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Brazilian plants with possible action on the central nervous system—A study of historical sources from the 16th to 19th century

Melina Giorgetti, Giuseppina Negri, Eliana Rodrigues *

CEBRID, Department of Psychobiology at UNIFESP, Sao Paulo, Brazil

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Abstract

Brazil is a country rich in biodiversity, endemism, and cultural diversity, inhabited by different types of population. European expeditions and the migratory processes that began in the 16th century greatly contributed both to cultural diversity and to Brazilian popular therapeutics, and produced the first records on medicinal plants in Brazil. This study comprises a bibliographical survey of historic books found in Sao Paulo libraries (16th through 19th centuries) on medicinal plants exerting effects on the central nervous system (CNS). Thirty-four plants native to Brazil were selected from the reading of the books. Of these 34 plants, 13 were also recorded in ethnopharmacological studies among modern Brazilian communities and 16 have been studied phytochemically. Only eight have been the object of pharmacological studies, six of these, recently, with a request for a patent. Results showed that most of the species recorded in this study have been reported as medicinal for centuries, but have never been the object of pharmacological investigation down to the present time. Such results provide ideas for a selection of these species as potentially bioactive to be included in future pharmacological studies.

Keywords: Medicinal plants; Central nervous system; Ethnopharmacology; Historic literature; Popular knowledge; Ethnobotany

1. Introduction

Brazil is a country rich in diversity and endemism, with a territory that includes five main biomas: the Amazon rain forest, the Cerrado brushlands, the Mata Atlântica rain forest, the Pantanal wetlands, and the Caatinga semi-arid desert. Brazil is also rich in cultural diversity and is inhabited by several types of traditional communities and ethnic groups such as Indigenous ethnic groups, Quilombola communities, and other traditional populations (Caboclo/river dwellers, Caiçara fishermen, the Jangadeiro raftsmen, babaçu gatherers, and rubber tappers), the latter being the result of miscegenation between native Indian, European, and African elements. Descendants of Europeans and Asians settled in Brazil during colonization and migratory processes begun at the start of the 16th century. This miscegenation enhanced the culture and rituals of some Brazilian communities and ethnic groups, enriching them from the ethnobotanical point of view.

Little was known about Brazil at the time of the discoveries. The first Jesuits, scientists, explorers, and settlers to arrive in Brazil (such as Padre Anchieta, Guilherme Piso and Von Martius) reported on all the characteristics they could observe (Kury, 2001); these writings are today regarded as the first ethnobotanical records on Brazilian medicinal plants and their uses by different populations.

In time, this knowledge took different paths—in part passed on from one person to another as people moved on (migration, journeys, etc.) to be later re-transmitted, diffused and broadly utilized by several populations in all parts of the country. However, another part of the knowledge was not passed on: its use became less and less frequent over the course of time and, not having been awarded the attention it deserved by the population and scientific community, was wholly forgotten. Only a few written records survived in books from the past centuries. Some studies outside Brazil have focused at the history of plant use from an ethnopharmacological perspective (Fabre, 2003; Heinrich and Teoh, 2004; Kufer et al., 2005; Heinrich et al., 2006).

The main objective of this study is, from a bibliographical survey of historic Brazilian literature, to recover therapeutic uses of plants native to Brazil, going back over centuries, and, con-

* Corresponding author at: Department of Psychobiology, UNIFESP, R. Botucatu, 862 Ed. Ciências Biomedicas (1° Andar), CEP 04023-062 Sao Paulo, Brazil. Tel.: +55 11 21490155; fax: +55 11 50842793.
E-mail address: elirodri@psicobio.epm.br (E. Rodrigues).

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comitantly, to search for phytochemical and pharmacological investigations. The data obtained in this study may serve as a basis to select the species to be investigated in future pharmacological and phytochemical studies.

Therefore, the aim of the present study matches the recent concept for ethnopharmacology, which is an "Interdisciplinary study of the physiological actions of plant, animal and other substances used in indigenous medicines of past and present cultures" (International Society of Ethnopharmacology, 2005).

2. Methodology

The investigation focused on historic books on popular use of medicinal plants found in Sao Paulo institutions. Included were: the University of Sao Paulo libraries, the Botanical Institute of the State of Sao Paulo, the Padre Anchieta Museum, and private collections owned by researchers José Ribeiro do Valle and Elisaldo Luís de Araújo Carlini, with over 40 years of their academic life devoted to the study of medicinal plants. The search yielded six books of great interest to the project, published between the 16th and the 19th centuries. Reports on plant species with therapeutic uses that might affect the central nervous system (CNS) were obtained by reading the books. This article focuses on the CNS, based on the fact that 450 million people in all of the world experience mental, neurological, or behavioral problems at some time (WHO, 2006).

The geographical origin of the species selected was verified using the six-volume Pio Corrêa (1926); books by Lorenzi (1992, 1998, 2003), Lorenzi and Matos (2002), Missouri Botanical Garden Website (2006) and specific flora found in large herbaria.

Bibliographical surveys concerning ethnopharmacological studies were made to verify if species recorded in the present study have uses in modern Brazilian communities. It was searched in Pubmed and in UNIFESP collection. This research was carried out in June 2006.

Efforts were made to identify modern pharmacological studies that might partially validate some of the possible effects related to uses encountered in the historical sources. Bibliographical surveys were carried out in Pubmed (August 2005) and in all of the Annals of the Brazilian Symposium of Medicinal Plants (from 1968 until 2004), one of the most relevant sources for Brazil. In 2006 (May), a survey was also conducted in Dr. Duke's Phytochemical and Ethnobotanical Database.

The bibliographical research on all of the chemical classes found in the plants selected was carried out in the Web of Science (July 2006) utilizing the scientific name of each plant. Results of the survey were evaluated to certify that the article contained the chemical constituents analyzed in order to discard false results. Information was classified in "phytochemical classes" present in each plant: the chemical constituent was not mentioned so that comparisons and results might be visualized more clearly.

Every attempt was made, also, to verify whether the species identified in this study are available on the market in Brazil as pharmaceutical products. ANVISA (National Agência for Sanitary Vigilance) – a regulatory agency for Brazilian medication with a complete list of these products – was consulted (http://www.anvisa.gov.br/ July 2005). DEF (Dicionário de Especialidades Farmaceuticas 2004/2005), an up-to-date listing of medication legally approved in Brazil was also consulted.

Finally, a survey verified the existence of any patent related to the species recorded in the present study. Sites for registry of patents in Brazil, the United States, and Europe, were consulted, namely, the Instituto Nacional da Propriedade Industrial—INPI (http://www.inpi.gov.br), the United States Patent Office—USPTO (http://www.uspto.gov) and the European Patent Office—ESPACENET, 2005 (http://www.ep.espacenet.com). This survey was conducted during August 2005.

3. Results

Only a few books were found on the subject of medicinal plants in the institutions researched, written in former centuries and in good enough condition for reading. Books in a poor state of conservation were not included in this study, due to difficulties in interpreting data. The books on medicinal plants of greatest relevance belonged to private collections or museum libraries. All books utilized in this research are new editions, published in the 20th century, of original books.

The six books selected were from the 16th century (one book), the 17th century (one), the 18th century (one), and the 19th century (three):

- Book 1: Notícia do Brasil (1587). Sousa, G.S. Brasiliensia Documenta. Volume VII. Sao Paulo, 1974.
- Book 2: "Zoobiblion" (Livro de Animais do Brasil (1654). Wagener, Z. Brasiliensia Documenta. Volume IV. Sao Paulo, 1964.
- Book 3: Plantas Fluminenses Descritas por Frei Veloso (1741–1811). Veloso, J.M.C. Separata de Anais da Biblioteca Nacional Volume 96. Rio de Janeiro, 1976.
- Book 4: Plantas Medicinais do Brasil (1801–1812). Gomes, B.A. Brasiliensia Documenta. Volume V. Sao Paulo, 1972.
- Book 5: Viagem pelo Brasil (1817–1820). Spix and Martius. Volume III. Editora Melhoramentos. Sao Paulo, 1976.
- Book 6: Natureza, Doenças, Medicina e Remédios dos Índios Brasileiros (1844). Martius. Companhia Editorial Nacional. Sao Paulo, 1939.

The books were read and 93 plants with effect or uses possibly related to the CNS recorded as reported by the respective authors. Uses most cited were: to combat fever (febrifuges—20.4%), against pain (analgesic—20.4%) and those that alter consciousness (that produce "drunkenness", that produce "numbness"—16.1%).

Bignonia chica Humb. and Bonpl. used as blood depurative was also included. Even though this category of use has no direct relationship with the CNS, it might well be related to a reduction in viscosity of the blood thereby improving memory, as for example in case of *Ginkgo biloba* L. (Santos et al., 2003).

Plants not identified up to the species level in the books were not included in the study. This decision was based on the fact that the attempt to establish a correlation between the plants cited only by their vernacular names or by genus and possible

Table 1
Thirty-four species native to Brazil cited in historic literature with possible uses/effects on the central nervous system

Species (family)	Vernacular name	Indications in historic literature [part utilized]	Indications by Brazilian communities nowadays
Anacardium occidentale L. (Anacardiaceae)	Cajú (cashew)	"Intoxicating, inebriating" [fruit] (Martius, 1939)	Hemorrhoids, serious diarrhea [bark]—coastal Caiçara fishermen (Di Stasi and Hiruma-Lima, 2002); lower extremity pain, skin injury [bark]—Pataxó Indians (Thomas, 2001); to treat inflammations [bark] (Albuquerque and Andrade, 2002); inflammation—Xucuru Indians (Silva and Andrade, 1998)
Aristolochia grandiflora Sw (Aristolochiaceae)	Mil-homens	"Febrifuge" [stem] (Gomes, 1972)	No data
Bertholletia excelsa Bompl. (Lecythidaceae)	Castanhero-do-pará (brazil-nut-tree)	"Smoke" [bark] (Spix and Martius, 1976)	Anemia [fruit]—Amazonian river-dwellers (Amorozo and Gély, 1988); gastrointestinal disturbances, fever, body strengtheners [bark and fruit]—Amazonian river-dwellers (Rodrigues, 2006); to treat dysentery, colic, liver [bark and fruit]—Amazonian rubber tappers (Ming, 1995)
Bignonia chica Humb. and Bonpl. (Bignoniaceae)	Carajuru	"Blood purifier" [leaf] (Spix and Martius, 1976)	Gastrointestinal disturbances, body strengtheners [leaf]—Amazonian river-dwellers (Rodrigues, 2006); conjunctivitis [leaf]—Amazonian inhabitants (Estrella, 1995)
Cecropia palmata Willd. (Cecropiaceae)	No record	"Becalms the need for food and sleep" [leaf] (Spix and Martius, 1976)	No data
Couratari guianensis Aubl. (Lecythidaceae)	Tauiri	"Cigarette" [bark] (Spix and Martius, 1976)	No data
Cryptocarya pretiosa Mart. ex Nees (Lauraceae)	Casca-preciosa	"To counteract weakness in the nerves" [bark] (Spix and Martius, 1976)	No data
Dorstenia brasiliensis Lam. (Moraceae)[a]	Contraherva	"Febrifuge" [root and leaf] (Gomes, 1972)	To treat snake bites, fever and others infections (Lorenzi and Matos, 2002)
Echites cururu Mart. (Apocynaceae)	Cipó-cururu	"Counteracts fever, headache, and loss of appetite" [stem] (Spix and Martius, 1976; Martius, 1939)	No data
Echites grandiflorus G. Mey. (Apocynaceae)	Cipó-cururu	"Counteracts fever, headache, and loss of appetite" [stem] (Spix and Martius, 1976)	No data
Erythroxylon coca Lam. (Erythroxylaceae)[a]	Ipadú	"Inebriates" [leaf] (Spix and Martius, 1976; Martius, 1939)	Stimulant and narcotic—Amazonian Indians (Plowman, 1979; Cooper, 1987), to treat heart disorders—Amazonian Inhabitants (Van den Berg and Silva, 1988)
Hura crepitans L. (Euphorbiaceae)	Assacú	"Cigarette (numbs)" [sap] (Spix and Martius, 1976)	Ray sting [latex]—Amazonian river-dwellers (Amorozo, 1993); ichthyotoxic (Heizer, 1987; Schultes and Raffauf, 1990)
Manihot utilissima Pohl (Euphorbiaceae)	Mandioca (manioc)	"Intoxicates, inebriating" [root] (Martius, 1939)	No data
Musa sapientum L. (Musaceae)	Banana	"Intoxicates, inebriating" [fruit] (Martius, 1939)	No data
Nicotiana langsdorffii Weinmann (Solanaceae)	Nicotina (nicotine)	"Same use as *Nicotiana tabacum* and *N. rustica* (narcotic)" [whole plant] (Martius, 1939)	No data
Ocotea cujumary Mart. (Lauraceae)	Cujumari	"Combats rheumatic pain" [seed] (Spix and Martius, 1976)	No data
Ocotea opifera Mart. (Lauraceae)	No record	"Combats rheumatic pain" [seed] (Spix and Martius, 1976)	"Enhances the 'strength' of the coca" [fruit]—Amazonian Indians (Schultes and Raffauf, 1990)
Paullinia cururu L. (Sapindaceae)	Guaraná	"Affects the emotions, uncommon excitement, double vision, insomnia, aphrodisiacs" [seed] (Spix and Martius, 1976)	No data

Table 1 (*Continued*)

Species (family)	Vernacular name	Indications in historic literature [part utilized]	Indications by Brazilian communities nowadays
Paullinia pinnata L. (Sapindaceae)	Guaraná/Curuapé/Cruapé-Vermelho	"Affects emotions, uncommon excitement, double vision, insomnia, aphrodisiac" [seed] (Spix and Martius, 1976)	No data
Paullinia sorbilis Mart. (Sapindaceae)	Guaraná	"Affects the emotions, uncommon excitement, double vision, insomnia, aphrodisiac" [seed] (Spix and Martius, 1976)	No data
Piper nodosum C. DC. (Piperaceae)	No record	"Combats toothache" [root] (Martius, 1939)	No data
Piptadenia colubrina (Vell.) Benth. (Fabaceae)	Paricá	"Tonic" [seed] (Martius, 1939)	No data
Psychotria ipecacuanha (Brot.) Stokes (Rubiaceae)	Ipecacuanha	"Antidote to opium" [root] (Gomes, 1972)	Antiemetic [root] (Lorenzi and Matos, 2002); stimulant (snuff)—Amazonian Indians (Cooper, 1987)
Selaginella convoluta (Arn.) Spring (Selaginellaceae)	No record	"Arouses vital forces that are dormant (analeptic)" [whole plant] (Martius, 1939)	No data
Tachia guianensis Aubl. (Gentianaceae)	Raiz-de-jacaré-aru/coferana	"Febrifuge" [root] (Spix and Martius, 1976)	To treat "sore stomach" [root]—Amazonian Indians (Schultes and Raffauf, 1990)
Theobroma bicolor Bonpl. (Sterculiaceae)	Cacau (cacao)	"Bitter principle comparable to caffeine" [whole plant] (Spix and Martius, 1976)	No data
Theobroma cacao L. (Sterculiaceae)	Cacau (cacao)	"Bitter principle comparable to caffeine" [whole plant] (Spix and Martius, 1976)	Osteomuscular problems [fruit]—Amazonian river-dwellers (Rodrigues, 2006); to treat liver problems—Amazon Inhabitants (Van den Berg and Silva, 1988)
Theobroma microcarpum Mart. (Sterculiaceae)	Cacau (cacao)	"Bitter principle comparable to caffeine" [whole plant] (Spix and Martius, 1976)	No data
Theobroma speciosum Willd. ex Spreng. (Sterculiaceae)[a]	Cacau (cacao)	"Bitter principle comparable to caffeine" [whole plant] (Spix and Martius, 1976)	Diuretic, stimulant [seed] (Lorenzi and Matos, 2002)
Theobroma subincanum Martius in Buchner (Sterculiaceae)	Cacau (cacao)	"Bitter principle comparable to caffeine" [whole plant] (Spix and Martius, 1976)	Hallucinogenic snuff [bark ashes]—Indians living in the Northwestern Amazon (Schultes, 1969)
Theobroma sylvestre Aubl. ex Mart. in Buchner (Sterculiaceae)	Cacau (cacao)	"Bitter principle comparable to caffeine" [whole plant] (Spix and Martius, 1976)	No data
Trimezia lurida Salisb. (Iridaceae)	Manciçó	"Febrifuge" [root] (Gomes, 1972)	No data
Vandellia difusa L. (Scrophulariaceae)	Erva-da-mata-cana	"Febrifuge" [root] (Spix and Martius, 1976)	No data
Zea mays L. (Poaceae)	Milho (maize)	"Inebriates" [fruit] (Martius, 1939)	Antiemetic [straw-fibers]—Terena Indians (Carvalho, 1996); kidney pain, measles [straw-fibers]—Amazonian rubber tappers (Ming, 1995)

[a] Species that present coincidence between the uses described in historic literature and in the current ethnopharmacological studies.

species would be of little value since the descriptive material on these species did not contain enough information to distinguish precisely to what species the authors were referring. Thus, of the 93 plants recorded, 39 were excluded from the present study, because they were described by their vernacular names or were identified on a genus level, while 54 were identified on a species level. Of these 54 plants, 34 are native to Brazil and the results referred in the present article are related to these species (Tables 1 and 2).

Ethnopharmacological studies showed that only 13 of the 34 species have been recorded in modern ethnopharmacological studies in traditional communities (Table 1). Most of the uses reported in former centuries do not coincide with those today. Only three cases were reported in which a use coincided as can be noted ([a]) in Table 1. Thus, *Dorstenia brasiliensis* Lam. and *Theobroma speciosum* Willd. ex Spreng. were cited for their febrifuge and stimulating action, respectively (Lorenzi and Matos, 2002) and these uses were also reported in previous centuries. Also, *Erythroxylon coca* Lam. has been cited as "inebriating" in the nineteen century (Martius, 1939; Spix and Martius, 1976), and nowadays its stimulant and narcotic effects have been reported by Plowman (1979) and Cooper (1987), among Amazonian Indians.

A bibliographical survey showed that up to the present time, only eight of these 34 species were the focus of pharmacological investigation (Table 2). Two coincidences between uses reported

Table 2
Thirty-four species native to Brazil cited in historic literature with possible uses/effects on the central nervous system, as well as their phytochemical and pharmacological studies found in present-day literature

Species (family)	Phytochemical data found in present-day literature	Pharmacological studies found in present-day literature	Pharmacological use in the patent
Anacardium occidentale L. (Anacardiaceae)	Anacardic acids, cardanols and cardols (Trevisan et al., 2006; Olatunji et al., 2005); steroids (Phillips et al., 2005; Alexander-Lindo et al., 2004); terpenes, tannins, flavonoids and saponins (Gonçalves et al., 2005); carotenoids and ascorbic acid (Assunção and Mercadante, 2003); ketones, lactones and norisoprenoids (Bicalho et al., 2000); tannins (Mota et al., 1985); long-chain phenols (Tyman et al., 1984); acylated flavanone glycoside (Rahman et al., 1978)	Antioxidant (Melo Cavalcante et al., 2003; Trevisan et al., 2006); anti-inflammatory (Mota et al., 1985); anti-diabetic effects (Olatunji et al., 2005)	Antioxidant, anti-obesity
Aristolochia grandiflora Sw (Aristolochiaceae)	No data	No data	No data
Bertholletia excelsa Bompl. (Lecythidaceae)	Saponin, phenolic compounds and quinazolinic alkaloids (Campos et al., 2005); amyrines and tocopherols (De Siqueira et al., 2003)	No data	No data
Bignonia chica Humb. and Bonpl. (Bignoniaceae)	No data	No data	No data
Cecropia palmata Willd. (Cecropiaceae)	No data	No data	No data
Couratari guianensis Aubl. (Lecythidaceae)	No data	No data	No data
Cryptocarya pretiosa Mart. ex Nees (Lauraceae)	No data	No data	No data
Dorstenia brasiliensis Lam. (Moraceae)	Seco-adianane-type triterpenoids, isopimarane-type diterpenoid and coumarins (Uchiyama et al., 2002); steroids and furocoumarins (Kuster et al., 1994)	No data	No data
Echites cururu Mart. (Apocynaceae)	No data	No data	No data
Echites grandiflorus G. Mey. (Apocynaceae)	No data	No data	No data
Erythroxylon coca Lam. (Erythroxylaceae)	Tropane alkaloids (Hammerschmidt, 1999; Leete, 1983); alkaloids (Turner et al., 1981)	Anesthesic (Bedford et al., 1984)	Anoretic
Hura crepitans L. (Euphorbiaceae)	Flavonoids (Freixa et al., 1998)	Ichthyotoxic (Pires, 1978)	Neuronal regeneration
Manihot utilissima Pohl (Euphorbiaceae)	Flavonoids (Chariandy et al., 1999; Kamil et al., 1974)	Antioxidant (Rahmat et al., 2004)	No data
Musa sapientum L. (Musaceae)	Essential oils (Pino et al., 2003; Pannangpetch et al., 2001); flavonoids (Lewis et al., 1999; Pari and Maheswari, 1999); cycloartane triterpenes (Akihisa et al., 1998); tannins (Ali and Bhutani, 1993); steroids (Knapp et al., 1972)	Antioxidant (Goel et al., 2001); muscle paralysis (Singh and Dryden, 1985)	Antidepressant
Nicotiana langsdorffii Weinmann (Solanaceae)	No data	No data	No data
Ocotea cujumary Mart. (Lauraceae)	No data	No data	No data
Ocotea opifera Mart. (Lauraceae)	Essential oils (Lorenzo et al., 2001)	No data	No data
Paullinia cururu L. (Sapindaceae)	No data	No data	No data
Paullinia pinnata L. (Sapindaceae)	Polyphenols (Zamble et al., 2006); flavone glycosides (Abourashed et al., 1999)	Ichthyotoxic (Pires, 1978)	No data
Paullinia sorbilis Mart. (Sapindaceae)	No data	No data	Antidepressant
Piper nodosum C. DC. (Piperaceae)	No data	No data	No data

Table 2 (*Continued*)

Species (family)	Phytochemical data found in present-day literature	Pharmacological studies found in present-day literature	Pharmacological use in the patent
Piptadenia colubrina (Vell.) Benth. (Fabaceae)	Indole alkaloids (Pachter et al., 1959)	No data	No data
Psychotria ipecacuanha (Brot.) Stokes (Rubiaceae)	Alkaloids (Garcia et al., 2005)	No data	No data
Selaginella convoluta (Am.) Spring (Selaginellaceae)[a]	No data	Antidepressant (Santos et al., 1994)	No data
Tachia guianensis Aubl. (Gentianaceae)	Flavonoids (Carvalho et al., 1991)	No data	No data
Theobroma bicolor Bonpl. (Sterculiaceae)	Fatty acids (Jee, 1984); phenolic acids (Torres et al., 2002)	No data	No data
Theobroma cacao L. (Sterculiaceae)[a]	Catechins (Gotti et al., 2006; Kelm et al., 2006); flavonoids (Ramiro et al., 2005; Osman et al., 2004); flavonoids O-glucosides and C-glucosides (Sanchez-Rabaneda et al., 2003); tannins (Falade et al., 2005); essential oils (Chee et al., 2005); alkaloids (Stark et al., 2005); polyphenols (Edwards et al., 2005); proanthocyanidin glycosides (Hatano et al., 2002); carboxylic acids, purine alkaloids, fatty acids (Bucheli et al., 2001)	Anti-inflammatory (Schewe et al., 2002); psychoactive (Melzig et al., 2000)	Anti-inflammatory; antioxidant; appetite regulator
Theobroma microcarpum Mart. (Sterculiaceae)	No data	No data	No data
Theobroma speciosum Willd. ex Spreng. (Sterculiaceae)	No data	No data	No data
Theobroma subincanum Martius in Buchner (Sterculiaceae)	Tocopherol, fatty acids, steroids (Bruni et al., 2000, 2002)	No data	No data
Theobroma sylvestre Aubl. ex Mart. in Buchner (Sterculiaceae)	No data	No data	No data
Trimezia lurida Salisb. (Iridaceae)	No data	No data	No data
Vandellia difusa L. (Scrophulariaceae)	No data	No data	No data
Zea mays L. (Poaceae)	Terpenoids (Yan and Wang, 2006); polyamines (Moreau and Hicks, 2005); fatty acids, primary alcohols, diacids, omega-hydroxy fatty acids, and 2-hydroxy fatty acids, with omega-hydroxy fatty acids (Schreiber et al., 2005); phenolic acids (Fontaine et al., 2005; Funk et al., 2005); alkylresorcinol (Gembeh et al., 2001); sesquiterpene hydrocarbon (Köllner et al., 2004); polyphenols (Del Pozo-Insfran et al., 2006)	No data	No data

[a] Species that present coincidence between the uses described in historic literature and their effects observed in the nowadays pharmacological studies.

in historic literature and the pharmacological data described in contemporary scientific literature were noted also in Table 2. *Selaginella convoluta* (Arn.) Spring and *Theobroma cacao* L. were cited in historic literature for its arousing “vital forces that are dormant (analeptic)” (Martius, 1939) and for its “Bitter principle comparable to caffeine” (Spix and Martius, 1976), respectively (Table 1). The current pharmacological studies showed antidepressant (Santos et al., 1994) and psychoactive (Melzig et al., 2000) effects, respectively (Table 2).

Of the 34 species cited in the present study, only 16 were studied from a phytochemical point of view (Table 2). The main chemical constituents found in these plants in decreasing order were: flavonoids (eight plants), alkaloids (six), phenolic acids (four), tannins (four) essential oils (three), pentacyclic triterpenes (three), steroids (two) and saponins (two).

In the survey on possible requests for patents, six species were found to be registered (*Anacardium occidentale* L., *Erythroxylon coca* Lam., *Hura crepitans* L., *Musa sapientum* L., *Paullinia sorbilis* Mart., and *Theobroma cacao* L.). However, no patent shows any coincidence in plant use and the possible effects described in historic literature (Tables 1 and 2).

No information was found concerning medication registered in Brazil and developed as from these plants.

4. Discussion

This study presents data that allows us to verify not only ethnopharmacological data but also social and cultural aspects of Brazilian cultures of the past century, in compliance with a recent ethnopharmacological concept as a transdisciplinary exploration that spans the biological and social sciences (Etkin and Elisabetsky, 2005).

Some limitations must be considered in spite of the careful survey. For instance, use of a scientific name as a key word in databases will not bring results if the orthography of the scientific name published has been subject to alteration. Also, it was not checked on all the botanic synonyms in this survey. Finally, maybe not all Brazilian studies have been consulted as desired, since most of them have been published in periodic not indexed.

From the ethnopharmacological point of view, the results showed the different paths traveled by plants over the course of history, confirming the hypothesis that some of them were used for the same purposes for centuries (*Dorstenia brasiliensis* Lam.; *Erythroxylon coca* Lam. and *Theobroma speciosum* Willd. ex Spreng.). For others, uses were modified, as can be observed in the recent ethnopharmacological studies described in Table 1 (*Anacardium occidentale* L.; *Bertholletia excelsa* Bompl.; *Bignonia chica* Humb. and Bonpl.; *Hura crepitans* L.; *Ocotea opifera* Mart.; *Psychotria ipecacuanha* (Brot.) Stokes; *Tachia guianensis* Aubl.; *Theobroma cacao* L.; *Theobroma subincanum* Martius in Buchner and *Zea mays* L.). In other cases, uses were completely forgotten in the course of time (*Aristolochia grandiflora* Sw; *Cecropia palmata* Willd.; *Couratari guianensis* Aubl.; *Cryptocarya pretiosa* Mart., ex Nees; *Echites cururu* Mart.; *Echites grandiflorus* G. Mey.; *Manihot utilissima* Pohl; *Musa sapientum* L.; *Nicotiana langsdorffii* Weinmann; *Ocotea cujumary* Mart.; *Paullinia cururu* L.; *Paullinia pinnata* L.; *Paullinia sorbilis* Mart.; *Piper nodosum* C. DC.; *Piptadenia colubrina* (Vell.) Benth.; *Selaginella convoluta* (Arn.) Spring; *Theobroma bicolor* Bonpl.; *Theobroma microcarpum* Mart.; *Theobroma seylvestre* Aubl. ex Mart. in Buchner; *Trimezia lurida* Salisb. and *Vandellia difusa* L.).

From the phytochemical point of view, the most recurrent chemical constituents in the plants under study were the flavonoids, alkaloids, phenolic acids, tannins and essential oils. As has been reported in several articles, these substances exert activity on the CNS. Some flavonoids present anticonvulsive and sedative effects (Dos Santos et al., 2005; Fernandez et al., 2004), have the effect of protecting against neurodegeneration of the CNS (Nagase et al., 2005; Heitzman et al., 2005; Marder et al., 2003) and antidepressant activity (Juergenliemk et al., 2003). Many tannins showed an anticonvulsive effect (Dos Santos et al., 2005). Pentacyclic triterpenes also presented activity on the CNS (Heitzman et al., 2005). Alkaloids of the matrine type exert an antinociceptive effect through many mechanisms of action (Yin and Zhu, 2005), such as an increase in activation of the cholinergic system (Breining, 2004). Alkaloids thus possess pharmacological activity and may be relevant in the treatment of cognitive disorders, including an increase in the cholinergic function in the CNS (Howes and Houghton, 2003).

Phenolic compounds protect neurons from oxidative stress (Scapagnini et al., 2004). Aromatic plants possess high concentrations of essential oils and are utilized in the treatment of diseases related to the CNS, common in tropical regions (Freire et al., 2006; Ozturk et al., 2002).

The reduced number of pharmacological studies found for the species surveyed shows that they obviously did not focus on medicinal plants cited in historic literature. Hopefully this article contributes to a new appreciation of such historical documents, since researches which reinstate historic medicinal uses of plants are rare or difficult to carry through (because of difficult access to books), so that few species have been the subject of investigation up to the present time. The main difficulty concerns to the lack of a location which concentrates these books or even information about them, since they are dispersed in few museums and other institutions; often in bad conditions of conservation. Also, sometimes they are only available as microfilms, and usually are contaminated by fungus, jeopardizing the reading. A wider search has been conduced by the authors in other Brazilian cities, in order to verify the general conditions of the historic literature deposited in Institutions outside Sao Paulo.

Only six species were found to have a registered patent in the patent database consulted (Table 2). With the exception of *Paullinia sorbilis* Mart., all five other plants have been studied from a pharmacological point of view. *Paullinia sorbilis* Mart. was also the only species related to the CNS with a patent registered in Brazil (INPI, 2005); all others have been patented in the United States or in Europe. In Brazil, only methods or inventions are patentable—not species and their constituents. When a substance is isolated, or effects of one particular species reported, this register can only be made outside Brazil, in countries that accept this type of patent. Many species are taken to other countries and studied in foreign laboratories. These two facts may explain the number of patents of Brazilian species registered in international offices and the absence of patents for Brazilian species in the country.

The fact that no records have been found of medications in Brazil for the species under study comes as no surprise. With the exception of one phytomedicine registered by ANVISA in 2004, Acheflan®, Brazil does not possess any registered phytomedicine derived from Brazilian resources. This is due to several reasons, ranging from the lack of financial incentive from the government for the study of natural products, to the recent difficulties in the Brazilian legislation concerning the study of medicinal plants. Some of these obstacles have been reverted over the last years. Firstly, through incentive provided by university-business company partnerships, financing wide-scale projects and training groups of professionals of great importance to Brazil (Rodrigues, 2005). Secondly, registration of one particular phytomedicine takes years to pass all of the pre-clinical and clinical pharmacological tests. For such, the phytomedicine would have to show its pharmacological safety and effectiveness – in itself, not a very simple matter – since many studies are not carried through because the species do not present the desired pharmacological effect in the first pharmacological tests.

5. Conclusion

This study shows the importance and ethnopharmacological potential of bibliographical surveys of historic texts in providing a record of plants with possible bioactive properties, often forgotten over the course of time. The species of greatest importance are those which have not been the object of pharmacological investigation in spite of their historic uses reported.

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