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Identification and evaluation of Peruvian plants used to treat malaria and leishmaniasis

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Abstract

Households in eleven geographically and ethnically distinct areas in Loreto, Peru, were interviewed about their knowledge and use of plants, for the treatment of malaria and leishmaniasis. The survey resulted in 988 use records representing 118 plant-taxa for malaria and 289 use-records representing 85 plant-taxa for leishmaniasis. In both cases the 10 most frequently reported taxa accounted for about half of all the use-records. Plant material was collected and extracts were screened for in vitro inhibition of *Plasmodium* and *Leishmania* parasites. In the case of *Plasmodium*, extracts of 11 of the 13 most frequently reported plants showed significant growth inhibitory activity, while only a few plant extracts inhibited the growth of *Leishmania* parasites.

Keywords: In vitro screening; Leishmaniasis; Loreto; Malaria; Peru; Use-records

1. Introduction

The global extent and consequences of diseases such as malaria and leishmaniasis are alarming. With a rising number of clinical cases malaria is, at present, among the world's most devastating infectious diseases, infecting hundreds of millions of people and causing up to 3 million deaths annually (Sachs and Malaney, 2002). The increasing resistance of malaria causing *Plasmodium* parasites towards the drugs of first choice adds to the severity of the problem. In the case of leishmaniasis only one new drug (miltefosine) (Croft et al., 2005) has been registered for decades. Antiparasitic compounds found in plants used in tribal medicine can be valuable as templates for new drugs. In fact most of the drugs that have been used against malaria are directly or indirectly derived from natural products (Christensen and Kharazmi, 2001). In this study the emphasis has been put on malaria because the different populations in the Loreto department of Peru use more herbal medicines to treat malaria than leishmaniasis. Also the literature on malaria is more extensive and the impact of malaria on society is far more severe than that of leishmaniasis.

Malaria was introduced to the Americas by the Europeans. The introduction led to a dramatic reduction of indigenous populations during the first centuries after the European arrival (Denewan, 1976). Malaria has since been one of the principal health hazards in tropical America (Newman, 1976). Consequently indigenous people and descendants of Europeans have experimented with local plants in order to find efficient treatments for the disease. Due to limited exchange of knowledge and because of lower levels of infection, relatively isolated groups of indigenous people typically use fewer medicinal plants than groups with more outside contact. The Waorani of the Ecuadorian Amazon presently use far more medicinal plants than they did before the first peaceful contact in the 1970s (David and Yost, 1983; Céron and Montalvo, 1998). The Yanomami along the Venezuela-Brazil border were first exposed to malaria in the early 1930s and obviously had no need for drugs against the disease before that time. A recent study has demonstrated, that they currently use at least 10 medicinal plants specifically against malaria (Milliken and Albert, 1996).

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Since western tropical South America is the floristically richest regions in the world (Myers et al., 2000), the search by native populations for efficient drugs ought to lead to a higher number of effective remedies than similar searches in floristically poorer regions an hence could yield diverse new templates for drug development. Numerous Latin American plants have been reported used to treat malaria or to reduce malarial fevers (Blair et al., 1991; Milliken, 1997). Few of these plants have been reported, however, as part of studies performed with the specific goal of mapping the use of herbal medicine against malaria. Anti-malarial plants have been investigated in two areas populated by Mestizos in the Amazon basin of Brazil (Brandão et al., 1992), and among various indigenous groups in the lowlands of Bolivia (Muñoz et al., 2000a,b,c; Deharo et al., 2001; Bourdy et al., 2004), and in French Guiana (Bertani et al., 1995; Vigneron et al., 2005). Many more anti-malarial plants have been recorded as part of general surveys of medicinal plants used in specific geographical areas or by specific ethnic groups. In the case of Peru surveys of medicinal plants covering the entire country (Brack, 1999), the Amazon region (Rutter, 1990), the southeastern Amazon department Madre de Dios (Desmarchelier and Witting, 2000), and the northeastern Amazon Department Loreto (Rutter, 1990; Duke and Vasquez, 1994; Mejia and Rengifo, 1995; Silva et al., 1995; Pinedo et al., 1997) have been published. Among the Peruvian ethnic groups the medicinal plants used by the Shipibo Amerindians in the Ucayali department have been reviewed (Arevalo, 1994), and Lewis (Lewis et al., 2000) discuss plants used by the Aguaruna Amerindians in the Amazon department but does not refer to specific plant species.

After being almost eradicated in the 1960s the incidence of malaria in Peru has increased dramatically. In the Loreto department malaria increased 50-fold from 1992 to 1997, and in 1997 a total of 121,268 cases were reported out of a population of approximately 800,000 (Guarda et al., 1999). Compared to the overwhelming number of malaria cases the incidents of leishmaniasis are much fewer. In Peru the average annual number of cases recorded between 1996 and 1998 were 2668 (Davies et al., 2000). The effect of a leishmaniasis infection on the individual, however, should not be underestimated. Visceral leishmaniasis caused by *L. donovani* can be lethal if not treated. Much fewer Latin American plants have been reported as useful for the treatment of leishmaniasis than for treatment of malaria. A few studies focusing on herbal remedies for this disease have been undertaken in Bolivia (Fournet et al., 1994; Weniger et al., 2001) and in Colombia (Weniger et al., 2001). General studies of medicinal plants rarely provide more than a few records regarding leishmaniasis. Informants have to be asked specifically in order to recall any plants used to treat this fairly uncommon disease.

The present work investigates plants used against malaria and leishmaniasis by both native and non-native people of the Loreto department in Peru (Fig. 1). Loreto, located in northeastern Peru, is the largest Peruvian department covering ca. 269,000 km^2. With ca. 800,000 inhabitants the department is sparsely populated, and it remains covered with extensive lowland Amazonian rainforest. The rural population is made up of nearly 30 indigenous groups speaking different native languages

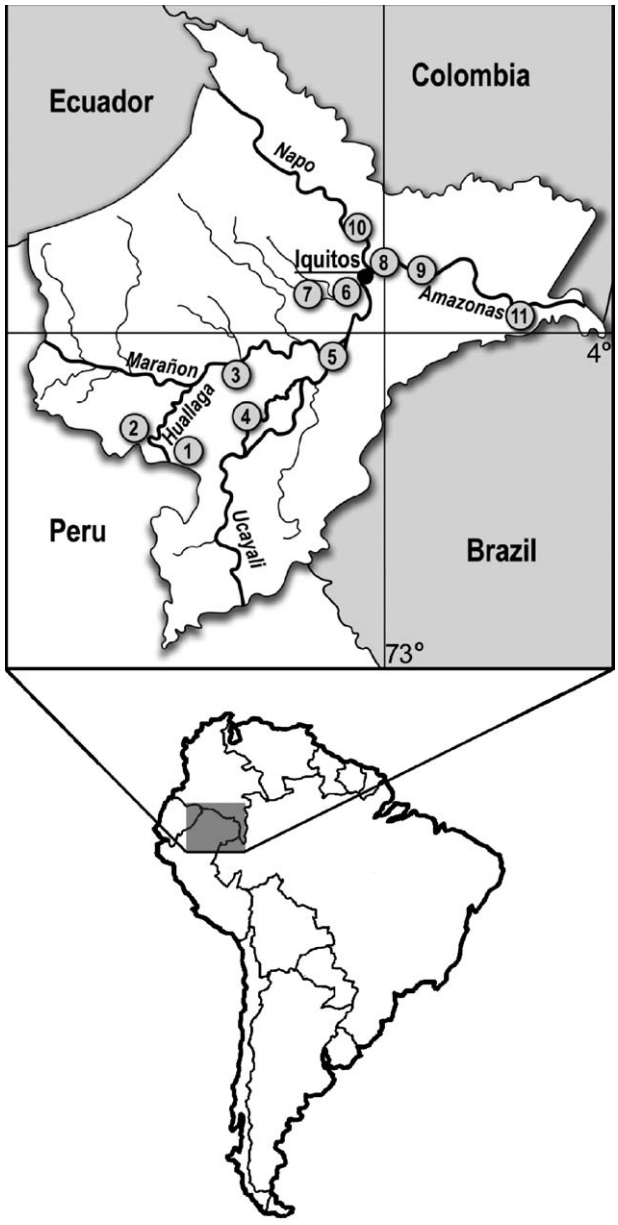

Fig. 1. Location of the study area in South America; and detail map of the study area Loreto constituting North Eastern Peru. The show shows the location of the 11 study zones where plants used to treat malaria and leishmaniasis were studied by interviewing individual households. The names of the major rivers and the location of the departmental capital Iquitos also appear.

and a Spanish-speaking majority. Since the latter are predominantly descended from indigenous people, they also preserve much traditional knowledge. The lack of roads in the region necessitated that this study focused on communities located along, or easily accessed from the major rivers of the region (Fig. 1, Table 1). On the other hand, these communities are interesting because this accessibility has resulted in a long history of involvement with the outside world and an equally long history of exposure to malaria. Furthermore, communication with the outside world has taught these communities the use of non-local herbal medicines. The population mostly knows malaria as paludismo, and leishmaniasis as uta or chagas.

The present study is based on the hypothesis that positive experiences with medicinal plants gradually diffuse throughout local and regional areas. As a consequence the more frequently used and widely known medicinal species are more likely to have an effect and hence contain active substances. More specifically it was envisioned that the project would both serve to investigate the regional knowledge of anti-protozoan medicines, and help discover potential new drug leads. Fieldwork was performed in separate zones throughout the Loreto Department. Within each of the study zones informants were asked about their knowledge and experiences regarding herbal remedies. Frequently reported plant species were collected for phytochemical analysis, and plant-extracts were screened for ability to inhibit growth of *Plasmodium* and *Leishmania* parasites in vitro. Finally isolation and characterization of active principles were undertaken for the more potent extracts.

The fieldwork was performed through 1996–1997; extraction and in vitro screening of plant materials during 1997–1998, and the phytochemistry of species have been investigated until the present. Part of the field work performed in the areas near Iquitos has been published (González et al., 1999, 2000) (nos. 6–10 in Table 1), but this paper for the first time collates the entire material and makes it available to a wider international forum.

2. Methodology

2.1. Field program

Plants reported used to treat malaria and leishmaniasis were identified and collected throughout northeastern Peru. The studies were undertaken in 11 geographically distinct research areas distributed throughout the Loreto Department (Fig. 1). Non-native populations live in six of the areas and predominantly indigenous people in the remaining five. Some of the areas are flooded each year by rising rivers and others are uplands that never flood (Table 1). A number of villages were visited in each research zone.

2.1.1. Survey of plant uses

The same sequence of structured interviews was undertaken in each of the villages. Initially village leaders and health promoters were contacted and interviewed using standardized forms. The questions related to socio-economic variables (e.g. size of village, migrations, ethnicity, and languages) and the occurrence of the two studied diseases in the local area (e.g. history, frequency, health facilities, and local responses). Subsequently, between 10 and 30 individual households were visited, they being either nuclear or extended families. The inhabitants present at the time of the visit were interviewed in one group. Standardized forms concerning their personal experiences with malaria and leishmaniasis were always completed, and what plants they used to alleviate the symptoms of or cure the two diseases. For each plant-taxa reported used alone, or as a part of a herbal remedy, a form was completed regarding the plant parts used, the preparation, application and effect of the herbal medicine.

We define a use-record as 'one household describing the usefulness of one specific plant taxon against malaria or leishmaniasis', corresponding to the use-records defined for interviews with individual informants (Phillips and Gentry, 1993). The number of use-records and their distribution indicate if few or many people know the potential of particular remedies and if the use is restricted to certain areas or is more widely distributed. Most of the reported plants were botanically identified based on the popular names given by the informants. Previous ethnobotanical studies conducted by the first author and collaborators in Loreto (Kvist et al., 2001a,b) had helped to determine the vernacular names used for the different scientific species in the region. The anti-parasitic plants most often have vernacular names that clearly match well-delimitated scientific species, but a few correspond to several related species or even species belonging to different genera (see discussion of these cases below).

2.1.2. Plant materials

When informants provided vernacular names unknown to the researchers the relevant plants were collected locally with the

Table 1
Survey of study zones in Loreto, Peru, where plants used for malaria and leishmaniasis were studied

	Study zone	Affluent river	Dominant forest habitat	Dominant ethnicity	Numbers of use-records		Malaria vs. Leishm. use-records
					Malaria	Leishm.	
1	Yanayacu	Huallaga	Upland	Mestizo	75	22	3.4
2	Paranapura	Huallaga	Upland	Chayahuito	122	47	2.6
3	Samiria	Marañon	Flood plain	Cocama	117	11	10.6
4	Puinahua	Ucayali	Flood plain	Cocama	23	40	0.6
5	Jenaro Herrera	Ucayali	Flood plain	Mestizo	73	64	1.1
6	Nanay	Amazonas	Upland	Mestizo	129	35	3.6
7	Momón	Amazonas	Upland	Mestizo	93	17	5.5
8	Indiana	Amazonas	Upland	Mestizo	78	26	3.0
9	Manití	Amazonas	Upland	Mestizo	103	3	34.3
10	Mazán	Napo	Upland	Quechua	35	11	3.1
11	Caballococha	Amazonas	Upland	Ticuna	140	13	10.8

For each zone appear the major river this is located along/drain to; whether the dominant landscape are annually inundated floodplains or uplands (terra firme); the prevalent ethnic group with mestizo defining Spanish speaking people not perceiving themselves as indigenous; the number of use-records regarding the two diseases (defined as one household describing the usefulness of one specific plant against malaria or leishmaniasis); and, the relative frequency of malaria vs. leishmaniasis use-records.

informants in order to obtain material for confident botanical determination. At least one voucher collection of anti-parasitic plants with known vernacular names was made to make sure they corresponded to well-defined scientific species. Voucher specimens were identified and deposited at the herbarium in Iquitos (AMAZ) and in Aarhus, Denmark (AAU). Material for phytochemical screening was collected as the fieldwork progressed. Species for phytochemical analysis were selected based on the geographical distribution and number of use-records. Dried plant material (ca. 50 g) was initially exported to Copenhagen for in vitro screening. Larger quantities (ca. 700 g) of dried material of the most potent plants were then exported for characterization of the active principles.

2.2. Methodology for extraction and in vitro screening

2.2.1. Plant extracts

The dried plant material (200 mg) was finely ground and extracted with ethanol overnight with agitation. The ethanol was removed in vacuo and the residue dissolved in DMSO. The yield (% of dry weight) appear in Table 2.

2.2.2. Antiplasmodial screening

The antiplasmodial assay was performed by a modified Desjardin's radioisotope protocol (Desjardins et al., 1979; Ziegler et al., 2002). A chloroquine susceptible strain of *Plasmodium falciparum* (3D7) kindly provided by D. Walliker (Edingburgh, Scotland) was incubated at for 24 h in a standard RPMI medium supplemented with 5% human serum containing [^{3}H]hypoxanthine and DMSO stock solutions of the plant extracts to give final concentrations of 100, 50, 25 and 12 μg/ml. The DMSO concentration was always kept below 1%. The parasites were harvested after incubation for 24 h and the incorporation of [^{3}H]hypoxanthine measured. Chloroquine was used as positive control. All experiments were performed in triplicate. If the IC_{50} value of the residue of the ethanolic extract was higher than 100 μg/ml the activity was given the value 0 (no activity), if $100 > IC_{50} > 50$ μg/ml the activity was given the value 1 (low activity), if $50 > IC_{50} > 10$ μg/ml the activity was given the value 2 (medium activity), and if the IC_{50} value was less then 10 μg/ml, the activity was given the value 3 (high activity) (Table 3).

2.2.3. Antileishmanial screening

A World Health Organization reference vaccine strain of *Leishmania major*, originally isolated from a patient in Iran was used. Promastigotes were cultured at 26 °C in the presence of concentrations of 100, 50, 25 and 12 μg/ml of the extracts according to a previously published procedure (Chen et al., 1993). Pentostam was used as a positive control. The DMSO concentration in the assay was kept below 1%. After 2 h 1 μCi of [^{3}H]thymidine was added to each cell. Parasites were harvested after 18 h and [^{3}H]thymidine incorporation measured. All cultures were performed in triplicate. To rank activity the same IC_{50} intervals as above was used (Table 4). Since no local strains of leishmania parasites were available for this study, the results of the present antileishmanial screening should be interpreted with some caution, since local strains might differ in sensitivities towards some of the plant extracts. The broad field of extracts tested, however, makes it unlikely that different sensitivities of local strains would change the overall tendency of the study.

2.2.4. Lymphocyte proliferation assay

The effects of the compounds on the phytohaemagglutinin A-stimulated human peripheral blood lymphocytes proliferation was determined as previously described (Bygbjerg and Flachs, 1986). This assay reveals the ability of the extracts to inhibit phytohaemagglutinin A induced proliferation of human lymphocytes. Since lymphocytes are involved in the immune response in humans, inhibition of their growth should be minimized. In addition, if the extract inhibited both mammalian lymphocytes and malaria parasites it would indicate that the extract exhibit general cytotoxic activity rather than a specific inhibition of the parasites (results are shown in Table 2 under the heading Toxicity).

3. Results

Table 2 is an alphabetic list of the genera and species reported by informants in Loreto and/or screened for in vitro inhibition in Copenhagen. The list presents both malaria and leishmaniasis results indicated by M and L (and also include plant families, species authors and plant families). The numbers following M and L in Table 2 refer to the order of these taxa in Tables 3 and 4, where the taxa are listed according to number of use-records reported for malaria and leishmaniasis treatment, respectively. Not all taxa in Table 2 appear in Table 3 and/or Table 4. These taxa were investigated for in vitro inhibition of *Leishmania* and/or *Plasmodium* parasites because previous studies in tropical America (reviewed by Blair et al., 1991) have reported their use against malaria or leishmaniasis, but in the present study these taxa were never mentioned by the informants. Table 2 contains for each plant taxon the following results: the number of use-records for malaria and leishmaniasis treatment; results from in vitro screenings (IC_{50} values); results from a toxicity test (vide supra); the plant part(s) used; the most common vernacular name in Loreto; the number of literature references reporting the application of the species/genus for fever/malaria treatment in Latin America (Milliken, 1997); and the number of literature references reporting the use against malaria and leishmaniasis in Peru. It appears that most of the frequently reported taxa also have been cited as useful for malaria or leishmaniasis treatment by other workers.

3.1. Malaria

Table 3 shows the number of malaria use-records per study zone. In spite of geographical distances and ethnic differences the use-records were relatively uniformly distributed across the 11 study zones, showing that many of the anti-malarial plants are known throughout most of Loreto (Fig. 1, Table 3). In addition, some of the observed variation in the distribution of use-records can be explained by habitat requirements. *Curarea tecunarum* and *Aspidosperma rigidum* are limited to upland forests, and are therefore absent from (not used in) three study zones dominated

Table 2
Alphabetic list of the taxa investigated for in vitro inhibition of *Plasmodium* and *Leishmania* parasites, and/or reported to be useful for malaria or leishmaniasis by at least six/five households, respectively

Plant family, species with author(s)	M/L, No. (Tables 3 and 4)	Use-records	Inhib. act.	Toxic.	Yield % dry	Part used	Ame. ref. sp./gen.	Peru ref.	Local name	Voucher specimen
Anacardiaceae										
Mangifera indica L.	M 28	10	>100	–	5.8	Cortex	5/5	1	Mango	G-021
	L 11	5	>100			Cortex	–	0		
Spondias mombin L.	L 3	28	–	–	9.2	Cortex	–	2	Ubos	G-042
Annonaceae										
Unonopsis floribunda Diels	M 41	2	65	51	6.3	Cortex	0/0	0	Icoja	K-1870
	L 20	0	51			Cortex	–	0		
Apiaceae										
Eryngium foetidum L.	M 18	17		–	6.1	Leaf	7/7	3	Sacha culantro	G-013
Apocynaceae										
Aspidosperma excelsum Benth.	M 4	49	42	>100	1.9	Cortex	1/11	1	Remo caspi (de baja)	K-1733
	L 23	1	>100			Cortex	–	0		
Aspidosperma rigidum Rusby	M 2	74	<10	75	3.2	Cortex	0/11	0	Remo caspi (de altura)	K-1728
	L –	0	20			Cortex	–			
Himatanthus succuba (Spruce ex. Müll. Arg.) Woodson	M 29	8	>100	–	9.8	Cortex	1/5	1	Bellaco caspi	None
Rauwolfia sp.	M 40	2	35	>100	3.7	Root	0/2	0	Udchu sanango	K-1736
	L –	0	15			Root	–	0		
Tabernaemontana sp.	L 12	5	15	>100	2.3	Root	–	0	Lobo sanango	K-1712
Araceae										
Dieffenbachia sp.	M –	0	40	–	6.7	Leaf	0/0	0	Patiquina	G-061
	L 14	4	>100			Leaf	–	0		
Pistia stratiotes L.	L 5	8	–	–	7.3	Leaf	–	0	Puto puto	
Arecaceae										
Astrocaryum chonta C. Martius	M 35	6	–	–	4.9	Fruit	0/0	0	Huicungo (de altura)	G-019
Euterpe precatoria Mart.	M 1	102	45	–		Root	0/4	3	Huasai	G-027
Oenocarpus bataua Mart.	M 31	8	18	>100	4.6	Root	0/2	1	Ungurahua	G-033
	L –	0	>100			Root	–	0		
	M		18			Fruit				
Bignoniaceae										
Mansoa standleyi (Steyerm.) A. Gentry	M 11	30	15	30	4.9	Root	1/8	1	Ajo sacha (macho)	G-046
	L 21	2	18			Root	–	0		
Bombacaceae										
Pseudobombax munguba (Mart. and Zucc.) Dugand	M 39	2	>100	>100	6.4	Cortex	0/0	0	Punga colorado	None
	L –	0	>100			Cortex	–	0		
Caesalpinaceae										
Campsiandra angustifolia (Benth.) Sandwith	M 13	21	<10	>100	10.7	Cortex	0/2	3	Huacapurana	G-026
	L 18	2	>100			Cortex	–	0		
Copaifera pauperi (Herzog) Dwyer	M –	0	35	80		Resin	0/2	0	Copaiba	K-1785
	L 15	3	17			Resin	–	0		
Senna reticulata Willd.	M 9	30	>100	>100	5.3	Flower	2/28	2	Retamo	G-022
	L –	0	>100			Flower	–	0		
Caprifoliaceae										
Sambucus mexicana Presl. ex A.DC.	M 17	19	>100	–	3.5	Leaf	2/9	3	Sauco	G-043
Celestraceae										
Maytenus spp.	M 7	33	<10	48	21.1	Cortex	0/0	0	Chuchuhuasi (del bajo)	K-1731
	L 1	62	<10			Cortex	–	1		
	M		14	40		Cortex			Chuchuhuasi (del altura)	G-001
	L		20			Cortex				

Table 2 (*Continued*)

Plant family, species with author(s)	M/L, No. (Tables 3 and 4)	Use-records	Inhib. act.	Toxic.	Yield % dry	Part used	Ame. ref. sp./gen.	Peru ref.	Local name	Voucher specimen
Chenopodiaceae										
Chenopodium ambrosioides L.	M 38	2	>100	–	7.3	Shoot	4/5	1	Paico	K-1256
	L 24	1	>100			Shoot	–	0		
Clusiaceae										
Tovomita sp.	L –	0	>100	–	3.4	Cortex	–	0	Chulla chaqui caspi	K-1750
Euphorbiaceae										
Croton lechleri Muell.-Arg.	M –	0	<25	–		Resin	0/16	1	Sangre de drago	None
	L 4	8	>100			Resin	–	0		
Hura crepitans L.	L 8	7	>100	–		Resin	–	1	Catahua	None
Fabaceae										
Machaerium floribunda Benth.	M 37	4	87	–	1.6	Stem	0/0	0	Uña de gato (resina roja)	G-036
	L –	0	>100			Stem	–	0		
Icacinaceae										
Poraqueiba sericea Tulasne	M –	0	70	–	3.6	Cortex	0/0	0	Umarí	None
	L 26	1	>100			Cortex	–	0		
Lecythidaceae										
Couroupita guianensis Aubl.	M 42	1	55	>100	1.9	Cortex	0/0	0	Aya huma	None
	L 16	3	>100			Cortex	–	0		
	M		>100	–		Fruit	–	0		
	L		>100			Fruit	–	0		
Grias neuberthii J.F. Macbr.	M 15	20		–	4.7	Seeds	1/1	1	Sacha mangua	G-054
Loganiaceae										
Potalia amara Aubl.	M 22	12	–	–	6.5	All parts	2/2	0	Curarino del bajo	G-035
Malpighiaceae										
Burdachia prismatocarpa A. Juss.	M –	0	23	>100	20.7	Cortex	0/0	0	Engaina	K-1714
Malvaceae										
Malachra alceifolia Jacq.	M 30	8	77	–	6.0	Shoot	4/4	2	Malva	G-030
Meliaceae										
Carapa guianensis Aubl.	M 19	16	–	–	2.9	Cortex	8/8	2	Andiroba	K-1754
Cedrela odorata L.	M 14	20	75	>100	6.0	Cortex	7/8	2	Cedro	G-045
	L 19	2	60			Cortex	–	1		
Menispermaceae										
Abuta rufescens Aubl.	M –	–	–	–		Cortex	1/5	2	Abuta	None
Curarea tecunarum Barneby and Krukoff	M 3	61	<10	87	2.1	Stem	0/0	0	Abuta	G-025
	L 13	4	>100			Stem	–	0		
Moraceae										
Brosimum lactescens S. Moore	M 36	6	>100	>100	6.9	Cortex	0/1	0	Tamamuri	K-1852
	L –	0	>100			Cortex	–	0		
Ficus insipida Willdenow	M 8	31	>100	–		Resin	1/2	1	Ojé	G-032
	L 17	3	>100			Resin	–	2		
Maquira coriacea (Karsten) C.C.Berg	M 43	1	>100	–		Cortex	0/0	0	Capinuri	None
	L –	0	>100			Cortex	–	0		
Olacaceae										
Minquartia guianensis Aublet	M 5	38	<10	<10	4.3	Cortex	0/0	2	Huacapú	G-014
	L 22	2	<10			Cortex	–	0		
Poaceae										
Cymbopogon citratus (DC.) Stapf	M 27	10	–	–	4.9	Leaf	7/7	3	Yerba luisa	G-028
Panicum trichoides Sw.	L 9	6	–	–	5.2	Shoot	–	0	Lapakunga	K-1715
Polygonaceae										
Triplaris weigeltiana (Rchb.) Kuntze	M 34	7	>100	–	2.8	Cortex	1/2	1	Tangarana	G-008
	L 28	1	>100			Cortex	–	0		

Table 2 (*Continued*)

Plant family, species with author(s)	M/L, No. (Tables 3 and 4)	Use-records	Inhib. act.	Toxic.	Yield % dry	Part used	Ame. ref. sp./gen.	Peru ref.	Local name	Voucher specimen
Polypodiaceae										
Polypodium decumanum (Willd.) J.Sm.	M –	0	>100	–	4.5	Rhiz.	1/2	2	Coto chupe	K-1722
	L 25	1	>100			Rhiz.	–	0		
Rubiaceae										
Calycophyllum spruceanum (Benth.) Hook. f.ex Schuman	L 10	5	–	–	4.3	Cortex	–	0	Capirona	K-1643
Remijia peruviana Standl.	M 33	8	<10	>100	6.4	Cortex	1/7	1	Cascarilla	G-051
	L –	0	75			Cortex	–	0		
Uncaria guianensis (Aublet) Gmelin	M 25	11	–	–	5.2	Cortex	0/0	0	Uña de gato	G-052
Rutaceae										
Citrus limon (L.) Burm.f.	M 10	30	<10	–	3.2	Root	2/8	1	Limón	G-028
	L 7	7	70			Root	–	0		
Citrus paradisi Macfadyn.	M 21	13	20	–	2.4	Root	0/8	0	Toronja	G-023
	L 20	2	95			Root	–	0		
Salicaceae										
Salix humboldtiana Willd.	M –	0	32	>100	2.9	Cortex	3/5	1	Sauce	K-1729
	M –	–	42			Leaf	–	0		
Sapotaceae										
Pouteria caimito (Ruiz & Pav.) Radlk.	M 32	8	>100	–	2.9	Leaf	0/1	0	Caimito	G-048
	L 27	1	>100			Leaf	–	0		
Smilacaceae										
Smilax sp.	M –	0	>100	70	3.6	Root	0/2	0	Zarzaparilla	None
	L 2	28	>100			Root	–	0		
Solanaceae										
Brunfelsia grandiflora D. Don	M 20	13	64	100	2.5	Root	1/4	1	Chiric sanango	G-005
	L 6	7	53			Root	–	2		
Physalis angulata L.	M 16	20	–	–	5.4	Shoot	3/6	3	Mullaca	G-009
Verbenaceae										
Stachytarpheta cayennensis (Rich.) Vahl	M 24	11	–	–	4.8	Shoot	6/8	2	Verbena negro	G-015
Verbena litoralis Kunth	M 6	38	37	60	6.1	Shoot	4/5	3	Verbena blanca	G-044
Zingeberaceae										
Costus arabicus L.	M 26	10	–	–	4.6	Stem	1/4	0	Caña agria	G-050
Curcuma longa L.	M 12	26	<10	50		Bulb	1/1	1	Guisador	G-038
	L –	0	16			Bulb	–	0		
Zingeber officinale Roscoe	M 23	12	–	–	4.7	Rhizome	1/1	0	Jenjibre	G-037
	L –	0	–			Rhizome	–	1		

Included is the following information: scientific name; plant family; use for malaria and/or leishmaniasis (M/L followed of the number of the species in Tables 3 and 4 surveying malaria and leishmaniasis data, respectively); the number of use-records regarding malaria and leishmaniasis; the in vitro screening results (IC_{50} values varying from >100 to <10 μg/ml with small figures indicating strong inhibition of parasites); the toxicity test results (same range of IC_{50} values); the extraction yield in % of dry weight; the plant part(s) used to treat malaria/leishmaniasis; the numbers of literature references reporting use of species/genus for fever/malaria according to Milliken (1997); the number of literature references reporting use against malaria or leishmaniasis in Peru (based on Rutter, 1990; Duke and Vasquez, 1994; Mejia and Rengifo, 1995; Silva et al., 1995; Pinedo et al., 1997); the common vernacular name in Loreto; and voucher-numbers of plant taxa with G and K representing Gonzalez- and Kvist-collections located in AMAZ and in AMAZ and AAU, respectively.

by flood plain forests (nos. 3–5 in Table 3). Vice versa *Aspidosperma excelsum* are limited to flood plain forests, and its use has predominantly been recorded within the mentioned three zones (Table 3). Habitat requirements or restricted distributions cannot explain the fact that *Carapa guianensis* (a widespread forest tree) and *Sambucus mexicana* (a widely cultivated shrub) are apparently only used in the extreme eastern and southwestern parts of Loreto, respectively (Fig. 1, Table 3).

Table 3 also shows that the fieldwork led to a total of 988 use-records for the treatment of malaria representing 118 plant taxa corresponding to 8.4 use-records per taxon. The most frequently reported species was the palm *Euterpe precatoria*, reported by 102 households, corresponding to ca. 10% of the use-records. The 10 most frequently reported taxa accounted for 50% of the malaria use-records and the 20 most frequently reported taxa for 70% of all records. Table 3 lists all 36 taxa reported by more than five households, as well as seven of the taxa reported by one to five households (above/below the 36th entry). The latter seven taxa were also screened for their ability to inhibit *Plasmodium falciparum* parasites, in con-

Table 3
Plant-taxa screened for their ability to inhibit *Plasmodium* parasites and/or represented with at least five malaria use-records

	Species	Family	Use-records per study zone											Sum	
			1	2	3	4	5	6	7	8	9	10	11	U-rec.	Activity
1	*Euterpe precatoria*	Arec	4	5	25	2	9	10	17	5	18	3	4	102	2
2	*Aspidosperma rigidum*	Apoc	8	9				18	9	10	11	2	7	74	3
3	*Curarea tecunarum*	Meni	13	12			1	19	9		5		2	61	3
4	*Aspidosperma excelsum*	Apoc		1	33	4	8					3		49	2
5	*Minquartia guianensis*	Olac	4	2	5		1	1	2		4	1	18	38	3
6	*Verbena litoralis*	Verb	3	15	1	4	1	3	2	1	2		6	38	2
7	*Maytenus* spp.	Cele	2	12					5	5	3	1	5	33	3
8	*Ficus insipida*	Mora	2	5	4	5	4		2	1			8	31	0
9	*Senna reticulata*	Caes			5	1	1	6	2	2	7	2	4	30	0
10	*Citrus limon*	Ruta	4	13	1		1	1	1		5		4	30	3
11	*Mansoa standleyi*	Bign	1	2	4		2	6		5	4	5	1	30	2
12	*Curcuma longa*	Zing			1	2	2	3	3	6	4	3	2	26	3
13	*Campsiandra angustifolia*	Caes					4		5	1	4	2	5	21	3
14	*Cedrela odorata*	Meli	7	2				2		1	6	1	1	20	1
15	*Grias neuberthii*	Lecy	1	4	5			2	3	1	4			20	–
16	*Physalis angulata*	Sola			2			7		7	3	1		20	–
17	*Sambucus mexicana*	Capr	5	13							1			19	0
18	*Eryngium foetidum*	Apia		2	3			1	2	1	3		5	17	–
19	*Carapa guianensis*	Meli											16	16	–
20	*Brunfelsia grandiflora*	Sola	1		2		3		1	4		2		13	1
21	*Citrus paradisi*	Ruta	1	1			1	2		1	6	1		13	2
22	*Potalia amara*	Loga							3	1		2	6	12	–
23	*Zingeber officinale*	Zing						6	1	3	1		1	12	–
24	*Stachytarpheta cayennensis*	Verb					1		5	1	1			11	–
25	*Uncaria guianensis*	Faba	1					4				1	5	11	–
26	*Costus arabicus*	Zing	2				1	2	2		1	1	1	10	–
27	*Cymbopogon citratus*	Poac		1			2	2	2		2	1		10	–
28	*Mangifera indica*	Anac	4	1	2		1		1				1	10	0
29	*Himatanthus succuba*	Apoc			5		1						2	8	0
30	*Malachra alceifolia*	Malv	1	1			4	1		1				8	1
31	*Oenocarpus bataua*	Arec					3		1	1			3	8	2
32	*Pouteria caimito*	Sapo					1	4		2	1			8	1
33	Remijia peruviana	Rubi		4			1	2			1			8	3
34	*Triplaris weigeltiana*	Poly			1			1	1				4	7	1
35	*Astrocaryum chonta*	Arec						2	2	2				6	–
36	*Brosimum lactescens*	Mora	2	1	2		1							6	1
37	*Machaerium floribunda*	Faba	1	1			2							4	1
38	*Chenopodium ambrosioides*	Chen												2	0
39	*Pseudobombax munguba*	Bomb					1			1				2	0
40	*Rauwolfia* sp.	Sola	1										1	2	2
41	*Unonopsis floribunda*	Anno			1		1							2	1
42	*Couroupita guianensis*	Lecy				1	1							1	1
43	*Maquira coriaceae*	Mora												1	0
75 species with one to five 5 use-records			7	12	15	4	14	24	12	15	6	3	28	138	
Use-records per area and total			75	122	117	23	73	129	93	78	103	35	140	988	

The plants are ordered and numbered according to the numbers of use-records (sum), and the distribution of the use-records across the 11 study zones in Loreto, Peru, also appear. To the right appears the anti-plasmodial activity (with 3, 2, 1, 0 representing high, medium, low, and none activity, respectively, and a - (hyphen) that the activity not were determined).

trast to another 75 taxa equally represented with one to five use-records.

Extracts of 32 of the 43 plant taxa appearing in Table 3 were screened for their ability to inhibit the growth of *Plasmodium falciparum*, and it is indicated if they demonstrated high (3), medium (2), low (1) or no (0) activity (according to the IC_{50} intervals defined above). The screening results of 14 taxa with more than 20 use-records were compared with those of 18 taxa represented with 1–19 use-records (appearing above/below the 17th entry). Among the former 7, 4, 1, and 2 taxa demonstrated high, medium, low or no inhibition of *Plasmodium falciparum* growth, while the corresponding numbers for the latter were 1, 3, 8 and 6. The average activity (summing activities and dividing with number of taxa) of the two groups were 2.1 versus 0.9, suggesting that commonly used species are more active against malaria than the lesser-known taxa.

Table 4
Plant-taxa screened for their ability to inhibit *Leishmania* parasites and/or represented with at least four leishmaniasis use-records

	Species	Family	Use-records per study zone											Sum	
			1	2	3	4	5	6	7	8	9	10	11	U-rec.	Activity
1	*Maytenus* spp.	Cele	6	14	2	10	16	4	2	4	2		2	62	3
2	*Smilax* sp.	Smil	2	16		1	3	4	1	1				28	0
3	*Spondias mombin*	Anac	3			7	11	2	1	4				28	–
4	*Croton lechleri*	Euph	2	2			1	2			1			8	0
5	*Pistia stratiotes*	Arac				1		2	1	3			1	8	–
6	*Brunfelsia grandiflora*	Sola		4	1	1		1						7	1
7	*Citrus limon*	Ruta		1			4	2						7	1
8	*Hura crepitans*	Euph	1		2		2	2						7	0
9	*Panicum trichoides*	Poac					1		4		1			6	–
10	*Calycophyllum spruceanum*	Rubi				2	1		1		1			5	–
11	*Mangifera indica*	Anac				3		1		1				5	0
12	*Tabernaemontana* sp.	Apoc	1					1		2			1	5	2
13	*Curarea tecunarum*	Meni			1		2		1					4	0
14	*Dieffenbachia* sp.	Arac			1	1	1		1					4	0
15	*Copaifera pauperi*	Caes	1			1		1						3	2
16	*Couroupita guianensis*	Lecy			1	1	1							3	0
17	*Ficus insipida*	Mora				1	1			1				3	0
18	*Campsiandra angustifolia*	Caes								1			1	2	0
19	*Cedrela odorata*	Meli					1			1				2	1
20	*Citrus paradisi*	Ruta					1		1					2	1
21	*Mansoa standleyi*	Bign						2						2	1
22	*Minquartia guianensis*	Olac					1				1			2	3
23	*Aspidosperma excelsum*	Apoc											1	1	0
24	*Chenopodium ambrosioides*	Chen					1							1	0
25	*Polypodium decumanum*	Fili					1							1	0
26	*Poraqueiba sericea*	Icac					1							1	0
27	*Pouteria caimito*	Sapo						1						1	0
28	*Triplaris weigeltiana*	Poly					1							1	0
57 species with one to four use-records			6	10	3	11	13	10	4	8	5	3	7	80	
Use-records per area and total			22	47	11	40	64	35	17	26	11	3	13	289	

The plants are ordered and numbered according to the numbers of use-records (sum), and the distribution of the use-records across the 11 study zones in Loreto, Peru, also appear. To the right appears the anti-leishmanial activity (with 3, 2, 1, 0 representing high, medium, low, and none activity, respectively, and a - (hyphen) that the activity not were determined).

3.2. Leishmaniasis

Table 4 shows that the fieldwork led to a total of 289 use-records for the treatment of leishmaniasis representing 85 plant taxa corresponding to only 3.4 use-records per taxa. Three taxa were mentioned frequently, viz. *Maytenus* spp. with more than 20% of the 289 records, and *Spondias mombin* and *Smilax* sp. each with about 10% of the records, while nine taxa also appearing in Table 4 were reported by five to eight households, and 73 taxa were reported by one to four households. Sixteen of the latter taxa screened for their ability to inhibit *Leishmania major* parasites appear below the 12th entry.

Table 4 includes screening results for 24 taxa reported to be used for leishmaniasis, and 2, 2, 5 and 15 of them demonstrated high (3), medium (2), low (1) and none (0) antileishmanial activity, respectively. The average activity (summing activities and dividing with 24) were 0.6 showing that plants used for leishmaniasis is much less active than plants used for malaria (average activity of 32 taxa being 1.5). The average activity of taxa reported by at least five/less than five house-holds were 0.9 versus 0.5, suggesting little correlation between numbers of leishmaniasis use-records and inhibitory activities. The most frequently reported taxon *Maytenus* spp. did demonstrate high antileishmanial activity as well as high antiplasmodial activity (Table 3) and a moderate toxicity (Table 2). The other strongly antileishmanial species, *Minquartia guianensis*, is also strongly antiplasmodial and provided the most toxic of all the investigated assays (Table 2). The latter species is rarely used for leishmansiais (Table 4) but more frequently for malaria (Table 3).

4. Discussion

4.1. Field results

The results clearly show that, in Loreto, more plants are used for the treatment of malaria than to treat leishmaniasis. The fieldwork resulted in 988 versus 289 use-records for the treatment of malaria versus leishmaniasis. In only one of the 11 areas studied more use-records were found for the treatment of leishmaniasis than for malaria (no. 4 in Table 1). In individual villages the knowledge varied greatly between households. Some families would mention up to 10 plants for treating malaria while

their neighbors did not report any. An equally large variation between villages was observed. The average number of malaria use-records reported per interviewed households varied from more than three to less than one (including families not reporting any plants). The corresponding figures for leishmaniasis were far lower, with most families showing no knowledge of plants useful for treating leishmaniasis.

According to Table 3 the 20 most frequently reported species in the study constituted ca. 70% of the malaria use-records, and Table 4 demonstrate that just three species represent ca. 50% of the leishmaniasis use-records. Had more fieldwork been conducted throughout Loreto the same commonly used taxa would probably have continued to represent the majority of the use-records. The number of sporadically reported taxa, however, would almost certainly have increased. Most use-records regarding the rarely reported taxa are probably due to misinformation. This may happen unintentionally because of poor recollection or insufficient knowledge on the part of the informant. Informants may also prefer to fabricate information rather than admit to their ignorance, and a few may even have fun trying to fool investigators. Such use-records are considered as "noise", and most of the infrequently reported plant-taxa have not been included in Tables 2–4 (e.g. pineapple, sugarcane, banana, coffee, coco and avocado represented with 1, 3, 4, 5, 5 and 5 malaria use-records, respectively).

Infrequently reported plant-taxa were evaluated critically before being dismissed as "noise". A limited geographical distribution and/or scarcity may limit the use of an ethno-botanically and phytochemically interesting species. A case in point is *Remijia peruviana*, which was only reported by eight informants but demonstrated high in vitro inhibition of *Plasmodium* (Tables 2 and 3) in accordance with the presence of quinine and cinchonine (Ruiz-Mesia et al., 2005). *Cinchona* is limited to forests at the eastern Andean slopes, while *Remijia peruviana* occurs in the Amazon basin limited to patches of low-stature forests on extremely infertile white sands (known as varillal). *Remijia* is referred to as Cascarilla, which is also the common name for different *Cinchona* species in Peru. The low number of use-records for *Remijia* in Loreto reflects the fact that only immigrants from the eastern Andean slopes already familiar with *Cinchona* have tried to use and thereby recognized that *Remijia peruviana* is useful against malaria. Ethno-pharmacologically interesting species may also be little known because only certain ethnic groups recognize their potential, e.g. *Carapa guianensis* and *Sambucus mexicana* are apparently used for malaria treatment only by the Ticuna and Chayahuito Amerindians, respectively (Tables 1 and 3). The use of these plants may not yet have spread to other populations.

It appears from Table 2, that nearly all commonly reported taxa used against malaria in the present study, have also been reported for this purpose by other investigators in Loreto, and many of them have also been reported used elsewhere in South- and Central-America. It is remarkable that extracts of nearly all these frequently reported species inhibit the in vitro growth of *Plasmodium*, while few of the less frequently reported species show any significant activity (Table 3). This may lend credence to the hypothesis that ethno-pharmacological criteria are more successful as a basis for selecting plants than random screening. The same conclusion has been reached previously (Balick, 1990; Cox, 1994; Farnsworth, 1994; Lewis et al., 2000). The investigators in this study did not choose plants randomly but it cannot be ruled out, that some of the infrequently reported plant-taxa have been suggested at random by the informants.

A lack of clinical double blind studies makes it questionable to evaluate the efficacy of traditional herbal treatments of malaria and leishmaniasis, even though many informants claim they have been cured using plants. Initially informants were also queried about plants which were useful for treatment of intestinal parasites such as *Ascaris* during this study. Most use-records referred to three commonly known and easily accessible species: *Carica papaya*, *Chenopodium ambrosioides*, and *Ficus insipida*, which are all renowned for eliminating intestinal parasites (Duke and Vasquez, 1994; Mejia and Rengifo, 1995; Pinedo et al., 1997; Brack, 1999). This is in contrast to the broader spectrum of plants used against malaria and leishmaniasis, implying that the local population may use many different plants, because they have not yet identified any highly efficient and easily accessible species to treat these two diseases.

Plants used for the treatment of malaria are mainly drunk as an infusion, prepared by boiling the plant material in water. Woody material and cortex, however, is mostly steeped in locally prepared sugar-cane brandy before being ingested. In contrast, leishmaniasis is predominantly treated topically. Leaves are typically macerated and resins and latex tend to be applied directly to the visible wounds with no further treatment. The topical treatment of wounds caused by leishmaniasis indicate that the disease is not recognized as a systemic infection with a parasite, but as an outbreak of wounds. Consequently a number of plants that are commonly used to disinfect and heal wounds also are applied for leishmaniasis, in particular *Maytenus* spp., *Spondias mombin* and *Croton lechleri* (Rutter, 1990; Silva et al., 1995; Pinedo et al., 1997). The general lower activity of plants used against leishmaniasis (Tables 2–4) could relate to this lack of understanding of the cause of the disease. The only species frequently reported as taken orally for treatment of leishmaniasis is *Smilax* sp., the extract of which did not show any activity against *Leishmania* parasites (Tables 2 and 4). The identity of the *Smilax* species has not been determined since we failed to collect it in the field. The analyzed material was bought at the medicinal plant market in Iquitos, and was not fertile. The quantity was too small to prepare voucher specimens. *Smilax* should therefore be collected for further investigation.

Even though most well known folk-species used to treat malaria and leishmaniasis correspond to a single botanic species, some vernacular names e.g. Remo caspi, Chuchuhuasi and Abuta apparently encompass more than one species. Remo caspi is used for various species of *Aspidosperma*, particularly *Aspidosperma excelsum* and *Aspidosperma rigidum*. The former only grows in flood plain forests whereas the latter as well as at least one additional unidentified species are found in upland forests. Chuchuhuasi may refer to one or both of the species *Maytenus macrocarpa* and *Maytenus amazonica*, with the former found mostly, but not exclusively, in flood plain forests and the latter in upland forests. Finally in the existing literature the

vernacular name Abuta refers to the genus *Abuta* and particularly the species *Abuta rufescens*. We were consequently surprised when our two field collections of Abuta were later identified as *Curarea tecunarum*, making it unclear whether informants mentioning the folk-species Abuta have *Abuta rufescens* and/or *Curarea tecunarum* in mind. Surveying the literature on phytochemical analyses of *Abuta* it became apparent, that very different compounds were isolated from what was claimed to be the same species (*Abuta grandifolia*). In different studies either bis-benzyltetrahydroisoquinoline or azafluoranthene type alkaloids were isolated but both were never found together. From a chemotaxonomic point of view this would suggest that the plants were actually different, at least on the species if not on the genus level. Looking at other *Abuta* spp. it was found that azafluoranthenes seem to be the common type alkaloids found in this genus.

4.2. Antiplasmodial activities

The collected *Curarera tecunarum* was initially misidentified as *Abuta rufescens*. Whereas reports of the use of the latter to treat malaria exist (Milliken, 1997; Duke and Vasquez, 1994), no similar reports have been found for *Curarera tecunarum*. However, the phyto-chemical results are consistent with existing information regarding the chemistry of the genus *Curarea* rather than *Abuta*. Azafluoranthene alkaloids have been isolated from *Abuta* sp. (Cava et al., 1975) and curare type bis-benzyltetrahydroisoquinoline alkaloids from *Curarea* sp. (Lavault et al., 1985). These alkaloids have been found to be potent inhibitors of the growth of *Plasmodium falciparum* in vitro (Angerhofer et al., 1999) but the in vivo effects are less convincing (Christensen and Kharazmi, 2001).

Species belonging to the genus *Aspidosperma* were extensively reported as being useful for the treatment of malaria (Milliken, 1997). Problems in identifying the collected plant material on a species level precluded in-depth phytochemical studies. Several aspidosperma alkaloids have been found in this genus, some of which show modest antiplasmodial activities (Mitaine-Offer et al., 2002), but again in vivo experiments have been less encouraging (Milliken, 1997).

Species belonging to the genus *Maytenus* are widely used in folk-medicine all around the tropics (Kennedy et al., 2001). In the Amazonian and Andean areas chuchuhuasha or chuchuhuasi is used for several purposes (Duke and Vasquez, 1994), but several different species might be used for the preparation of the remedies. An authoritative Flora (Vasquez, 1997) mentions that two species *Maytenus macrocarpa* and *Maytenus amazonica* are found in the areas studied. In spite of this fact several papers describe phytochemical examinations of *Maytenus chuchuhuasha*, including a report on the isolation of pristimerin (Martinod et al., 1976). This latter species name has never been validly published and the investigated materials may represent *Maytenus macrocarpa*. *Maytenus amazonica* in addition to pristimerin contain a series of other quinone-methide triterpenes (Chavez et al., 1999). The specimen of *Maytenus macrocarpa* collected in 1997 in the lowlands (baja) did contain 0.1% pristimerin (Jensen, 2003). Pristimerin and some other quinone-methide triterpenes are known to be antiplasmodial even though they also are toxic towards mammalian cells (Figueiredo et al., 1998). Dihydro-β-agarofuran sesquiterpenes inhibiting the P-glycoprotein pump that makes *Leishmania tropica* resistant towards daunomycin have also been found in *Maytenus macrocarpa* (Perez-Victoria et al., 1999).

Roots of *Euterpe precatoria* was the most regularly mentioned remedy for the treatment of malaria. The undeveloped leaves found apically in its trunks, and referred to as the heart of the palm is used for food (Duke and Vasquez, 1994), and indigenous groups in Bolivia (Bourdy et al., 2000; Deharo et al., 2004), Colombia (as *Euterpe* sp.) (Schultes and Rauffauf, 1990) and French Guiana (Bertani et al., 1995) have also been reported to use decoctions of the roots against malaria. An extract of *Euterpe precatoria* roots showed only modest antiplasmodial activity. Phytochemical studies revealed the presence of *p*-hydroxybenzoic acid, which showed no significant antiparasitic activity, and the lignan dehydrodiconiferyl dibenzoate showing modest antiplasmodial activity. The lignan was, however, only present in amounts of 10 ppm in the dried roots (Jensen et al., 2002), but maybe concentration takes place during the preparation of the remedy. *Euterpe* roots is sliced in several liters of water, and boiled until a concentrated extract remains.

The bark of *Minquartia guianensis* is used as an anthelmintic by the Quijos Quichua of Ecuador's Amazonian lowlands (Marles et al., 1989). Phytochemical studies have revealed the presence of the toxic polyacetylene minquartynoic acid in large amounts (Marles et al., 1989; El-Seedi et al., 1994; Rasmussen et al., 2000b).

The three curcumins isolated from *Curcuma longa* show only moderate growth inhibition of leishmania and malaria parasites (Rasmussen et al., 2000a) and high doses control a malaria infection in mice (Reddy et al., 2005). The use of *Curcuma longa* for malaria treatment has recently also been reported from French Guiana (Vigneron et al., 2005).

5. Conclusion

Many different plants are used to treat malaria in Loreto. Frequently reported anti-malarial plants tend to be well-known throughout Loreto and are also used for this purpose elsewhere, and extracts from most of these species inhibit *Plasmodium falciparum* in vitro. Of the less frequently reported taxa only a few inhibited *Plasmodium falciparum*, and most of these taxa are probably not ethno-pharmacologically interesting. Some interesting taxa may be reported rarely due to limited geographical distribution, or the fact that only small, distinct, ethnic groups recognize the potential of these plants. This suggests that future field-investigations should target areas with a higher concentration of endemic and/or rare plants and ethnic groups that still treat the relevant diseases according to their own plant-medicinal traditions. Although informants also reported a large number of potentially useful plant-taxa in the case of leishmaniasis, few are widely known and most of them do not inhibit *Leishmania major* parasites. The reason may be that the population recognize leishmaniasis as a skin disease, and only treat the resulting wounds—not the infection causing them. Several

substances inhibiting malaria parasites were identified during the present study and other active substances are known from previous ethno-pharmacological studies. The efficacy of the plant-medicinal treatments of the two diseases still remains to be investigated.

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