ACTA
AMAZONICA

http://dx.doi.org/10.1590/1809-4392201701191

Ethnobotanical study of antimalarial plants in the middle region of the Negro River, Amazonas, Brazil

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ABSTRACT

The middle Rio Negro region is an interesting place to seek novel antimalarial compounds because of the traditional knowledge of the Amazon population in conjunction with the high biodiversity of the region. The objective of this work was to study the use of antimalarial plants in Barcelos, state of Amazonas, Brazil. Fifty-two local specialists from eight different communities were interviewed over one year. The identified plants were collected with the assistance of local specialists, classified to species level and deposited in herbarium. In total, 55 antimalarial plants were identified in use in the region, of which 16 had not been previously reported in other published studies. Many factors could be involved with the use of antimalarial plants by the Barcelos population, such as the accessibility of these medicinal plants, efficiency and safety of using these plants, the accessibility to drugs or other medical treatments, plant bitterness, and the gender of the interviewees. Our results indicate that the population of Barcelos possesses an extensive knowledge on the use of a diverse array of antimalarial plants, and may contribute to the development of novel antimalarial compounds.

KEYWORDS: malaria, ethnobotany, Amazonia, medicinal plants, traditional knowledge

Etnobotânica de plantas antimaláricas no médio Rio Negro, Amazonas, Brasil

RESUMO

O conhecimento tradicional da população amazônica, associado à grande biodiversidade da região, faz do médio Rio Negro um lugar propício para a pesquisa de novos remédios antimaláricos. O objetivo deste trabalho foi estudar o uso de plantas antimaláricas no município de Barcelos, Amazonas, Brasil. Ao longo de um ano foram entrevistados 52 especialistas de oito comunidades de Barcelos. As plantas indicadas foram coletadas com o auxilio dos especialistas, identificadas e depositadas em herbário. Foram mencionadas 55 plantas antimaláricas, das quais 16 nunca foram citadas em outros trabalhos previamente publicados. Muitos fatores podem estar associados ao uso destas plantas antimaláricas, tais quais o acesso a estas plantas, sua eficiência e segurança, o acesso a outros tratamentos médicos, o amargor das plantas e o gênero das pessoas entrevistadas. Nossos resultados indicam que a população de Barcelos é detentora de um rico conhecimento sobre o uso de plantas medicinais antimaláricas e pode contribuir para o desenvolvimento de novas drogas antimaláricas.

PALAVRAS-CHAVE: malária, etnobotânica, Amazônia, plantas medicinais, conhecimento tradicional

INTRODUCTION

Malaria remains as one of the major tropical diseases worldwide (Bremen 2011). In 2015, 214 million cases and 438,000 deaths were reported, most of them children less than five years old (WHO 2015). Malaria is considered as one of the neglected diseases, which are usually present in poor populations in tropical areas, and which receive little attention from governments and the pharmaceutical industry (Krettli 2008). Malaria is caused by an infection with protozoans of the genus *Plasmodium*, and is transmitted by female mosquitos *Anopheles* spp. Clinical symptoms of malaria include cycles of fevers, chills, and headaches, and infection can affect the liver, kidneys, and nervous system, causing brain damage, which can lead to serious complications in infected individuals and result in death (WHO 2010; WHO 2015).

Malaria has a large economic and social impact in its endemic areas in Brazil. In 2013, 143,000 cases and 30 deaths were reported in the country. The Amazon region concentrated 99% of malaria cases in Brazil. *Plasmodium vivax* is the most frequent infection agent in Brazil, identified in 84% of all cases, followed by *P. falciparum*, identified in 16% of cases (SVS 2015; WHO 2015). Although Brazil has a universal public health system, eradication of the disease across the country is difficult due to factors such as the incorrect administration of drugs, the presence of isolated populations in the forest, the movement of people, particularly in border areas, and the expanding colonization fronts in the Amazon region (Melo 1985; Coimbra 1998; Singer and Caldas 2001).

Incorrect use of drugs and the evolution of *Plasmodium* spp. contribute to the development of increasing resistance to currently available antimalarial drugs, which creates an urgent need to identify novel therapeutic antimalarial compounds (Alecrim *et. al.* 1999, Krettli 2008, WHO 2010; WHO 2015). Ethnobotanical research of medicinal plants remains as one of the most important means for the identification of new, efficient, and safe compounds for the control of malaria (Ginsburg and Deharo 2011; Graz *et al*. 2011; Willcox *et al* 2010).

The populations that live along the Negro River, in the western Brazilian Amazon, use a wide variety of plants for the treatment of numerous diseases (Silva *et al*. 2007). The Negro River region is suitable for the survey of novel drugs, because the region has a conserved forest, several endemic plant species, and the largest indigenous population of Brazil, comprising 24 ethnic groups (Sufredine and Daly 2001).

Therefore the objective of this study was to profile the use of antimalarial plants by traditional communities in the municipality of Barcelos, in the middle Negro River, Amazonas, Brazil.

MATERIALS AND METHODS

For this study, approval was obtained from all the involved communities, from the Ethics Research Committee (CEP) of São Paulo State University (UNESP/FMB nº 3425-2010) and from the Brazilian National Genetic Heritage Council (CGEN nº111 / 2012).

The fieldwork was carried out between July 2012 and July 2013 in eight communities in the municipality of Barcelos, state of Amazonas, Brazil (Figure 1), on the margins of the Negro River, the largest blackwater river of the Amazon basin, that originates in the Colombian Andes and crosses Amazonas from its northwestern border to the capital city of Amazonas, Manaus, where it joins with the Amazonas River. Barcelos is located in the middle region of the Negro River, 496 km upriver from Manaus.

The municipality of Barcelos covers an area of 123,000 km^2 and has a population of 27,000 inhabitants, the majority of them (56%) being indigenous (IBGE 2016). The Human Development Index (HDI) of Barcelos is considered low (0,500) (IBGE 2016). The incidence of malaria in the city is high, with more than 100 cases per thousand inhabitants registered each year (Suarez-Muttis and Coura 2007; SVS 2015). The surveyed communities were indicated by the Barcelos Municipal Health Office according to their incidence of malaria (Table 1). Fifty two persons from the eight target communities were identified by locals according to their knowledge of medicinal plants using the snowball method (Alexiades, 1996). Semi-structured interviews were conducted in order to understand socio-cultural aspects, the comprehension of malaria, and the use of medicinal plants for treatment of the disease (Supplemental Material, Annex S1).

The identified plants were collected with assistance of the local specialists, identified to the lowest possible taxonomic level and deposited in the herbarium of the Instituto Federal de Educação, Ciência e Tecnoclogia do Amazonas (EAFM/IFAM) (Manaus, Amazonas). The curator of the herbarium Valdely F. Kinupp identified all plant species. The geographical origin of the species (native or exotic to Amazonia), was determined in accordance with Flora do Brasil 2020 em construção (2017). We reviewed available information about the phytochemical composition of and biological essays carried out for each of the surveyed species in online databases BIOMED, Scopus, SciDirect and GoogleSchoolar, as well as in related literature (Milliken 1997a).

RESULTS

The 52 interviewees were 18 women and 34 men, with an average age of approximately 52 years. In terms of ethnicity, 73% of interviewees considered themselves indigenous, including 26 (50%) Baré, three Tukano, two Baniwa, two

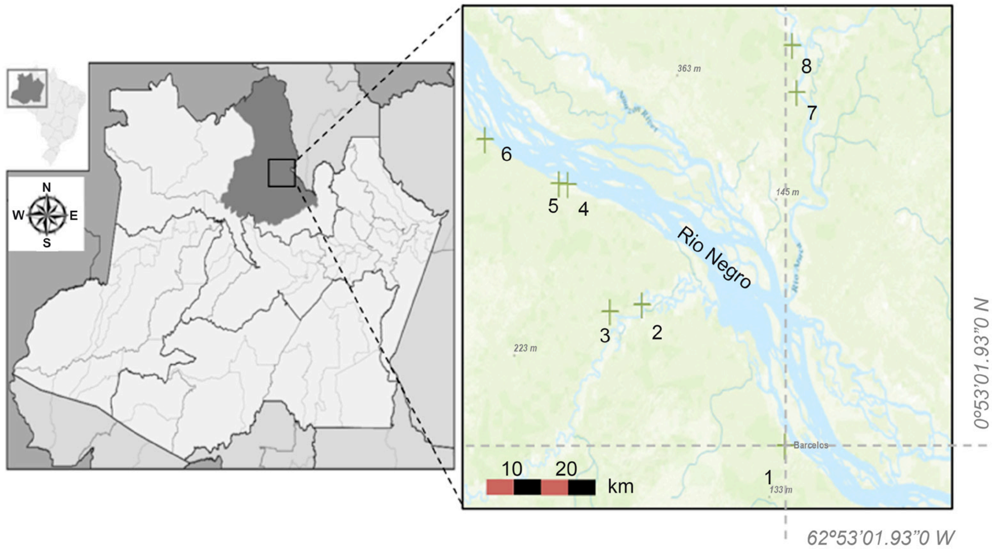

Figure 1. Location of the municipality of Barcelos, Amazonas, Brazil. Numbers indicate the communities surveyed in this study: Barcelos (1), Ponta da Terra (2), Santa Inês (Bulixu) (3), São Luís (4), Cumaru (5), Baturité (6), Bacabal (7), and Romão (8). This figure is in color in the electronic version.

Table 1. Communities visited for the survey of antimalarial plants in the municipality of Barcelos, Amazonas, Brazil

Community	Location		Population	Specialists interviewed
	Coordinates	River		
Barcelos (urban zone)	0º58'30''S, 62º55'26''W	Negro	27,110[1]	4
Ponta da Terra	0°45'59"S; 63°11'55"W	Quiuini	78[2]	9
Santa Inês (Bulixu)	0°50'54"S; 63°18'24"W	Quiuini	56[2]	8
Cumarú	0°36'10"S; 63°23'6"W	Negro	128[2]	7
São Luíz	0°37'49"S; 63°17'54"W	Negro	63[2]	5
Baturité	0º31'41''S, 63º32'46''W	Negro	10	6
Romão	0°20'44"S; 62°59'11"W	Aracá	39[2]	7
Bacabal	0°22'29"S; 62°55'40"W	Demeni	79[2]	6

Source: [1]IBGE, 2013; [2]Barra and Dias, 2013

Yanomami, two Kaxinawá, one Tariano, one Urubu Tapira, and one Arapaço.

Concerning the incidence of malaria, only three people reported that they never contracted the disease. All interviewees claimed that their last cases of malaria were contracted in other communities, particularly those in the urban zone of Barcelos. Regarding disease transmission, 53% of interviewees believed that transmission is via mosquitoes, known locally as *carapanã*, 6% believed that transmission is through the water, 25% believed that both water and mosquitoes facilitate transmission, and 16% claimed not to know how transmission occurs. Almost half of the interviewees (44%) reported they did not know any preventive method against contracting malaria. Most interviewees (67%) said they use pharmaceutical drugs in addition to medicinal plants to treat malaria, 18% said they only use pharmaceutical drugs, and 15% said they only use plants and natural remedies.

Our survey resulted in the identification of 55 species belonging to 29 botanical families that are used for the treatment of malaria (Table 2). Some plants referred locally by the same name have been classified by botanical specialists as distinct species. These included açaí (*Euterpe* spp.), which was later identified as three different species of the same genus; carapanaúba (*Aspidosperma* spp.), which turned out to be three different species; and sucuúba (*Himatanthus* spp.), which was represented by two distinct species. Herein these species were considered in accordance with their common local denomination, since species under the same local name belonged to the same genus and were morphologically similar.

The families identified most frequently for the treatment of malaria were Apocynaceae (41 times), Simaroubaceae (15 times),

Table 2. Antimalarial plants used in the municipality of Barcelos, Amazonas, Brazil. Species marked with an asterisc (*) were tested in biological essays. Voucher number refers to the identification of the EAFM herbarium. N citations=number of interviewed specialists that cited this plant followed by the percentage of total interviewees in parentheses; Other sources=other published works that cited the same use; NA=not available. N citations and rank for *Aspidosperma*, *Euterpe* and *Phanera* species are presented as one value because they were considered as only one species by the interviewees.

Family	Species	Herbarium voucher nr	Local name	Part used / preparation method	N citations	Citation rank	Origin	Other sources
Amaranthaceae	*Alternanthera sessilis* (L.) R.Br.	10546	*cibalena*	leaf as infusion	1 (2%)	9	Amazonia	NA
Apocynaceae	*Aspidosperma nitidum* Benth. Ex Müll. Arg.	10561	*carapanaúba*	bark decoction	-	-	Amazonia	1, 2
Apocynaceae	*Aspidosperma schultesii* Woodson*	10607	*carapanaúba*	bark decoction	-	-	Amazonia	3
Apocynaceae	*Aspidosperma* sp.	10551	*carapanaúba*	bark decoction	36 (69%)	1	Amazonia	1, 4, 5
Apocynaceae	*Geissospermum* sp.	NA	*quina*	bark decoction	1 (2%)	9	Amazonia	1, 2, 4, 6, 7, 8
Apocynaceae	*Himatanthus stenophyllus* Plumel	10654	*sucuuba*	latex and bark decoction	3 (6%)	7	Amazonia	NA
Apocynaceae	*Himatanthus sucuuba* (Spruce ex Müll.Arg.) Woodson	10504	*sucuuba*	bark decoction	3 (6%)	7	Amazonia	1, 9
Arecaceae	*Astrocaryum aculeatum* G.Mey	NA	*tucumã*	toasted palm heart as infusion	1 (2%)	9	Amazonia	3, 5
Arecaceae	*Euterpe catinga* Wallace	NA	*açai-caatinga*	root decoction	11 (21%)	2	Amazonia	3
Arecaceae	*Euterpe oleracea* Mart.	NA	*açai-do-pará*	root decoction	-	-	Amazonia	1, 4, 5
Arecaceae	*Euterpe precatoria* Mart.*	NA	*açaí; iwapixuna*	root decoction	-	-	Amazonia	1, 3, 5, 9
Arecacea	*Socratea exorrhiza* (Mart.) H.Wendl	NA	*paxiubinha*	leaf stalk infusion	1 (2%)	9	Amazonia	5
Asteraceae	*Artemisia vulgaris* L.*	10556	*cibalena*	shoot infusion	1 (2%)	9	Europe, Asia, Africa	1, 9
Asteraceae	*Bidens cynapiifolia* Kunth	10563	*picão, picão preto*	whole plant infusion	1 (2%)	9	Amazonia	1, 5
Asteraceae	*Gymnanthemum amygdalinum* (Delile) Sch.Bip.*	10611	*boldo-de-árvore*	leaf infusion	1 (2%)	9	Tropical Africa	1, 5, 6, 10
Asteraceae	*Mikania psilostachya* DC.	10562	*lingua-de-onça*	leaf infusion	2 (4%)	8	Amazonia	NA
Asteraceae	*Unxia camphorata* L.f.	10623	*são-joão-caá*	leaf infusion	1 (2%)	9	Amazonia	3
Bignoniaceae	*Handroanthus barbatus* (E.Mey.) Mattos	10657	*caapitari*	leaf infusion	2 (4%)	8	Amazon	NA
Caricaceae	*Carica papaya* L.*	NA	*mamão*	leaf inhalation	1 (2%)	9	Central America	1, 3, 4
Convovulaceae	*Bonamia ferruginea* (Choisy) Hallier f.	10582	*cipó-tuira*	leaf infusion	2 (6%)	7	Amazonia	5, 9, 11, 12
Dilleniaceae	*Doliocarpus magnificus* Sleumer	10603	*Cipó d'água*	leaf infusion	1 (2%)	9	Amazonia	NA
Euphorbiaceae	*Croton cajucara* Benth.*	10537	*sacaca*	leaf infusion	8 (15%)	3	Amazonia	1, 5
Euphorbiaceae	*Jatropha curcas* L.*	10543	*pinhão-branco*	seed infusion as emetic	1 (2%)	9	Amazonia	1
Euphorbiaceae	*Manihot esculenta* Crantz	NA	*mandioca*	root flour	1 (2%)	9	Amazonia	5
Fabaceae	*Copaifera* sp.	NA	*copaíba*	resin in alcohol extract	1 (2%)	9	Amazon	1, 4
Fabaceae	*Phanera* sp.	10589	*escada-de-jabuti*	stalk decoction	3 (6%)	7	Amazonia	1, 9
Fabaceae	*Phanera splendens* (Kunth) Vaz*	10554	*escada-de-jabuti*	stalk decoction	-	-	Amazonia	1, 3

Table 2. Continuation.

Family	Species	Herbarium voucher nr	Local name	Part used / preparation method	N citations	Citation rank	Origin	Other sources
Fabaceae	*Phaseolus vulgaris* L.	NA	*feijão*	seed soup	2 (4%)	8	Central America	NA
Fabaceae	*Senna occidentalis* (L.) Link*	10662	*feijãozinha*	seeds toasted as coffee	1 (2%)	9	Amazonia	1, 6, 9, 11, 13
Gentinaceae	*Potalia resinifera* Mart.	10590	*surucucu-mirá*	bark decoction	7 (13%)	4	Amazonia	14
Icacinaceae	*Poraqueiba sericea* Tul.	10599	*umari*	seeds cooked	1 (2%)	9	Amazonia	NA
Lamiaceae	*Plectranthus amboinicus* (Lour.) Spreng.	10640	*hortelã*	leaf infusion	1 (2%)	9	Africa	NA
Lamiaceae	*Plectranthus ornatus* Codd	10610	*boldo*	leaf infusion	3 (6%)	7	Europe, Asia	NA
Lauracea	*Persea americana* Mill.*	NA	*abacate*	toasted leaf infusion	1 (2%)	9	Central America	1, 3, 5, 9
Lecythidaceae	*Bertholletia excelsa* Bonpl.*	10553	*castanheira*	bark decoction	7 (13%)	4	Amazonia	1, 5, 6
Lecythidaceae	*Eschweilera* sp.	10596	*mata-mata*	bark decoction	1 (2%)	9	Amazonia	NA
Meliaceae	*Guarea pubescens* (Rich.) A.Juss.	10655	*jatoá*	bark and liber decoction	3 (6%)	7	Amazonia	5
Menispermaceae	*Abuta grandifolia* (Mart.) Sandwith	10598	*pitombinha*	leaf infusion	2 (4%)	8	Amazonia	1, 4
Menispermaceae	*Abuta imene* (Mart.) Eichler	10615	*cipó-abuta*	root decoction	4 (8%)	6	Amazon	NA
Myristicaceae	*Iryanthera hostmannii* (Benth.) Warb.	10595	*ucuí*	sap	2 (4%)	8	Amazonia	NA
Myrtaceae	*Eucalyptus* sp.*	NA	*eucalipto*	leaf infusion	1 (2%)	9	Australia	1, 11
Poaceae	*Paspalum gardnerianum* Nees	10547	*pacuã*	whole plant infusion	1 (2%)	9	Amazonia	NA
Rhamnaceae	*Ampelozizyphus amazonicus* Ducke*	10567	*saracura mirá*	root and liber decoction	7 (13%)	4	Amazonia	1, 3, 5, 6, 9
Rubiaceae	*Coffea* sp.	NA	*café*	toasted leaf infusion	1 (2%)	9	Africa	1, 7, 9
Rutaceae	*Citrus limon* (L.) Osbeck	10581	*limão*	dried fruit peel infusion	1 (2%)	9	Asia	1, 3, 5
Rutaceae	*Citrus* sp.	NA	*laranja*	dried fruit peel infusion	1 (2%)	9	Asia	1, 3, 5
Selaginellaceae	*Selaginella* sp.	10538	*samambaia*	leaf decoction	1 (2%)	9	Amazonia	NA
Simaroubaceae	*Quassia amara* L.*	10569	*quina*	leaf infusion	8 (15%)	3	Amazonia	1, 5, 9
Simaroubaceae	*Simaba cedron* Planch.*	10591	*pau-pra-tudo*	bark decoction	7 (13%)	4	Amazonia	1, 5, 9
Solanaceae	*Capsicum frutescens* L.	10641	*malagueta*	whole plant infusion	4 (8%)	6	America	1
Solanaceae	*Physalis angulata* L.*	10549	*camapu*	root decoction	5 (10%)	5	America	1, 3, 9
Solanaceae	*Solanum stramoniifolium* Jacq.	10574	*jurubeba*	root decoction	2 (4%)	8	Amazonia	NA
Urticaceae	*Cecropia ficifolia* Warb. ex Snethl.	10604	*embaúba-branca*	leaf inhalation	1 (2%)	9	Amazonia	NA
Verbenaceae	*Stachytarpheta cayennensis* (Rich.) Vahl*	10571	*gervão*	leaf infusion	1 (2%)	9	Amazonia	1, 5, 9
Zingiberaceae	*Alpinia zerumbet* (Pers.) B.L.Burtt & R.M.Sm.	10639	*vindicá*	leaf infusion	1 (2%)	9	China, Japan	NA

1- Milliken (1997a), 2- Steele *et al*. (2002), 3- Kffuri *et al*. (2016), 4- Ferreira *et al*. (2015), 5- Frausin *et al*. (2015), 6- Brandão *et al*. (1992), 7- Botsaris (2007), 8- Deharo and Ginsburg (2011), 9- Hidalgo (2003), 10- Madureira (2008), 11- Caraballo *et al* (2004), 12- Idowu *et al*. (2010), 13- Nguta *et al*. (2010), 14- Ruiz *et al*. (2011)

Asteraceae (14 times), Arecaceae (13 times), and Rhamnaceae (12 times). Regarding the origin of the identified species, 82% are native to the Amazon region and 18% are exotic.

Of the 52 plants identified for the treatment of malaria, 16 have not been previously described in other published works (*Alternanthera sessilis*, *Himatanthus stenophyllus*, *Mikania pilostachya*, *Handroanthus barbatus*, *Phaseolus vulgaris*, *Doliocarpus magnificus*, *Poraqueiba sericea*, *Eschweilera* sp., *Plectranthus amboinicus*, *Plectranthus ornatus*, *Abuta imene*, *Iryanthera hostmannii*, *Paspalum gardnerianum*, *Solanum stramoniifolium*, *Cecropia ficifolia* and *Alpinia zerumbet*) (Table 2). Only 25 of the plants identified in the present study have been characterized pharmacologically (Table 2).

The interviewees considered that approximately 65% of the plants reported for malaria treatment are bitter and eleven of the 12 most frequently identified plants for malaria treatment were considered bitter. A wide variety of plant parts were used, as well as several preparation methods (Table 2).

On average, the interviewed women identified eight antimalarial plants while men identified six. Among the plants indicated by women, 54% grow in intensively managed (domesticated) environments, such as backyards and small fields, while 61% of the plants indicated by men grow in wild environments, such as terra firme and floodplain forests.

DISCUSSION

More than 30% of interviewees believed that water was the sole or partial transmission agent of malaria. This association of malaria transmission with water can be explained by the higher incidence of the disease during the rainy season (November to March) (SVS 2015), when the breeding and consequent abundance of the *Anopheles* vectors increases significantly. The still widespread misconception about the transmission mode of the disease, as well as the widespread ignorance about preventative methods reflects the low effectiveness of awareness campaigns by local health officials, which makes the control of the disease more difficult. The use of medicinal plants may also be related to the ineffective coverage of health provision services. The majority of interviewees stated that they relay on pharmaceuticals for malaria treatment, and medicinal plants were used mainly for the treatment of malaria symptoms such as headache, fever, body aches, liver problems, and anemia. However, the use of plants for the treatment of the malaria infection in itself, occurred specially in communities with low access to conventional public health providers.

The most frequently identified species for the treatment of malaria in the present study were carapanaúba (*Aspidosperma* spp.), saracura-mirá (*Ampelozizyphus amazonicus*), açaí (*Euterpe* spp.), picão (*Bidens pibinatifolia*), sacaca (*Croton crajucara*), and quina (*Quassia amara*) (Table 2), which is in agreement with other similar studies carried out in the Amazon region (Brandão *et al.* 1992; Milliken 1997b; Hidalgo 2000; Frausin *et al.* 2014; Ferreira et al 2015; Kffuri *et al.* 2016). All of these plants have proven effective in the control of malaria *Plasmodium* (Milliken 1997a; Mariath *et al.* 2009; Nunomura and Pohlit 2010), except for *B. bipinatifolia* that has not yet been tested. Thus our results support the notion that the species more commonly used, and therefore empirically approved by more people, are also those proven to be efficient for disease treatment when tested scientifically.

The use of these medicinal plants was also influenced by their accessibility. For instance, saracura-mirá (*Ampelozizyphus amazonicus*), the second most frequently cited plant in this study, occurs only in specific places according to the interviewees, sometimes far from their home, and is only used when they have access to it. Some plants were rather used as substitutes for prefered plants, like paxiubinha (*Socratea exorrhiza)*, that was used when the interviewees could not find carapanaúba (*Aspidosperma* ssp.).

Apocynaceae was the botanical family with the greatest number of species (six) used to treat malaria, followed by Arecaceae (five), Asteraceae (five), and Fabaceae (four), as has been observed in other antimalarial plant surveys in the Amazon region (Brandão *et al.* 1992; Hidalgo 2000; Frausin *et al.* 2014; Ferreira *et al.* 2015; Kffuri *et al.* 2016). These families are among those with the highest species diversity in the Amazon region (Flora do Brasil 2020 em construção 2017). However, when considering the ratio of total species number by family to those of antimalarial value in traditional pharmacopeia, Simaroubaceae would be the most important plant family for the treatment of malaria, since 20% of all Simaroubaceae species that occur in the Amazon were reported to be used for the treatment of this disease, while only 3.4% of Apocynaceae species occurring in the region were reported as antimalarial (Milliken 1997a; Mariath *et al.* 2009; Flora do Brasil 2020 em construção 2017). The relatively high use of exotic species in popular pharmacopoeia is a result of population influx of other regions, which is common in northern South America (Bennet and Prance 2000) and in Barcelos (Barra and Dias 2013).

The predominance of bitter taste in plants used for malaria treatment was observed in other studies (Brandão *et al.* 1992; Hidalgo 2000). This may result from the relationship with the bitter taste of the real quina (*Cinchona* spp.) and its active component (quinine) that is used in the allopathic medicine, or with other antimalarial plants used by local populations that are considered bitter and have been proven effective in parasite control, such as sacaca (*Croton cajucara*), carapanaúba (*Aspidosperma* spp.), or quina (*Quassia amara*) (Milliken 1997a; Mariath *et al.* 2009).

Which plant part is used for treatment reflects the variety of growing habits of the species used. Commonly used materials from trees were bark and timber, while that from herbs were leaves. The plant part used largely determines the preparation method. Seeds and bark are usually decocted, while leaves are rather used in infusion. These aspects are important for the evaluation of the sustainable exploration of these plants, but should be considered on an individual case basis.

The generally higher number of antimalarial plants identified by women is probably due to the fact that, traditionally, women are responsible for the family's health. In the northeast of Brazil women have been found to have more knowledge about the use of medicinal plants (Voeks 2007). The differential association of men and women with domesticated and wild medicinal plant species likely stems from the role partition between the genders. Men fish and hunt, having more contact with the wild areas around the communities, while women spend most of their working hours in backyards and farm fields (Ribeiro 1995). The interviewees who identified a higher number of plants for malaria treatment had some form of written record of the use of medicinal plants, which suggests that the knowledge of medicinal plants should also be related to the memory of each person.

CONCLUSIONS

The knowledge of the use of antimalarial plants is well developed in communities of the Barcelos municipality at the middle Negro River, where the incidence of malaria is still high. We report 55 plants used to treat malaria infection, among them 16 species that had not been previously mentioned in other publications as antimalarial. Local women specialists cited more antimalarial plants than men, and cited more plants related to domestic environments, while men cited more plant species found in surrounding forests. Most antimalarial plants used by local people were bitter tasting. The exclusive use of plants for malaria treatment tends to be higher where conventional health providers are absent. Other factors could be involved with the use of antimalarial plants, but must be more studied, such as the accessibility of these plants and thei efficiency and safety. Of the 55 reported species, only 25 have been characterized through biological essays, which highlights the importance of ethnobotanical research for the identification of potential novel antimalarial drugs.

ACKNOWLEDGEMENTS

The authors are grateful to the population of Barcelos, and, in particular, to the Association of Indigenous Communities of Barcelos (ASSIBA), to the Foundation for Health Vigilance of Barcelos (FVS), to the Barcelos Health Secretary, and to the Special Secretary for Indigenous Health from the National Health Ministry (DSEI/Barcelos). This research was funded by Fundação CAPES, Fundação de Amparo à Pesquisa de São Paulo (FAPESP), and Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq).

REFERENCES

Alecrim, M.G.C.; Alecrim, W.; Macedo, V. 1999. *Plasmodium vivax* resistence to chloroquine (R2) and mefloquine (R3) in Brazilian Amazona Region. *Revista da Sociedade Brasileira de Medicina Tropical,* 32: 67-68.

Alexiades, M. 1996. *Selected Guidelines for ethnobotanical research: a field manual*. The New York Botanical Garden, New York, 306p.

Barra, C.S.; Dias C. 2013. *Barcelos indígena e ribeirinha: um perfil socioeconômico*. ASIBA/FOIRN/ISA, São Paulo, 82p.

Bennet, B.C.; Prance, G.T. 2000 Introduced plants in the indigenous pharmacopoeira of northerns South America. *Economic Botany,* 54: 90-102.

Botsaris, A.S. 2007. Plants used traditionally to treat malaria in Brazil: the archives of Flora Medicinal. *Journal of Ethnobiology and Ethnomedicine,* 65: 3-18.

Brandão, M.G.L.; Grandi, T.S.M.; Rocha, E.M.M.; Sawyer, D.R.; Krettli, A.U. 1992. Survey of medicinal plants used as antimalarials in the Amazon. *Journal of Ethnopharmacology,* 36: 175-82.

Bremem, J. 2011. The ears of the hippopotamus: manifestations, determinants, and estimates of the malária burden. *American Journal of Tropical Medicine and Hyggene.* 64: 1-11.

Caraballo, A.; Caraballo, B.; Rodrigues-Acosta, A. 2004. Preliminary assessment of medicinal plants used as antimalarials in the southeastern Venezuelan Amazon. *Revista da Sociedade Brasileira de Medicina Tropical,* 37: 186-188.

Carvalho, L.H.; Krettli, A.U. 1991. Antimalarial chemotherapy with natural products and chemically defined molecules. *Memórias do Instituto Oswaldo Cruz,* 86: 181-184.

Coimbra Jr, C.E.A. 1998. Human factors in the epidemiology of malaria in the Brazilian Amazon. *Human Organization,* 47: 254–260.

Deharo, E.; Ginsburg H. 2011. Analyses of additivity and synergism in the anti-plasmodial effect of purified compounds from plant extracts. Malaria Journal 10(S1): S5. (http://www.malariajournal.com/content/10/S1/S5)

Ferreira, A.; Ming, L.C.; Haverroth, M.; Daly, D.; Caballero, J.; Ballesté, A. 2015. Plants Used to Treat Malaria in the Regions of Rio Branco-Acre State and Southern Amazonas State - Brazil. *International Journal of Phytocosmetics and Natural Ingredients,* 2015: 2-9.

Flora do Brasil 2020 em construção. 2017. Jardim Botânico do Rio de Janeiro (Rio de Janeiro Botanical Garden). (http://floradobrasil.jbrj.gov.br/). Accessed on 19 Feb 2017.

Frausin, G.; Hidalgo, A.F.; Lima, R.B.S.; Kinupp, V.F.; Ming, L.C.; Pohlit, A.M.; Milliken, W. 2015. An ethnobotanical study of anti-malarial plants among indigenous people on the upper Negro River in the Brazilian Amazon. *Journal of Ethnopharmacology,* 215: 238-252.

Frits, F.J.; Franssen, F.F.J.; Smeijters, L.J.J.W.; Berger, I.; Aldana, B.E.M. 1997. *In vivo* and *In vitro* antiplasmodial activities of some plants traditionally used in Guatemala against malaria. *Antimicrobial Agents and Chemotherapy,* 41: 1500-1503.

Ginsburg, H.; Deharo, E. 2011. A call for using natural compounds in the development of new antimalarial treatments – an introduction. *Malaria Journal* 10(S1): S1. (http://www.malariajournal.com/content/10/S1/S1)

Graz, B. 2004. Observational methods for assissing Traditional antimalarial. In; Willcox, M., Bodeker, G., Rasoanauvi, P. (Ed.). Traditional Medicinal Plants and Malaria. CRC Press, New York, p.240-276.

Graz, B.; Kitua, A; Maledo, H.M. 2011. To what extent can traditional medicine contribute a complementary or alternative solution to malaria control programmes. *Malaria Journal* 10(S1): S6. (http://www.malariajournal.com/content/10/S1/S6)

Hidalgo, A.F. 2003. *Plantas de uso popular para o tratamento da malária e males associados da área de influência do rio Solimões e região de Manaus – AM*. Doctoral Dissertation, Department of Horticulture, Faculdade de Ciências Agronômicas, Universidade Estadual Paulista, Botucatu. 192p.

IBGE. 2016. *Informações sobre o município de Barcelos, Amazonas*. (http://www.cidades.ibge.gov.br/xtras/perfil.php?lang=&codmun=130040). Accessed on 01 Feb 2016.

Idowu, O.A.; Soniran, O.T.; Ajana, O.; Aworinde, D.O. 2010. Ethnobotanical survey of antimalaria plants used in Ogun State, Southwest Nigeria. *African Journal of Pharmacy and Pharmacology*, 4: 55-60.

Jensen, J.F.; Kvist, L.P.; Christensen, S.B. 2002. An antiplasmodial lignan from *Euterpe precatoria*. *Journal of Natural Products,* 65: 1915-1917.

Kffuri, C.W.; Lopes, M.A.; Ming, L.C.; Odonne, G.; Kinupp, V.F. 2016. Antimalarial plants used by indigenous people of the Upper Rio Negro in Amazonas, Brazil. *Journal of Ethnopharmacology,* 178: 188-198.

Krettli, A.U. 2008. Grandes Endemias no Brasil. *Gazeta Médica da Bahia,* 78: 74-78.

Krettli, A.U.; Aandrade-Neto, V.F.; Brandão, M.G.L.; Ferrari, F. 2001. Search for new antimalarial drugs from plants used to treat fever and malaria or plants randomly selected: a review. *Mem*órias do *Instituto. Oswaldo Cruz,* 96: 1033-1042.

Lima, R.B.; Rocha e Silva, L.F.; Melo, M.R.; Costa, J.S.; Picanço, N.S.; Lima, E.S.; *et al.* 2015. In vitro and in vivo anti-malarial activity of plants from the Brazilian Amazon. *Malaria Journal*, 14: 508. (DOI: https://doi.org/10.1186/s12936-015-0999-2)

Mariath, I.R.; Flacão, H.S.; Barbosa-Filho, J.M.; Sousa, L.C.F.; Tomaz, A.C.; Diniz, M.F. *et al.* 2009. Plants of the American continent with antimalarial activity. *Brazilian Journal of Pharmacology,* 61: 1401-1433.

Mello, D.A. 1985. Malária entre populações indígenas do Brasil. *Cadernos de Saúde Pública,* 1: 25-34

Milliken, W. 1997a. *Plants for malaria, plants for fever: medicinal species in Latin America – a bibliographic survey.* The Royal Botanic Gardens, Kew Gardens, 116p.

Milliken, W. 1997b. Traditional anti-malarial medicine in Roraima, Brazil. *Economic Botany,* 51: 212-237.

Muñoz, V.; Sauvain, M.; Bourdy, G.; Arrázola, S.; Callapa, J.; Ruiz, G.; Choque, J.; Deharo, E. 2000. A search for natural bioactive compounds in Bolivia through a multidisciplinary approach: Part III. Evaluation of the antimalarial activity of plants used by Alteños Indians. *Journal of Ethnopharmacology*, 71: 123-131.

Nguta, J.M.; Mbaria, J.M.; Gakuya, D.W.; Gathumbi, P.K.; Kiama, S.G. 2010. Traditional antimalaria phytotherapy remedies used by the South Coast community, Kenya. *Journal of Ethnopharmacology,* 131: 256-267.

Nunomura, S.M.; Pohlit, A.M. 2010. Alcalóides indólicos de casca de *Aspidosperma vargasii* e *A. desmanthum. Quimica Nova,* 33: 284-287.

Oliveira, F.Q.; Junqueira, R.G.; Sthemann, J.R.; Brandão, M.G.L. 2003. Potencial das plantas medicinais como fonte de novos antimaláricos: espécies indicadas na bibliográfica etnomédica brasileira. *Revista Brasileira de Plantas Medicinais,* 5: 23-31.

Ribeiro, B. 1995. *Os índios das águas pretas*. Companhia das Letras, São Paulo, 270p.

Sá, M.S; Menzes, M.N.; Krettli, A.U; Tomassini, R.T.C.B; Santos, R.R; Azevedo, J.R.W.F; Soares, M.B.P. 2011. Antinalarial activity of Physalins B, D, F and G. *Natural Products,* 74: 2269–2272.

Silva, A.L.; Tamashiro, J.; Begossi, A. 2007. An ethnobotany of the riverine population from the Rio Negro, Amazonia (Brazil). *Journal of Ethnobiology,* 27: 46-72.

Singer, B.H.; Caldas, M.C. 2001. Agricultural colonization and malaria on the Amazon frontier. *Annals of the New York Academy of Sciences,* 954: 184-222.

Spencer, C.F.; Koniuszy, F.R.; Rogers, E.F.; Shavel Junior, J.; Easton, N.R.; Kaczka, E.A.; *et al*. 1947. Survey of plants for antimalarial activity. *Lloydia,* 10: 145-174.

Suárez-Muttis, M.C.; Coura, J.R. 2007. Mudanças no padrão epidemiológico da malária em área rural do médio rio Negro, Amazônia brasileira: análise retrospectiva. *Cadernos da Saúde Pública,* 23: 785-804.

Suffredini, I.B.; Daly, D.C. 2001. O rio Negro como cenário na busca de novos medicamentos. In: Oliveira, A.A., Daly, D.C. (Ed.). *Florestas do rio Negro*. Companhia das Letras, São Paulo, p.340-365.

SVS. 2015. *Boletim epidemiológico.* Ministério da Saúde 46(25). (http://portalsaude.saude.gov.br/images/pdf/2015/agosto/18/2015-009---Mal--ria-para-publica----o.pdf). Accessed on 19 Nov 2015.

Voeks, R.A. 2007. Are women reservoirs of traditional plant knowledge? Gender, ethnobotany and globalization in northeast Brazil. *Singapore Journal of Tropical Geography,* 28: 7-20

WHO. 2010. *Global report on antimalarial drug efficacy and drug resistance.* 2000-2010. World Health Organization, Geneve, 843p.

WHO. 2015. *World Malaria Report 2015.* (http://www.who.int/malaria/publications/world-malaria-report-2015/report/en/). Accessed on 8 Feb 2016

Willcox, M.; Benoit-Vical, F.; Fowler, D.; Bourdy, G.; Burford, G.; Giani, S., *et al.* 2010. Do ethonobotanical and laboratory data predict clinical safety and efficacy of anti-malaria plants? *Malaria Journal, London* 10(S1): S7. (http://www.malariajournal.com/content/10/S1/S7)

Received: 18/04/2017
Accepted: 08/06/2017

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http://dx.doi.org/10.1590/1809-4392201701191

SUPPLEMENTARY MATERIAL

TOMCHINSKY *et al*. Ethnobotanical study of antimalarial plants in the middle region of the Negro River, Amazonas, Brazil.

Annex S1. Questionnaire used in the survey

First section - life history of the interviewee:
a) name;
b) gender;
c) birthplace;
d) date of birth;
e) ethnicity.

Second section - knowledge of the interviewee about malaria and its treatment:
f) description of disease symptoms;
g) mode of transmission;
h) alternate names for the disease;
i) if he/she had suffered malaria in the past and how frequently;
j) how is access to medical treatment;
k) which *Plasmodium* strain was responsible for the infection when clinical exam was made;
l) information about known prevention and treatment methods (drugs, medicinal plants, and other methods);
m) which medicinal plants are used or known to used for the treatment of malaria.

Third section - information about each plant described as a means of treating malaria:
n) name of the plant;
o) where it occurs and where it is collected;
p) plant parts used;
q) preparation methods;
r) taste.