demonstration of malaria parasite in the peripheral blood were excluded from the study. The clinical features of falciparum and vivax malaria were tabulated separately and compared. All cases were initially treated with chloroquine with the WHO recommended dose. Response to treatment was noted and recorded clinically in each case. Those cases which did not respond to the above regime clinically or where the condition specially the level of consciousness in *P. falciparum* cases were deteriorating, were treated with quinine 600 mg thrice daily for 7 days orally or I/V in cases in coma (or artemisinin in selected cases) but with change to oral medication as soon as the level of consciousness permitted.

RESULTS

It is evident from the Table 1, all the cases of both *P. vivax* and *P. falciparum* were febrile but 36 cases (60%) of *P. falciparum* had intermittent temperature compared to 120 cases (72.73%) of vivax. It is also noted that 24 (40%) cases of *P. falciparum* and 45 (27.27%) cases of *P. vivax* had continued or remittent fever. Chill and rigor were ob-

served in 48 (80%) and 24 (40%) cases of *P. falciparum* and 150 (90.90%) and 78 (47.27%) cases of *P. vivax* respectively. Headache was associated in 80% cases of *P. vivax* and 100% cases of *P. falciparum.* Dizziness was more common in *P. falciparum* (60% cases) than in *P. vivax* (38.18% cases). Cough and cold was present in 32 (53.33%) cases with *P. falciparum* and 75 (45.45%) cases with *P. vivax.* Coma or convulsion was observed in 5 (8.33%) cases of *P. falciparum* and none with *P. vivax.* Stupor with bilateral extensor planter response and sluggish pupillary response were found in two cases which proved to be vivax only.

Jaundice was remarkably common in *P. falciparum* in 24 (40%) as opposed to 15 (9.09%) of *P. vivax* cases. Splenomegaly was recorded in 24 (40%) cases of *P. falciparum* as compared to 30 cases (18.18%) of *P. vivax* cases. Hepatomegaly was present in 48 (80%) cases of *P. falciparum* and 105 (63.63%) cases of *P. vivax* . Only two cases (3.33%) of *P. falciparum* had purpuric spots with evidence of disseminated intravascular coagulation, while black water fever was also observed in only two cases of *P. falciparum* (3.33%). Amongst falciparum cases 3 (5%) had oliguria with renal impairment, 4 (6.6%) had acute respiratory distress. Enteric fever was associated with 2 (3.33%) cases of *P. falciparum* and 4 (2.6%) cases of *P. vivax* malaria. All the cases of *P. vivax* responded to the standard chloroquine regime but 55 cases (91.66%) of *P. falciparum* malaria clinically responded to chloroquine therapy, the remaining cases needed quinine oral or I/V, or artemisinin in cases complicated with ischaemic heart disease with atrio-ventricular conduction defect where quinine was avoided.

DISCUSSION

Fever was encountered in all patients with either *P. falciparum* or *P. vivax* malaria. But typical paroxysm at the time of diagnosis was present in 40% cases with *P. falciparum* malaria and 47.27% of *P. vivax* malaria though the difference was not statistically significant. This finding, however, indicates that more than 50% of the cases do not develop typical paroxysm at the time of aetiological diagnosis, and this is a deviation from the frequent description of common classical paroxysm in text book. Periodicity however with alternate day fever was more commonly encountered with 60% although this is not statistically significant. A sizable proportion, of *P. falciparum* (40%) cases had continued or remittent temperature and the percentage with *P. vivax* being 27.27% (Table 1). This type of temperature raises confusion with the common enteric fever in tropical countries like ours, causing a clinical diagnostic dilemma, specially with an associated splenomegaly which may be common in both the conditions. This is why co-prescription with ciprofloxacin and chloroquine are frequently seen in clinical practice. Moreover the present series has encountered co-existing enteric fever in 3.3% cases of falciparum malaria and 2.6% of vivax malaria. It is worth mentioning that nine cases of cerebral malaria with co-existent enteric fever has been reported by Singh[7]. Positive widal test in 15.2% cases of cerebral malaria in Loni areas in Ahmednagar district of western Maharashtra has also been reported dur-

Table 1. Relative incidence of symptoms and signs of *P. falciparum* and *P. vivax* cases

Systems	Symptoms and signs	No. of cases (%)		Statistical significance between the two groups
		Group A *Pf* (n = 60)	Group B *Pv* (n = 165)	
General	Fever	60 (100)	165 (100)	
	Intermittent fever	36 (60)	120 (72.73)	NS
	Continued or remittent	24 (40)	54 (27.27)	NS
	High rise of temperature	20 (33.33)	60 (36.36)	NS
	Low grade fever	40 (66.66)	105 (63.63)	NS
	Typical paroxysm	24 (40)	78 (47.27)	NS
	Chill	48 (80)	150 (90.90)	*
	Rigor	24 (40)	78 (47.27)	NS
	Associated enteric fever	2 (3.33)	4 (2.6)	NS
	Sweating	48 (80)	90 (54.54)	**
	Headache	60 (100)	132 (80)	**
	Dizziness	36 (60)	63 (38.18)	**
	Arthralgia	32 (53.33)	105 (63.63)	NS
Gastro-intestinal	Nausea and/or vomiting	36 (60)	75 (45.45)	*
	Abdominal pain/Diarrhoea	6 (10)	15 (9.09)	NS
	Jaundice	24 (40)	15 (9.09)	**
	Splenomegaly	24 (40)	30 (18.18)	**
	Hepatomegaly	48 (80)	105 (63.63)	*
Respiratory	Cough and cold	32 (53.33)	75 (45.45)	NS
	Acute respiratory distress	4 (6.6)	0 (0)	**
Neurology	Convulsion/Coma	5 (8.33)	9 (0)	**
	Stupor with neurological sign		2 (1.3)	
Haematology	Anaemia	48 (80)	75 (45.54)	**
	Purpuric spots in legs with DIC	2 (3.33)	0 (0)	*
Renal	Oliguria with impairment of renal function	3 (5)	0 (0)	*
	Black urine	2 (3.33)	0 (0)	*
	Response to chloroquine	55 (91.66)	165 (100)	**

*Significant at 95% level of confidence; ** Significant at 99% level of confidence; NS — Not significant; *Pf* — *P. falciparum*; *Pv* — *P. vivax*.

ing January 1993 to December 1994 by Khubnani *et al.*[8] In our series chill was present in 80 and 90.90% cases of *P. falciparum* and *P. vivax* malaria respectively, but rigor was found in less than 50% in both groups and the difference is statistically significant. It becomes evident that sensation of chill with fever has a strong association with both types of malaria.

The next important clinical feature is headache which was found in 80% cases with *P. vivax* and 100% cases with *P. falciparum* but this has no diagnostic value, being non-specifically present in any febrile condition. Another important clinical feature was associated with cough and cold, mimicking respiratory tract infection which was encountered in 53.3% of *P. falciparum* and 45.45% of *P. vivax* malaria and this interferes with clinical diagnosis and even after aetiologically, diagnosis of malaria becomes established. The question remains about the pathogenesis of such respiratory symptoms in almost 50% cases of malaria. It is also not clear whether there is associated respiratory tract infection and hence other antibiotic needs to be added along with treatment of malaria. Convulsion and coma were not encountered in *P. vivax* malaria but it was seen in 8.33% in *P. falciparum* cases and this has statistical significance of 99% level of confidence and it appears that alteration in level of consciousness is a strong clinical pointer to the probable clinical diagnosis of *P. falciparum* malaria. However, we had the experience of *P. vivax* malaria presenting with stupor and bilateral extensor planter response with sluggish pupillary reaction in two cases (1.3%). This could be due to co-existent falciparum infection which was probably missed or it could be due to heavy parasitaemia which was not studied in our case. Then again it justifies thorough clinical and ancillary investigation to differentiate from intracranial infections.

Jaundice was found in 40% cases with *P. falciparum* and 0.09% of *P. vivax* cases and the difference in the two groups is statistically significant at 99% level of confidence, and this in association with hepatomegaly in 80% cases with *P. falciparum* and 63.63% of *P. vivax* specially in association with nausea or vomiting brings the possibility of infective hepatitis as the differential diagnosis which needs to be excluded prior to institution of antimalarial therapy, with the help of appropriate liver function tests. Splenomegaly, however, was obtained in only 18.18% cases of *P. vivax* and 40% cases of *P. falciparum* in contradiction to the common description of splenomegaly in 85 to 100% of all malaria cases[9,10] and the difference in two groups in statistically significant at 99% level of confidence. Also this is in agreement with the description of the 'small spleen' in malaria by Chauhan *et al.*[11], who were unable to elicit splenomegaly during an acute attack of malaria specially in cases who had already suffered from earlier malaria disease. In general splenomegaly appears after two or three episodes. Greater number of splenomegaly in falciparum cases raised the suspicion of quicker rate of enlargement of spleen. Hepatomegaly was more frequent than splenomegaly in all cases of malaria. This could be explained by the pre-

existing causes of hepatomegaly like amoebiasis etc. which were not excluded in all the cases. Detection of purpuric spots vasculitis due to disseminated intravascular coagulation passage of black urine in 3.33% cases of *P. falciparum* indicate that they are rate accompaniments of *P. falciparum* malaria which are amenable to antimalarial therapy after early diagnosis . In two cases of black water fever, there was history of intake of primaquine without prior G-6-PD screening test.

Acute respiratory distress was seen in 6.6% of falciparum malaria. Oliguria with renal impairment was noted in 5% cases of *P. falciparum* malaria only as compared to 50% patients of complicated falciparum malaria reported with renal dysfunction by Nand *et al.*[12] in Rohtak. Jaundice was present in 40% of *P. falciparum* and 9.09% of *P. vivax* malaria as compared to its presence in 100% cases of complicated falciparum malaria[12].

The present study has also revealed that all cases of *P. vivax* responded to the schedule chloroquine dose but 8.34% of *P. falciparum* cases needed therapy other than chloroquine to have clinical cure of their ailment indicating either severe falciparum infection or perhaps the evolving chloroquine resistance in the studied group, which was not proved before switching to alternative therapy. It is note worthy to mention that clinicians often feel shaky whenever predicted clinical response is not obtained in falciparum cases and switch over to other antimalarials. We also did not think it is ethical to deny our patient the effect of alternative antimalarials whenever the clinical response was not a text book picture. Costly alternative antimalarials were rarely required, only in individualised cases depending on status of other vital organs.

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Short Note

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Factors Influencing the Larvicidal Activity of Bacterial Toxin

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Keywords : Bacteria, Factors, Larvicidal activity, Toxin

Many species of mosquito play the important role as being the vectors carried diseases to man, which remain the public health problems in Thailand[1]. Control measures for those vectors providing effectiveness and cause less harmful effects to people and environment have to be critically selected. Mosquito control by using biological control agents has been accepted as the most safe larval control among the available control measures[2]. Current bacterial larvicides for controlling mosquito larvae and related species has gained more interest during the past few decades. However, there are many factors concerning the virulence of bacterial toxin which can be summarized as follows.

Bacterial toxin

The bacterial toxin can actually be divided into five major groups which consisted of delta endotoxin, beta exotoxin, alpha exotoxin, gamma exotoxin and louse factor[3,4]. Exotoxin is the water soluble toxic protein which is gradually produced and released during bacterial growth. It can be inactivated by unappropriate temperature. Endotoxin is solubilized in alkaline solution but stable to heat and chemicals.

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Some exotoxin particularly a water soluble, thermostable exotoxin or thuringiensis, at high dosage had adverse effects on birds and mammals while at low dosage had a broad spectrum effects on invertebrates since they could interfere the biosynthesis of RNA and some inhibited the function of RNA polymerase[5]. Thus, the bacterial strains to be used for commercial productions must be those that do not produce beta exotoxin.

The toxin produced by bacteria is encoded by the gene which results in the variation on gene type of bacterial toxin. Normally, the structure of toxin consists of primary and tertiary structure. Toxin of primary structure are encoded by *cry* gene and *cyt* gene such as *cry I*, *cry II*, *cry III* and *cry IV*. Gene products can express their specific biological activity against different groups of insect. For example, products of *cry I* gene are toxic to lepidopterans while toxin encoded by *cry IV* are active toward dipterans[6].

Bacterial toxins are glycoprotein[7]. The N- and O-glycosylation can occur at multiple sites of the primary structure which glycosylated moieties are believed to play an important role in toxicity to insects[8].

Influence of media on virulence of bacterial toxin

The delta endotoxin of *B. thuringiensis* are packaged into parasporal inclusions. The structure of parasporal inclusions are different among subspecies. It is believed that conditions used for cultivation of bacteria influences the structure of parasporal inclusion[6] for example it was reported that among the six media compositions proposed for production of *B. thuringiensis*, basal medium containing 0.2% yeast extract, 0.1% K_2HPO_4 and 0.1% KH_2PO_4 with 1% greengram and 1% cane sugar provided the highest potency of toxin[9].

Formulation of bacterial larvicide products

As mode of action of bacterial toxin is through oral ingestion, so formulations of the bacterial larvicide are the tools to convey toxin to insect larvae. Formulation can support and increase the ease of handling, provide long shelf life and protect the toxin protein from UV light. Moreover, it can maximize contact of target larvae to bacterial toxin and prolong residual activity[10].

The study on efficacy of aqueous formulation and slow release formulation of *B. sphaericus* against *Cx. quinquefasciatus* indicated that the slow release in briquet formulation provided the best larval reduction for three weeks while reduction of the other suspension and pellet formulations were only three days[11]. Since depth of water showed remarkable influence on persistence of bacterial larvicides in the breeding sites, once application, the bacterial cells would gradually sink down. Upon the behaviour of larval feeding, any formulation that could bring the bacterial toxin directly to larvae and remained lethal dose at the feeding zone, would be considered as important factor rather than

the dosage at the time of application.

Effect of larval instar

Most of the previous studies agreed that susceptibility of mosquito larvae decreased with increasing instar[13-15] but later study[16] reported that larval instar was not the reason since it was indicated that each larval instar of *Ae. aegypti* was susceptible to *B. sphaericus* at nearly the same level.

Effect of food on larvicidal activity

Food also influenced the activity of bacterial larvicide. It was observed in the laboratory that the larval mortality decreased with the increasing availability of foods[17]. The consumption rate was different among mosquito species[18]. Thus, concentration of bacterial larvicide when applied, was not considered as important factor as compared to the time consuming for toxin accumulation and proceeding lethal dose[17].

Temperature

The relation between temperature and mortality of mosquito larvae has been remarkably observed. As the temperature decreased about 10°C, the increase in 5-6 fold of LC_{50} value could be observed[16]. This decrease in temperature might have resulted in increased rate of ingestion as well as rate of release and uptake of bacterial toxin in larval gut[14-16].

Effect of pH

pH had a great effect on the activity of bacterial toxin[19] because insecticidal activity was dependent upon the solubilization and ingestion of protoxin under alkaline environment of larval midgut[20]. It was reported that each bacterial toxin could be solubilized at specific pH[6]. However, the activity of endotoxin could be suppressed if pH was reversed to low alkalinity[21].

Effect of sewage affluent

The activity of microflora as well as solids suspending in the water were found affecting the effectiveness of bacterial larvicide. In the presence of microflora, larval mortality became very low as compared to those observed in the tap water although the same concentration was performed[19]. By treating microflora with autoclave, the mortality remained lower than those in tap water. It could be explained that the degree of pollution affected the persistence of bacterial toxin which agreed to the above report[22]. With increasing degree of pollution, larval reduction became short. However, the persistence and recycling potential of pathogenic bacteria depended upon the degree of water pollution because bacteria used the cadavers as medium for growth and complete the lifecycle then the later bacterial generation would be released to the surroundings after decomposition of the cadavers which occurred rapidly in the sewer waters[23]. Contrary to the above mentions, it was reported that *B. sphaericus* was found more effective against mosquito larvae in polluted water than in clean water[24]. It was believed that not only *B. sphaericus* caused mortality to larvae but also some certain chemicals in those water might be toxic to larvae.

Influence of soil constituents and silt particle on toxin

It was proposed that persistence of *B. thuringiensis israelensis* in nature was so low because bacterial toxin was probably adsorbed to silt particle[25]. However, this conclusion was supported by the studies reported by Van Essen and Hembree[26] that in the presence of clay particle, the persistence sharply dropped as compared to the absence of clay particle.

Effect of sunlight to bacterial toxin

Sunlight has lesser degree of influence on the activity of bacterial toxin. The light intensity of 7.3 lux for normal laboratory would not have any affect on the activity of bacterial toxin. Only six hours exposure to 22,000 lux of direct sunlight inhibited the activity of pathogenic bacteria which could be due to the occurrence of damage on protein composition[19,27].

Effects of bioassay procedure on mortality

Result from toxicity tests using individual and grouped larvae were different. It was reported that the concentration of bacterial larvicide required to provide median lethal concentration to larvae testing individually was rather high about 2-folds as compared to 25 grouped larvae eventhough exposure times were the same. Moreover, volume also affected the mortality. Under the conditions of larval number per volume of bacterial suspension such as one larva per 1 ml, one larva per 6 ml and 25 larvae per 150 ml, it was indicated that the former condition required 300 µg/ml to provide LC_{50} while only 70 and 30 µg/ml were enough to induce LC_{50} to the two latter conditions[28].

Recycling potential

It has been suspected that the bacterial larvicide can survive and grow in the natural environment or not. Although bacterial larvicides were generally the spore-crystal complex and after larval feeding, the spores could germinate and complete its life cycle within the cadavers but unfortunately cadavers were not suitable as sources of essential nutrients so toxin produced became irregular[25,29].

Resistance to bacterial toxin

Resistance to certain chemicals among insect population has caused big problem for control programme of target species. It has not been doubtful whether resistance to bacterial toxin can be risen among the insect larvae. Resistance to *B. thuringiensis israelensis* in the population of *Ae. aegypti* was observed. Results indicated that after 15 generations of selection, no resistance was noticed[30]. But resistant ratio to bacterial larvicide among the chemical-resistant strains remarkably varied[31].

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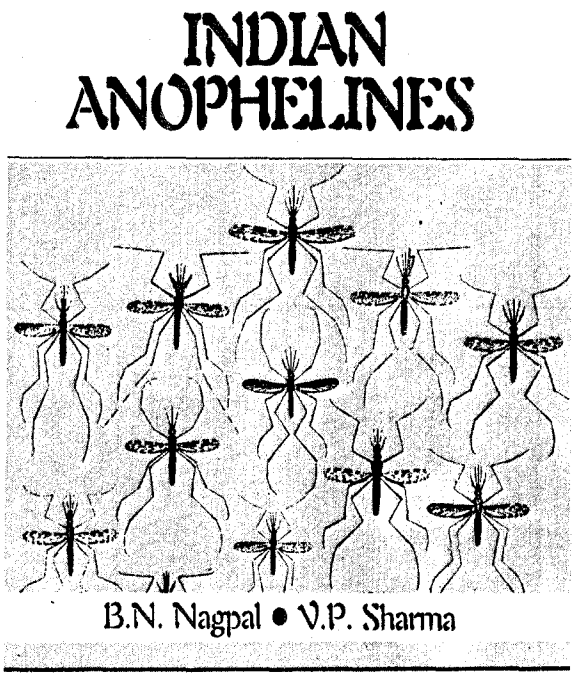

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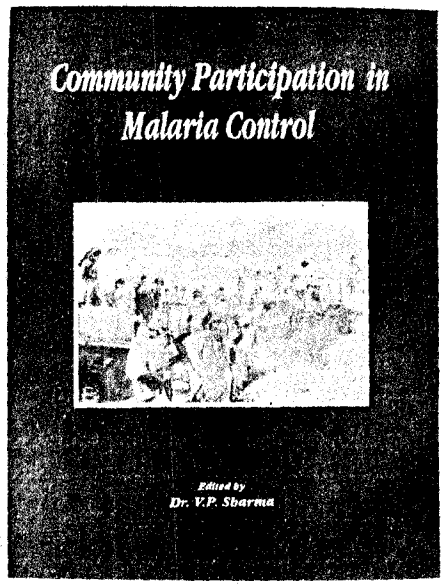

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