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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

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Abstract: Ethnopharmacological research when grounded on historic literature has for its objective retrieving traditional knowledge compiled throughout history by early cultures. The current study has used literature from the 16th to the 19th centuries to assess reports that include accounts of Brazil's native plants, with possible reports of disorders of the Central Nervous System (CNS). Visits were paid to 27 institutions located in four Brazilian states. This resulted in raising 529 publications, out of which 65 were read, revealing that 33 of them contained reports of plants exerting effects on CNS ailments. These plants' scientific names underwent an updating process. The updating process resulted in 788 species names (129 correct scientific names and their 659 synonyms) out of which 66 hold current ethnopharmacology, pharmacology studies and/or patent application. Coincidences among past and present data have been observed in 46 cases. Only three of them carried applications for patents all of which coincided with past uses. There have hardly been any studies whatsoever throughout the centuries for many of the species currently being studied. Although of very seldom use, research in ethnopharmacology and historic literature can be promising tools for the selecting of new pharmaco products, further to contributing with retrieving traditional knowledge.

Introduction

Ethnopharmacology can be defined as a multidisciplinary study of the physiological effects of plants, animals and other substances used by ethnic groups in traditional medicine of past and present cultures (ISE, 2005).

In accordance with Rodrigues et al. (2005), ethnopharmacological studies utilize at least two sources when selecting plants to be submitted to pharmacological and phytochemical studies. One of these sources is based on performing ethnopharmacological surveys during field work, or through observations and interviews. The other gathers folk knowledge published in literature - be it specific for a certain human group (whose publication often does not make any reference as to the origin of the knowledge) or still those pieces of information that have been broadly divulged among populations of different regions.

Ethnopharmacological research based on historic literature carries for its main objective the retrieval of traditional knowledge shown by ethnic cultures in the course of history. In Brazil, this retrieval is only possible due to the great number of works resulting from the inquisitiveness shown by foreigners who arrived here in the 15th century. Pero Vaz de Caminha's letter (written in 1500 and now considered the country's first official register) includes 118 direct or indirect referrals to plants or vegetal associations, further to 43 citations of plants or their respective parts. Of these, 24 are native from Brazil (Filgueiras & Peixoto, 2002). Since then, colonists, priests, travelers and naturalists have compiled a diversity of records in separate timelines and regions, portraying customs displayed by assorted Brazilian populations (Kury, 2001).

In the 16th century, the existing literature on Brazil was based only on accounts given by travelers, colonists and Jesuits. The Maurício de Nassau's expedition was the first scientific expedition to take place in Brazil during the 17th century. This expedition was only possible on account of the Dutch invasion of Northeastern Brazil. It also brought to the country two naturalists accountable for the first perusal of the native fauna and flora: Guilherme Piso and George Marcgraf (Mello-Leitão, 1941). In the 18th century another scientific expedition studied Brazil's wealth of natural resources. The latter had been sent by Portugal in 1783 under the command of Alexandre Rodrigues Ferreira (Mello-Leitão, 1941).

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The following scientific expeditions made to Brazil were to be made only in the 19th century for, prior to that, any visit paid to the country by citizens of any nationality with the exception of the Portuguese, was deemed as "unpleasant affairs" (Mello-Leitão, 1941). According to the same author, the arrival in Brazil of the King of Portugal, D. João VI, the Royal family and consequent opening of the ports to other countries allowed for the first scientific expeditions made by foreign explorers authorized by the Portuguese crown, further to permitting many naturalists to visit Brazil. Among these we can quote some that were of major botanical importance: Alexander von Humboldt, Aimeé Bonpland, Auguste de Saint-Hillaire, Karl Friedrich Phillip von Martius, Johann Baptiste von Spix, Francisco Freire Allemão, among several others. All of them studied the country's natural and cultural wealth providing detailed accounts of the country's fauna, flora, ethnography, geography, geology, hydrographs and astronomy.

These studies are fundamental tools in ethnopharmacology and historic literature works, for, as of them reports on medicinal plants and animals are obtained, including their usage among a diversity of populations that existed in the past.

Researches that focus on the use of medicinal substances used by populations in the past have been conducted in several countries. We can quote many studies grounded on old literature from Greece (Merlino, 1989; Heinrich, & Teoh, 2004; Tsoulogiannis & Spandidos, 2007), India (Narayana & Kumaraswamy, 1996; Narayana, 1996), China (Peigen et al., 1984), Poland (Trojanowska, 2005), Constantinople, currently Istanbul (Tricot, 2004), Mediterranean communities (Lev, 2002; Lev, 2006; Lev, 2007), Peru (Bussmann & Sharon, 2006) and Mexico (Heinrich et al., 2006). Among research grounded on old literature on Brazil, we may quote Camargo (1994; 2000), Brandão et al. (2006) and Botsaris (2007); among others.

Brazil is inhabited by myriad types of cultures, namely: around 220 native indigenous ethnic groups (ISA, 2007), around 740 quilombola communities (IBGE, 2007), further to traditional populations: known as caboclos/ribeirinhos Amazon river dwellers, non-Amazon riverside dwellers; caiçaras: seaside dwellers, caipiras-midland areas dwellers; jangadeiros: raft conductors; babaçueiros: babuaçu pickers; seringueiros: rubber tree pickers; pantaneiros: swamp dwellers; pastoreios: herd shepherds; praieiros: beachside dwellers, varjeiros riverside flooded areas dwellers; sitiante: small country property dwellers; pescadores: fisherman; southern Brazil colonists, sertanejos/vaqueiros: backwoods dwellers and cowhands (Diegues et al., 2000) - resulting from the mix among Native Brazilian Indians, Europeans and Africans. Furthermore, Brazil is still home to descendents from Europeans and Asians resulting from colonization and migration processes that have been occurring since the 16th century. This cultural diversity has promoted wealth from an ethnopharmacological point of view since in such processes, there was an exchange of knowledge (Rodrigues et al., 2005).

This collection of knowledge may have taken at least two separate paths in the course of time. A first path was the cascading of information as people moved about from region to region being later transmitted, becoming increasingly diffused and broadly utilized by the country's different populations; in a second path, the information was not passed on and thus its use became increasingly less frequent until falling into complete oblivion in the course of time.

The current study aims at an ethnopharmacological survey, based on reading of 16th and 19th centuries´ publications that focus on reporting Brazilian plants indicated for eventual disorders of the Central Nervous System (CNS), extending an earlier study (Giorgetti et al., 2007).

Methodology

Giorgetti et al. (2007) set off on an investigation of old literature focusing on reports of medicinal plants. This literature was found with private collectors, in institutional libraries and museums in the city of São Paulo. In this study, the investigation has been expanded to three more Brazilian cities (Belem, Salvador and Rio de Janeiro). During the survey the search was for works on Brazil, be they simply descriptions given by the country's inhabitants, travelers' or naturalists' journals or literature itself. This research's conduction is in an ongoing process and results shall be discussed in future studies (Scalco et al., 2010).

This current research has taken the previously used methodology (Giorgetti et al., 2007) into consideration, however having made adaptations due to the large number of publications encountered in those above mentioned capitals. The following criteria have been used for the selection of the publications to be read, ranking them in a relevance sequence: a) the publication's state of preservation, b) language, including only publications in Portuguese, English and Spanish c) presence of Brazilian native species whose scientific names were listed - including a detailed botanical description enabling the specie's nomenclature to be reviewed and updated. The updating of the names has been done in accordance with the International Botanical Nomenclature Code, via consultations with taxonomists and specialized studies predominantly facilitated by virtual online taxonomic databanks that include bibliography and carry information on a wide variety of species. In the updating process, among

other things, there was a verification to check whether the species' names cited in early publications are still accepted currently. Should that not be the case, they were then substituted by their correct current scientific names. Furthermore, there was a check for any synonyms these species may have and if the botanical names used in ancient publications indeed corresponded to the species of interest. For this, there was observation of botanical descriptions in the respective publications. During this updating process, the species' geographical origins were also checked in order to exclude those that were not native from Brazil.

From the reading of the selected publications, only plants that possess any probable effect/action over CNS were selected since hundreds of millions of people throughout the world are affected by CNS disorders (WHO, 2008). Highlight goes to the fact that exclusively Brazilian plants documented in bibliography about Brazil (written both by Brazilians or foreigners) have been singled out.

Botanical species selected at this stage of the study have all been submitted to bibliographical surveys in current literature for purposes of checking whether there are ethnopharmacological and pharmacologic studies performed on the said species, be they on the internet international database - *Scopus e Dr. Duke's Phytochemical and Ethnobotanical Database*, or in searches from the Annals of 19 Brazil Medicinal Plants Symposiums (from 1968 to 2006), further to articles kept at the Ethnopharmacological Studies Center collection from the São Paulo Federal University and São Paulo State University. Further to that there was one last bibliographical survey to USA patent application sites (United States Patent Office) – www.uspto.gov; and Europe (European Patent Office) - www.ep.espacenet.com, with the objective of checking any existing application for patents on the species studied up to the present moment. It is worth stressing that the latter site encompasses records of applications made by multiple countries, Brazil included.

All searches were made using the currently accepted scientific name for each plant as well as for their respective synonyms, thereby verifying if they have been investigated in the past decades and if their uses have been proven. Please observe that the surveys have been made seeking exclusively effects (or reports of their uses in the case of ethnopharmacology) referent to CNS disorders. Other effects, if found, have not been mentioned herein. Tables and graphs have been used to format the gathered data with highlight to those that deserve more profound discussions.

The present research has been conducted in accordance with Federal University of São Paulo, Brazil, ethical principles having received approval from the Research Ethics Committee from the São Paulo Federal University (CEP 0601/06).

Results and Discussion

During the field work 27 collections were visited in the states of São Paulo, Rio de Janeiro, Para and Bahia. In those locations 529 publications were found. Out of this total, 65 have been read (36 scientific articles, twelve theses and seventeen books). Some of these works are re-publications facsimile of the original titles. Of these 65 works, 33 include reports of Brazil indigenous plants that act over CNS disorders (Table 1).

Resulting from the reading of these publications, 191 plants with possible action/effects for CNS have been singled out. These plants underwent an updating of their scientific names further to determining their geographic sources, resulting in 129 Brazil-native species which, together with their synonyms, account for 788 scientific names. During this updating it was verified that one species may carry up to 82 synonyms. By including these synonyms it has become possible to find references about studies that may have been otherwise ignored, had only the original or current names or still the name used in the study have been searched.

These 129 species belong to 36 taxonomic families. The ones appearing more often are: Fabaceae s.l. (24 species); Asteraceae (14), Aristolochiaceae (12), Rubiaceae (10), Arecaceae (7), Menispermaceae (7), Rutaceae (7) and Solanaceae (7) (Figure 1).

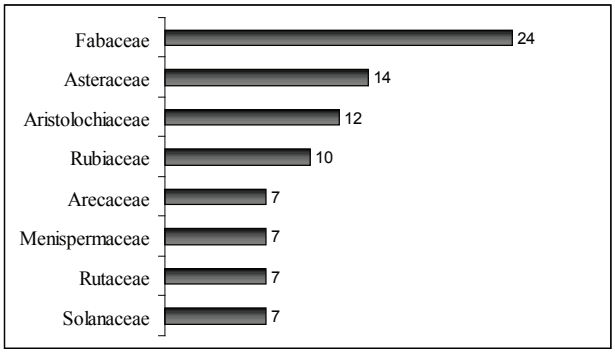

Figure 1. Major botanical families corresponding to the 129 species extracted from the reading of the 33 historic publications (only those represented herein by seven or more species).

Some of these taxonomic families have also been the most frequently mentioned in other studies. In a review focused on plants possibly acting/having effect on CSN indicated by 26 native Brazilian ethnicities (Rodrigues et al., 2006), it was observed that families with the highest frequency of reporting were Fabaceae, Asteraceae, Rubiaceae and Solanaceae, among others. Two other ethnopharmacological studies with the same focus as this review verified that the Fabaceae, Sterculiaceae, Asteraceae and Rubiaceae families

Table 1. Author, title, city, publisher and year of the read publications, plus the place where they were taken out from.

Author	Title	City/Publisher	Year	Collection
1 – no author defined	Gazeta Médica do Rio de Janeiro Tomo I (1862)	São Paulo. Brasiliensia Documenta (X)	1976	CPRV
2 – no author defined	Gazeta Médica do Rio de Janeiro Tomo II (1863)	São Paulo. Brasiliensia Documenta (X)	1976	CPRV
3 – no author defined	Gazeta Médica do Rio de Janeiro Tomo III (1864)	São Paulo. Brasiliensia Documenta (X)	1976	CPRV
4 – no author defined	Gazeta Médica da Bahia. Tomo I: (julho de 1866 - junho de 1867).	São Paulo. Brasiliensia Documenta (IX)	1974	CPRV
5 – no author defined	Gazeta Médica da Bahia Tomo II: (julho de 1867 - julho de 1868).	São Paulo. Brasiliensia Documenta (IX)	1974	CPRV
6 – no author defined	Gazeta Médica da Bahia Tomo III: (agosto de 1868 - julho de 1869).	São Paulo. Brasiliensia Documenta (IX)	1974	CPRV
7 – no author defined	Gazeta Médica da Bahia. Tomo IV: (Agosto de 1871 – Julho de 1872).	Bahia, Typographia de J. G. Tourinho. Salvador	1872	UFBA
8 – no author defined	Gazeta Médica da Bahia. Tomo V(1): (Julho de 1872 – Junho de 1873).	Bahia, Typographia de J. G. Tourinho. Salvador	1873	UFBA
9 – no author defined	Gazeta Médica da Bahia. Tomo V(2): (Julho de 1873 – Junho de 1874).	Bahia, Typographia de J. G. Tourinho. Salvador	1874	UFBA
10 – no author defined	Gazeta Médica da Bahia. Tomo VI: (Julho de 1874 – Junho de 1875).	Bahia, Typographia de J. G. Tourinho. Salvador	1875	UFBA
11 – no author defined	Gazeta Médica da Bahia. Tomo VII: (Julho de 1875 – Junho de 1876).	Bahia, Typographia de J. G. Tourinho. Salvador	1876	UFBA
12 – no author defined	Gazeta Médica da Bahia. Tomo IX: (Julho de 1877 – Junho de 1878).	Bahia, Typographia de J. G. Tourinho. Salvador	1878	UFBA
13 – no author defined	Gazeta Médica da Bahia. Tomo X: (Julho de 1878 – Junho de 1879).	Bahia, Typographia de J. G. Tourinho. Salvador	1879	UFBA
14 – no author defined	Gazeta Médica da Bahia. Tomo XI: (Julho de 1879 – Junho de 1880).	Bahia, Typographia de J. G. Tourinho. Salvador	1880	UFBA
15 – no author defined	Gazeta Médica da Bahia. Tomo XII: (Julho de 1880 – Junho de 1881).	Bahia, Typographia de J. G. Tourinho. Salvador	1881	UFBA
16 – no author defined	Gazeta Médica da Bahia. Tomo XIII: (Julho de 1881 – Junho de 1882).	Bahia, Typographia de J. G. Tourinho. Salvador	1882	UFBA
17 – no author defined	Gazeta Médica da Bahia. Tomo XIV: (Julho de 1882 – Junho de 1883).	Bahia, Typographia de J. G. Tourinho. Salvador	1883	UFBA
18 - no author defined	Gazeta Médica da Bahia. Tomo XV: (Julho de 1883 – Junho de 884).	Bahia, Typographia de J. G. Tourinho. Salvador	1884	UFBA
19 – no author defined	Gazeta Médica da Bahia. Tomo XVI: (Julho de 1884 – Junho de 1885).	Bahia, Typographia de J. G. Tourinho. Salvador	1885	UFBA
20 – no author defined	Gazeta Médica da Bahia. Tomo XVII: (Julho de 1885 – Junho de 1886).	Bahia, Typographia de J. G. Tourinho. Salvador	1886	UFBA
21 – no author defined	Gazeta Médica da Bahia. Tomo XXV: (Julho de 1893 – Junho de 1894).	Bahia, Typographia de J. G. Tourinho. Salvador	1894	UFBA
22 – Carvalho, Bonifácio Ferreira de.	Da Coca, seu princípio activo e sua acção physiotherapeutica.	Tese Inaugural de Doutoramento. FAMEB. Salvador	1889	UFBA
23 - Carvalho, José Eduardo Freire de.	Estudo do Ziziphus Joazeiro em suas Aplicações na Medicina.	Tese Inaugural de Doutoramento. FAMEB. Salvador	1899	UFBA
24 - Gardner, George.	Viagem ao Interior do Brasil (1836-1841).	Belo Horizonte. Itatiaia	1975	CPRV
25 - Gomes, Bernardino Antônio.	Plantas medicinais do Brasil.	São Paulo. Brasiliensia Documenta (V)	1972	CPRV
26 - Martius, Karl Friedrich Phillip von.	Natureza, doença, medicina e remédios dos índios brasileiros. 1844	São Paulo. Companhia Editora Nacional	1939	CPRV
27 - Pereira, Francisco Bráulio.	Leguminosas Medicinaes Brazileiras: sua Acção Physiologica e Therapeutica.	Tese de Concurso, FAMEB. Salvador	1886	UFBA

28 - Rodrigues Ferreira, Alexandre.	Viagem filosófica. Tomo I.	Rio de Janeiro. Conselho Federal de Cultural	1971	MN
29 - Siqueira, Augusto Calmon de.	Descripção, Acção Physiologica e Therapeutica de Necotiana Tabacum.	Tese Inaugural de Doutoramento. FAMEB. Salvador	1858	UFBA
30 – Spix, Johan Baptiste von; Martius, Karl Friedrich Phillipp von.	Viagem Pelo Brasil (1817-1820). Tomo I. 2ª Edição	São Paulo. Melhoramentos	1976	CPRV
31 – Spix, Johan Baptiste von; Martius, Karl Friedrich Phillipp von.	Viagem Pelo Brasil (1817-1820). Tomo II. 4ª Edição	São Paulo. Melhoramentos	1976	CPRV
32 - Spix, Johan Baptiste von; Martius, Karl Friedrich Phillipp von.	Viagem Pelo Brasil (1817-1820). Tomo III. 4ª Edição	São Paulo. Melhoramentos	1938	UFBA
33 - Zama, Aristides Cezar Spínola.	Sciencias Medicas – Bebidas Aromáticas	Tese Inaugural de Doutoramento. FAMEB. Salvador	1858	UFBA

CPRV: Ribeiro do Valle's Private Collection, Sao Paulo; MN: Nacional Museum of Brazil, Rio de Janeiro; UFBA: Federal University of Bahia, Bahia State.

are also present among reports given by members of the Krahô tribe (Rodrigues & Carlini, 2005); while Asteraceae is dominant among the Sesmaria Mata-Cavalos quilombola (Rodrigues & Carlini, 2004). In a review study on psychoactive plants used by Mexican indian tribes (Díaz, 1977), it was also observed that among the most frequently mentioned families, the Solanaceae, Asteraceae and Fabaceae families were to be found.

A factor that may influence significant frequency in the presence of these taxonomic families is the large amount of species belonging to them. Fabaceae and Asteraceae families carry from 18000 to 20000 species respectively (Woodland, 1997). Moreover, these families are broadly spread in their geographical distribution, not only in Brazil but also around the world (Schultes & Raffauf, 1990), which in itself facilitates its usage by numerous cultures, conversely to families with a restricted geographical distribution.

The fact that different cultures both inside and outside Brazil use plants from these families more often for disorders related to CNS makes these plants potential bioactive targets for studies whose focuses are on this therapeutic class.

Of plants singled out from the reading of the publications, 29.6% did not mention the utilized part. Among the remaining ones, a predominance of using the entire plant was observed (17.5%), followed by the root (15.7%), root bark (15%) and the part under the root bark (12.2%), among others. Some species were quoted for more than one part of the plant for its use. For those cases, they have been listed separately for the above mentioned percentages.

The publications in their majority, do not list recipes for preparing the plants. They simply list their use such as: "*analeptic, nevrosthenia*" (Ferreira, 1886). Therefore, 66 uses have been recorded, and among the most often cited: fever (22.1%) tonics (21.6%) and narcotics (9.5%). Our decision was to use the terms in the same manner as they had been originally described. Furthermore, some uses are quoted using synonyms. For purposes of streamlining the analysis, uses have been grouped into fifteen categories separated by their therapeutical similarities (Table 2).

Table 2. Uses possibly acting over the CNS, referent to 129 vegetal species extracted from 33 historic publications, grouped into fifteen categories of usage.

No.	Uses for CNS disorders	Category
1	antidote for intoxicating and inebriating effects	1. overall abstinence
2	against *delirium tremens*	
3	aphrodisiac	2. aphrodisiac
4	altering	3. alters perception
5	powerfully effective altering substance	
6	drunkenness	
7	fermented alcoholic beverage	
8	intoxicates	
9	alcoholic intoxication	
10	inebriating	
11	same application as *Nicotiana tabacum* and *N. rustica*	
12	narcotic	
13	wine	
14	analgesic	4. analgesic
15	combats headaches	
16	toothaches	
17	anesthetic	5. anesthetic
18	general anesthetic	
19	sedative baths	6. anxiolytic
20	calming	
21	"nevroseante"	
22	convulsive nevroses	
23	nevrosthenia	
24	pupil dilating	7. anti-cholinergic
25	eyesight scintillation	

26	disturbance to sight	
27	double vision	
28	antigen for *Gelsemium sempervirens**	8. cholinergic
29	combats lack of appetite	9. weight control
30	less need for food	
31	support for food abstinence	
32	nausea	10. emetic/anti-emetic
33	vomitive	
34	vomit-inducer	
35	vomit	
36	calms needs for feed and sleeping	11. stimulant
37	analeptic	
38	wakens vital sleeping strength	
39	energetic	
40	stimulates brain, cerebellum and marrow	
41	excites breathing	
42	abnormal excitement	
43	light excitement trending to insomnia	
44	exciter	
45	CNS exciter	
46	causes insomnia	
47	bitter principle comparable with caffeine	
48	anti-fever	12. fever
49	combats fever	
50	fever	
51	malignant fever	
52	febrifuge	
53	combats nerve weakness	13. restorative
54	combats state of weakness	
55	fortifies the nerves	
56	tonic	
57	fixed tonic	
58	hypnotic	14. hypnotic
59	narcotic	
60	mild acting narcotic principle	
61	sedative	
62	toxic substances (stupor, narcotics)	
63	affects emotions	15. others
64	antidote for opium	
65	good medicine for all illnesses	
66	acts against CNS disorders	

**Gelsemium sempervirens* was cited earlier in the same historic publication as "*pupil dilating*".

In spite of some of the terms being synonyms: "*intoxicates, inebriates, causes drunkenness, alters, altering, powerful effectiveness, befuddled, fermented alcoholic beverage, same use as* Nicotiana tabacum *and* N. rustica, *narcotizing, wine*" they have all been grouped in category 3 (alters perception). Certain uses were not capable of being classified due to countless possible interpretations in the reports. One such example is the Ipecacunha plant cited by Bernardino Antônio Gomes as an "*antidote for opium*" (Gomes, 1972). This indication may carry several different meanings in that which refers to possible pharmacological effects. On account of its being considered historic literature, it becomes impossible to go deeper into an investigation in order to find out exactly what is referred to in a certain report of its use. The investigator is left with nothing except a lexical significance of such an account. Therefore these uses have been grouped in category 15 (others). Plants with more than one report for its use have been included in more than one single category.

Being so, categories that comprised the largest amount of cited species were the following: 12. fever (63 cited species); 11. stimulants (44) and 13. restorative (34) (Figure 2). The fact that temperature accounts for one of the categories with the largest amount of citations can be explained if we observe that the accounts have predominantly been given by people from North and Northeastern Brazil. These locations account for great incidences of malaria and other tropical illnesses which carry fever as their major symptom.

A review performed by Rodrigues et al. (2006) raised some species utilized by Native Brazilian Indians, also analyzing scientific literature for these species. This study pointed out that species cited as "*fever*" display a greater occurrence of flavonoids, essential oils and triterpenoids; species cited as "*tonics*" display a greater occurrence of alkaloids, cumarins and triterpenoids; while the "*hallucinogen*" category (that in the research includes species cited as narcotics) displays a greater occurrence of alkaloids and lignin. It would therefore be very interesting to verify if botanical families more often cited within each category also display these chemical constituents or not. This data permits the establishing of the chemotaxonomic relationship among some therapeutic categories and chemical constituents or still between botanic families and chemical constituents. However, since the current research has for its focus the use of plants and their maintenance or not by populations throughout time, the option was not to investigate plants from a phytochemical point of view.

Uses that convey to narcotics may be related not only to an exclusively hypnotic effect, but also to a psychotropic one, *i.e.*, further to providing a psychoactive effect, it can also cause addiction. In this sense, depending upon the context of the citation in the consulted publication, these uses were placed in categories: 3 (alters perception) or 14 (hypnotic).

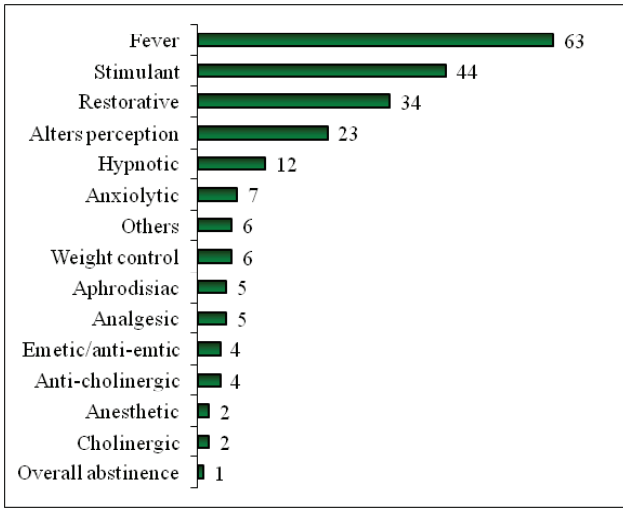

Figure 2. Categories of usage (left) referent to 129 plants (right), extracted from the reading of the 33 historic publications. Some of the plants have been indicated for more than one use so they are therefore present in more than one category simultaneously.

As to the *Erythroxylum coca* Lam. species, among uses attributed to it, the following are also part of the same publication: "*excitement, narcotic*"; in this case it is believed that the mention of "*narcotic*" refers to an addicting effect that is already accompanied by the "*excitement*" use. Therefore, the option was to include this use as narcotic, in category 3 (alters perception) (Table 2). Another study claimed that for the *Physalis angulata* L. species there are reports of "mild acting narcotic principle", "*calming*" use. In this context it is believed that the term "*narcotic*" is related to a hypnotic effect. Therefore, the option was to include this use as mild acting narcotic principle, in category 14 (hypnotic).

Since therapy in earlier centuries commonly caused vomiting, it is not known for certain if the cited plants for the following uses: "*nausea, vomit-inducer, vomitive, vomit*" have an effect of causing or fighting nausea\vomit. Therefore, these two therapeutic effects have been placed together in one single category 10 (emetic\anti-emetic).

As shown in Table 2, some uses, although having been categorized, doubts still exist in reference to their actual effect. For example: the plant *Nicotiana langsdorffii* Weinm. reports the use as "*the same as with* Nicotiana tabacum *and* N. rustica" and that has also been included in the category 3 (alters perception) since some authors consider that this plant is used to alter perception (Prance, 1973). Schultes (1984) explains that tobacco is definitely psychoactive in any method of use; the enigma persists in how in certain conditions and several methods of use, *Nicotiana* may produce a strong psychoactive effect on aborigine societies.

Mostly, authors do not make specific references to the cultures whose understanding has been described in their work. When mentioned, these populations were referred to with the following terms: "*indians, Sao Paulo backwoods men, Minas Gerais backwoods men, Bahia backwoods men, mazombos (Creoles- Portuguese>Brazilian mix), Black women, whites hailing from Portugal, inhabitants of the region between Paranaguá and Saco do Tanque, Vila de Arraias inhabitants, farmland dwellers*"; further to generic terms such as: "*people*" and "*known by all*". Only in the book *Viagem Pelo Brasil* (*Traveling in Brazil*) (Spix & Martius, 1976) was a reference made to the Maué and Baré Inidáo Native Brazilian Indians.

In current literature, studies for 66 species have been found (Table 3). For some plants, few studies were found in current literature with the correct use of the present nomenclature, using only with their synonyms. Out of the total studies found, only 44 refer to the currently accurate nomenclature while the other 22 use their synonyms. When a study refers to a synonym, its currently correct name is listed as a sub-item (Table 3).

Current ethnopharmacological studies were found for 61 of the 66 above mentioned species while pharmacologic studies were found for 31 of them and patent applications for fourteen. One same species may hold ethnopharmacology, pharmacology and patent applications studies. The number of studies per plant may vary from one to fifteen. Being so, the *Nicotiana tabacum* L. plant displayed six ethnopharmacological studies, eight pharmacology studies and one patent applications process; in reference to *Passiflora maliformis* L., only one ethnopharmacological study was found.

In that which refers to coincidences among reports of past usage compared with studies in current literature, coincidences have been observed for 46 species, all stressed on Table 3, underlined and in bold print. Of these, 41 displayed coincidences in usage for old reports and current ethnopharmacological studies, eight for current pharmacologic studies and three for patent applications. The underscored numbers next to each old use listed on the table refer to the book where this use was found. In order to check for which book contains the referral please check Table 1.

Upon observing coincidences contained in the data of usage found in historic and current literature, we have noticed that some species call attention in that which refers to two different aspects: while some plants display a great deal of studies, some plants on the other hand have been scarcely studied.

An example is *Nicotiana tabacum* L. that holds indications of possible effects listed in categories 7 (anticholinergic) "*disturbance to sight*", 10 (emetic\

anti-emetic) "*nausea, vomit*", 3 (alters perception) "*drunkenness*" and 11 (stimulant) "*stimulates brain, cerebellum and marrow*". These effects are widely known to traditional populations given the great number of current ethnopharmacological studies detected plus coincidences in reports for the three last above mentioned categories (Table 3). There are however, neither current pharmacological studies nor patent applications that make any reference to these past indications, nor do they make any attempt to directly prove these possible effects.

Yet *Pterodon emarginatus* Vogel has been reported in old literature as 4 (pain killer) "*against tooth aches*" that carries pharmacological studies that proves this effect for three of its synonyms (*P. polygalaeflorus* (Benth.) Benth.; *P. polygaliflorus* (Benth.) Benth. and *P. pubescens* (Benth.) Benth). There is however, no ethnopharmacological research or patent application for this species. There is also the *Mikania cordifolia* Willd., species reported in old literature as "febrifuge" (12 fever), this use having been confirmed in current ethnopharmacological studies without however any pharmacology study or patent applications to investigate this effect.

In a general sense, it has been observed that the species of interest herein have been scarcely studied throughout the years with only three of them holding patent applications that coincide with older day uses. The low number of requests for patent applications of the studied species may be a consequence of the number of pharmacological studies. Depending upon the country, in order to obtain a patent for some substance or method, it is advisable that you obtain proven effect (in the case of pharmacos).

Ethnopharmacology research grounded on old literature presents problems that should be taken into consideration. The first of these is that many of the plants cited herein have reports with no equivalent lexicon in the present. This on its own limits the analyses concerning knowledge exchange of a specific plant in the course of time (Voeks, 1997).

Still another problem is locating those books. When you are talking about a rare book, there are neither new editions nor are there many available copies which turns their location into something very restrictive. This becomes a twofold challenge for a researcher for, further to having to locate a book, there is still painstaking access considering that the country's main institutions in the country are located in different regions of the said country. Another downside is that not always does old literature specify the target culture of the study or the part of the plant used, nor do they explain the preparation of these plants. Furthermore, indications for the use are sometimes unspecific or have double meanings, leaving the researcher with the decision-making process. All of these factors represent hurdles in data analyses.

It is also a known fact that no matter how much effort has been placed on ethnopharmacology studies conducted among Brazilian cultures or in pharmacology after the 20th century - in order to establish a co-relation between "coincidence or not of use" of medicinal plants - we are perfectly aware that a bibliographic survey is never absolutely thorough. No matter how much you have looked up information on large-scope domestic and international publications, some researches may have been conducted yet only published in magazines of limited distribution. Further to that, there is always the possibility of negative pharmacological data never having been published at all. There is a significant number of communities in Brazil that have never been the target of ethnopharmacological research, or even those communities that have become extinct, which makes it even more difficult to observe if reports of past uses have been preserved among the current ones. Last of all, we must consider that knowledge is dynamic and the process of cultural mix and migration through time may have caused alterations to the used part, to the method of preparation or objective of the use of these plants.

Conclusions

In spite of all the limitations listed above, an ethnopharmacology survey using historic literature as a strategy to arrive at new potential bioactives is a promising tool since many of these medicinal plants recorded in these usually rare publications have never been investigated from a pharmacological and phytochemical point of view. In this current study, what can be observed is that out of 129 species, 63 have not displayed any kind of CNS-oriented investigation whatsoever. On the other hand, 66 species carry investigations in current literature, some of those holding on to their uses through time and having been thoroughly studied, among those: *Jatropha curcas* L. and *Psychotria ipecacuanha* (Brot.) Stokes acting as "*vomit inducers*"; *Paullinia cupana* Kunth var. sorbilis (Mart.) Ducke and *Theobroma cacao* L. acting as "*stimulants*"; at whose studies others should be added with an aim at developing new phytotherapeutics.

The present study further tried to contribute with the retrieving of past traditional folk knowledge in Brazil, thereby incrementing knowledge held by its diverse culture.

Table 3. Species (represented by their currently correct scientific names and their synonyms) that carry current ethnopharmacology or pharmacology studies and/or patent application processes. For the first 46, the data (from historic publications and current literature) all coincide and are highlighted in bold print and underlined. The remaining 23 do not display coincidences.

Nº	Currently correct scientific names; their synonyms and Taxonomic Families	Uses in historic literature	Current ethnopharmacology studies	Current pharmacology studies	Patent application process
			Current studies which coincides with historic uses		
1	*Acacia farnesiana* (L.) Willd. [Fabaceae]	exciter[26]	emetic, nausea, toothache, altering, aphrodisiac, convulsions, delirium, calming, epilepsy, fever, insanity, stimulant (Dr. Duke, 2010).	-	-
2	*Angostura trifoliata* (Willd.) T.S. Elias [Rutaceae]				
	Sin. *Cusparia trifoliata* (Willd.) Engl.	febrifuge[10]	aperitif, fever, stimulant, tonic (Dr. Duke, 2010).	-	-
3	*Arachis hypogaea* L. [Fabaceae]	aphrodisiac[27]	aphrodisiac, lactagogue (Dr. Duke, 2010); tonic, aphrodisiac (Mendes & Carlini, 2007).	-	-
4	*Aristolochia anguicida* Jacq. [Aristolochiaceae]				
	Sin. *Aristolochia mexicana* Willd.	febrifuge, tonic, stimulant[9]	stimulant (Dr. Duke, 2010).	-	-
5	*Aristolochia cymbifera* Mart. & Zucc. [Aristolochiaceae]	febrifuge, tonic, stimulant[9]	stimulant (Dr. Duke, 2010).	-	-
6	*Aristolochia fragrantissima* Ruiz [Aristolochiaceae]				
	Sin. *Aristolochia reticulata* Seem.	febrifuge, tonic, stimulant[9]	stimulant (Dr. Duke, 2010).	-	-
7	*Aristolochia odoratissima* L. [Aristolochiaceae]	febrifuge, tonic, stimulant[9]	calming, fever, stimulant, tonic (Dr. Duke, 2010).	-	-
8	*Aristolochia ringens* Vahl [Aristolochiaceae]				
	Sin. *Aristolochia grandiflora* Vahl	febrifuge, tonic, stimulant[9]	fever, tonic (Dr. Duke, 2010).	-	-
9	*Aristolochia triangularis* Cham. [Aristolochiaceae]				
	Sin. *Aristolochia antihysterica* Mart. ex Duch.	febrifuge, tonic, stimulant[9]	emetic, exciter (Dr. Duke, 2010).	-	-
10	*Aristolochia trilobata* L. [Aristolochiaceae]	febrifuge, tonic, stimulant[9]	fever, pain (Dr. Duke, 2010).	-	-
11	*Baccharis articulata* (Lam.) Pers. [Asteraceae]	febrifuge[9]	to weight loss (Ghedini et al., 2002); tonic, febrifuge (Dickel et al., 2007).	antioxidant (De Oliveira et al., 2003; Charão et al., 2002)	-
12	*Baccharis tridentata* Vahl [Asteraceae]	febrifuge[9]	febrifuge (Dr. Duke, 2010).	-	-
13	*Baccharis trimera* (Less.) DC. [Asteraceae]	febrifuge[9]	fever (Castellucci et al., 2000); fever, obesity - cerrado habitants (Rodrigues & Carvalho, 2007); tonic, febrifuge - Porto Alegre habitants (Dickel et al., 2007).	antioxidant (Simões-Pires et al., 2005; Oliveira et al., 2004); weight loss (Biela et al., 2002); analgesic (Gené et al., 1996).	-
14	*Cissampelos pareira* L. [Menispermaceae]	tonic, narcotic[9]	convulsions, epilepsy, cough, delirium, fever, madness, stimulant, tonic (Dr. Duke, 2010); tonic, sedative, analgesic, febrifuge - Indians (Adesina, 1982); fever - cerrado habitants (Rodrigues & Carvalho, 2007).	antioxidant (Amresh et al., 2007c); analgesic (Amresh et al., 2007a; 2007b).	-

15	*Cissampelos glaberrima* A. St.-Hil. [Menispermaceae]	tonic, narcotic[9]	tonic (Mendes & Carlini, 2007).	-	-
16	*Coutarea hexandra* (Jacq.) K. Schum. [Rubiaceae]	febrifuge[10]	fever (Agra & Barbora-Filho, 1990; Dr. Duke, 2010) - Xucuru Indians (Silva & Andrade, 1998).	-	-
17	*Crescentia cujete* L. [Bignoniaceae]	febrifuge[10]	headache, calming, aperitif, aphrodisiac, cough, depurative, emetic, fever (Dr. Duke, 2010).	-	-
18	*Cucurbita pepo* L. [Cucurbitaceae]	febrifuge[10]	calming, fever, tonic (Dr. Duke, 2010); tonic in mental disorders and insanity - Indians (Adesina, 1982).	-	-
19	*Dipteryx odorata* (Aubl.) Willd. [Fabaceae]	analeptic, nevrosthenia[27]	anticoagulant, fever, narcotic, stimulant (Dr. Duke, 2010); tonic (Mendes & Carlini, 2007).	antioxidant (Suzuki et al., 2007).	-
20	*Dorstenia brasiliensis* Lam. [Moraceae]	fortifies the nerves[30]	cough, emetic, fever, stimulant, tonic (Dr. Duke, 2010); anesthetic for toothache - cerrado habitants (Rodrigues & Carvalho, 2007) tonic (Mendes & Carlini, 2007).	analgesic (Ruppelt et al., 1991).	-
21	*Elephantopus mollis* Kunth [Asteraceae]				
	Sin. *Elephantopus scaber* L.	febrifuge[10]	toothache, altering, aphrodisiac, cough, fever, nausea, tonic (Dr. Duke, 2010).	analgesic (Ruppelt et al., 1991).	-
22	*Erythrina crista-galli* L. [Fabaceae]	calming and hypnotic[16, 27]	narcotic (Dr. Duke, 2010).	analgesic (Miño et al., 2002; Fischer et al., 2007).	-
23	*Erythroxylum coca* Lam. [Erythroxylaceae]	"combats state of weakness; less need for food, CNS exciter." drunkenness; anesthetic; exciter, narcotic[10, 21, 22, 32.]	headache, anesthetic, calming, aphrodisiac, depression, depurative, hallucinogenic, hunger, melancholy, narcotic, jitters, psychedelic, stimulant (Dr. Duke, 2010); stimulant and narcotic – Marpie, Yukuna and Tanimuka Indians (Schultes, 1984); stimulant and narcotic (Plowman, 1979; Cooper, 1987).	CNS stimulant (Seidler, 2001); lack of appetite (Burczynski et al, 1986; Vee et al., 1983); anesthetic (Bedford et al., 1984).	supress appetite (European Patent Office, 2010).
24	*Geissospermum laeve* (Vell.) Miers [Apocynaceae]	tonic, anti-fever[10, 12]	fever (Dr. Duke, 2010).	potentiates action of serotonin on hippocampus (Barros et al., 2006).	-
25	*Ipomoea batatas* (L.) Lam. [Convolvulaceae]	inebriating [26]	toothache (Castellucci et al., 2000); altering, aphrodisiac, tonic (Dr. Duke, 2010), general pain (Ghedini et al., 2002).	antioxidant (Han et al., 2007); vasodilator (Runnie et al., 2004); antioxidant; improves cognition (Cho et al., 2003).	-
26	*Jatropha curcas* L. [Euphorbiaceae]	vomitive[21, 26]	toothache, convulsions, cough, depurative, emetic, fever, lactagogue, narcotic (Dr. Duke, 2010); analgesic (Rodrigues, 2006).	anticoagulant, coagulant (Osoniyi & Onajobi, 2003); neuroprotective (Kulkarni et al., 2005); causes nausea and vomiting (Abdu-Aguye et al., 1986).	-
27	*Manihot esculenta* Crantz *subsp. esculenta* [Euphorbiaceae]	antidote of the drunkenness and inebriating effects /drunkenness; inebriating [26]	fermented beverage - Totoboí Indians(Prance, 1970)	-	alcoholic fermentation (European Patent Office, 2010).
28	*Mikania cordifolia* Willd. [Asteraceae]	febrifuge[10]	fever (Dr. Duke, 2010).	-	-

29	*Mimosa verrucosa* Benth. [Fabaceae]	narcotic [9, 10]	hallucinogenic (Schultes, 1979).	antioxidant (Desmarchelier & Lisboa Romão, 1999).	-
30	*Nicotiana tabacum* L. [Solanaceae]	"drunkenness, disturbance to sight, nausea, vomit. Stimulates brain, cerebellum and marrow." [29]	headache, toothache, calming, anorectic CNS stimulant, cough, emetic, fear, hallucinogenic, narcotic, psychedelic, sedative, snuff (Dr. Duke, 2010); snuff – Dení Indians (Prance, 1972); hallucinogenic (Schultes, 1979; 1984). stimulant, sedative, narcotic, antipyretic, to treat convulsions, snuff - Indians. (Adesina, 1982), toothache (Castellucci et al., 2000).	neuroprotective (Qiao et al., 2005); improves cognition (Maskos et al., 2005), increases sensibility of behavioral effects of alcohol (Bowers et al., 2005); decreases sensibility to metanphetamine (Kuribara, 1999); increases dopaminergic activity (Pidoplichko et al., 1997); act on cholinergic receptors (Kobayashi et al., 1999); inhibits MAO B (Fowler et al., 1996); psychoactive (Cassels et al., 2005).	combats vascular headache (European Patent Office, 2010).
31	*Passiflora maliformis* L. [Passifloraceae]	Calms need for feed and sleeping[4]	sedative (Dr. Duke, 2010)	-	-
32	*Paullinia cupana* Kunth var. *sorbilis* (Mart.) Ducke [Sapindaceae]	affects emotions, abnormal excitement, double vision, insomnia, eyesight scintillation, aphrodisiac. [32]	stimulant, tonic (Dr. Duke, 2010) tonic (Mendes & Carlini, 2007).	antioxidant (Basile et al., 2005), psychostimulant (Otobone et al., 2007).	-
33	*Physalis angulata* L. [Solanaceae]	mild acting narcotic principle, calming, fixed tonic[2]	analgesic, fever, narcotic, nausea, sleep disease (Dr. Duke, 2010).	presents acetilcholine (Melo, 1982); anticholinergic (Fonteles et al., 1990); analgesic (Bastos et al., 2006); antioxidant (Choi & Hwang, 2005).	-
34	*Physalis pubescens* L. [Solanaceae]	mild acting narcotic principle, calming, fixed tonic[2]	cough, fever, sedative (Dr. Duke, 2010).	-	-
35	*Psychotria ipecacuanha* (Brot.) Stokes [Rubiaceae]	vomitive, antidote for opium [25, 26, 30]	stimulant (snuff) – Amazonian Indians (Cooper, 1987)	vomitive (Möller et al., 2007).	-
	Sin. *Cephaelis ipecacuanha* (Brot.) A. Rich.	vomitive, antidote for opium [25, 26, 30]	emetic (Van den Berg, 1982); aperitif, emetic (Dr. Duke, 2010).	-	sexual hypofunction (European Patent Office, 2010); help quit smoking (USPTO, 2008).
36	*Pterodon emarginatus* Vogel [Fabaceae]				-
	Sin. *Pterodon polygalaeflorus* (Benth.) Benth.	toothaches [24]	-	analgesic (Duarte et al., 1992).	-

36	Sin. *Pterodon polygaliflorus* (Benth.) Benth.	toothaches [24]	-	analgesic (Leal et al., 2000); antioxidant (Paula et al., 2005).	-
	Sin. *Pterodon pubescens* (Benth.) Benth.	toothaches [24]	-	analgesic (Coelho et al., 2005); decoagulation (Calixto et al., 2007; Spindola et al., 2010).	-
37	*Quassia amara* L. [Simaroubaceae]	febrifuge, tonic, energetic [10]	febrifuge, tonic (Van den Berg, 1982; Dr Duke, 2010); stimulant (Dr. Duke, 2010) tonic (Mendes & Carlini, 2007).	analgesic, sedative (Toma et al., 2003); affinity with D1 and D2 receptors (Luedtke et al., 2003).	-
38	*Senna occidentalis* (L.) Link [Fabaceae]	tonic [27]	general weakness (Agra & Barbosa-Filho, 1990).	-	-
	Sin. *Cassia occidentalis* L.	tonic [27]	headache, fever, nausea, tonic (Dr. Duke, 2010); fever – Roraima population (Van den Berg & Silva, 1988), tonic (Mendes & Carlini, 2007).	-	weight loss (European Patent Office, 2010); tranquilizer (European Patent Office, 2010).
39	*Simarouba amara* Aubl. [Burseraceae]				
	Sin. *Quassia simarouba* L. f	febrifuge, tonic, energetic [10]	fever (Rêgo, 1988).	-	-
	Sin. *Simarouba glauca* DC	febrifuge[10]	body ache, calming, emetic, fever (Dr. Duke, 2010).	-	treats insomnia (European Patent Office, 2010)
40	*Stachytarpheta jamaicensis* (L.) Vahl [Verbenaceae]	febrifuge[10]	Headache, calming, cough, depurative, emetic, fever, lactagogue, nausea, sedative (Dr. Duke, 2010).	antinociceptive (Sulaiman et al., 2009)	-
41	*Tachia guianensis* Aubl. [Gentianaceae]	fever [32]	fever (Dr. Duke, 2010).	-	-
42	*Theobroma cacao* L. [Sterculiaceae]	bitter principle comparable with caffeine; analeptic 26, 33	cough (Dr. Duke, 2010); tonic (Mendes & Carlini, 2007).	antioxidant (Sanbongi et al., 1998); canabinoids (Di Tomaso et al., 1996); theobromine and caffeine (Wiśniewski & Klepaczewska-Saluda, 1971); psychoactive (Melzig at al., 2000).	antidepresssant (European Patent Office, 2010).
43	*Theobroma subincanum* Mart. [Sterculiaceae]	bitter principle comparable with caffeine 26	snuff (exciting, nausea, hallucinogen, deep and disturbed sleep) – northwest Amazon (Schultes, 1969) - Dení Indians (Prance 1972; Dr. Duke, 2010).	-	-
44	*Zanthoxylum tingoassuiba* A. St.-Hil. [Rutaceae]	antigen for Gelsemium sempervirens [12*]	-	cholinergic blocker (Mehl de Menezes e Menezes & Pereira, 1990).	-
45	*Zea mays* L. *subsp*. Mays [Poaceae]	drunkenness [26]	pain, altering, stimulant (Dr. Duke, 2010).	-	-

46	*Ziziphus joazeiro* Mart. [Rhamnaceae]	general anesthetic [23]	cough (Albuquerque & Oliveira, 2007).	antinociceptive (Affonso et al., 1990), power benzodiazepines (Cruz et al., 1998).	-
		Current studies without coincidence with historic uses			
1	*Acosmium dasycarpum* subsp. glabratum (Benth.) Yakovlev [Fabaceae]	acts against CNS disorders; 20	-	sedative (*A. dasycarpum*) (Rocha et al., 1980)	-
2	*Anacardium occidentale* L. [Anacardiaceae]	drunkenness, inebriating[26]	nausea, toothache, cough, fever (Dr. Duke, 2010); tonic, aphrodisiac (Mendes & Carlini, 2007); combat pain in extremities – Pataxó Indians (Thomas, 2001).	antioxidant (Singh et al., 2004; Boscolo et al., 2007); vasodilator (Runnie et al., 2004).	inhibits nitric oxide (Espacenet, 2008); hypotensive (European Patent Office, 2010); antioxidant
3	*Astrocaryum aculeatum* G. Mey. [Arecaceae]				
	Sin. *Astrocaryum chambira* Burret	wine [28]	-	-	antioxidant (USPTO, 2008).
4	*Baccharis trimera* (Less.) DC. [Asteraceae]				
	Sin. *Baccharis genistelloides* var. *trimera* (Less.) Baker	febrifuge [10]	tonic (Dr. Duke, 2010); tonic, aphrodisiac (Mendes & Carlini, 2007).	-	-
5	*Caesalpinia echinata* Lam. [Fabaceae]	febrifuge, tonic [27]	-	-	antioxidant (European Patent Office, 2010); increases blood viscosity (USPTO, 2008).
6	*Cissampelos ovalifolia* DC. [Menispermaceae]	tonic, narcotic [9]	fever- cerrado habitants (Rodrigues & Carvalho, 2007).	-	-
7	*Copaifera officinalis* (Jacq.) L. [Fabaceae]	febrifuge [27]	stimulant (Dr. Duke, 2010).	-	-
8	*Elephantopus mollis* Kunth	febrifuge [10]	tonic (Dr. Duke, 2010)	-	-
9	*Euterpe oleracea* Mart. [Arecaceae]	wine [28]	restorative (Rodrigues, 2006).	antinociceptive (Marinho et al., 2000); vasodilator (Rocha et al., 2007); antioxidant (Arruda et al., 2004; Lichtenthaler et al., 2005).	-
10	*Hyptis spicigera* Lam. [Lamiaceae]	febrifuge [17]	-	sedative, anticonvulsant (Bum et al., 2009)	-
11	*Lindernia diffusa* (L.) Wettst. [Scrophulariaceae]	fever[4]	emetic (Dr. Duke, 2010)	-	-
12	*Mauritia flexuosa* L. f. [Arecaceae]	fermented alcoholic beverage [31]	tonic, restorative (Mendes & Carlini, 2007).	antioxidant (Silva et al., 2005).	-
13	*Myrciaria cauliflora* (Mart.) O. Berg [Myrtaceae]	wine [30]	-	antioxidant (Einbond et al., 2004).	-

14	*Ocotea odorifera* (Vell.) Rowher [Lauraceae]				
	Sin. *Ocotea pretiosa* (Nees) Mez	combats nerve weakness[10]	depurative (Van den Berg, 1982).	-	-
15	*Oenocarpus bataua* Mart. [Arecaceae]				
	Sin. *Jessenia bataua* (Mart.) Burret	wine [28]	headache (Russo, 1992).	-	-
16	*Paullinia pinnata* L. [Sapindaceae]	affects emotions, abnormal excitement, double vision, insomnia, eyesight scintillation, aphrodisiac [32]	emetic, fever (Dr. Duke, 2010)	-	-
17	*Peperomia pellucida* (L.) Kunth [Piperaceae]	exciter [9]	headache, calming, cough, calming, depurative, fever (Dr. Duke, 2010).	analgesic (Aziba et al., 2001; de Fátima Arrigoni-Blank et al., 2004).	-
18	*Senna quinquangulata* (Rich.) H.S. Irwin & Barneby [Fabaceae]				
	Sin. *Cassia quinquangulata* Rich.	calming [27]	-	-	weight loss (USPTO, 2008).
19	*Senna sophera* (L.) Roxb. [Fabaceae]	tonic [27]	-	-	decreases blood viscosity (European Patent Office, 2010).
	Sin. *Cassia sophera* L.	tonic [27]	fever, headache (Dr. Duke, 2010).	-	blood viscosity (European Patent Office, 2010).
20	*Solanum chenopodioides* Lam. [Solanaceae]				
	Sin. *Solanum gracile* Dunal	calming [2]	fever (Dr. Duke, 2010).	-	-
21	*Strychnos pseudoquina* A. St-Hil. [Loganiaceae]	febrifuge [24]	tonic, aphrodisiac (Mendes & Carlini, 2007).	-	-
22	*Theobroma bicolor* Bonpl. [Sterculiaceae]	bitter principle comparable with caffeine [32]	-	antioxidant (Torres et al., 2002).	-
23	*Zanthoxylum tingoassuiba* A. St.-Hil. [Rutaceae]				
	Sin. *Zanthoxylum articulatum* Engl. in Mart. (*Zanthoxylum tingoassiba* A. St.-Hil.)	antigen for *Gelsemium sempervirens* [12]	toothache, analgesic, calming, stimulant (Dr. Duke, 2010).	-	-
	Sin. *Zanthoxylum nitidum* A. St.-Hil. (*Zanthoxylum tingoassiba* A. St.-Hil.)	antigen for *Gelsemium sempervirens* [12]	stimulant (Dr. Duke, 2010)	analgesic (Hong & Zeng, 1983; Hu et al., 2006).	treats drug dependence (USPTO, 2008).

**Gelsemium sempervirens* was cited earlier in the same historic publication as "*pupil dilating*"
Obs.: The numbers on the side stand for the books wherefrom its use was extracted. In order to check each reference number, please refer to Table 1.

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