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Medicinal Plants of Brazil

Introduction

Brazil is the largest country in Latin America covering a territory of 8,514,876.599 km² that lies between central South America and the Atlantic Ocean. Brazil is named after the plant pau-brasil (*Caesalpinia echinata* L.), a member of the Caesalpinaceae family which was used in the past to obtain a dye-stuff known as “brasiline” (Goncalves De Lima *et al.*, 1961). Due to Brazil’s varied geographical environment ranging from the Amazonian rainforests to the dry semi-arid hinterland known to the Indians as the “Caatinga” (Anon1 1978), the country is botanically rich with 40 000–60 000 vegetal species (Jorge *et al.*, 2004). The five major biomes of Brazil include the Amazon rain forests that cloak an area larger than western Europe, Cerrado brushlands the home of the Krahô Indians, the Mata Atlântica rain forest, the Pantanal wetlands and the Caatinga semi arid desert (Giorgetti *et al.*, 2007). With the exception of the Amazon forests, there is a huge paucity of documented studies on the medicinal plants concerning other biomes such as the Mata Atlantica, the Pantanal, (Di Stasi *et al.*, 2002) and especially the Caatinga and the Cerrado (Almeida *et al.*, 2006). Historians believe that it was the richness of the flora and the highly prized wood from the forests of Brazil that had played a central role in enticing the early explorers to its shore (De Mello 1980). In Brazil, an ancient tradition where plants are looked upon as divine sources of healing still exists especially among the different ethnic groups like the Tupis in the north and the Guaranis in the south that inhabit the Amazon rain forests. Bertoni, a 19th century botanist held strong convictions that the wild Guaranis had a better knowledge of plants compared to that of the Europeans of the 16th century (Marini-Bettòlo 1977). Perhaps one way or

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another, many of us have been acquainted with the term “curare” coined by Margraff in 1648 which was originally used by different forest tribes from the French Guiana to the Mato Grosso, as an arrow poison, that paralyzed the skeletal muscles by blocking the effects of acetylcholine at the neuromuscular junction of the victim (Stejskal 2005). Arrow tips carrying this poison brought death to many Spanish soldiers who ventured out to explore and conquer Central and South America. Today, in the civilized world, among other uses, curare is used as an adjunct to general anesthesia (Stejskal 2005).

The healers in Brazil who practice the Indian traditional medicine are known as the pajés or the shamans. Pajés cultivate their own medicinal herbs, hold dancing and chanting rituals and enter into a trance like state to seek the support of benign spirits to exorcize the malevolent ones and drive away diseases (Finger 2003). The practice of the pajés amongst the Amayura tribe of the Alto Xingu in Mato Grosso have been reported by Carod-Artal and Vazquez-Cabrera (2001). Amongst the early publications on the plants of Brazil include the one written by the Bavarian von Martius entitled “Systema Materiae Medicae Vegetabilis Brasiliensis Vegetabilis Brasiliensis” which describes 470 plants belonging to 236 different types with commentaries on the therapeutic value of the medicinal plants (De Mello 1980). Other notable books on the medicinal plants of Brazil that have survived the ravages of time, include the (a) *Notícia do Brasil* (1587) Sousa, G.S. *Brasiliensia Documenta*. Volume VII, Sao Paulo, 1974 (b) “Zoobiblion” (*Livro de Animais do Brasil*, 1654 Wagener, Z. *Brasiliensia Documenta*, Volume IV, 1964, (c) *Plantas Fluminenses Descritas por Frei Veloso* (1741–1811), Veloso, J.M.C. *Separata de Anais da Biblioteca Nacional* Volume 96. Rio de Janeiro, 1976 (d) *Plantas Medicinais do Brasil* (1801-1812), Gomes, B.A. *Brasiliensia Documenta*, Volume V, Sao Paulo, 1972. (e) *Viagem pelo Brasil* (1817-1820) Spix and Martius, Volume III, Editora Melhoramentos, Sao Paulo, 1976 (f) *Natureza, Doencas, Medicina e Remedios dos Indios Brasileiros* (1844) Martius, Companhia Editorial Nacional, Sao Paulo, 1939 (Giorgetti *et al.*, 2007).

In this article, we have presented the medical properties of some medicinal plants from Brazil that are used as traditional medicine.

Medicinal Plants

Anacardium occidentale or Cashew is known as “Caju” (the fruit) in Brazil and the word is of Portuguese origin. *Anacardium occidentale* belongs to the family Anacardiaceae and the tree is native to Northeastern Brazil but is presently cultivated in many regions of the world that harbor a tropical climate (Konan and Bacchi 2007), such as East Africa, India and Vietnam (Santos *et al.*, 2007). The Portuguese took the cashew tree to East Africa and India sometime around 1750, which then spread to Sri Lanka and Malaysia (Maia *et al.*, 2000). *Anacardium occidentale* is an important crop of Brazil, occupying an estimated area of 700 000 ha (Oliveira *et al.*, 2006) and almost 96% of the cashew cultivation is located in the northeast region (Sousa de Brito 2007). Brazil is the major exporter of cashew nut to the world, with annual sales ranging from US\$ 140 million to US\$ 160 million (Oliveira *et al.*, 2006).

“Cajueiro” is a small evergreen tree with irregularly shaped trunk with a height of 10-12 m (Kamtchouing *et al.*, 1998). The leaves are spirally arranged, leathery in texture, elliptic to obovate in shape with a smooth margin. The flowers are small and bears five slender, acute petals, produced in a panicle and are pale green initially but changes to a reddish hue with maturity. The cashew apple is a pseudo-fruit (edible part of the tree connecting the fruit) formed by an enlarged peduncle, whilst the true fruit (cashew nut) is the kidney-shaped (reniform) achene, measuring 3 cm in length and possessing a hard gray-green pericarp (Vaughan and Geissler 1997). The peduncle is of high nutrient quality and includes tannins, mineral salts, organic acids, carbohydrates (FAO 1986) as well as vitamin C, that averages to 200 mg/100 g of juice which is four times higher than that of orange juice (Menezes and Alves 1995). Vitamin C is crucial for hydroxylation processes, corticoid and catecholamine biosynthesis, as well as blood and bone formation (Assunção and Mercadante 2003).

The antimicrobial property of *Anacardium occidentale* has been extensively made use of in the traditional folk medicine of South America where decoctions prepared from the leaves of the cashew tree are used to treat various diseases including ulcers (Taylor 2005) such as ulcers of the mouth, throat problems and gastrointestinal disorders (acute gastritis and diarrhea) (Akinpelu, 2001; Gonçalves *et al.*, 2005; Kudi *et al.*, 1999). The cardiovascular effects of the aqueous extract from cashew leaves on the arterial blood pressure of rabbits, have been documented, which was found to be significantly reduced by 89% on treatment with the extract (Tchikaya *et al.*, 2003). The leaves of the cashew tree are known to contain two main chemical groups viz. the flavonoids such as quercetin-3-O-rhamnoside, kaempferol-3-O-methyl-ether, myricetin-3-O-rhamnoside and kaempferol-3-O-rhamnoside as well as tannins (Konan *et al.*, 2007). Studies have also revealed that extracts prepared from the cashew bark are known to inhibit skin cancer, the cause of which has been attributed by Franca *et al.* (1996) to the presence of tannins and flavonoids. The Caiçara fishermen of coastal Brazil use the bark of the plant to treat hemorrhoids and severe diarrhea (Di Stasi and Hiruma-Lima 2002), the Pataxó Indians use it to treat lower extremity pains and skin injury (Thomas 2001) while the Xucuru Indians value the bark for its anti-inflammatory properties (Silva and Andrade 1998). Apart from South America, use of *Anacardium occidentale* for the treatment of inflammatory conditions such as arthritis has also been reported from Africa (Iwu 1993; Oliver-Bever 1986).

In addition to hydrolysable tannins (Pillai *et al.*, 1963), epicatechin and catechin are also among the major polyphenols present in the reddish brown testa that covers the kernel of the cashew nut (Mathew and Parpia 1970). Due to the presence of these polyphenols, the ethanolic extract of cashew skin has been reported to exhibit significant antioxidant activity by Kamath and Rajini (2007). Kamtchouing *et al.* (1998) have demonstrated the protective effect of *Anacardium occidentale* extract against streptozotocin (STZ)-induced diabetes in rats, the effect of which was attributed to the presence of glucose and epicatechin in the plant extract. Antidiabetic activity of *Anacardium occidentale* stem-bark in fructose-diabetic rats have

been reported by Olatunji *et al.* (2005). The exuded gum from *Anacardium occidentale* is a heteropolysaccharide that is synthesized in the epithelial cells bordering the gum ducts and usually used as a substitute for gum arabic in pharmaceutical uses (de Paula and Rodrigues 1995). The constituents of the gum has been reported to contain galactose (72–73%), glucose (11–14%), arabinose (4.6–5%), rhamnose (3.2–4%) and glucuronic acid (4.7–6.3%) (de Paula and Rodrigues 1995; de Paula *et al.*, 1998). Marques *et al.*, (1992) has reported on the antimicrobial and insecticidal properties of the gum.

Bertholletia excelsa or the Brazil nut tree or “Castanhero-do-pará” (Giorgetti *et al.*, 2007) is a member of the Lecythidaceae family and is regarded among one of the most economically successful non-timber forest products (NTFPs) in Brazil (Wadt *et al.*, 2005). *Bertholletia excelsa* is a canopy emergent tree scattered throughout the Amazon basin and is known to attain a height of 30–50 m (Mori and Prance 1990). The tree is usually distributed in the ‘tierra firma’ (non-flooded) parts of the forest, i.e. in sites that experiences about two months of dry season, an annual rainfall of 1400–2800 mm, and an annual mean temperature of 24.3–27.2°C (Mori and Prance 1990). The Brazil nut tree has been ranked as the 8th most productive nut tree besides almond, walnut, cashew, hazelnut, chestnut, pistachio, pecan, and macadamia (Rodrigues *et al.*, 2005). Brazil nuts are very high in selenium content however the selenium content of the nuts is highly dependent on the amount of the trace element present in the soil (Dumont *et al.*, 2006). Dietary selenium and Brazil nuts have been associated with protection against tumor development in laboratory animal studies (Chang *et al.*, 1995). Selenium is known to induce a cytotoxic effect on tumor cells (Alaejos *et al.*, 2000; Mugesh *et al.*, 2001). From a study by Caffrey and Frenkel (1991) it was apparent that brief exposure of HeLa cells to micromolar concentrations of selenite exhibited significant inhibition in tumor cell colony formation. Other than anticancer properties, selenium is an essential trace element required by the body for cell metabolism as a component of glutathione peroxidase an antioxidant enzyme (Arsenyan *et al.*, 2003) and hence has the ability to protect the cells against detrimental effects of free radicals. The fruit from the plant is mostly used as a part of traditional medicine by the Amazonian river dwellers to treat anemia (Amorozo and Gély 1988) whilst both the bark and the fruit are used by the Amazonian river-dwellers and the rubber-tappers for the treatment of gastrointestinal disturbances, fever, liver and colic problems, dysentery and as a body strengthener (Ming 1995; Rodrigues 2005).

Chagas’ disease caused by the flagellate protozoan *Trypanosoma cruzi* affects more than 18 million people in Latin America with a high annual death toll of approximately 400,000 deaths (Chiari *et al.*, 1991; WHO 1993). Blood transfusion-transmitted Chagas disease is a frequent case in Central and South America and the annual incidence in Brazil alone is about 20,000 cases. The only trypanosomicidal agent without major side effects available is a triarylmethane dye known as crystal violet, (Chiari *et al.*, 1991), however this dye suffers from the disadvantage of coloring and staining the patient’s blood and tissue and is thus avoided by the physicians for the routine

treatment of blood (Brener 1982; Docampo and Moreno 1985). Therefore it was considered imperative that a prophylactic therapeutic drug or a natural antiprotozoal agent harboring trypanocidal activity be found, in order to eradicate Chagas' disease. A study carried out by Campos *et al.* (2005) showed that acetone and methanol extracts prepared from the stem barks of *Bertholletia excelsa* exhibited significant *in vitro* trypanocidal activity against the trypomastigote form of *Trypanosoma cruzi*. The juice from the fruit is popularly used to treat hepatitis whilst the tea prepared with stem barks has also been deemed potent as an antimalarial agent (Vieira 1992).

Bixa orellana belongs to the family Bixaceae and is known as the annatto plant, "urucum" in Portuguese and more quaintly as the "Lipstick tree" because some of the Amazonian Indians use the vitamin C containing dye prepared from the plant to paint their bodies and the woman use it color their lips. It is a small 2 – 5 m high, evergreen tree (also considered as a tropical shrub) native to the rain forests of Central and Southern America and widespread among the tropics (Perry 1980). *Bixa orellana* is named in the honour of Francisco de Orellana, the Conquistador who first explored the Amazon River in 1541 (Preston and Rickard 1980). The tree bears attractive pink or white flowers and a burr like pod containing 10 - 50 seeds with a thin layer of soft, slightly sticky vermilion pulp (Preston and Rickard 1980) that yields 'annatto' a natural reddish-yellow extract (Ribeiro *et al.*, 2005). "Annatto" is widely used as a colorant in the food, cosmetic and pharmaceutical industries (Massarani *et al.*, 1992). The two main annatto colorant substances presented in extracts are the bixin, an oil-soluble carotenoid (Carvalho and Hein 1989) and the norbixin a water-soluble bixin hydrolyzed derivative (Bautista *et al.*, 2004). *Bixa orellana* is categorized as an adaptogen and the seeds are used widely in traditional medicine, either in the form of a powder or prepared into syrup and used as a tonic, a fortifier and as an aphrodisiac (Mendes and Carlini 2007). Besides being valued for its adaptogenic properties and an effective gastrointestinal tonic, the seeds of *Bixa orellana* are also used for the treatment of fevers, heartburn and asthma, as an aid in easing constipation (purgative), (Lorenzi and Matos 2002) as a gargle for sore throats, as an anti-pruritic and for treatment of buccal tumours and gonorrhea (Burkill 1985; Cáceres *et al.*, 1995; Pamplona-Roger 1998). Cáceres *et al.* (1995) found that amongst the 46 plants of American origin that were screened for *in vitro* activity against *Neisseria gonorrhoeae* (a bacterium responsible for gonorrhea), extract from the leaves of *Bixa orellana* was considerably active against the bacterium, thereby indicating the benefit of the plant in the control of gonorrhea. Besides treatment of gonorrhea the leaves are also used for oral hygiene and as an antiemetic (Burkill 1985; Cáceres *et al.*, 1995; Pamplona-Roger 1998). In another study, Fleischer *et al.* (2003) revealed that the ethanolic extracts of the leaves and seeds of *Bixa orellana* exhibited considerable antimicrobial activity against both the Gram-positive and Gram-negative bacteria (*Bacillus subtilis*, *Staphylococcus aureus*, *Streptococcus pyogenes*, *Salmonella typhi*, *Pseudomonas aeruginosa* and *Escherichia coli*) as well as against the yeast-like fungus *Candida albicans*. The activity appeared to be more pronounced in the use of leaf extract thereby indicating the benefits of *Bixa orellana* in traditional medicine

particularly as a gargle for sore throats and oral hygiene. In a study carried out by Otero *et al.* (2000), twelve out of 74 ethanolic extracts of plants used by traditional healers for snakebites in the northwest region of Colombia, were active against the lethal effect of *Bothrops atrox* (an Amazonian snake) venom when they were i.p. (intraperitoneal) injected into mice (18–20 g). Extract prepared from the leaves and the branches of *Bixa orellana* were among the 12 plants that were used in the study and the results showed that the extracts from the plant exhibited partial protection of mice with a mean survival rate varying from 45% to 80 % at 48 hours. According to Gowda (1997) Phospholipase A2 (PLA2) enzymes are important constituents of snake venoms with the capability to initiate several pharmacological effects such as neurotoxic, myotoxic, cardiotoxic, anticoagulant, hemorrhagic, hemolytic, edema-inducing, convulsant, hypotensive and platelet aggregation activities. However, some of the constituents of plants have the ability to bind to these proteins and inhibit both the enzymatic activity and the catalytic activity of the PLA2 present in the venom (Gowda 1997; Melo and Ownby 1999). Thus from the study it was concluded by Otero *et al.* (2000), that some of the plants including *Bixa orellana* had the ability to bring about an *in vitro* neutralizing effect (either absolute or partial) against the indirect hemolytic activity of *Bothrops atrox* venom, through inhibition of PLA2 enzymes.

Genipa americana is a fruit-tree species belonging to the family Rubiaceae and is distributed in the neotropical forests extending from Mexico to the north of Argentina (Carvalho 1994; Lorenzi 1992). In Brazil, it is known as “Jenipapo” (Mendes and Carlini 2007). The tree is tall and erect with a slender trunk and spreading branches with height ranging between 60–110 feet. The leaves are abundant, deciduous, short-petioled, opposite and clustered at the branch tips. The flowers are pale-yellow or white in colour, tubular in shape and possess five petals that are borne in short, branched, terminal clusters. The fruits are 9–15 cm long, elliptic or rounded-oval in shape tapering briefly at the stem with a short hollow tube at the apex (Anon 2 1999). In Brazil, the fruits are highly valued because of their richness in iron and are either consumed raw or in the processed forms, such as candies, jellies and liqueurs (Mielke *et al.*, 2003). The fruit is also popular as a source of beverages (Ueda and Iwahashi 1991). In traditional medicine, the ripe fruits are used as a treatment for anemia, asthma and diarrhea (Mielke *et al.*, 2003) however there are very little documented studies on its medicinal properties compared to other Brazilian plants. *Genipa americana* contains geniposide (Djerassi *et al.*, 1960) and geniposidic acid (Kasahara 1986) in the fruits and geniposidic acid (Kasahara 1986) in the leaves and on callus induction the plant synthesizes tarennoside, (Heyne 1950) geniposidic acid (Kasahara 1986) and gardenoside (Djerassi *et al.*, 1961) at high levels. Geniposide, is a major iridoid glycoside present in many plants including the Gardenia fruit in which it was shown to inhibit 5-lipoxygenase (Nishizawa *et al.*, 1988) thereby displaying its potency in antiasthma therapy. Although the ripe fruits of *Genipa americana* are generally used for the treatment of asthma, no such studies have been documented for this plant. Moreover many geniposide containing plants have also been attributed with antitumor activity although such studies have not been carried out in *Genipa americana*. The plant is considered as an adaptogen in Brazil and hence used as a tonic and a fortifier as well as an aphrodisiac (Mendes and Carlini 2007).

Hymenaea courbaril is known by many names such as stinking toe, “Jatobá” as well as the Kerosene tree because of its strong odor. The deciduous tree belongs to the family Fabaceae (Caesalpinaceae) and is widely distributed in the Caribbean and the Amazon basin (Jayaprakasham *et al.*, 2007), especially in the Brazilian forests (Lima *et al.*, 1995) and in Venezuela (Clamens *et al.*, 2000). The tree is tall and straight, with unbuttressed trunk and the leaves are alternate, compound, bearing two asymmetric leaflets (Anon 3 2007). The bark, resin and leaves of the tree are used for the treatment of arthritis, asthma, bronchitis and rheumatism (Jayaprakasham *et al.*, 2007). The resin (known as “Brazil copal”) is generally secreted into the rounded pockets found in the parenchyma cells lining of the leaves, floral parts and young stems (Martin *et al.*, 1972) and are a rich source of diterpene carboxylic acids (Jayaprakasham *et al.*, 2007). The resin of *Hymenaea courbaril* or the toasted leaves of *Piper auritum* are burned as incense by the Zapotecs of the Isthmus-Sierra (Oaxaca, Mexico) (Frei *et al.*, 1998). Both the bark and the resin from the tree is used as a tonic, fortifier and an energizer as it can restore organic strength and counteract weakness in general (Mendes and Carlini 2007). *Hymenaea courbaril* is classified as an adaptogen or a resistogen — a term coined by N. Lazarev in the Soviet Union to classify plants and other substances that boost non-specific resistance of the body to protect it from stressful factors (Brekhman and Dardymov 1969). Adaptogens are believed to enhance the body’s capacity to respond to stressful stimuli, a behavior, akin to some stress mediators such as corticosteroids, catecholamines and nitric oxide (Panossian *et al.*, 1999; Rege *et al.*, 1999) and may act non-specifically as an antioxidant, immunomodulator, hypoglycemic as well as a hypocholesterolemic (Baranov 1982; Davydov and Krikorian 2000; Panossian *et al.*, 1999; Rege *et al.*, 1999). Amongst the 15 known *Hymenaea* spp., only *Hymenaea courbaril* and *Hymenaea martiana* yield fruits (Lee and Langenheim 1975) that are about 10–20 cm in length and 4–6 cm in diameter containing a powdery pulp or flour (Jayaprakasham *et al.*, 2007). In a study carried out by Jayaprakasham *et al.*, (2007), it was revealed that the edible portion of the fruit primarily contained about 25% of sucrose and 0.067% of linolenic acid, in addition to the terpenoids. Jayaprakasham *et al.*, (2007) found that the presence of terpenoids contributed towards both specific COX-2 enzyme and lipid peroxidation inhibitory activities. The presence of linolenic acid in the fruit was also found to be a factor for COX enzyme inhibitory activity and was thus concluded that the fruits of *Hymenaea courbaril* had the potential of an anti-inflammatory agent and consumption of this fruit was deemed useful in alleviating some of the symptoms associated with inflammation. The two isoforms of Cyclooxygenase enzymes are Cyclooxygenase-1 (COX-1) and Cyclooxygenase-2 (COX-2). Both COX-2 and COX-2-derived prostaglandins are known to play a pivotal role in regulating inflammation and inflammatory pain (Wang and Dionne 2006).

Ilex paraguariensis is a member of the family Aquifoliaceae and is locally known as “Erva-maté” or “Yerba-maté” (Mendes and Carlini 2007). The plant is native to regions with temperate climate and its natural occurrence

is restricted to Brazil, Paraguay, and Argentina (Anuário Brasileiro da erva-mate 1999). The genus *Ilex* includes over 400 species (Alikaridis, 1987), which belong to the so-called holly plant — popular examples being *Ilex aquifolium* (European or English holly), *Ilex opaca* (American holly), *Ilex cornuta* (Chinese holly) and *Ilex cremata* (Japanese holly) (Baisch *et al.*, 1998). *Ilex paraguariensis* is a small evergreen tree (also considered as a shrub) about 4–7 m in height. The leaves are dark green in color, elliptic to obovate and the size of the leaves may range from 2.5–13 cm in length and 2–6.4 cm in width. The flowers occur in numerous small cymes and are usually 1–2 cm long (Wagner *et al.*, 1999). The green or dried leaves and stemlets of *Ilex paraguariensis* are often used to prepare maté a type of tea or a nutrient beverage, widely consumed in several South American countries, particularly Argentina, Paraguay, Uruguay, and the southern states of Brazil (Bates *et al.*, 2007). Preparation of maté from its aerial parts has made *Ilex paraguariensis* one of the most commercialized plant in South America (Filip *et al.*, 2000). Maté is rich in xanthine, polyphenols and flavonoids, saponins as well as minerals such as potassium and magnesium (Deladino *et al.*, 2007; Gugliucci 1996; Schenkel *et al.*, 1997) and is drunk for its acclaimed diuretic, anti-inflammatory and mild stimulant properties (Schinella *et al.*, 2000). The stimulatory effect of maté has been associated with the presence of methylxanthines, namely caffeine and theobromine (Rates 1999). Research has revealed that maté has a significant content of an important group of non-volatile compounds known as chlorogenic acids (CGA) (Clifford and Ramirez-Martinez 1990). However it is also noteworthy that some of the therapeutic properties of plants like *Ilex paraguariensis* can be attributed to the high content of caffeoyl-derivatives the plant may possess because Caffeic acid and its derivatives have been known to exhibit antioxidant properties in both biological and chemical systems (Kerry and Rice-Evans 1999; Kono *et al.*, 1997; Nardini *et al.*, 1997). Therefore there is a possibility that a nutrient beverage like maté prepared from *Ilex paraguariensis* can act as a benign source, in providing antioxidants to the body through the supply of caffeoyl-derivatives and other polyphenols (Filip *et al.*, 2000). Besides the preparation of mate, *Ilex paraguariensis* is widely used in the South American folk medicine for the treatment of gastrointestinal disorders as an eupeptic, and as choleric drugs (Alonso Paz *et al.*, 1992; Gorzalczy *et al.*, 2001), for treatment of arthritis, liver diseases, headache, rheumatism and obesity (Filip *et al.*, 2000). Dickel *et al.* (2007) has presented preclinical data from seven plants including *Ilex paraguariensis* that indicate a potential role of the plant in controlling certain conditions associated with obesity, such as hyperlipidemia. *Ilex paraguariensis* is considered as an adaptogen because the plant can enhance the physical resistance of the body and its ability to counteract stress (Mendes and Carlini 2007) and as mentioned earlier the plant also has the ability to alleviate mental and physical fatigue due to the presence of xanthines such as caffeine and theobromine (Filip *et al.*, 1998).

Maytenus ilicifolia is a member of the Celastraceae family and native to southern Brazil, Paraguay, Uruguay, and northern Argentina (Bruneton

1995). The Celastraceae family includes about 50 genus and 800 species that are distributed in tropical and subtropical regions (Cronquist 1981) The genus *Maytenus* Molina mostly include woody and shrubby species that are basically used in traditional medicine or investigated for its phytochemical and pharmacological purposes, some very good examples from the genus include *Maytenus aquifolium* Mart. (Corsino *et al.*, 2000), *Maytenus chuchuhuasha* Raymond-Hamet et Colas (Shirota *et al.*, 1994; Shirota *et al.*, 1998), *Maytenus evonymoides* Reiss. (Pullen *et al.*, 2003) *Maytenus hookeri* Loes. (Lu *et al.*, 2002) *Maytenus macrocarpa* (Ruiz et Pav.) Briq. (Chavez *et al.*, 1998), *Maytenus robusta* Reiss. (Niero *et al.*, 2001) and *Maytenus senegalensis* (Lam.) Exell. (Gessler *et al.*, 1994; El Tahir *et al.*, 1999; Hussein *et al.*, 1999a; Hussein *et al.*, 1999b).

Maytenus ilicifolia is a small medicinal evergreen shrub that grows to a height of five meters bearing leaves and berries that resemble holly and is commonly known as “*espinheira santa*” (holy spine), “*cancerosa*”, “*cangorosa*”, “*maiteno*” and “*espinheira divina*” (divine spine) (Cordeiro *et al.*, 2006). The plant is widely used as a traditional medicine in many countries of South America as a remedy for fertility control for e.g. infusion prepared from the leaves of the plant is used by the rural and indigenous populations of Paraguay as a contraceptive and an emmenagogue (Arenas and Azorero 1977). In Argentina, the plant is used as an abortive, an emmenagogue and an anticancer agent (Arenas and Azorero, 1977; Martinez-Crovetto 1987) whilst in Brazil the plant serves both as a contraceptive and an abortifacient (especially in southern Brazil) as well as a remedy against gastric disorders (Carlini 1988; Cruz 1982). In a study conducted by Montanari and Bevilacqua, 2002, for the verification of *Maytenus ilicifolia* as an abortifacient, lyophilized hydroalcoholic extract of its leaves was administered orally at a dose of 1000 mg/kg/day to mice between the first and third day of pregnancy (DOP), between the forth and sixth DOP, or between the seventh and ninth DOP. The study revealed that the extract caused a preimplantation embryonic loss, but had no effect on implantation or organogenesis. On the same token, with respect to male fertility, a study carried out by Montanari *et al.* (1998) on the effects of ethanolic extract of *Maytenus ilicifolia* Mart.ex. Reiss leaves on spermatogenesis in adult male Swiss albino mice revealed that the leaves did not contain substances that could lead to the arrest of spermatogenesis.

Tea known as “*abafado*” is prepared from the fresh or dry leaves of *Maytenus ilicifolia* by pouring boiled water over them (Balbach 1980; Cruz 1982) and the tea leaves are applied to wounds and rashes as well as to treat skin cancer (Taylor 1996). The antiulcer effectiveness of *Maytenus ilicifolia* extracts have been experimentally proven through studies carried out by Ferreira *et al.* (2004) in isolated frog gastric mucosa. Jorge *et al.* (2004) showed that extracts prepared from *Maytenus ilicifolia* had the potential to inhibit nociception and formaldehyde-induced paw oedema in mice and carrageenin-induced

paw oedema in rats. Souza-Formigoni *et al.* (1991) used boiling water extract of equal proportions of *Maytenus aquifolium* and *Maytenus ilicifolia* leaves against ulcer lesions induced by indomethacin and cold-restraint stress in rats and found that both the oral and intraperitoneal administration of the extract had a potent antiulcerogenic effect against both types of ulcers. From a study conducted by Velloso *et al.* (2006), it was apparent that the crude ethanolic extract of *Maytenus ilicifolia* had a powerful antioxidant potential due to the presence of polyphenols and flavonoids that are important for free radical scavenging action. Velloso *et al.* (2006) also concluded that apart from scavenging action, free radicals and reactive oxygen species are involved in a variety of pathological events like diabetes, cancer and aging. The presence of following chemicals have been revealed in the plant viz. maytenin and pristimerine (de Lima *et al.*, 1971; Pereira and Borges 1960), flavonoid glycosides (Leite *et al.*, 2001), an arabinogalactan (Cipriani *et al.*, 2004), catechin and epicatechin (Soares *et al.*, 2004), and triterpenes (Shirota *et al.*, 1994), as well as the new triterpenoids maytefolins A–C (1–3) and uvaol-3-caffeate (4) (Ohsaki *et al.*, 2004) in both leaves and roots of *Maytenus ilicifolia*. The plant is also categorized as an adaptogen and hence can be used as a tonic to counteract asthenia (Mendes and Carlini 2007).

Ptychopetalum olacoides found in the northern and northeastern parts of Brazil belongs to the family Olacaceae (Mendes and Carlini 2007), and has been traditionally used by Amazonian communities as a “nerve tonic” (Elisabetsky and Siqueira 1998). Alcoholic infusions prepared from *Ptychopetalum olacoides* known as “muirapuama” and “marapuama” are widely consumed in the Amazon as a treatment for central nervous system (CNS)-related conditions for e.g. by people recuperating from conditions associated with damage of the CNS (such as stroke) (Siqueira *et al.*, 2004) or to cope high stress (Elisabetsky 1987; Grenand *et al.*, 1987; Siqueira *et al.*, 1998). *Ptychopetalum olacoides* is believed to be endowed with the potential of a “brain tonic” because it can bring about the recovery of cognitive and motor deficits after brain injuries (such as stroke), as well as enhance cognitive functions, such as alertness and memory, in the elderly (Siqueira *et al.*, 2004). Cognitive impairment during normal aging as well as in neurodegenerative diseases such as Alzheimer’s disease is associated with the degeneration of the basal forebrain cholinergic neurons and one possible strategy for the enhancement of brain cholinergic activity is the use of acetylcholinesterase inhibitors (AChEIs) (Siqueira *et al.*, 2003). Novel acetylcholinesterase inhibitors such as donepezil and huperazine, have been made available in the European market (Rogers and Friedhoff 1996; Sugimoto *et al.*, 1992), however there is a need of a natural and potent long-acting AChE inhibitor with fewer side effects in patients with Alzheimer’s disease (Siqueira *et al.*, 2003). From a study carried out by Siqueira *et al.* (2003) it was evident that *Ptychopetalum olacoides* ethanol extract (POEE) had the potential to inhibit in vitro AChE activity significantly in a dose- and time-dependent manner in rat frontal cortex, hippocampus and striatum. This plant is also widely employed because of its aphrodisiac properties and has the ability to counteract impotence (Siqueira *et al.*, 2007). A herbal infusion called

Catuama® prepared from crude ingredient extracts of four Brazilian plants viz. *Paulinia cupana* ("guarana"; Sapindaceae), *Trichilia catigua* ("catuaba"; Meliaceae), *Ptychopetalum olacoides* ("muirapuama"; Olacaceae) and *Zingiber officinale* (ginger; Zingiberaceae) is commercially available in Brazil and is used as a body stimulant, energetic tonic for relief from physical and mental fatigue and as a sexual stimulant (aphrodisiac) (Oliveira *et al.*, 2005). Catuama® is administered orally sometimes on a long term basis and no adverse side effects from the use of this herbal infusion have been reported (Calixto and Cabrini 1997). *Ptychopetalum olacoides* is also considered as an adoptogen and therefore used as a remedy for asthenia and neurasthenia (Mendes and Carlini 2007) and have exhibited antioxidant properties both *in vitro* (Siqueira *et al.*, 2002) and *in vivo* (Siqueira *et al.*, 2007).

Schinus terebinthifolius or the Brazilian pepper tree or "Aroeira" is a member of the Anacardiaceae family (Braga *et al.*, 2007) and is considered as an aggressive weed in America especially in Florida (Medal *et al.*, 1999). This perennial tree with drooping branch tips and spreading crown is native to Brazil, Paraguay and Argentina (Barkley 1957). The leaves are 3 – 12 inches long, alternate and pinnately compound, the fruits are pink to red in color with a round, berry-like appearance (hence known as peppercorn berries) and ripens in midwinter. The bark is initially smooth and gray-brown, but becomes irregularly furrowed with reddish brown splits and grayish ridges with maturity (Anon 4 2006). The parts of the plant that are used for ethnomedical purposes include the leaves and the stem bark. Studies have also shown that ethyl acetate extracts of pink peppercorns (containing triterpenoids) have the ability to inhibit secreted phospholipase A2 (Jain *et al.*, 1995). Phospholipase A2 is known to control a variety of processes including the mobilization of eicosanoids and the metabolism of phospholipids and thus the inhibitors of Phospholipase A2 once identified from natural sources could prove very useful in the control of inflammatory processes that are involved in rheumatoid arthritis, asthma and psoriasis (Waite 1987; Wong and Dennis 1990). According to Lorenzi and Matos (2002) the leaves and the stem bark of the plant is used to treat urinary disorders, bronchitis and other superior respiratory problems, hemorrhages as well as excessive and bloody menstruations. Use of herbal medicine in dentistry, in the treatment of oral plaque, gingivitis, periodontitis and alveolitis (dry socket) is also becoming a major focus of research in Brazil (de Melo Júnior *et al.*, 2002). The initial symptom of alveolitis appears 36 – 72 hours after tooth extraction with signs of inflammation, and the pain is usually beyond the control of analgesics (Jensen 1978). de Melo Júnior *et al.*, (2002) screened the antimicrobial activity of ethanolic extracts prepared from 17 medicinal plants against the microorganisms isolated from alveolitis in rats. *In vitro* antibacterial tests showed that the extracts prepared from *Schinus terebinthifolius* were active against all gram-positive bacteria (*Bacillus corineforme*, *Proteus vulgaris*, *Pseudomonas aeruginosa*, *Citrobacter freundii* and *Escherichia coli*) and one gram-negative bacterium. The extract of *Schinus terebinthifolius* has also

displayed a good wound-healing activity by histological analysis. Studies by Xavier (1995) have shown that the plant has a potential for the treatment of stomatitis (inflammation of the mucous lining of mouth) and also possesses an anti-inflammatory effect allied with antihistamic action (de Melo Júnior *et al.*, 2002). The antioxidant activity of extracts prepared from aerial parts of *Schinus terebinthifolius* has been described in a study conducted by Velázquez *et al.*, (2003), with respect to its superoxide and DPPH radical scavenging activity. The essential oil of *Schinus terebinthifolius* has been found useful in the treatment of respiratory problems, mycosis and candidal infections (topical use), and the therapeutic property has been attributed to the high concentrations of monoterpenes present (Ferreira de Lima 2006). In a study carried out by Ferreira de Lima (2006), chemical analyses of the ethanolic extract of the stem bark of *Schinus terebinthifolius* revealed the presence of phenols, pentacyclic triterpenes and anthraquinones, whilst the hexane extract of the stem bark gave positive results for flavones, flavonoids and xanthenes, free steroids, anthraquinones and pentacyclic triterpenes. The ethanolic extract of the leaves was found to be positive for phenols, flavones, flavonoids, xanthenes and leucoanthocyanidins, flavanones and free steroids. Ferreira de Lima (2006) also found that the stem bark extract of the plant exhibited the highest anti-bacterial activity, particularly against the resistant strains of *Staphylococcus aureus* compared to that of the susceptible strain.

Strychnos pseudoquina belonging to the family Loganiaceae is a native cinchona-like tree that grows in the Brazilian Savannah (Cerrado) (Santos *et al.*, 2006) and is known as “Falsa-quina” in the local language (Mendes and Carlini 2007). There are about 200 plant species belonging to the genus *Strychnos* that are distributed throughout the tropical regions of the world (Philippe *et al.*, 2004; Thongphasuk *et al.*, 2003). The species belonging to this genus are not only known for their medicinal values but also for their powerful poisons some of which may occur as secondary metabolites (Santos *et al.*, 2006). Perhaps the most potent of these poisons is strychnine, one of many indole alkaloids produced by plants of this genus (Philippe *et al.*, 2004; Thongphasuk *et al.*, 2003). Strychnine is used chiefly in poison baits for rodents and birds (Barrueto 2005). *Strychnos pseudoquina* is popularly used in traditional medicine for the treatment of hepatic diseases and as a bitter folk medicine against stomach diseases (Correa 1926) as well as to treat fevers (febrifuge) and malaria (Andrade-Neto *et al.*, 2003). *Strychnos pseudoquina* has been investigated by da Silva *et al.* (2005) for its ability to protect the gastric mucosa against injuries caused by nonsteroidal anti-inflammatory drugs (piroxicam) and a necrotizing agent (HCl/EtOH) in mice. From the study, it was apparent that both the methanol extract and the enriched alkaloidic fraction (EAF) were orally effective against gastric damage induced by cytotoxic agents such as HCl and ethanol and also against ulcerogenic agents like the non-steroidal anti-inflammatory drugs (NSAIDs). For hundreds of years, malaria has been treated with the bark of plants like *Cinchona calisaya* and *Cinchona succirubra* popularly known as “quinas” in Brazil. However, according to Souza (1951) and Wasick (1944), *Cinchona* species, do not occur indigenously in Brazil, *Remijia ferruginea* known as “quina” is used as a substitute of quinine to treat malaria. Hence,

among the other species that has been categorized as “quinas” apart from the Cinchona species include the *Deianira erubescens* (roots and leaves), *Strychnos pseudoquina* (bark) and *Remijia ferruginea* (bark) (Andrade-Neto *et al.*, 2003). Quinine is an alkaloid that was first identified and isolated from the barks of the Peruvian plants *Cinchona calisaya* Wedd. and *Cinchona succirubra* Pav. ex Klotzsch (Rubiaceae) (Bruce-Chwatt 1988). *Strychnos pseudoquina* is also categorized as an adaptogen and thus infusion prepared from the bark is used as a tonic, aphrodisiac, restorative and to counteract nervous debility (Mendes and Carlini 2007).


Conclusion

When Brazil seeps into one’s thoughts, it instantaneously conjures up a picture of a country rich in both bio- and cultural diversity, the indigenous people of the upper Rio Negro region of the Amazon, the Txicao people of Brazil’s Mato Grosso, the Quilombola communities, the Caiçara fishermen, the Tupis and the Guaranis and of course the grand Mardi Gras parade of Brazil the melting pot of many cultures. Migration to Brazil began at the start of the 16th century (Giorgetti *et al.*, 2007) but it was only from the 17th century onwards that the culture, knowledge and traditions of the indigenous Indians mingled with that of the African and European races (De Mello 1980). The Europeans learnt more about the healing properties of the plant drugs and of the deadly hallucinogens like *Mimosa hostilis* and the members of the Malpighiaceae family that contain harmine and its derivatives from the natives that inhabited the deep, virgin, unexplored rain forests of the Amazon. They learnt of the “ayahuasca” a tea containing psychoactive chemicals from the Quechua people, of “balche” (*Lonchocarpus lonistylus*) the mythical plant of the Mayas, of “Açaí” a fruit from the Amazon region rich in polyphenols and at the same time were paralyzed to death when struck by arrow tips smeared with curare prepared from highly toxic plant extracts.

Today, as molecular medicine stands on the cross roads of radical advancement, it is apparent, on one hand, the immense contribution of the Amazonian rainforests towards global medicine, where the plants have served and are still serving as sources of direct therapeutic agents. A good example being the alkaloid D-tubocurarine isolated from the swinging lianas of *Chondrodendron tomentosum*, now popular in surgery as a muscle relaxant (Gurib-Fakim 2006). Whilst on the other, the contributions made by the empirical knowledge of the indigenous people of the Amazon and the healing rituals of the shamans involving plants of medicinal value as a part and parcel of global ethnopharmacology. Through centuries the Amazonian rainforests have not only lured the tribal shamans in search of magical plants but have also enticed the modern chemists in their quest for novel plants harboring compounds of pharmacological value. The area of research in medicinal plants is immense, it embraces: (a) sophisticated spectroscopic techniques such as Nuclear Magnetic Resonance (NMR) juxtaposed with

sound isolation methods using chromatographic techniques like Thin Layer Chromatography (TLC) and High Performance Liquid Chromatography (HPLC); (b) highly reliable bioassays for evaluating the activity of extracts both *in vitro* and *in vivo* using laboratory animal; models where not only economy but ethics is of prime importance (Gurib-Fakim 2006). (c) gene manipulation/ transformation and molecular biology techniques for the isolation and characterization of the many genes that may encode for the different proteins, transcription factors and enzymes crucial in imparting the healing potential of the plant; and (d) subsequently, the critical data obtained from all three above would finally reflect on the plant's potential as a source of new drugs and lay the platform for future clinical trials. Although new and sophisticated research centers are steadily emerging in Brazil through the years, the growth is comparatively sluggish when 55 000 plants species that are scattered throughout the country and the existing reports of a mere 0.4 % of its flora (Gurib-Fakim 2006) is taken into consideration.

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