Revista Brasileira de Farmacognosia 27 (2017) 135–142

Brazilian Journal of Pharmacognosy
REVISTA BRASILEIRA DE FARMACOGNOSIA
www.elsevier.com/locate/bjp

Original Article

Medicinal plants in the diet of woolly spider monkeys (*Brachyteles arachnoides*, E. Geoffroy, 1806) – a bio-rational for the search of new medicines for human use?

Liége M. Petroni[a], Michael A. Huffman[b], Eliana Rodrigues[a,*]

[a] Centro de Estudos Etnobotânicos e Etnofarmacológicos, Departamento de Ciências Biológicas, Universidade Federal de São Paulo, São Paulo, SP, Brazil
[b] Primate Research Institute, Kyoto University, Kyoto, Japan

ARTICLE INFO

Article history:
Received 15 April 2016
Accepted 18 September 2016
Available online 12 October 2016

Keywords:
Zoopharmacognosy
Ethnomedicine
Woolly spider monkeys
Diet
Atlantic forest
Medicinal plants

ABSTRACT

The present study aimed to compare the plant food diet of woolly spider monkeys (*Brachyteles arachnoides*) inhabiting Intervales State Park in São Paulo, Brazil, with medicinal plant species used by humans in the surrounding areas of the park. The diet of a group of woolly spider monkeys living in an Atlantic forest area was recorded during 43 months of fieldwork. Fifty-three species (87 food items) were recorded. Plant specimens were collected and identified at the University of São Paulo and the Botanical Institute of São Paulo State. Using semi-structured interviews, ethnomedicinal data were also collected from four preselected respondents regarding the human therapeutic value of these plants. The study showed that 24.5% (13/53) of these species are used by residents around the park for medicinal purposes. Of these thirteen, seven species also have validated pharmacological properties, and three are utilized by local residents for similar medicinal purposes. Overlap in the plant food/medicinal diet of woolly spider monkey populations elsewhere were also noted, suggesting potential overlap in their medicinal value for humans and primates. The similarities between the ingestion of plants by primates and their medicinal use by humans provide a bio-rational for the search of bioactive plants in the primate diet. Further detailed investigation of their pharmacological and phytochemical value is warranted.

Introduction

Most primates have a diverse plant based diet, from which they obtain the needed calories and nutrients necessary for survival and reproduction (Oats, 1987; Altmann, 1998; Lambert, 2011). The major plant dietary strategies are frugivory and folivory, supplementing this with seeds, sap, bark and flowers (Carvalho, 1996; Lambert, 2011). However, plants provide more then just nutrients. Plants also contain a variety of secondary metabolites that have largely been viewed as deterring primates from eat them (Glander, 1982). It has also been shown that many different primate species ingest plants containing both nutritional and medicinal value, suggesting that these secondary metabolites could actually be beneficial to the health of the user (*e.g.* Sifaka: Carrai et al., 2003; gorilla: Cousins and Huffman, 2002; chimpanzee: Huffman, 2003; Krief et al., 2005, 2006; Japanese macaque: MacIntosh and Huffman, 2010).

Building on the work of animal self-medication, an identified path for the discovery of new drugs of potential value to humans is based on the evaluation of the medicinal potential of the diet of great apes, Old World monkeys and prosimians (Ohigashi et al., 1994; Huffman et al., 1998; Krief et al., 2004). The basic premise of this process, also known as zoopharmacognosy (Rodriguez and Wrangham, 1993) is that animals utilize plant secondary metabolites and other non-nutritional substances in the diet as a form of passive prevention or treatment for diseases such as parasite infection (Huffman, 1997). Huffman points out that the challenge of interpreting self-medication in animals is to distinguish between possible indirect medicinal benefits derived from limited ingestion of plants rich in secondary compounds of biological significance (medicinal foods), *versus* the limited and situation specific ingestion of non-nutritional items that are processed solely for their therapeutic medicinal properties (*e.g.* Huffman and Seifu, 1989; Huffman et al., 1993). One thing, that sets medicinal foods apart from normal dietary food items high in nutritional value, is the biological properties present in dietary items eaten at seasonally limited periods in small amounts, with no signs of illness, that have use in human traditional medicine for ailments common to

* Corresponding author.
E-mail: e.rodrigues@unifesp.br (E. Rodrigues).

http://dx.doi.org/10.1016/j.bjp.2016.09.002

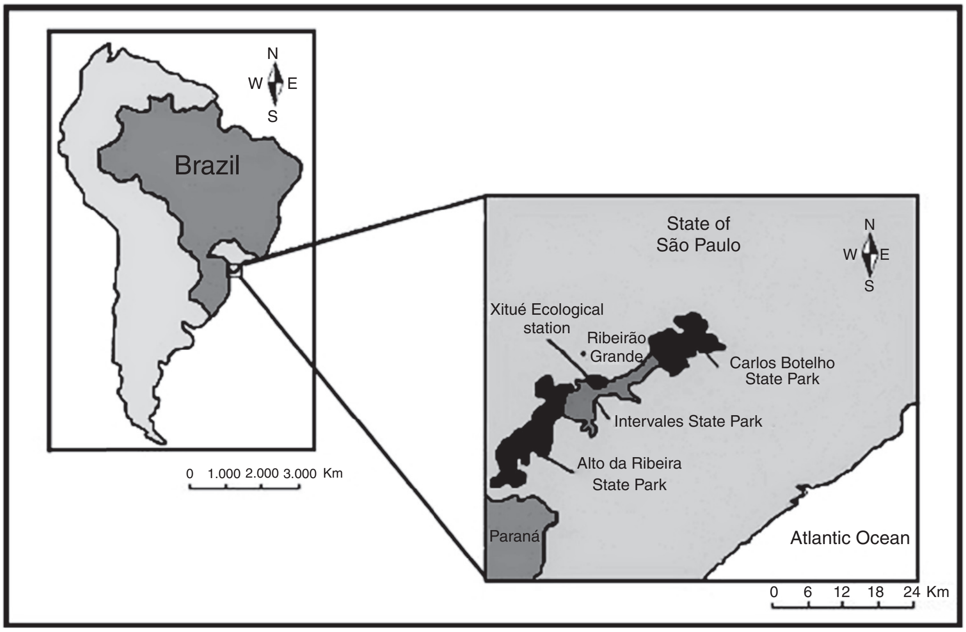

Fig. 1. Location of Intervales State Park, São Paulo state, Ribeirão Grande municipality (24°12′ to 24°25′ S and 48°03′ to 48°30′ W).

both humans and animals. The plant diet of neo-tropical primate has remained under-studied and under reported in these aspects (Janzen, 1978; Glander, 1994).

Brazil has an incalculable wealth of traditions, customs and cultural traits that still linger, especially in traditional societies. Plants comprise part of the identity of a group of people because they reflect what they are and what they think as well as their relationships with their surroundings (Medeiros et al., 2004). Therefore, the use of plants for therapeutic purposes is part of a social and ecological context, and most of the specificities of such use can only be understood in this context.

Understanding the role of plants in the diet of neo-tropical primates and how these plants may be used to promote health is a potential new avenue to help understand the biological bases and origins of traditional practices within efforts to develop potential bioactive compounds. Using this bio-rational, the present study aimed to compare the plants contained in the diet of woolly spider monkeys (*Brachyteles arachnoides*) inhabiting Intervales State Park in São Paulo, Brazil, to the plant species used in human medicine around the park.

Materials and methods

Ethics

This study was approved by the Unifesp Ethics Committee (CEP-UNIFESP) under the process number 031538/2016, and Terms of Consent (TCLE) were obtained from respondents.

Study area and groups

Intervales State Park (ISP) is located in the southern region of the state of São Paulo, headquartered in the municipality of Ribeirão Grande (24°12′ to 24°25′ S and 48°03′ to 48°30′ W). ISP has an area of 49,888 ha and is connected to three other Conservation Units: Carlos Botelho State Park, Xitué Ecological Station and Alto Ribeira State Park (Fig. 1).

According to The IUCN Red List of Threatened Species, *B. arachnoides* has been categorized as an endangered species since 1982. In Brazil, the distribution of woolly spider monkeys is currently restricted to isolated, scattered areas because of anthropogenic disturbances, ranging from deforestation to indiscriminate hunting (Lemos de Sá, 1988). The group of woolly spider monkeys reported here consisted of 39 individuals occupying an area of use of 1216.35 ha (Petroni, 1993, 2000).

Species and food items used by woolly spider monkeys

A behavioural study of woolly spider monkeys was conducted during 43 months of fieldwork, from 1989 to 1990 and from 1994 to 1997, by one of the authors (Petroni, L.M.). The daily activities of the woolly spider monkeys were recorded *ad libitum* (Altmann, 1974). The present study performed a qualitative analysis of the diet of the group studied. The calculation of the intake of each food item was based on the number of observations in which each item was consumed by woolly spider monkeys. The samples of plant specimens observed in the diet of monkeys were collected for identification purposes using the dry method (Mori et al., 1985) consisted of the following: branches, flowers or fruits knocked down or picked from treetops by the monkeys. Food items were classified into flower, fruit, and leaf categories. All of the plant specimens were identified by researchers from the Universidade de São Paulo, Department of Ecology and from the Botanical Institute of Sao Paulo State, and their exsiccates were deposited in the corresponding herbaria.

Ethnomedicine

Semi-structured interviews, field diary and participant observation were used during fieldwork (Bernard, 1988) to obtain knowledge of the people living around the park, regarding the medicinal use of the plants included in the diet of woolly spider monkeys. The authors selected four respondents in April 2016, based on their recognition by other local residents as holders of knowledge on medicinal plants. These correlations were performed using both the popular and scientific names of the plants because the respondents are also park rangers and have thus learned the scientific names of the plants through helping local botanical researchers.

The uses of plants by primates and humans were organized, and their biological activities as reported in the pharmacological scientific literature, as well as other studies on diet of woolly spider monkeys, were assessed to impart greater robustness to the data, enabling inferences on any potential bioactive compounds. One of the limitations of our study is that we did not collect specific data on the health of individuals when feeding. This was not a part of initial study.

Results and discussion

Plant food diet of woolly spider monkeys

The diet of woolly spider monkeys recorded at Intervales State Park contained 53 plant species, from which 87 different items were eaten; leaves, fruits and flowers. An equal number of leaves (45.5%) and fruit (45.5%) items were recognized, with flowers (9%) representing only a small proportion of the diet. These species belonged to 27 families (Box 1). Among them, Myrtaceae had the greatest number of food species (n = 10) represented, followed by Fabaceae s.l. (n = 8), Lauraceae (n = 4), Moraceae (n = 3), Celastraceae, Euphorbiaceae, Rubiaceae, Sapotaceae and Urticaceae (two species each). The remaining families were represented by one species each.

In order to analyze the diet of Intervales State Park woolly spider monkeys compared with that of *B. arachnoides* populations elsewhere, we compared our list with published records in the literature (Box 1). The sites for which literature was available included two states of southeastern Brazil: state of São Paulo: Intervales State Park, municipality of Ribeirão Grande (Vieira and Izar, 1999), Fazenda Barreiro Rico, municipality of Anhembi (Assumpção, 1983; Milton, 1984; Martins, 2008), Carlos Botelho State Park, municipality of São Miguel Arcanjo (Talebi et al., 2005; Bueno et al., 2013); and state of Minas Gerais: Fazenda Montes Claros, municipality of Montes Claros (Brozek, 1991). A complete comparison was difficult, as the part consumed was not always indicated and in some instances plant foods were only listed to the genus level or incomplete species were given.

Food items in species from the Myrtaceae family (n = 17), followed by those of Lauraceae (n = 5) and Fabaceae s.l. (n = 3) were recognized for *B. arachnoides* at Carlos Botelho State Park (Moraes, 1992). These families are among the most common in the region of the Intervales and Carlos Botelho State Parks (Hueck, 1972). In Minas Gerais state, food plant species from the families Fabaceae s.l., Myrtaceae and Moraceae were among the main dietary components of *B. arachnoides* there (Brozek, 1991).

Overall, fifteen species in the same genus were recorded in the diets of these different populations; seven of which were the same species (marked with an asterisk in Box 1). Ten out of the fifteen species had at least one part of the same plant consumed by monkeys at one or more other sites. The main items reported to be consumed were leaves, fruits and flowers. Among the plant food items mentioned in Box 1, whose ingested parts were reported, there was a predominance of fruit (70%), followed to a much lesser extent by leaves (20%), seeds (5%) and flowers (5%). The main food source of *Brachyteles* is fruit. However, Martins (2008) found that depending on location habitat, fruit consumption occupies between 21% and 71% of the average annual feeding time of *B. arachnoides*.

A study conducted by Milton (1984) in Barreiro Rico, São Paulo state, found a higher number of leaves in the diet of woolly spider monkeys than in a study conducted by Strier (1986) in Montes Claros, Minas Gerais state, where a higher number of fruits was observed. These dietary differences are mainly related to the existence of a higher number of species that provide fruits in Montes Claros than in Barreiro Rico (Strier, 1986).

Ethnomedicinal and pharmacological properties of the diet

Evidence for possible medicinal activity in the diet of woolly spider monkeys, either ethnomedicinally or pharmacologically validated, was recognized in 37.7% (20/53 species) of the species listed in Box 1. Of these, thirteen were reported by the four local respondents as being used for ethnomedicinal purposes, fourteen had reported pharmacological activity, while seven had both ethnomedicinal and pharmacological records.

The ethnomedicinal uses described for these species were; laxative/purgative (n = 5), wound healer, cold remedy (n = 3 each), stimulant, bronchitis, ulcers/gastritis, hoarseness, warms the body (n = 2 each). Other less frequently listed properties, represented by one species each were, asthma, fracture, hypotensive, aphrodisiac, postpartum weakness, hepatitis, rheumatism, cleanser, infection, clotting agent, digestive (n = 1 each). Some species had multiple uses reported, *e.g. Tapirira guianensis* was used as a purgative, wound healer and other treatment for cuts. The fact that the indication *to fight a cold* is almost always accompanied by the expression *warms the body* stands out. According to respondents, the sensation imparted is that of comfort because the body becomes warm, mitigating the undesirable cold symptoms.

Twenty-six percent (14/53) of the food plant species in Box 1 have pharmacological properties. However, of the thirteen ethnomedicinal plant species reported by the respondents, only seven had reported pharmacological uses. Of these, three have uses similar to the biological activity reported in the scientific literature (marked with two asterisks in Box 1). The human use of aroeira (*Tapirira guianensis* Aubl.) as a wound and cut healer matched its anti-bacterial pharmacological activity (Roumy et al., 2009). The species *Croton urucurana* Baill., known as pau-sangue (dragon's blood) used as a wound healer, was studied by Peres et al. (1997), who found antimicrobial activity. While jatobá (guapinol), *Hymenaea courbaril* L., indicated for cold symptoms, has shown immunomodulatory activity (Rosário et al., 2008), although the plant parts studied in the pharmacological literature and the parts indicated by the respondents of this study were not always the same (Box 1).

Zoopharmacognosy and ethnomedicine

As mentioned before, among the 53 plants consumed by primates in the present study, thirteen are also used in local human medicine. However, we observed little similarity when comparing the parts of the thirteen plants used by both by the respondents and primates. Humans use the following plant parts for medicinal purposes: bark (four plant species), seeds (3), leaves (2), root, fruit, sap, oil, resin, core, latex and vine (one each); while for these thirteen plants, the primates mostly consumed fruits (nine species) and/or leaves (8).

One possible explanation for this difference is that folk medicine has many plants preparation forms, predominating is the use of leaves and bark in their recipes. While primates have a consistently frugivorous diet when inhabiting less disturbed habitats, as is the case here. Their predominant food item is fruit. Moreover, the fruits are rarely used in human medicine. In this sense, a convergence was not expected.

Still, it is not possible to claim that the bioactive properties are not present in different parts of the plants to establish a broader discussion. Future chemical studies could and should investigate these properties, expanding our understanding and bringing more data to light.

Box 1: The 53 plant food species present in the diet of woolly spider monkeys (*Brachyteles arachnoides)* at Intervales State Park, São Paulo, Brazil. Plant part(s) consumed, their local ethnomedicinal, pharmacological properties and food items reported at other *B. arachnoides* study sites.

Family	Species [voucher] – plant part consumed	Vernacular name	Ethnomedicinal uses (plant part)	Pharmacological properties	Plant foods reported at other sites
Anacardiaceae	*Tapirira guianensis* Aubl. [256464] – Le	Aroeira, roeirão, roeira-brava	*Laxative/purgative, wound healer*[b] (Ba)	Anti-protozoal and anti-bacterial[b] (Roumy et al., 2009)	N.d.f.
Annonaceae	*Guatteria australis* A. St-Hil. [262336] – Fr, Le	Reticueiro	–	Antiplasmodial activity (Fischer et al., 2004)	N.d.f.
Araceae	*Philodendron imbe* Schott *ex* Endl. hort. ex Engl. [249754] – Fr, Le	Trucuá	–	N.d.f.	*Philodendron appendiculatum, P. corcovadense* Kunth., *P. crassinervium* Lindl., *P. exymium* Schott., *P. martianum* and *P. obliquifolium* – Fr (Vieira and Izar, 1999)
Araliaceae	*Schefflera calva* (Cham.) Frodin & Fiaschi [347509] – Le	Mandioqueiro	–	N.d.f.	N.d.f.
Boraginaceae	*Cordia sellowiana* Cham.[a] [263105] – Le	Louro	–	N.d.f.	*Cordia sellowiana*[a] – Fr (Martins, 2008)
Canellaceae	*Cinnamodendron dinisii* Schwacke [397239] – Fr, Le	Pimenteira	–	Antibacterial, Antifungal and Trypanocidal activity (esssential oil) (Andrade et al., 2015)	N.d.f.
Celastraceae	*Cheiloclinium serratum* (Cambess.) A.C. Sm. [252697] – Fr, Le	Cipotá	–	N.d.f.	N.d.f.
	Maytenus cestrifolia Reissek [309097] – Fr	Carrapateiro	–	N.d.f.	N.d.f.
Combretaceae	*Buchenavia kleinii* Exell [129533] – Fr, Le	Amarelinho	–	N.d.f.	N.d.f.
Euphorbiaceae	*Alchornea triplinervia* (Spreng.) Müll. Arg.[a] [205189] – Le	Tapiaeiro-miúdo, tapiá	–	Anti-inflammatory activity (Lopes et al., 2010); Antibacterial activity – Le (Calvo et al., 2010); Gastroprotective effect (Lima et al., 2008)	*Alchornea triplinervia* (Spreng.) Müll. Arg.[a] – n.d.f. (Milton, 1984)
	Croton urucurana Baill. [291906] – Le, Fl	Pau-sangue, sangueiro	*Wound healer*[b] (Sa)	Alleviate pain associated with gastrointestinal and other related disorders – Sa (Rao et al., 2007); Antidiarrhoeal effect – Sa (Gurgel et al., 2001); Antimicrobial activity[b] (Peres et al., 1997)	*Croton floribundus* Spreng. – Fl (Milton, 1984)
Fabaceae s.l.	*Copaifera trapezifolia* Hayne[a] [254711] – Le	Pau-óleo, capaúva, capaúba	*Bronchitis, laxative/purgative, ulcers/gastritis and infection* (Oil)	N.d.f.	*Copaifera langsdorfii* Desf. – n.d.f. (Milton, 1984); *C. langsdorfii* – Se (Assunção, 1983); *Copaifera trapezifolia*[a] – Fr (Bueno, 2013)
	Hymenaea courbaril L.[a] [251741] – Fr, Le	Jatobá	*Clotting agent* (Ba), *cold remedy*[b], *bronchitis, rheumatism, laxative/purgative* (Ba, Re)	Immunomodulatory activity[b] (Rosario et al., 2008) – Se	*Hymenaea courbaril*[a] – Fr (Martins, 2008); *H. courbaril*[a] – n.d.f. (Milton, 1984); *H. courbaril*[a] – Le (Assunção, 1983)
	Inga marginata Kunth. [254729] – Fr, Le	Ingá-mirim, inga-feijão	–	N.d.f.	*Inga striata* – Fr (Martins, 2008); *I. striata* – Se (Milton, 1984); *I. sessilis*[a] – Le (Talebi et al., 2005)
	Inga sessilis (Vell.) Mart.[a] [256195] – Fr, Le	Ingá-macaco	–	N.d.f.	
	Piptadenia adiantoides (Spreng.) .J.F. Macbr. [373254] – Fr	Gambaeiro	–	Leishmanicidal (Campos et al., 2008)	*Piptadenia gonoacantha* – n.d.f. (Milton, 1984)
	Pseudopiptadenia warmingii (Benth.)G.P.Lewis e M.P.Lima [285783] – Le	Calvin	–	N.d.f.	N.d.f.
	Swartzia acutifolia Vogel [159775] – Le	Terereca	–	N.d.f.	N.d.f.

Box 1: (*Continued*)

Family	Species [voucher] – plant part consumed	Vernacular name	Ethnomedicinal uses (plant part)	Pharmacological properties	Plant foods reported at other sites
	Tachigali denudata (Vogel) Oliveira-Filho [254424] – Le	Pascoré, pasquaré	–	N.d.f.	N.d.f.
Lauraceae	*Beilschmiedia emarginata* (Meisn.) Kosterm. [101743] – Fr, Le	Canela-batalha, canela-bataia	–	N.d.f.	N.d.f.
	Ocotea diospyrifolia (Meissn.) Mez [331471] – Fr, Le	Canela-nhutinga	*Aphrodisiac, warms the body, cold remedy, hoarseness* (Fr, Se)	Acaricidal activity (Dos Santos et al., 2013)	*Ocotea corymbosa* – Fr (Martins, 2008); *O. odorifera* (Vell.) Rohwer[a] – Le (Talebi et al., 2005); *O. spixiana* Nees., *O. acutifolia* Nees., *Ocotea* sp. – Le (Milton, 1984); *O. spixiana* – Fr (Assunção, 1983)
	Ocotea odorifera Rohwer[a] [300387] – Fr, Le	Canela-sassafrás	*Stimulant, cold remedy, hoarseness, warms the body* (Ba, He)	Antifungal effects – Le (Yamaguchi et al., 2011); Antimicrobial (De Souza et al., 2004)	
	Ocotea porosa (Nees & Mart.) Barroso [204129] – Fr, Le	Canela-amarela	–	N.d.f.	
Magnoliaceae	*Magnolia ovata* A.St.-Hill. [253046] – Le	Pinho-bravo	–	Antipyretic and anti-inflammatory (Kassuya et al., 2009); Insecticidal activity (Coelho et al., 2006); Hypoglycemic effect – Le (Morato et al., 1989)	N.d.f.
Malvaceae	*Spirotheca rivieri* (Decne.) Ulbr. [13075] – Fr, Le, Fl	Figueira-mata-pau	–	N.d.f.	N.d.f.
Melastomataceae	*Tibouchina pulchra* (Cham.) Cogn. [286821] – Le, Fl	Manacá-da-serra	–	N.d.f.	N.d.f.
Meliaceae	*Cabralea canjerana* (Vell.) Mart. [248092] – Le	Canjarana, canharana	–	N.d.f.	*Cabralea* sp. – n.d.f. (Milton, 1984)
Menispermaceae	*Abuta selloana* Eichler [318838] – Fr	Grão-de-mico, buta	*Postpartum weakness* (Li)	N.d.f.	n.d.f.
Moraceae	*Ficus insipida* Willd. [247888] – Fr, Le	Figueira-branca	–	Anthelmintic activity – La (de Amorim et al., 1999)	*Ficus* sp. – Fr (Milton, 1984)
	Ficus organensis Miq. [374561] – Fr, Le	Figueira	–	N.d.f.	
	Sorocea bonplandii (Baill.) W.C. Burger, Lanj. & Wess. Boer. [318828] – Fr	Laranjinha	*Ulcers/gastritis* (Le)	N.d.f.	N.d.f.
Myristicaceae	*Virola bicuhyba* (Schott ex Spreng.) Warb. [288360] – Fr, Le	Bucúva, bucuveira	*Laxative/purgative and digestive* (Se)	Analgesic activity – Le (Kuroshima et al., 2001)	N.d.f.
Myrtaceae	*Campomanesia guaviroba* (DC.) Kiaersk. [304809] – Fr, Le	Guabirova, guabiroba	–	N.d.f.	*Campomanesia* sp. – Fr (Martins, 2008)
	Eugenia burkartiana (D.Legrand) D.Legrand [312083] – Fr	Murta	–	N.d.f.	*Eugenia pyriformis, E. ligustrina, Eugenia* sp. – Fr (Martins, 2008); *Eugenia* sp. – Fr (Talebi et al., 2005); *Eugenia* sp. – Fr (Assunção, 1983)
	Eugenia pruinosa D.Legrand [262439] – Fr	Murta	–	N.d.f.	
	Myrceugenia myrcioides (Cambess.) O.Berg [262327] – Fr	Cafeeiro	*Stimulant* (Se)	N.d.f.	N.d.f.
	Myrcia anacardiifolia Gardner [313862] – Fr	Goiabinha	–	N.d.f.	N.d.f.
	Myrcia grandifolia Kiaersk [254610] – Fr, Le, Fl	Murta	–	N.d.f.	N.d.f.
	Myrcia macrocarpa Barb. Rodr. [246584] – Fr	Goiabinha, murta	–	N.d.f.	N.d.f.
	Myrcia pubipetala Miq. [250041] – Fr	Murta	–	N.d.f.	N.d.f.
	Myrciaria floribunda (H.West *ex* Willd.) O.Berg [292773] – Fr, Le, Fl	Araçazinho	–	N.d.f.	*Myrciaria* sp. – Fr (Milton, 1984)
	Psidium longipetiolatum D.Legrand [293823] – Fr, Le, Fl	Araçá-piranga	–	N.d.f.	N.d.f.
Nyctaginaceae	*Guapira opposita* (Vell.) Reitz [246573] – Le	Abobreiro, carne-de-vaca	–	N.d.f.	N.d.f.

Box 1: (*Continued*)

Family	Species [voucher] – plant part consumed	Vernacular name	Ethnomedicinal uses (plant part)	Pharmacological properties	Plant foods reported at other sites
Ochnaceae	*Quiina glaziovii* Engl. [290593] – Fr	Jerivazinho	–	N.d.f.	N.d.f.
Phyllanthaceae	*Hyeronima alchorneoides* Allemão [296596] – Fr, Le, Fl	Recurana, aricurana	–	N.d.f.	N.d.f.
Phytolaccaceae	*Phytolacca dioica* L. [288761] – Fr, Le, Fl	Embueiro	–	Antifungal activity – Fr (Di Liberto et al., 2010)	N.d.f.
Rubiaceae	*Bathysa australis* (A.St.-Hil.) K.Shum. [358307] – Le	Fumo-bravo, fumeiro	–	N.d.f.	N.d.f.
	Posoqueria latifolia (Rudge) Roem & Schult. [350771] – Fr	Laranja-de-macaco	–	N.d.f.	N.d.f.
Sapotaceae	*Chrysophyllum viride* Mart. & Eichler [275282] – Fr, Le, Fl	Bujoeiro, pau-marfim	–	N.d.f.	N.d.f.
	Pouteria bullata (S. Moore) Baehni[a] [32105] – Fr	Guapeva-branca	*Wound healer and hepatitis* (La and Fr)	N.d.f.	*Pouteria bullata*[a] – Fr (Bueno et al., 2013)
Solanaceae	*Solanum rufescens* Sendtn. [305753] – Le	Quina-branca	*Laxative/purgative* (Ba, Ro)	N.d.f.	N.d.f.
Urticaceae	*Cecropia glaziovii* Snethl. [309099] – Fr, Le	Embaúba	*Asthma, fracture, cleanser, hypotensive* (Br)	Antisecretory and antiulcer activities (Souccar et al., 2008); Antidepressant-like effect (Rocha et al., 2007); Anxiolytic-like effects (Rocha et al., 2002)	N.d.f.
	Coussapoa microcarpa (Schott) Rizzini [268699] – Fr, Le	Figueira-mata-pau	–	N.d.f.	N.d.f.

[a] The matches between the plant species consumed by woolly spider monkeys observed in the present study and reported at other *B. arachnoides* study sites.

[b] Local ethnomedicinal value is consistent with reports from the pharmacological literature.

Ba, bark; Sa, sap; Br, bract; Ro, root; La, latex; Li, liana; He, heartwood; Fr, fruit; Re, resin; Le, leaves; Fl, flowers; Se, seeds; N.d.f., no data found.

While pharmacological literature corroborated some of the biological activity obtained from our interviews, this overlap is not the most outstanding aspect of this study. Rather, it is notable that thirteen species of a total of 53 plants present in the diet of monkeys are included in the medicinal repertoire of people living around the park. Several studies have previously shown a strong correlation between the plants used by primates for self-medication and plant species used in the traditional medicines of local communities (Baker, 1996; Gottlieb et al., 1996; Huffman, 1997; Cousins and Huffman, 2002; Krief et al., 2005).

Krief et al. (2005) also found that several plant species included in the diet of chimpanzees are used by traditional healers in local communities in Africa. When correlating these plants with the ethnomedicinal literature, those authors found that at least 35 (21.5%) of the 163 species included in the diet of chimpanzees are used in traditional medicine, including in the treatment of intestinal parasites, skin infections and respiratory diseases. Huffman (1997, 2003) also reported in two studies of chimpanzees, that 22% of the diet contained medicinal plants used specifically against parasites by people in Africa. Also, a study conducted by MacIntosh and Huffman (2010) verified that 21.9% of the plant food items of ten Japanese macaque troops also contained antiparasitic and other medicinal properties. The results of the present study are similar to that reported above; *i.e.* 24.5% (13/53) of the plants in the diet of the woolly spider monkeys matched the plants used in local human medicine.

These studies show that almost one quarter of plants found in the diets of primates have some medicinal value to humans. This is interesting as it indicates a commonality between humans and non-human primates in their selection of plants. Further studies should investigate the relative medicinal and nutritional value of these plants.

Cousins and Huffman (2002) indicated a strong correlation between the plants used by gorillas and the plants used by local communities to treat parasitic, fungal, viral, cardiac and respiratory diseases. These uses corroborate the data found in the present study because many of those therapeutic uses were also reported herein.

It is interesting that five (38.5%) of the plants recognized by respondents in our study as being medicinal are used as laxatives and purgatives, *i.e. Tapirira guianensis* Aubl., *Copaifera trapezifolia* Hayne, *Virola bicuhyba* (Schott ex Spreng.) Warb., *Solanum rufescens* Sendtn. and *H. courbaril* L. Another five species have anti-parasitic activities in the literature (Box 1), including the following activities; leishmanicidal: *Piptadenia adiantoides* (Spreng.) J.F. Macbr., (Campos et al., 2008), anthelmintic: *Ficus insipid* Willd. (de Amorin et al., 1999), antiplasmodial: *Guatteria australis* A. St-Hil. (Fischer et al., 2004), trypanocidal: *Cinnamodendron dinisii* Schwacke (Andrade et al., 2015) and acaricidal: *Ocotea diospyrifolia* (Meissn.) Mez (Dos Santos et al., 2013) (Box 1).

Our data indicate the importance of plants with laxative and purgative activities in the diet of woolly spider monkeys. Such therapeutic uses in humans may be related to anti-parasitic activities in primates, as was also observed in previous studies (Huffman and Seifu, 1989; Huffman et al., 1993, 1996, 1997; Huffman and Caton, 2001). These studies established a direct link between parasite infection and 'self-medication' in chimpanzees. In our study it was not possible to establish such a correlation, since faecal parasitological analysis of the monkeys were not conducted. For this reason, in the present study we could only make inferences considering their potential as medicinal foods. The physiological balance existing between primates and parasites is a known phenomenon, and it is even more relevant in animals inhabiting less anthropised environments (Kowalewski et al., 2010), as in the case of our study. Accordingly, the use of plants with antiparasitic activity is important and, therefore, could explain their use not only among humans but also among primates, strengthening their pharmacological potential.

Among the plants present in the diet of woolly spider monkeys, in addition to the therapeutic uses outlined above, we found two toxic plants, *Phytolacca dioica* L. (Ashafa et al., 2010) and *Ficus insipida* Willd (de Amorin et al., 1999). The same plant parts shown to be toxic are the parts consumed most by the woolly spider monkeys while they are actively avoided by other primates such as chimpanzees (Gustafsson et al., 2016). This should be examined more closely in future studies.

Conclusion

The relationships between plants, primates and humans observed in the present study indicate potential bioactive compounds to be examined in future pharmacological and phytochemical studies, especially those plants with antiparasitic activity. Both aspects could significantly contribute to improving the quality of life of local communities and to the sustainability of the Atlantic Forest, especially at the study site.

Ethical disclosures

Protection of human and animal subjects. The authors declare that no experiments were performed on humans or animals for this study.

Confidentiality of data. The authors declare that no patient data appear in this article.

Right to privacy and informed consent. The authors declare that no patient data appear in this article.

Authors' contributions

LP and ER have together idealized this study. LP has collected data among the muriquis and ER has collected the ethnomedicinal data among the interviewees. MAH contributed to the writing, analysis and literature search. All authors have read the final manuscript and approved submission.

Conflicts of interest

The authors declare no conflicts of interest.

Acknowledgements

We thank the people living around Intervales State Park who participated in the interviews for providing their knowledge on the medicinal use of plants and helping to collect and identify the species included in the diet of woolly spider monkeys: Luís Avelino, Ditinho, João Vaz and Tonico. We thank Sônia Aragaki, Eduardo Gomes and Waldir Mantovani for help with identifying the plant species. We thank the Fundação Florestal para a Conservação e a Produção Florestal do Estado de São Paulo for the logistical support and for allowing us to conduct this study at Intervales State Park. We thank FAPESP, CNPq, CAPES, Fundação O Boticário de Proteção à Natureza, and the World Wide Fund for Nature for their financial support. We also thank two anonymous referees for their helpful suggestions in improving this paper.

References

Altmann, J., 1974. Observational study of behavior: sampling methods. Behaviour 49, 227–267.

Altmann, S.A., 1998. Foraging for Survival, Yearling Baboon in Africa. Chicago University of Chicago Press.

Andrade, M.A., Cardoso, M.d.G., Gomes, M.d.S., de Azeredo, C.M.O., Batista, L.R., Soares, M.J., Rodrigues, L.M.A., Figueiredo, A.C.S., 2015. Biological activity of the essential oils from *Cinnamodendron dinisii* and *Siparuna guianensis*. Braz. J. Microbiol. 46, 189–194.

Ashafa, A.O., Sunmonu, T.O., Afolayan, A.J., 2010. Toxicological evaluation of aqueous leaf and berry extracts of *Phytolacca dioica* L. in male Wistar rats. Food Chem. Toxicol. 48, 1886–1889.

Assumpção, C.T., 1983. Ecological and behavioural information on *Brachyteles arachnoides*. Primates 24, 584–593.

Baker, M., 1996. Fur rubbing: use of medicinal plants by capuchin monkeys (*Cebus capucinus*). Am. J. Primatol. 38, 263–270.

Bernard, H.R., 1988. Research Methods in Cultural Anthropology. Sage Publications, London.

Brozek, R.M., 1991. Observações sobre a ecologia alimentar e a dispersão de sementes pelo muriqui (*Brachyteles arachnoides* E. Geoffroy, 1806 – Cebidae, Primates). Graduate thesis presented to Universidade Estadual Paulista, Rio Claro – SP.

Bueno, R.S., Guevara, R., Ribeiro, M.C., Culot, L., Bufalo, F.S., Galetti, M., 2013. Functional redundancy and complementarities of seed dispersal by the last neotropical megafrugivores. PLoS ONE 8, e56252.

Calvo, T.R., Demarco, D., Santos, F.V., Moraes, H.P., Bauab, T.M., Varanda, E.A., Cólus, I.M., Vilegas, W., 2010. Phenolic compounds in leaves of *Alchornea triplinervia*: anatomical localization, mutagenicity, and antibacterial activity. Nat. Prod. Commun. 5, 1225–1232.

Campos, F.F., Rosa, L.H., Cota, B.B., Caligiorne, R.B., Rabello, A.L., Alves, T.M., Rosa, C.A., Zani, C.L., 2008. Leishmanicidal metabolites from *Cochliobolus* sp., an endophytic fungus isolated from *Piptadenia adiantoides* (Fabaceae). PLoS Negl. Trop. Dis. 2, 348.

Carrai, V., Borgognini-Tarli, S.M., Huffman, M.A., Bardi, M., 2003. Increase in tannin consumption by sifaka (*Propithecus verreauxi verreauxi*) females during the birth season: a case for self-medication in prosimians? Primates 44, 61–66.

Carvalho Jr., O., 1996. Dieta, padrões de atividades e de agrupamento do monocarvoeiro (*Brachyteles arachnoides*) no Parque Estadual de Carlos Botelho, SP. Master's degree thesis presented to Universidade Federal do Pará.

Coelho, A.A., de Paula, J.E., Espíndola, L.S., 2006. Insecticidal activity of cerrado plant extracts on *Rhodnius milesi* Carcavallo, Rocha, Galvão & Jurberg (Hemiptera: Reduviidae), under laboratory conditions. Neotrop. Entomol. 35, 133–138.

Cousins, D., Huffman, M.A., 2002. Medicinal properties in the diet of gorillas: an ethno-pharmacological evaluation. Afr. Study Monogr. 23, 65–89.

de Amorin, A., Borba, H.R., Carauta, J.P., Lopes, D., Kaplan, M.A., 1999. Anthelmintic activity of the latex of *Ficus* species. J. Ethnopharmacol. 64, 255–258.

De Souza, G.C., Haas, A.P., von Poser, G.L., Schapoval, E.E., Elisabetsky, E., 2004. Ethnopharmacological studies of antimicrobial remedies in the south of Brazil. J. Ethnopharmacol. 90, 135–143.

Di Liberto, M., Svetaz, L., Furlán, R.L., Zacchino, S.A., Delporte, C., Novoa, M.A., Asencio, M., Cassels, B.K., 2010. Antifungal activity of saponin-rich extracts of *Phytolacca dioica* and of the sapogenins obtained through hydrolysis. Nat. Prod. Commun. 5, 1013–1018.

Dos Santos, L.B.D., Souza, J.K., Papassoni, B., Borges, D.G.L., Junior, G.A.D., Souza, J.M.E.D, Carollo, C.A., Borges, F.D.A., 2013. Efficacy of extracts from plants of the Brazilian Pantanal against Rhipicephalus (Boophilus) microplus. Rev. Bras. Parasitol. Vet. 22, 532–538.

Fischer, D.C., de Amorim, G.N.C., Bachiega, D., Carvalho, C.S., Lupo, F.N., Bonotto, S.V., Alves Mde, O., Yogi, A., Santi, S.M., Avila, P.E., Kirchgatter, K., Moreno, P.R., 2004. In vitro screening for antiplasmodial activity of isoquinoline alkaloids from Brazilian plant species. Acta Trop. 92, 261–266.

Glander, K.E., 1982. The impact of plant secondary compounds on primate feeding behavior. Am. J. Phys. Anthropol. 25 (Suppl. 3), S1–S18.

Glander, K.E., 1994. Nonhuman primate self-medication with wild plant foods. In: Etkin, N.L. (Ed.), Eating on the Wild side: The Pharmacologic, Ecological, and Social Implications of Using Noncultigens. University of Arizona Press, Tuscon, pp. 239–256.

Gottlieb, O.R., de Borin, M.R., Bosisio, B.M., 1996. Trends of plant use by humans and nonhuman primates in Amazonia. Am. J. Primatol. 40, 189–195.

Gurgel, L.A., Silva, R.M., Santos, F.A., Martins, D.T., Mattos, P.O., Rao, V.S., 2001. Studies on the antidiarrhoeal effect of dragon's blood from *Croton urucurana*. Phytother. Res. 15, 319–322.

Gustafsson, E., Saint Jalme, M., Kamoga, D., Mugisha, L., Snounou, G., Bomsel, M.C., Krief, S., 2016. Food acceptance and social learning opportunities in semi-free Eastern chimpanzees (*Pantroglodytes schweinfurthii*). Ethology 122, 158–170.

Hueck, K., 1972. As florestas da América do Sul. Editora Polígono S.A., São Paulo.

Huffman, M.A., Seifu, M., 1989. Observations on the illness and consumption of a possibly medicinal plant *Vernonia amygdalina* by a wild chimpanzee in the Mahale Mountains, Tanzania. Primates 30, 51–63.

Huffman, M.A., 1997. Current evidence for self-medication in primates: a multidisciplinary perspective. Yearbk. Phys. Anthropol. 40, 171–200.

Huffman, M.A., 2003. Animal self-medication and ethnomedicine: exploration and exploitation of the medicinal properties of plants. Proc. Nutr. Soc. 62, 371–381.

Huffman, M.A., Gotoh, S., Izutsu, D., Koshimizu, K., Kalunde, M.S., 1993. Further observations on the use of the medicinal plant, *Vernonia amygdalina* (Del) by a wild chimpanzee, its possible effect on parasite load, and its phytochemistry. Afr. Study Monogr. 14, 227–240.

Huffman, M.A., Page, J.E., Sukhdeo, M.V.K., Gotoh, S., Kalunde, M.S., Chandrasiri, T., Towers, G.H.N., 1996. Leaf-swallowing by chimpanzees, a behavioral adaptation for the control of strongyle nematode infections. Int. J. Primatol. 17, 475–503.

Huffman, M.A., Gotoh, S., Turner, L.A., Hamai, M., Yoshida, K., 1997. Seasonal trends in intestinal nematode infection and medicinal plant use among chimpanzees in the Mahale Mountains National Park, Tanzania. Primates 38, 111–125.

Huffman, M.A., Ohigashi, H., Kawanaka, M., Page, J.E., Kirby, G.C., Gasquet, M., Murakami, A., Koshimizu, K., 1998. African great ape self-medication: a new paradigm for treating parasite disease with natural medicines. In: Ebizuka, Y. (Ed.), Towards Natural Medicine Research in the 21st Century. Elsevier Science B.V., Amsterdam, pp. 113–123.

Huffman, M.A., Caton, J.M., 2001. Self-induced increase of gut motility and the control of parasitic infections in wild chimpanzees. Int. J. Primatol. 22, 329–346.

Janzen, D.H., 1978. Complications in interpreting the chemical defenses of trees against tropical arboreal plant-eating vertebrates. In: Montgomery, G.G. (Ed.), The Ecology of Arboreal Folivores. Smithsonian Institute Press, Washington, DC, pp. 73–84.

Kassuya, C.A., Cremoneze, A., Barros, L.F., Simas, A.S., Lapa, F. da R., Mello-Silva, R., Stefanello, M.E., Zampronio, A.R., 2009. Antipyretic and anti-inflammatory properties of the ethanolic extract, dichloromethane fraction and costunolide from *Magnolia ovata* (Magnoliaceae). J. Ethnopharmacol. 124, 369–376.

Kowalewski, M.M., Salzer, J.S., Deutsch, J.C., Raño, M., Kuhlenschmidt, M.S., Gillespie, T.R., 2010. Black and gold howler monkeys (*Alouatta caraya*) as sentinels of ecosystem health: patterns of zoonotic protozoa infection relative to degree of human-primate contact. Am. J. Primatol. 71, 1–9.

Krief, S., Martin, M., Grellier, P., Kasenene, J., Sévenet, T., 2004. Novel antimalarial compounds isolated in a survey of self-medicative behavior of wild chimpanzees in Uganda. Antimicrob. Agents Chemother. 48, 3196–3199.

Krief, S., Hladik, C.M., Haxaire, C., 2005. Ethnomedicinal and bioactive properties of the plants ingested by wild chimpanzees in Uganda. J. Ethnopharmacol. 101, 1–15.

Krief, S., Wrangham, R.W., Lestel, D., 2006. Diversity of items of low nutritional value ingested by chimpanzees from Kanyawara, Kibale National Park, Uganda: an example of the etho-ethnology of chimpanzees. Soc. Sci. Inf. 45, 227–263.

Kuroshima, K.N., de Campos, F., de Souza, M.M., Yunes, R.A., Delle Monache, F., Cechinel Filho, V., 2001. Phytochemical and pharmacological investigations of *Virola oleifera* leaves. Z. Naturforsch. C 56, 703–706.

Lambert, J.E., 2011. Primate nutritional ecology. Feeding biology and diet at ecological and evolutionary scales. In: Campbell, C., Fuentes, A., MacKinnon, K., Panger, M., Bearder, S. (Eds.), Primates in Perspective. University of Oxford Press, Oxford, pp. 512–522.

Lemos de Sá, R.M., 1988. Situação de uma população de mono-carvoeiro, Brachyteles arachnoides, em fragmento de Mata Atlântica (MG), e implicações para sua conservação. Master's degree thesis presented to Universidade de Brasília, Brasília.

Lima, Z.P., Calvo, T.R., Silva, E.F., Pellizzon, C.H., Vilegas, W., Brito, A.R., Bauab, T.M., Hiruma-Lima, C.A., 2008. Brazilian medicinal plant acts on prostaglandin level and *Helicobacter pylori*. J. Med. Food 11, 701–708.

Lopes, F.C., Calvo, T.R., Vilegas, W., Carlos, I.Z., 2010. Anti-inflammatory activity of *Alchornea triplinervia* ethyl acetate fraction: inhibition of HO, NO and TNF-α. Pharm. Biol. 48, 1320–1327.

MacIntosh, A.J.J., Huffman, M.A., 2010. Towards understanding the role of diet in host–parasite interactions in the case of Japanese macaques. In: Nakagawa, F., Nakamichi, M., Sugiura, H. (Eds.), The Japanese Macaques. Springer, Tokyo, pp. 323–344.

Martins, M.M., 2008. Fruit diet of *Alouatta guariba* and *Brachyteles arachnoides* in Southeastern Brazil: comparison of fruit type, color, and seed size. Primates 49, 1–8.

Medeiros, M.F.T., da Fonseca, V.S., Andreata, R.H.P., 2004. Plantas medicinais e seus usos pelos sitiantes da Reserva Rio das Pedras, Mangaratiba, RJ, Brasil. Acta Bot. Bras. 18, 391–399.

Milton, K., 1984. Habitat, diet, and activity patterns of free-ranging woolly spider monkeys (*Brachyteles arachnoides* E. Geoffroy 1806). Int. J. Primatol. 5, 491–514.

Moraes, P.L.R.d., 1992. Espécies utilizadas na alimentação do mono-carvoeiro (*Brachyteles arachnoides* E. Geoffroy, 1806) no Parque Estadual de Carlos Botelho. In: Anais do 2° Congresso Nacional sobre Essências Nativas, São Paulo 3., pp. 1206–1208.

Morato, G.S., Calixto, J.B., Cordeiro, L., de Lima, T.C., Morato, E.F., Nicolau, M., Rae, G.A., Takahashi, R.N., Valle, R.M., Yunes, R.A., 1989. Chemical and pharmacological studies on *Talauma ovata* St. Hil. (Magnoliaceae). J. Ethnopharmacol. 26, 277–286.

Mori, S.A., Silva, L.A.M., Lisboa, G., Coradin, L., 1985. Manual de manejo do herbário fanerogâmico. Centro de Pesquisas do Cacau, Ilhéus.

Oats, J.F., 1987. Food distribution and foraging behavior. In: Smuts, B.B., Cheney, D.L., Seyfarth, R.M., Wrangham, R.W., Struhsaker, T.T. (Eds.), Primate Societies. University of Chicago Press, Chicago.

Ohigashi, H., Huffman, M.A., Izutsu, D., Koshimizu, K., Kawanaka, M., Sugiyama, H., Kirby, G.C., Warhurst, D.C., Allen, D., Wright, C.W., Phillipson, J.D., Timmon-David, P., Delmas, F., Elias, R., Balansard, G., 1994. Toward the chemical ecology of medicinal plant use in chimpanzees: the case of *Vernonia amygdalina*, a plant used by wild chimpanzees possibly for parasite-related diseases. J. Chem. Ecol. 20, 541–553.

Peres, M.T., Delle Monache, F., Cruz, A.B., Pizzolatti, M.G., Yunes, R.A., 1997. Chemical composition and antimicrobial activity of *Croton urucurana* Baillon (Euphorbiaceae). J. Ethnopharmacol. 56, 223–226.

Petroni, L.M., 1993. Aspectos da ecologia e comportamento do mono-carvoeiro *Brachyteles arachnoides* (E. Geoffroy, 1806) (Cebidae, Primates), na Fazenda Intervales, Serra de Paranapiacaba, São Paulo. Master's degree thesis presented to Pontifícia Universidade Católica do Rio Grande do Sul. Porto Alegre.

Petroni, L.M., 2000. Caracterização da área de uso e dieta do mono-carvoeiro (*Brachyteles arachnoides*, Cebidae-Primates) na Mata Atlântica, Serra de Paranapiacaba, SP. Doctorade thesis presented to Universidade de São Paulo. São Paulo.

Rao, V.S., Gurgel, L.A., Lima-Júnior, R.C., Martins, D.T., Cechinel-Filho, V., Santos, F.A., 2007. Dragon's blood from *Croton urucurana* (Baill.) attenuates visceral nociception in mice. J. Ethnopharmacol. 113, 357–360.

Rocha, F.F., Lapa, A.J., De Lima, T.C., 2002. Evaluation of the anxiolytic-like effects of *Cecropia glazioui* Sneth in mice. Pharmacol. Biochem. Behav. 71, 183–190.

Rocha, F.F., Lima-Landman, M.T., Souccar, C., Tanae, M.M., De Lima, T.C., Lapa, A.J., 2007. Antidepressant-like effect of *Cecropia glazioui* Sneth and its constituents – *in vivo* and *in vitro* characterization of the underlying mechanism. Phytomedicine 14, 396–402.

Rodriguez, E., Wrangham, R.W., 1993. Zoopharmacognosy: the Use of Medicinal Plants by Animals. In: Downum, K.R., Romeo, J.T., Stafford, H. (Eds.), Recent Advances in Phytochemistry, Phytochemical Potential of Tropic Plants. Plenum Press, New York, pp. 89–105.

Rosário, M.M., Noleto, G.R., Bento, J.F., Reicher, F., Oliveira, M.B., Petkowicz, C.L., 2008. Effect of storage xyloglucans on peritoneal macrophages. Phytochemistry 69, 464–472.

Roumy, V., Fabre, N., Portet, B., Bourdy, G., Acebey, L., Vigor, C., Valentin, A., Moulis, C., 2009. Four anti-protozoal and anti-bacterial compounds from *Tapirira guianensis*. Phytochemistry 70, 305–311.

Souccar, C., Cysneiros, R.M., Tanae, M.M., Torres, L.M., Lima-Landman, M.T., Lapa, A.J., 2008. Inhibition of gastric acid secretion by a standardized aqueous extract of *Cecropia glaziovii* Sneth and underlying mechanism. Phytomedicine 15, 462–469.

Talebi, M., Bastos, A., Lee, P.C., 2005. Diet of southern muriquis in continuous Brazilian Atlantic forest. Int. J. Primatol. 26, 1175–1187.

Vieira, E.M., Izar, P., 1999. Interactions between aroids and arboreal mammals in the Brazilian Atlantic rainforest. Plant Ecol. 145, 75–82.

Yamaguchi, M.U., Garcia, F.P., Cortez, D.A., Ueda-Nakamura, T., Filho, B.P., Nakamura, C.V., 2011. Antifungal effects of Ellagitannin isolated from leaves of *Ocotea odorífera* (Lauraceae). Antonie Van Leeuwenhoek 99, 507–514.