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Review

Trichilia catigua: therapeutic and cosmetic values

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ABSTRACT

Medicinal plants play an important role in human health care. It is estimated that about 25–30% of all drugs are evaluated as therapeutic agents derived from natural products. Research in the pharmaceutical industry has demonstrated that for complex diseases, natural products still represent a valuable source for the production of new chemical compounds, since they possess privileged structures. Among Brazilian biodiversity, "catuaba" is popularly used as a tonic to treat fatigue, stress, impotence, memory deficits, and digestive disorders. Studies show antibacterial, trypanocidal, antioxidant, antiarrhythmic, antidepressant, improvement of memory, anti-inflammatory and antinociceptive activities, as well as phytocosmetic activity in cellulite treatment and in anti-ageing. The Brazilian plants known and used as catuaba are represented by more than twenty different species; however, the plant most commonly found in Brazil as "catuaba" is the species *Trichilia catigua* A. Juss., Meliaceae. Thus, the aim of this paper is to present a review of *T. catigua*, with emphasis on biological activities, chemical and analytical development and formulations in order to provide a broader and deeper insight, seeking a herbal medicine and/or phytocosmetic as well as future prospects for commercial exploitation and directions for future studies.

Introduction

Brazilian biodiversity consists of a large arsenal of natural resources, with huge potential for the production of new drugs and herbal medicines. Among the representatives of the flora there is "catuaba", which is widely distributed in Brazilian territory and popularly used as an aphrodisiac, sexual and nervous system stimulant, and as a tonic in the treatment of fatigue, stress, memory deficits (Pizzolatti et al., 2002b; Beltrame et al., 2004; Silva, 2004a) and digestive disorders (Ming and Correa-Junior, 2002).

The plants popularly known as catuaba belong to different genera and families, respectively: *Anemopaegma* (Bignoniaceae), *Erythroxylum* (Erythroxylaceae), *Phyllanthus* (Phyllanthaceae), *Micropholis* (Sapotaceae), *Secondatia* (Apocynaceae), *Tetragastris* (Burseraceae), *Ilex* (Aquifoliaceae), *Trichilia* (Meliaceae), and species of Myrtaceae (Corrêa, 1931; Ducke, 1966).

The specie *Trichilia catigua* A. Juss., Meliaceae, is the unique know and used in Brazil as "catuaba". The plants distributed in Brazil known as "catuabas", but not the true catuaba are: *Eriotheca candolleana* (K. Schum.) A. Robyns, Malvaceae, *Anemopaegma arvense* (Vell.) Stellfeld ex J.F. Souza, Bignoniaceae, *Temnadenia violacea* (Vell.) Miers, Apocynaceae, *Tetragastris catuaba* Soares da Cunha, Burseraceae, *Secondatia floribunda* A. DC., Apocynaceae, *Pouteria* sect. *Micropholis* (Griseb.) Baehni, Sapotaceae, and *Phyllanthus nobilis* (L. f.) Müll. Arg., Phyllanthaceae, as well as two species of the family Erythroxylaceae, *Erythroxylum catuaba* da Silva ex Hamet and *E. vacciniifolium* Mart. (Pereira, 1982; Patrício and Cervi, 2005; Lorenzi, 2008).

Due to the large number of species popularly used for therapeutic purposes and known as "catuaba", the definition of what a species is that truly meets therapeutic purposes is difficult.

The confusion has a long history, and the first report is from 1906. A.J. da Silva studied the barks of catuaba from Bahia, identified botanically as *Erythroxylum catuaba* A.J. da Silva, of the Erythroxylaceae family. However, some years later, through botanical reviews, it was confirmed that this species does not exist and the plant under study had characteristics of the Meliaceae family. In the first edition of the Brazilian Pharmacopoeia (Farmacopeia-Brasileira, 1926) characteristics of the roots of *Anemopaegma arvense* (Vell.) Stellfeld ex J.F. Souza, belonging to the Bignoniaceae family, and marketed as catuaba in southern Brazil, were included, thus *A. arvense* has established itself as the official species. However,

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the difficulty in obtaining the roots of *A. arvense* and the search for cheaper alternatives with greater potential for therapeutic effectiveness led to the emergence of several samples commercialized as catuaba (Marques, 1998).

Currently the vegetable raw material sold as "catuaba" mostly corresponds to stem bark of *T. catigua* (Marques, 1998; Daolio et al., 2008), whose identification and pharmacognostic characterization were performed and published by Marques in 1998. However, after more than 14 years of explanation, lots of catuaba (bark) have the botanical name *A. arvense*, a species registered in the Brazilian Pharmacopoeia (1929), which was recently repealed by publishing its fifth edition (Farmacopeia Brasileira, 2010), whose description matches the whitish roots and not the bark. In this case, is clear the influence of the drug included in the pharmacopoeia, in the case of a distortion that needs to be tackled gradually and modified. In fact, the correct identification of the species and the existence of studies proving its effectiveness should be worth more than the mere inclusion in the official compendium, especially in the case of the first edition published in 1926 (Marques, 1998).

Therefore, the objective of this study was to conduct a review pointing out the therapeutic value of *T. catigua* species, popularly known as catuaba, emphasizing their biological and chemical properties that justify their current use as the most favourable species in relation to the challenges involved in the production technology of a herbal medicine.

Some species used as catuaba in Brazil

Anemopaegma arvense (Vell.) Stellfeld ex J.F. Souza

This species belongs to the Bignoniaceae family. It was described and published initially as *Bignonia arvensis* by José Mariano da Conceição Vellozo in Florae Fluminensis in 1829; it is a perennial shrub, deciduous, upright, slightly branched and xylopodium light-coloured, with pubescent stems, 30–40 cm high, native to the grasslands of central Brazil. The leaves are trifoliate, with hard leathery leaflets, with lighter colour on the underside, 10–20 cm long. Large flowers, campanulate, white or yellow, solitary, arranged in the stem apex of the armpits. The fruits are dehiscent capsules, flat, grey in colour, with a few whitish membranous seeds (Lorenzi and Matos, 2002).

The species is used for medicinal purposes in all savannah areas and is particularly popular for its "aphrodisiac action". A powerful tonic is prepared from the roots that stimulate the nervous system. It is also used in treating insomnia, neurasthenia, nervousness, hypochondria and poor memory and in recovery from serious illness. The bark of the stem and of the xylopodium is employed in cases of asthenia, anxiety, chronic bronchitis and bronchial asthma in the form of tea. The roots are used in aphrodisiac preparations, in the treatment of sexual impotence (Lorenzi and Matos, 2002).

Tabanca et al. (2007) isolated from this species catuabin A, cinchonain Ia and IIa, and kandelin A1, which shows antioxidant activity. The authors also evaluated the anti-inflammatory, anti-malarial and antimicrobial activity, in addition to that of cytotoxicity, but none showed significant activity or cytotoxicity to mammalian non-cancerous cells (Vero and LLC-PK_{11}) and human tumour cells of the liver, malignant melanoma, ovarian carcinoma, breast carcinoma, squamous cell carcinoma and promyelocytic leukaemia (HepG2, SK-MEL, SK-OV3, BT-549, KB at 13.51–22.12 μM and HL-60 at 16.89–27.65 μM, respectively).

The unregulated use of *A. arvense* for long periods caused the disappearance of this plant from markets, and other plants, known locally as catuaba, were sold instead (Daolio et al., 2008).

Erythroxylum vacciniifolium Mart.

Shrub or small tree 3–5 m tall. Belongs to Erythroxylaceae family, described and published by Karl Friedrich Philipp von Martius in Beit. *Erythroxylon* 1840. Its crown is thin and the foliage is semi-deciduous. Leaves simple, membranous, 5–7 cm long. Flowers yellow-orange colour, gathered in terminal and axillary inflorescences. Fruits of drupe type, oval form and dark yellow colour. It is native to the North-east and *Planalto Central*, extending to the Pará and Maranhão, Brazil (Lorenzi and Matos, 2002).

Popularly used as a stimulant, a practice introduced by the Tupi Indians. The barks are used as tea or decoction, with stimulating properties of the central nervous system (CNS) and proven by ethnopharmacological surveys. Thus, the decoction of its bark is used against sexual impotence, as well as for other types of nervous problems, such as agitation, neurasthenia, nervousness, poor memory, insomnia, hypochondria and sexual weakness. Its use is continuous, even though its efficacy and safety of use have not been scientifically proven (Lorenzi and Matos, 2002).

The main constituents found in their extracts include substances of classes of alkaloids, tannins, bitter substances, aromatic oils, resin, grease, phytosterols and ciclolignanas (Lorenzi and Matos, 2002). Zanolari et al. (2003a,b) isolated eight tropane alkaloids from the bark of *E. vacciniifolium*: catuabine D, E, F and G, 7β-hydroxycatuabine D, E and F, and 7β-acetylcatuabine E. The same group, but in another article, investigated the alkaloid content in extract using combination of HPLC with DAD, mass spectrometry and nuclear magnetic resonance (Zanolari et al., 2003b). The interpretation of data obtained spectroscopic online of these extracts led to structural elucidation of six new alkaloids and the partial identification of eighteen others that were potentially original, giving the direction of the same tropane skeleton esterified in positions 3 and 6 by 1-methyl-1-*H*-pyrrol-2-carboxylic acid and/or 4-hydroxy-3,5-dimethoxybenzoic acid (Zanolari et al., 2003b). In 2005, the group obtained nine new tropane alkaloids, elucidated as tropanediol or tropanetriol alkaloid esterified by 1-methyl-1*H*-pyrrole-2 carboxylic acid. One isolate compound was identified as a tropane alkaloid *N*-oxide (Zanolari et al., 2005).

Erythroxylum catuaba da Silva ex Hamet

The stimulant property of the CNS and aphrodisiac was also attributed to *E. catuaba*, missing description of the properties and type of specimen. The botanically correct identity may be *Erythroxylum vacciniifolium* Mart., Erythroxylaceae, *Anemopaegma mirandum* (Cham.) Mart. ex DC., Bignoniaceae, *T. catigua* A. Juss., Meliaceae, or others (Adams et al., 2007). The dubious or even erroneous nomenclature is probably due to the papers of Silva (Silva, 2004a,b, 2005).

A detailed description of the Erythroxylaceae family including history, habitat, synonymy, pharmaceutical forms, applications, clinical observations and chemical composition is well described and reviewed by Silva (2004a,b, 2005).

Meliaceae family

The Meliaceae family has pantropical distribution, including 52 genera and 699 species accepted (List, 2010) and distributed predominantly in the tropics worldwide (Joly, 2002; Souza and Lorenzi, 2005).

They are shrubs or trees, sometimes large, with alternate compound leaves (pinnate or bipinnate), in general large, apical growth, without stipules, rarely with translucent scores (some *Trichilia*),

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sometimes with pulvinus at the base. Small flowers on paniculate terminal inflorescences or in the upper axils, bisexual or unisexual (monoecious, dioecious or polygamous plants), cyclic, diclamideas, radial symmetry. Sepals and petals free. Stamens double the number of the petals, in general, with fillets welded, with fixed anthers on the inside top portion, nectary usually present, gynoecium gamocarpelar. Superior ovary with 4–5 carpels and many other locules, each with 1 or 2 ovule. Dried fruit, in general, loculicidal capsule or baciforme. Seeds often with aryl or winged (Joly, 2002; Souza and Lorenzi, 2005).

Among examples of genus distributed in Brazil stand out *Cedrela*, a popular cedar, *Carapa*, *Trichilia* and *Guarea*, which are also common trees of the rain forest, generally known as "canjeranas", a good quality wood (Joly, 2002).

Plants belonging to the Meliaceae family have long been used in folk medicine. Antiviral, anthelmintic, anti-inflammatory, antiparasitic, immunomodulatory, anti-ulcer, antirheumatic, healing and antioxidant activities, among others, have been reported (Mackinnon et al., 1997; Bray et al., 1990; Nunes et al., 2003; Omar et al., 2003; Lagos, 2006; Matos, 2006; Paiva et al., 2006; Shi et al., 2006; Resende, 2007; Valmorbida, 2007; Akhtar et al., 2008; Gouvêa et al., 2008; Nebo, 2008; Lima et al., 2009; Nayak et al., 2010). The anti-inflammatory and antirheumatic properties of some members of this family, such as *Azadirachta indica* A. Juss., *Melia azedarach* L. and *Cedrela tubiflora* Bertoni, have been explained by their action on the immune response (Benencia et al., 2000).

Genus *Trichilia*

The *Trichilia* genus was described by Browne in 1756, and comprises 71 species distributed in Tropical America, Africa and the Indo-Malaysian region, of which 47 species occur in Brazil (List, 2010; Pennington et al., 1981; Sakuragui et al., 2012). Belonging to the Meliaceae family, it has the largest number of species in the family and also the most anatomical characteristics of the Meliaceae family. The main secondary metabolites isolated are limonoids. On the site The Plant List it can be seen that there are 485 names of species of the genus *Trichilia*; however, among these there are 92 species unresolved, 286 synonyms and 107 species accepted. In the Missouri Botanical Garden (www.tropicos.org; MBG) the classification found is 192 genus for the Meliaceae family and for the *Trichilia* genus there are eighteen legitimate species, sixteen illegitimate species, twelve valid species and 328 species accepted. The data presented in The Plant List are based on the WCSP (World Checklist of Selected Plant Families) and differ from the MBG, which features 374 species in total compared to 485 on The Plant List (www.theplantlist.org).

Many species of the *Trichilia* genus are noted for possessing biological activity, mainly insecticide. These and other activities are summarized in Box 1.

Several species of *Trichilia* have been used in folk medicine in the treatment of diseases such as liver disorders, purgative, antiepileptic, antipyretic, antimalarial, physical and mental tonic, aphrodisiac and sexual stimulants (Ducke, 1966; Ming and Correa-Junior, 2002; Pizzolatti et al., 2002b; Beltrame et al., 2004; Silva, 2004a).

About the phytochemical the *Trichilia* gender, many secondary metabolites derived primarily from the biosynthetic route of terpenes were isolated. Several terpenoid classes have been described, among which stand out sesquiterpenes, triterpenes and tetranortriterpenes, which may be related to insecticidal activity (Beltrame, 2005; Matos, 2006; Akhtar et al., 2008; Souza, 2008; Matos et al., 2009; Rodrigues, 2009; Figueiredo, 2010). Also reported was the presence of steroids, coumarins, pregnans, lignans, lactones, flavonoids, limonoids, tannins, fatty acids, vitamin E, amino acids and ω-phenyl alkanoic acids and alkenoics (Burkill, 1997; Ramírez et al., 2000; Hantos et al., 2001; Rodriguez, 2003; Zhang et al., 2003; Krief et al., 2004; Beltrame, 2005; Beltrame et al., 2006; Krief et al., 2006; Lagos, 2006; Matos, 2006; Resende, 2007; Tang et al., 2007; Nebo, 2008; Souza, 2008; Tissot, 2008; Matos et al., 2009; Rodrigues, 2009; Rodrigues et al., 2009; Cala, 2010; Fang et al., 2010; Figueiredo, 2010; Martinelli, 2010; Resende et al., 2011; Viana et al., 2011). Some isolated and identified substances of species of the genus are presented in Box 2.

Komane et al. (2011) carried out a detailed review of *T. emetica*, covering aspects of traditional use, biological activities and phytochemicals. They showed that some of the traditional use data were evaluated and proven and the chemical basis found was responsible for these activities.

A review of the phytochemical of Meliaceae can be seen in Paritala et al. (2015).

Trichilia catigua A. Juss.

The *T. catigua* species (Fig. 1) is found in semi-deciduous and in part of the Atlantic Forests, and is widely distributed in South and Central America (Klein, 1984). However, according to Brazil's Flora database, the species is endemic to Brazil (Stefano et al., 2011). It is also known as catiguá, catiguá vermelho, catuama, pau-ervilha, and catuaba-do-norte (Garcez et al., 1997). It is a tree up to 10 m high, and the young twigs become glabrous with age and have grey colouration. The leaves are compound with 5–7 leaflets, and they are short pedicellate, oblong-elliptic, acuminate leaf apex, acute at the base, up to 7 cm in length. The flowers may be whitish-yellow and the fruit consists of a narrow oblong capsule, and is reddish, with long, stiff, yellowish hairs approximately 2 cm in length, and only one seed, appearing from December to January. The flower season is from September to October; however, the capsules may remain on the tree for 5 to 6 months before flowering (Souza et al., 2001; Lagos et al., 2007).

The macroscopy of the bark of *T. catigua* (Fig. 2) shows a greyish outer surface, ranging from light to dark tones, with a coarse granular appearance, small circular lenticels, and short and surface longitudinal cracks. The internal surface is reddish with finely striated fibres. The fracture is externally granulosa and internally fibrous. The odour is not characteristic and the taste is strong and bitter (Marques, 1998; Oliveira et al., 2011).

Marques (1998) also described the microscopic characteristics of this plant and verified the presence of thick suber, with about 30–40 cell layers, followed by 2–3 layers of stone cells forming a discontinuous strip. The cortical and phloem regions are extensive with numerous bundles of elongated sclerenchyma fibres transversely distributed. In the phloem region, the beams are interspersed with medullary rays 1–2 cells wide. The bark has cell rows with isolated crystals and a reddish-brown secretion in the intercellular spaces and secretory cells that are usually isolated, and oval to oblong (Tabanca et al., 2007). Fibres with crystal sheaths, prismatic crystals of calcium oxalate and simple or compound starch grains 2–8 μm in diameter can also be observed (Marques, 1998; Tabanca et al., 2007). Oliveira et al. (2011) developed a comparative study of *T. catigua* species collected in two different regions in Brazil, Bahia and Paraná, and also observed the same microscopic characteristics described above.

Lagos et al. (2007) investigated the anatomical characteristics of the leaf and stem bark of *T. catigua*, for pharmacognostic application purposes. Desiccated plant samples were portrayed, free-hand sectioned and stained. On the limbs of leaflets, the epidermal cells of both sides show polygonal to undulating outline in the front

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Box 1: Biological activities observed in some *Trichilia* genus.

Species	Biological activities	References
T. americana (Sesse & Moc.) T.D. Penn.	Antifeedant and toxic activity against the larvae of *Spodoptera litura*.	Wheeler and Isman (2001)
T. casaretti C. DC.	Antimicrobial activity against strains of *Staphylococcus aureus*, cytotoxic activity in *Artemia salina* Leach and evidence of antitumour activity.	Almeida et al. (2009), Figueiredo (2010)
T. catigua A. Juss.	Insecticidal activity against the caterpillar of cartridge-of-corn (*S. frugiperda*), affecting larval development, pupal weights and larval mortality. Trypanocidal activity against epimastigotes and trypomastigotes forms of *Trypanossoma cruzi*. Relaxing effect on rabbit corpus cavernosum. Antidepressant-like effect and improvement of memory in mice. Antinociceptive, anti-inflammatory, antiarrhythmic and antioxidant actions. Antibacterial activity against gram-positive such as *Bacillus cereus* and *Staphylococcus aureus*, and gram-negative such as *Escherichia coli* and *Pseudomonas aeruginosa*. Antiviral activity against poliovirus type 1, bovine herpes virus and poliovirus in HEp-2 cells. Neuroprotective activity.	Albrecht et al. (2006), Antunes et al. (2001), Barbosa et al. (2004), Bogorni and Vendramim (2005), Brighente et al. (2007), Calixto and Cabrini (1997), Campos et al. (2005), Chassot et al. (2011), Espada et al. (2015), Faccin-Galhardi et al. (2008), Lonni et al. (2012a), Matos et al. (2006), Matos et al. (2009), Nebo (2008), Pizzolatti et al. (2002a), Pizzolatti et al. (2002b), Pontieri et al. (2007), Quintão et al. (2008), Resende (2007), Resende et al. (2011), Tang et al. (2007), Truiti et al. (2015), Vaz et al. (1997), Viana et al. (2011)
T. claussenii C. DC.	Toxic activity against larvae and pupae of *S. frugiperda* and anthelmintic activity against gastrointestinal nematodes of sheep.	Cala (2010), Cala et al. (2012), Matos et al. (2006), Nebo et al. (2010)
T. dregeana Sond.	Antibacterial activity against gram-positive and gram-negative bacteria and cyclooxygenase-1 and acetylcholinesterase inhibitory effect. Antimicrobial activity and cytotoxicity.	Eldeen et al. (2005), Naidoo et al. (2013)
T. elegans A. Juss.	Insecticidal activity against larvae and pupae of *S. frugiperda*. Inhibitory effects on various components of the immune system.	Matos et al. (2006), Matos et al. (2009), Nores et al. (1997)
T. emetica Vahl	Inhibitory activities of cyclooxygenase and prostaglandin biosynthesis and antifungal activity against strains of *Candida glabrata*. Schistosomicidal activity against *Schistosoma haematobium*. Trypanocidal activity against *T. brucei rhodesiense* and antiplasmodial activity against *Plasmodium falciparum*. Antitrypanosomal activity against *Trypanosoma brucei brucei* and *Leishmania mexicana mexicana*. *In vivo* and *in vitro* antioxidant activity by inhibiting lipid peroxidation. Hormonal influences on prostate cancer cells. Ethnobotanical study for treatment of malaria. Antidiarrhoeal and antimicrobial activities. Larvicidal activity against *Anopheles arabiensis*. Popularly used to treat gynaecological and obstetric disorders. Hepatoprotective and antibacterial effects. Antioxidant properties and intestinal absorption of phenolic acids. Antifungal activity. DNA-damaging activity.	Atindehou et al. (2004), Bero et al. (2009), Bobach et al. (2014), Diarra et al. (2015), Germanò et al. (2006), Germanò et al. (2005), Geyid et al. (2005), Gunatilaka et al. (1998), Hoet et al. (2004), Kolaczkowski et al. (2009), Konaté et al. (2015), List (2010), Mavundza et al. (2013), Mcgaw et al. (1997), Shai et al. (2008), Sparg et al. (2000), Wet and Ngubane (2014)
T. glabra L.	*In vitro* anticomplementary and immunomodulatory activities. Anti-inflammatory activity.	Benencia and Coulombie (1998), Benencia et al. (2000)
T. lepidota Mart.	Cytotoxic activity against the MOLT-4 and U937 leukemic cell lines.	Terra et al. (2013)
T. monadelpha P. Browne.	Child health care. COX-1 inhibitory effect. Antiplasmodial activity against *Plasmodium falciparum*	Asase and Kadera (2014), Atindehou et al. (2004), Larsen et al. (2015)
T. pallens C. DC.	Insecticidal activity against caterpillar and larvae of *S. frugiperda*.	Bogorni and Vendramim (2003)
T. pallida Sw.	Insecticidal activity against caterpillar of *S. frugiperda*, acaricidal activity against the ectoparasitic *Rhipicephalus sanguineus* and antifungal activity.	Amaro (2007), Bogorni and Vendramim (2003), Pinto et al. (2010)
T. pleeana (A. Juss.) C. DC.	Antifungal activity.	Ficker et al. (2003)
T. quadrijuga (Miq.) Kunth	Antimicrobial activity against strains of *Staphylococcus aureus* and *S. epidermidis*.	Rodrigues (2009)
T. ramalhoi Rizzini	Trypanocidal activity.	Ambrozin et al. (2004)
T. rubescens Oliv.	Antimalarial activity against intra-erythrocytic forms of *Plasmodium falciparum*.	Krief et al. (2006), Krief et al. (2004)
T. silvatica C. DC.	Antimicrobial activity against strains of *S. aureus*, *Streptococcus salivarius* and *S. mutans* and evidence of antitumour activity.	Almeida et al. (2009), Figueiredo (2010)

Source: Adapted from Sereia (2013).

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Box 2: Isolated and identified compounds from *Trichilia* genus.

Species	Isolated and identified substances	References
T. americana (Sesse & Moc.) T.D. Penn.	Trichiliasterones A and B.	Hantos et al. (2001)
T. catigua A. Juss.	Stigmasterol, β-sitosterol, β-3-*O*-β-D-glucopyranosyl sitosterol, 11β-methoxycedrelone, cinchonains Ia, Ib, Ic, Id, IIa and IIb, apocynin, catechin, ent-catechin, epicatechin, chlorogenic acid, catiguanins A and B, procyanidins B2, B4 and C1, cedrelone, methylangolensate and epimeric mixture of photogedunin.	Beltrame et al. (2006), Lagos (2006), Martinelli (2010), Matos (2006), Matos et al. (2006), Matos et al. (2009), Nebo (2008), Resende (2007), Tang et al. (2007), Viana et al. (2011)
T. casaretti C. DC.	Aromadendrane-4β,10α-diol, 8-*epi*-sclareol, 24-methylenecycloartane-12-oxo-3β,22-diol, 24-methylenecycloartane-3β,22-diol, trichiliol, 24,25-dihydroxycycloart-22-enol, 22-hydroxycycloart-24-enol, lupeol, phytol, β-sitosterol, stigmasterol, stigmata-5,20(22)-dien-3β-ol, itesmol, scopoletin, β-elemen, germacren D, elemol, ledol, espatulenol, caryophyllene oxide, viridiflorol.	Figueiredo (2010), Souza (2008)
T. claussenii C. DC.	Cryptomeridiol, 24-methylene-26-hydroxycycloartan-3-one, α-amyrin, β-amyrin, lupeol, lupenone, β-sitosterol, stigmasterol, campesterol, sitostenone, 24-methylene-3β,4β,22α-trihydroxy-cholesterol3-β-*O*-β-D-glucopyranosyl sitosterol and ω-phenyl alkanoic and alkenoic acids.	Cala (2010), Matos (2006), Nebo (2008)
T. connaroides (Wight & Arn.) Bentv.	Trijugin C, 3β,4α-dihydroxypregnan-16-one; $\Delta^{8,14}$-2-hydroxy-6-deoxyswietenine and trichiliton A. Limonoids: trichagmalin A, B, C, D, E and F; 15-acetyltrichagmalin C, E; 1,2-diacetyltrichagmalin C; 30-acetyltrichagmalin F; 1,30-diacetyltrichagmalin F; trichanolide.	Fang et al. (2010), Zhang et al. (2003), Zhang et al. (2011)
T. elegans A. Juss.	11β-acetoxyobacunone, 1,2-dihydro-1α-acetoxy-11β-acetoxy-14,15-epoxycneorin, stigmasterol, β-sitosterol, sitostenone, campesterol, 3-β-*O*-β-D-glucopyranosyl sitosterol, scoparone, scopoletin, umbelliferone, 6,7-dimethoxycoumarin, 6-methoxy-7-hydroxycoumarin and 7-hydroxycoumarin.	Matos (2006), Matos et al. (2009), Nebo (2008)
T. emetica ssp. suberosa J.J. de Wilde	1-methoxy-pregnan-17(*R*)-1,4-dien-3,16-dione; 1-methoxy-pregnan-17-(*S*)-1,4-dien-3,16-dione; 1-methoxy-androstan-1,4-dien-3,16-dione; 2,3-seco-pregnan-17(*S*)-2,3-dioic acid-16-oxo-dimethyl ester; 2,3-seco-androstan-2,3-dioic acid-16-oxo-dimethyl ester; 3-methoxycarbonyl-2,3-seco-androstan-3-oic acid-16-oxo-2,19-lactone; 2,3,16-trihydroxy-5-pregnan-17(*R*)-20-yl acetate; 2α,3α,16α,20-tetrahydroxy-5α-pregnane; 2β,3β-dihydroxypregnan-16-one; 2β,3α-dihydroxypregnan-16-one. Monosaccharide (arabinose, galactose, galacturonic acid, mannose, glucose, rhamnose, xylose). Caffeic acid, ferulic acid, *p*-coumaric acid, syringic acid, vanillic acid, protocathecuic acid, gallic acid, chlorogenic acid. Limonoids: nymania 1, drageana 4, trichilin A, rohituka 3, Tr-B, *seco*-A protolimonoid.	Diallo et al. (2003), Germanò et al. (2006), Gunatilaka et al. (1998), Malafronte et al. (2013)
T. havanensis Jacq.	3,7-di-*O*-acetyl-14,15-deoxyhavanense, 1,7-di-*O*-acetyl-14,15-deoxyhavanense, azadirone and γ-hydroxybutenolide.	Rodriguez (2003)
T. hirta L.	Trichiliasterones A and B.	Hantos et al. (2001)
T. lepidota Mart.	β-Sitosterol, stigmasterol, scopoletin, lepidotrichilins A and B, 21,23-epoxy-7α-21α-dihydroxyapotirucalla-14,24-dien-3-one, 21,23-epoxy-7α-21β-dihydroxyapotirucalla-14,24-dien-3-one, dysoronea D and deoxyflindissone.	Terra et al. (2013)
T. pallida Sw.	Naphtalene, α-cubebene, α-copaene, β-elemene, caryophyllene, α-humulene, γ-muurolene, viridiflorene, α-selinene, Δ-cadinene, germacrene B, 10-*epi*-γ-eudesmol and 1-epi-cubenol.	Tissot (2008)
T. quadrijuga (Miq.) Kunth	Quadrijugol, kudithyol, spathulenol, bourjotinolone B, nilocitin, piscidinol, dihydronilocitin, 3β,4β-dihydroxypregn-16-one, β-sitosterol, 3-*O*-β-D-glicopyranosyl itesmol, stigmasterol and 2β,3β,4β-trihydroxypregn-16-one.	Rodrigues (2009), Rodrigues et al. (2009)
T. rubescens Oliv.	Trichirubines A and B.	Krief et al. (2006), Krief et al. (2004)
T. silvatica C. DC.	Ethyl palmitate, α-tocopherol, spathulenol, veridiflorol, humulene oxide, (2*S*,3*S*,6*R*,7*R*)-humulene-2,3,6,7-diepoxide, (2*R*,3*R*,6*R*,7*R*)-humulene-2,3,6,7-diepoxide, mustakone, β-sitosterol and a mixture containing triterpenes α-amyrin, β-amyrin, pseudotaraxasterol and lupeol. δ-elemene, isoledene, α-copaene, α-gurjunene, aromadendrene, α-humulene, alloaromadendrene, germacrene D, bicyclogermacrene, germacrene A, δ-cadinene, elemol, germacrene B, δ-cadinol, β-sitosterol, stigmasterol, ambrosanoli-11,10-diol and scopoletin.	Figueiredo (2010), Souza (2008)
T. trifolia L.	1,3,7,11,12-dolabella-3,7,18-trien-17-oic acid, 1,3,6,7,11,12-dolabella-3,7,18-trien-6,17-olide and (1,3,4,7,11,12)-3-hydroxydolabella-7,18-dien-4,17-olide.	Ramírez et al. (2000)
T. welwitschii C. DC.	dregeanin DM4; rohituka 3; trichilia lactone D5; 28,29-dinorcycloart-24-ene-3,4,6-triol; sitosterol-3-*O*-β-D-glucoside; 4-hydroxy-*N*-methyl-l-proline; stigmasterol and sitosterol.	Tsamo et al. (2013)

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Fig. 1. Leaves, flowers, and fruits of *Trichilia catigua*.
Source: Ismar Sebastião Moscheta (1993) and Cláudio Roberto Novello (2009).

Fig. 2. Macroscopic aspects of intact and ground bark of *Trichilia catigua*.
Source: Ana Luiza Sereia (2011).

view. Anomocytic stomata occur exclusively on the abaxial surface. Simple tector trichomes, uni- or multicellular, uniseriate, long and erect, are present. The mesophyll is dorsiventral. The midrib is biconvex and traversed by a collateral vascular bundle, arranged in a circle and surrounded by a complete sclerenchymaticous sheath. Oval secretory cells and calcium oxalate drusen are distributed in the leaves. In the stem bark, the periderm consists of suber, phellogen and phelloderm, the multiseriate cortex containing drusen, and phloem. This comprises sieve elements, stone cells, obliterated fibres and cells, amid numerous parenchyma cells. The fibres are grouped together in small groups and contain several prisms of calcium oxalate. The authors concluded that these structural data of *T. catigua* are compatible with the Meliaceae family and contribute to the knowledge of this species, which has been investigated very little from the morphological point of view.

The seedlings and tirodendros of *T. catigua*, *T. elegans* and *T. pallida* have already been studied morphologically and anatomically by Mourão et al. (2002), with the aim of understanding the life cycle and germination and growth processes of species.

Beltrame (2005) carried out a microscopic analysis, evaluating the anatomical characteristics of commercial samples acquired as catuaba. He used barks and powder of *T. catigua* and rhizomes of *A. arable* as standard plant material. Of the seven samples analyzed, six were consistent with the anatomical characteristics of standard *T. catigua*, and one sample analyzed did not conform with either and still had impurities (presence of sand).

T. catigua timber is red, compact, solid, flexible, very weather resistant, suitable for external works, joinery, bodywork, clamps and carpentry and makes excellent firewood. The bark is thin, smooth, bitter and astringent, suitable for tanning and gives an appreciable yellow colour to the leather. It is possible to obtain a colouration ranging from intense yellow-orange to red and violet (Corrêa, 1984). Lorenzi (2008) describes *T. catigua* timber as lightweight (density 0.43 g/cm^3). It is also used as the core for doors and panels, liners, and toys, among others. The tree is very ornamental, with a narrow crown and delicate foliage, and is used for

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landscaping, especially for afforestation of squares and avenues. As a fast-growing plant, it is useful in the planting of degraded areas for permanent preservation (Lorenzi, 2008).

Castellani et al. (2006) studied the volatile oil production obtained from leaves and branches of *T. catigua* according to the harvest season and found that the highest yields were observed in winter, while the volatile oil content was 0.21% in the leaves and 0.16% in the branches. The samples were collected in the Silviculture Forest, a secondary Atlantic Forest fragment located on the campus of the Federal University of Viçosa, Minas Gerais, Brazil. The chemical composition of the essential oils at different times of year has not been determined and remains open for future studies.

Chemical constituents and biological activities of *Trichilia catigua*

Marques (1998) conducted a phytochemical screening from crude extract of *T. catigua* and observed the presence of steroids, hydrolysable and condensed tannins, and saponins. In this study, the author found a foam index of 250 in the plant drug. Later on, Lagos (2006) determined the preliminary phytochemical profile of the bark and leaves of *T. catigua*. The aqueous extract of the leaves showed positive reaction for anthocyanin glycosides and tannins, both hydrolysable and condensed; for the aqueous extract of the bark of the same chemical groups were identified, as well as of saponins. The results of the phytochemical profile of the alcoholic extract of the bark and leaves were similar, revealing the presence of flavonoids and steroids, demonstrating the similarity of the composition of the two parts of the plant in this extract. Oliveira et al. (2011) carried out a preliminary phytochemical analysis of barks of *T. catigua*, and they established the presence of anthocyanins and anthracenics in addition to the groups already described above, and not observed the presence of alkaloids, mucilages, essential oils, and coumarins.

The extract and semi-purified fractions of *T. catigua* are composed of tannins (Burkill, 1997; Braz et al., 2012), ciclolignans, alkaloids, flavonoids and sesquiterpenes (Beltrame, 2005; Braz et al., 2012). Chemical studies have also indicated the presence of ω-phenyl alkanes, ω-phenyl-alkanoic acids, ω-phenyl-γ-lactones, γ-lactones alkyl, alkenyl γ-lactones and fatty acids of varying chain from C14 to C26, and β-sitosterol, stigmasterol, campesterol (Pizollatti et al., 2004) and a mixture of flavalignans isolated from barks (Pizzolatti et al., 2002b).

Studies have shown that substances contained in the crude extract of barks of *T. catigua*, as well as in fractions, contain condensed tannins, such as catechin, epicatechin, procyanidin (Beltrame, 2005), catiguanine A and B (Tang et al., 2007), and also flavolignans: cinchonains Ia (Pizzolatti et al., 2002b) and Ib (Beltrame et al., 2006), IIa and IIb, and apocynin E (Resende, 2007). It is worth noting that Resende and colleagues isolated the cinchonains IIa and IIb, and apocynin E, the latter for the first time in the *Trichilia* genus (Resende, 2007; Resende et al., 2011).

Some chemical substances of the *T. catigua* species have already been isolated and elucidated. Among them are: epicatechin (**1**), procyanidins B_2 [epicatechin-(4β → 8)-epicatechin] (**2**), B_4 [catechin-(4α → 8)-epicatechin] (**3**) and C_1 [epicatechin-(4β → 8)-epicatechin-(4β → 8)-epicatechin] (**4**), cinchonains IIa (**5**) and IIb (**6**), (Lagos, 2006; Resende, 2007; Resende et al., 2011), cinchonains Ia (**7**), Ib (**8**), Ic (**9**) and Id (**10**) (Pizzolatti et al., 2002b; Beltrame, 2005; Resende, 2007; Tang et al., 2007; Martinelli, 2010; Resende et al., 2011), catiguanine A (**11**) and B (**12**) (Tang et al., 2007), coumarins and triterpenes (Beltrame, 2005), chlorogenic acid (**13**), catechin (**14**), the steroids β-sitosterol and stigmasterol (Lagos, 2006), and apocynin E (**15**) (Resende et al., 2011).

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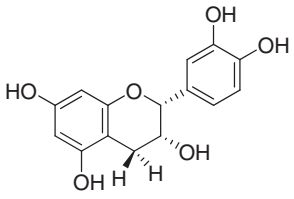

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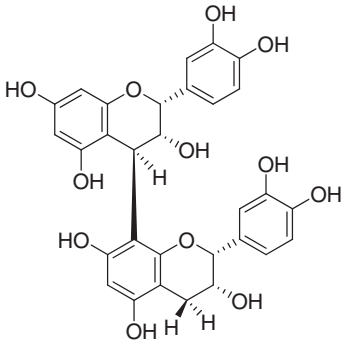

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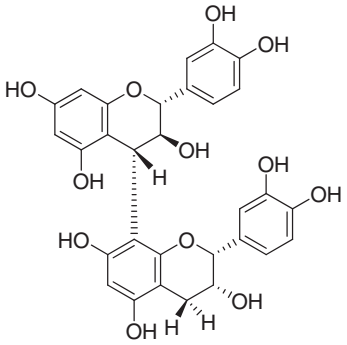

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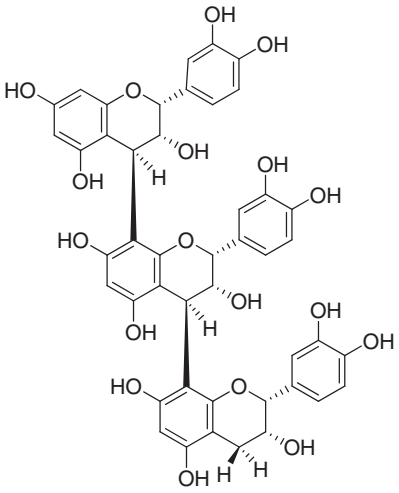

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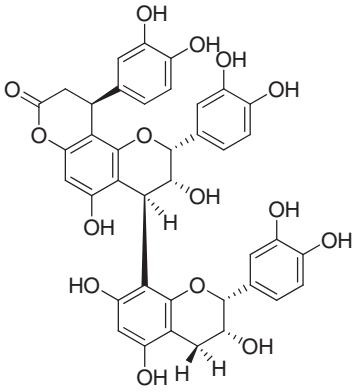

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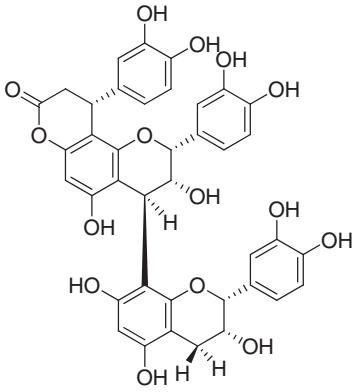

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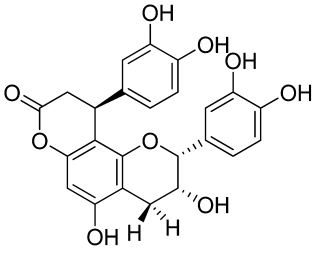

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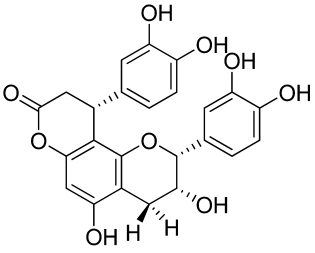

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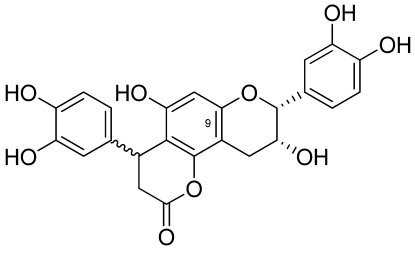
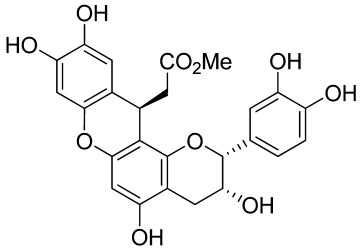


9 → 9*R*
10 → 9*S*



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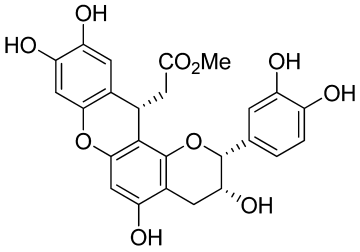

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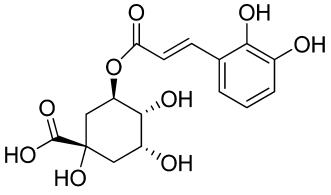

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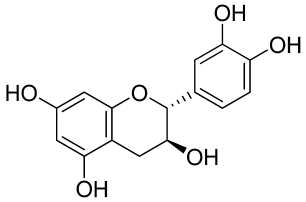

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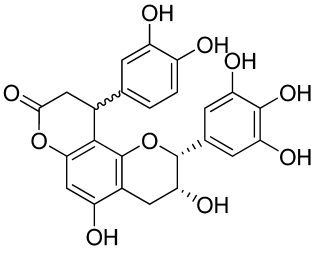

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Matos et al. (2009) isolated the limonoid cedrelone, methylangolensate and epimeric mixture of photogedunin of the methanolic extract of the fruit of *T. catigua*.

The presence of cinchonains, gallic acid derivatives, polyphenols, flavonoids, catechins and epicatechins in extracts from the barks of *T. catigua*, using as extractant a liquid mixture of water-methanol-acetone-ethanol (1:1:1:1), was analyzed by statistical methods, such as principal component analysis, and hierarchical clustering of the chromatographic peaks obtained from HPLC-DAD spectra (Lonni et al., 2012a).

Kamdem et al. (2013) identified the presence of gallic, chlorogenic, caffeic, rosmarinic and ellagic acids, quercetin, isoquercitrin, quercitrin, rutin, kaempferol and catechin, by HPLC fingerprinting of *T. catigua* bark macerated extract with 70% ethanol.

Antimicrobial

The hydroalcoholic extracts and ethyl-acetate fractions obtained from *T. catigua* barks showed significant antimicrobial activity. The ethyl-acetate fraction showed the best inhibitory activity of bacterial growth, by inhibiting the growth of Gram-positive bacteria such as *Bacillus cereus* and *Staphylococcus aureus*, and Gram-negative species such as *Escherichia coli* and *Pseudomonas aeruginosa*. Two flavolignans were isolated from fraction, identified as cinchonains Ia and Ib, which also showed significant antibacterial activity. All the isolated substances were more active against Gram-positive bacteria than against Gram-negative bacteria, showing a bactericidal effect, with minimal inhibitory concentrations, and minimal bactericidal concentrations ranging from 0.31 to 0.62 and 0.31 to 1.25 mg/ml, respectively (Pizzolatti et al., 2002b).

The antiviral activity was shown to be promissory for the discovery of active molecules. Faccin-Galhardi et al. (2008) evaluated the antiviral activity against poliovirus type 1 in HEp-2 cells. The crude extract, aqueous fraction and ethyl-acetate fraction were tested. The samples were non-toxic at the concentrations tested (12.5–100 μg/ml) and showed virucidal activity, reducing the infection in all cases. These results suggested that the extract and fractions derived from *T. catigua* interfered with the initial replication phase of poliovirus.

Later, Bernardi et al. (2010) assessed the effects of crude extract, aqueous fraction and ethyl-acetate fraction obtained from barks of *T. catigua* on the replication of bovine herpesvirus. The tested concentrations varied from 12.5 to 100 μg/ml, with the samples being added 1 and 2 h before, during (zero time – 0 h) and 1 and 2 h after the viral infection. Cytotoxicity was observed in Hep-2 cells at higher concentrations than 400 mg/ml for all samples. At time zero and in the virucidal test of crude extract, inhibition was 100% at all concentrations. Inhibition of the virus was total at concentrations of 50 and 100 mg/ml aqueous fraction and ethyl-acetate, both at time zero. The results suggest that extracts and fractions of *T. catigua* act in the initial phase of replication of bovine herpesvirus and also directly on the viral particles.

The same group evaluated the antiviral activity of *T. catigua* (crude extract, aqueous and ethyl-acetate fractions) in the replication of the herpes simplex virus (HSV-1), bovine herpesvirus (BoHV-1) and poliovirus (PV-1). All samples showed a low toxicity (CC_{50} >400 μg/ml) and low inhibitory concentration (IC_{50}), Thus, it presents a high virucidal effect and the ability to inhibit viral adsorption (Espada et al., 2015).

Trypanocidal

In a study by Pizzolatti et al. (2002a), the trypanocidal activity of some extracts and fractions of thirteen species of Brazilian plants, including *T. catigua*, was evaluated. The extracts were tested *in vitro* against cultures epimastigotes of *T. cruzi*. In the case of *T. catigua*, the extract that showed activity was hydroalcoholic, obtained from barks as well as the fractions hexane, dichloromethane and ethyl acetate, with an LD50 of 10 μg/ml. The dichloromethane fraction still has activity against trypomastigotes present in the blood, with a reduction of 74% in a concentration of 500 μg/ml.

Antioxidant

Evidence suggests that diseases caused by oxidative reactions in biological systems can be delayed by the intake of natural antioxidants found in the diet, particularly phenolic compounds, which include flavonoids and tannins (Dattner, 1999). This motivates the search for new antioxidants. Some studies involving *T. catigua* species are described below.

Bruyne et al. (1999) demonstrated the antioxidant properties of condensed tannins, front of DPPH radical (2,2-diphenyl-1-picryl-hidrazila), superoxide anion and the hydroxyl radical. Cinchonain Ib, obtained from the ethyl-acetate fraction of the barks from *T. catigua*, showed the best antioxidant activity in the DPPH method.

Tang et al. (2007) observed antioxidant activity in methanolic extract of the bark and six compounds isolated from *T. catigua*, catiguanine A and B, and cinchonains Ia, Ib, Ic and Id. The methanolic extract showed 48% inhibition at a concentration of 10 μg/ml in the DPPH test. The isolated substances that showed the highest DPPH radical scavenging activity were cinchonains Ic and Id with IC_{50} (50% inhibitory concentration) values of 2.5 and 2.3 μM, respectively.

Resende (2007) evaluated the antioxidant capacity of acetone crude extract, aqueous fraction and ethyl-acetate fraction of the barks from *T. catigua*. All extracts had high antioxidant capacity, and the ethyl-acetate fraction showed higher capacity than vitamin C and Trolox (with recognized antioxidant substances) against the free radical DPPH and total capacity reduction of Fe^{3+} to Fe^{2+}. The author observed that the higher the total polyphenol and total tannin content present in the extract, the greater its antioxidant capacity. This would explain the higher antioxidant capacity of the ethyl-acetate fraction, since it would be an extract enriched in phenolic compounds, mainly tannins.

Resende (2007) isolated nine substances of ethyl-acetate fraction of barks from *T. catigua*, and evaluated the antioxidant activity of seven of them against the DPPH method. The substances were epicatechin, procyanidin B2, cinchonains Ia, Ib, IIa and IIb, and procyanidin C1, all of which have higher antioxidant capacity than vitamin C and Trolox. The most significant antioxidant activity was procyanidin C1 (IC_{50} 4.08 ± 0.01 μM); for other substances the IC_{50} value ranged from 5 to 10 μM, while Trolox and vitamin C showed IC_{50} of about 30 μM. In addition, the author evaluated the reducing power of the complex Fe^{+3}/ferrocyanide ferrous form for the same substances above. Similarly to the DPPH, procyanidin C1 showed the greatest activity, followed by cinchonains Ib, IIa, IIb and Ia, procyanidin B2, and epicatechin. Resende (2007) also noted that the activity of sequestering phenolic free radical is largely influenced by the number of hydroxyl groups present in the aromatic ring: the greater the number of hydroxyl groups, the higher the radical scavenging activity. Procyanidin C1 has 12 hydroxyls, while in the other compounds the number varies from 4 to 9 hydroxyl groups.

Other groups also evaluated the antioxidant activity through free-radical DPPH. Brighente et al. (2007) investigated eight different extracts and fractions, including alcoholic extract of barks of *T. catigua*, and found that the activity against DPPH radical was significant, with IC_{50} of 2.1 μg/ml, compared to the values obtained for ascorbic acid (IC_{50} 8.4 μg/ml) and gallic acid (IC_{50} 2.6 μg/ml).

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Albrecht et al. (2006) evaluated the antioxidant activity of the acetone crude extract, aqueous phase and ethyl-acetate fraction obtained from the bark of *T. catigua*, showing IC_{50} values of the samples of 5.48, 8.67 and 3.79 μg/ml, respectively. Based on the results, the authors concluded that the ethyl-acetate fraction showed the best hydrogen atom donor capacity, thereby reducing free radical DPPH. The authors evaluated the antioxidant activity by DPPH radical of cinchonains Ia and Ib, with IC_{50} values of 7.87 and 7.64 μg/ml, respectively.

Recently, Chassot et al. (2011) compared the antioxidant capacity of ethyl-acetate fraction, crude extract and reference substances, Trolox, ascorbic acid and vitamin C, with the ethyl-acetate fraction showing the most significant antioxidant power.

With the help of statistical tools, specifically the use of a mixture of planning, like simplex-centroid type, principal component analysis, hierarchical cluster analysis and response surface, Lonni et al. (2012a) worked towards the optimization of extracts of the barks from *T. catigua*, which had the highest yield, high content of total polyphenols and antioxidant activity higher than vitamin C and E.

Anti-cellulite

The association between crude extract of *T. catigua*, *Ptychopetalum olacoides* and *Pfaffia* sp. has been used in topical formulations for the treatment and prevention of gynoid lipodystrophy (cellulite). This raw material is marketed as Slimbuster H® (Chemyunion, Brazil), which consists of a standardized extract with a content of 1.02% (w/w) of total flavonoids, expressed as rutin. The concentration used in semi-solid dosage forms is 5%. The lipolytic effect is due to the standardization of total flavonoids and saponins contained in the extract (Baby et al., 2006; Baby et al., 2007); however, the efficacy for topical use has not been proven so far in the literature.

Photoprotector

Natural products that have phenolic substances in their composition have been considered as potential resources for working synergistically with chemical and physical sunscreens to expand the sun protection factor (SPF) in sunscreens. Thus, Munhoz et al. (2012) analyzed the crude extract of *T. catigua* as to its FPS increase, and its correlation with the total polyphenol content and antioxidant capacity. The results demonstrate that the formulations were stable after the addition of the extracts, the physicochemical characteristics (macroscopic characteristics, centrifugation and pH test), when compared to control. The antioxidant capacity was directly proportional to the total polyphenol content. However, the *in vitro* SPF test showed decay of the FPS increased formulations of *T. catigua* extract.

Aphrodisiac

T. catigua is a plant popularly used as an aphrodisiac in Brazil, and is used to treat sexual impotence, stress, fatigue and memory deficits (Pizzolatti et al., 2002b).

Catuama is a product marketed by Catarinense Laboratory, and is registered by the Brazilian National Health Surveillance Agency as a phytomedicine, in the category of a drug psychoanaleptic or stimulant. Currently, the composition consists of a mixture of extracts of *T. catigua*, *Paullinia cupana* Kunth and *Croton heliotropiifolius* Kunth, and is available as capsules or as an oral solution. But its previous formulation was based on the hydroalcoholic extracts of *P. cupana*, *T. catigua*, *Zingiber officinale* and *Ptychopetalum olacoides* Benth. This tonic has been on the market for over 20 years and is indicated for some disorders, such as mental and physical fatigue, stress and muscular asthenia.

Calixto and Cabrini (1997) demonstrated that the product produced a vasorelaxation response, was concentration-dependent significant in vessels isolated from different animal species (mice, guinea pigs and rabbits) and showed that these effects are largely dependent on the release of nitric oxide and substances derived from nitric oxide. The concentrations from the study ranging from 1 to 3000 μg/ml. They also demonstrated that the vasorelaxant action of the product appears to be due to the action of the active ingredients present mainly in *P. cupana*, *T. catigua*, and to a smaller extent *Z. officinalis*.

Antunes et al. (2001) and Gomes (2007) evaluated the effects of Catuama considering its old formula. Its effect on the relaxation of the corpus cavernosum of rabbits was investigated, as well as the effect of hydroalcoholic extracts isolated from each species present in the product. The product and extract isolates produced a dose-dependent relaxation of short duration in isolated corpus cavernosum. Extracts of *T. catigua* barks produced a prolonged and sustained relaxation. The relaxation of the corpus cavernosum is the key step in penile erection (Antunes et al., 2001).

Neither aqueous nor methanolic extracts of the *T. catigua* reference material nor alkaloid-enriched fractions of commercial samples showed any effect on the rabbit corpus cavernosum in an *in vitro* test (Kletter et al., 2004).

Gomes (2007) evaluated the effects of extracts of *T. catigua* (aqueous infusion) and solution of the product on corporal biometric values, vesicular gland, seminiferous tubules and components of the testicular interstitial space of adult Wistar rats. Aqueous infusion doses of 36 and 72 mg/animal/day were administered, and the solution of the commercial product at 0.7 ml/kg/animal/day, for 56 days. In all treatments there was maintenance of body masses, testicular and vesicular glands, and the GSI (gonadosomatic index) increased significantly in animals treated with the product solution, compared to the group treated with the highest concentration of "catuaba". When considering the testicular parenchyma, there were no significant variations with respect to diameter, length and volume of the seminiferous tubules, as well as the height of the seminiferous epithelium. The extracts and solution administered promoted a significant decrease in the proportion of Leydig cells (responsible for the production of testosterone) and macrophages in all treated animals. The nuclear and cytoplasmic volumes of the Leydig cells underwent significant reductions in the treated groups, along with the total volume occupied by these cells and testicular per gram total weight. These results showed that infusions administered during the experiment had a deleterious effect on the population and the volume of Leydig cells in the testes of treated animals.

Antiarrhythmic

In other studies with Catuama, according to Pontieri et al. (2007) it was observed that this drug was able to reverse ventricular fibrillation, avoiding the reinduction and prolonged intraventricular conduction in isolated heart rabbits, and this may act as an antiarrhythmic effect. This same effect was observed for *T. catigua* extracts. The researchers pointed out that *T. catigua* extract was mainly responsible for this action assigned to the product.

Antidepressant-like effects

The antidepressant-like effect (tonic CNS) commonly assigned to "catuaba" is a very promising activity and constant research target.

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Campos et al. (2004) investigated the antidepressant-like effect of Catuama and suggested pharmacological and neurochemical evidence for antidepressant action. It was demonstrated that chronic and acute oral treatment resulted in a significant reduction in the immobility time in two models of depression in rats, forced swimming and tail suspension, when using a dose of 200 mg/kg administered orally.

In vivo experiments indicated that treatment with alcoholic extract of *T. catigua* barks produced a significant reduction in the immobility time in the classical model of forced swimming in rats and mice, indicating a potential antidepressant-like effect. These studies provide evidence that the antidepressant-like effect is modulated by dopamine. The concentrations that demonstrated the activity were doses of 200–400 mg/kg administered orally 6 h prior to the assay (Campos et al., 2005).

Recently, Chassot et al. (2011) evaluated the possible antidepressant-like effect, as well as anxiolytic, motor and cognitive effects, of the crude extract and ethyl-acetate fraction (EAF) of *T. catigua* barks in doses of 200–400 mg/kg and 100–400 mg/kg, respectively. The authors concluded that a single administration of different doses did not change the behaviour of animals submitted to the elevated plus maze or their motor activity in the open field test. The antidepressant effect was detected with a dose of 400 mg/kg EAF, after acute administration. Both extract and fraction improved memory in mice.

In 2012, continuing the work, the same group assessed whether the subchronic administration of EAF maintained the antidepressant-like effect and this effect was related to neurogenesis. Oral doses of 200–400 mg/kg were administered for 14 days. The results confirm that the dose of 400 mg/kg promoted an EAF antidepressant effect and this effect was accompanied by an increase in cell proliferation in the dentate gyrus of the hippocampus after 24 h treatments were discontinued. However, the proliferative effect did not affect cell survival or neurogenesis (Bonassoli et al., 2012).

Grosso et al. (2015) evaluated *in vitro* anti-MAO-A activity of the herbal teas of *T. catigua*, *Annona muricata* L., *Cereus grandiflorus* (L.) Mill. and *Hyssopus officinalis* L., as well as of their binary mixtures. The most active was *T. catigua* with an IC_{50} value of 7.25 μg/ml, but two effects were presented: a concentration-dependent enzyme inhibition in lower concentrations, while in higher concentrations this effect decreased. This was attributed to the antioxidant/prooxidant effect of catechins.

Anti-inflammatory and analgesic effect

The analgesic effect was first studied in Catuama product and the hydroalcoholic extracts that comprised this preparation. The research was conducted in chemical and thermal models of nociception in male Swiss mice (Vaz et al., 1997). The authors also evaluated the acute (200–5000 mg/kg, orally) and subchronic (500–1000 mg/kg, orally, for 15 consecutive days) toxicity in Swiss mice, male and female, and there was no sign of toxicity. The 200 mg/kg (orally) product produced antinociceptive time-dependent and long-lasting. In general, for all tests (contraction induced by acetic acid, capsaicin- and formalin-induced licking, tail-flick and hot-plate assays) the maximum analgesic effect was achieved after 6 h of oral administration. The hydroalcoholic extracts inhibited the pain induced by acetic acid (*T. catigua* 82 ± 2%; *P. cupana* 66 ± 2%, *P. olacoides* 42 ± 2%, *Z. officinale* 30 ± 4%). In the formalin test hydroalcoholic extracts of *T. catigua*, *P. cupana*, *P. olacoides* and to a lesser extent *Z. officinale* (200 mg/kg, orally, 6 h before) also inhibited both phases of formalin-induced pain. Based on the results, the authors concluded that the antinociceptive action caused by the product seems to involve a synergistic interaction of the active ingredients present in all plants that compose it, and the mechanism seems to be involved, at least in part, with the opioid system.

The mobilization of arachidonic acid (AA) by the enzyme phospholipase A2 (PLA2) and subsequent synthesis of prostaglandins are considered primary events in the inflammatory process. Thus, drugs that inhibit PLA2, thereby blocking the cyclooxygenase enzyme pathways of AA in the cascade, could be effective in the treatment of inflammatory processes. In this regard, new strategies for the treatment of inflammatory processes can be achieved in the research of active substances of plant origin that control the production of lipid mediators by inhibition of PLA2. A wide exploratory investigation of the effects of *T. catigua* demonstrated that PLA2 activity was completely inhibited by the hydroethanolic extract of the bark of this plant at a concentration of 120 μg/ml in radioenzymatic assays *in vitro* with human platelets, suggesting that this plant may produce substances with anti-inflammatory activity (Barbosa et al., 2004).

Quintão et al. (2008) demonstrated that the antinociceptive effect of the product in models of inflammatory and neuropathic pain in rats, orally administered, in both acute and chronic treatment, consistently inhibits the mechanical allodynia (pain by motion) induced by intraplantar injection of complete Freund's adjuvant (CFA). In another series of experiments, the product caused a notable reduction of mechanical allodynia induced by *Escherichia coli*. However, it was not effective in altering the production of the pro-inflammatory mediators IL-1β, TNFα, PGE_2 or LTB_4 after intraplantar administration of saline containing *E. coli* in rat paws. The results show that the product reduces the inflammatory nociceptive response, but not in neuropathic rats, with the mechanism involving interference with the dopaminergic pathways.

Viana et al. (2011) evaluated the effect of hydroalcoholic extract of *T. catigua* peels in a behavioural model of nociception in Swiss male mice and assessed the possible mechanisms involved in this action. The animals were subjected to the hot plate test, abdominal contraction and the von Frey test after oral treatment with the extract in a dose of 200 mg/kg. The extract exhibited an antinociceptive effect in the three models. For the hot plate test, the extract showed antinociceptive effect 3 h after oral administration. The authors attributed the possible action of the extract to the dopaminergic system, which was supported by augmented data regarding hypothermia induced by apomorphine and the prevention of haloperidol-induced catalepsy.

Other activities

Catuama was able to significantly alleviate the symptoms manifested by patients with burning mouth syndrome (Spanemberg et al., 2012).

Another interesting effect is the adaptogenic effect. Galvão et al. (1996), obtained preliminary pharmacological data of *T. catigua* drugs (stem bark of catuaba), *Pfaffia paniculata* (Mart.) Kuntze and *P. iresinoides* (Kunth) Spreng. (roots of Brazilian ginsengs), *Ptychopetalum uncinatum* Anselmino (stem bark of Muira Pauma-of-northeast) and *Vernonia cognata* Less. (rhizome of no-de-cachorro), synonym of *Chrysolaena platensis* (Spreng.) H. Rob. For this experiment, male Swiss mice were intraperitoneally treated acutely with hydroalcoholic extracts (50%) lyophilized in doses of 1–100 mg/kg, and were submitted to pharmacological screening to evaluate motor coordination and pentobarbital-induced sleep time. *T. catigua* had impaired locomotor activity and stereotyped behaviour. In the sleep time test, the extracts did not change parameter significantly and did not affect the coordination of animals. In pharmacological screening, *T. catigua* extract produced a stimulating effect depending on the dose.

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In simultaneous studies, the group assessed the effect of these drugs on motor activity and reversing the amnesic effect induced by scopolamine in a passive avoidance model in male Swiss mice treated intraperitoneally acutely. The motor activity was evaluated in boxes equipped with photoelectric sensors, and the *T. catigua* only drugs test caused a significant increase in the handling of animals in a dose of 10 mg/kg. Passive avoidance was accomplished in a light/dark chamber, subjecting the animals to the task after administration of scopolamine (2 mg/kg) and/or lyophilized extract after 24 h and a retention test was carried out. *T. catigua*, *P. paniculata* and *V. cognata* did not affect these parameters, damaged learning and memory in mice (Dias et al., 1996).

Mendes and Carlini (2007) pointed to *T. catigua* as one of the adaptogenic effects of participants, comprising anti-stress effects, improving memory, and increasing physical and sexual performance, alongside other plants such as: *Heteropterys aphrodisiaca* Machado (Malpighiaceae), *P. cupana* Kunth (Sapindaceae), *P. olacoides* (Olacaceae) and *Turnera diffusa* Willd. (Passifloraceae). The species *Pfaffia glomerata* (Spreng) Pedersen and *P. paniculata* (Amaranthaceae) are objects of pharmacological studies aimed at confirming this possible activity.

The neurodegenerative processes induced by global brain ischaemia in mice were attenuated by treatment with *T. catigua* ethyl-acetate fraction, so the fraction promoted functional recovery and decreased the delayed hippocampal cell loss, thereby conferring neuroprotection (Truiti et al., 2015).

With the results of antioxidant activity against DPPH radical, Tang et al. (2007) showed an important potential of *T. catigua* for the treatment of neurodegenerative diseases. Thus, they examined the neurotropic activity of two compounds isolated from the ethyl-acetate fraction, and catiguanine A and cinchonain Ia. For this, PC12 cells were used; however, neither compound showed any effect for these cells and or for PC12 cells mediated by factor nerve growth at concentrations of 1–100 μmol/l.

Bogorni and Vendramim (2005) sought alternatives for pest management on the leaves of corn and found in aqueous extracts of leaves and twigs of *T. catigua* a potential insecticidal activity against larvae and pupae of *Spodoptera frugiperda*, as well as in other species of *Trichilia*. They found that the extract of leaves of *T. catigua* 1% (w/v) affected insect development.

Matos et al. (2006) also evaluated the biological activity of organic extracts of leaves and branches of three species of *Trichilia* (*T. catigua*, *T. claussenii* and *T. elegans*) on *S. frugiperda*. The leaves and branches were dried and ground separately. The solvents used to obtain the hexane extracts were methanol and methanol/water (1:1). The extracts were incorporated into an artificial diet in a proportion of 100 mg of extract per 100 g of diet and offered to *S. frugiperda* larvae. The hexane extracts of leaves of methanol and hexane branches of *T. claussenii* were the most efficient, presenting a high larval mortality rate (exceeding 60%). All extracts affected insect development, delaying larval development in 2, 1.3 and 3.2 days, respectively, but did not affect the pupal period.

Furthermore, the same group evaluated the biological activity of fruit organic extracts of *T. elegans* and *T. catigua* on *S. frugiperda*. The hexane extracts, methanol and hydromethanolic of *T. catigua* seeds caused moderate larval mortality (approximately 50%). The highest larval mortality rate (100%) was obtained from the hexane and methanol extracts of fruits of *T. elegans* (Matos et al., 2009).

Toxicology

Toxicological studies about *T. catigua* have been few and far between, leaving a wide open field, a gap that our group has been seeking to meet with new toxicity studies whose data have not been published. Some of the results can be seen in Lonni (2012), where the safety of a topical formulation-type multiple emulsion W/O/W containing *T. catigua* extract for cosmetic use was assessed through analysis of toxicity, comedogenicity and histopathology in rabbits (New Zealand). The determination of *ex vivo* permeation of the formulation was carried out by means of photoacoustic spectroscopy technique. After 14 days of treatment, the histological, biochemical and hematologic results showed that the formulations are safe and there is no reaction in the tissue, which demonstrates the absence of toxicity and the formulations showed no comedogenicity. The permeation formulation made by photoacoustic test showed that the extract is present both in the epidermis and in the dermis (Lonni, 2012).

Galvão et al. (1996) administered doses of 1000 mg/kg in mice and the hydroalcoholic extract of *T. catigua* caused death within 4 h after administration.

The study of clinical toxicology was of the commercial preparation Catuama. The authors investigated the chronic administration of 25 ml of Catuama twice daily for 28 days to evaluate any evidence of toxic effects in healthy human volunteers of both sexes. No severe adverse reactions or hematologic and biochemical changes were recorded (Oliveira et al., 2005). Added to this, the product has been marketed in Brazil since 1995.

The behaviour of mice treated with crude extract and ethyl-acetate fraction of *T. catigua* barks appeared normal. There was no evidence of toxic effects at doses up to 5000 mg/kg and 3000 mg/kg of crude extract and ethyl-acetate fraction, respectively. No death was observed in any study group, and it was not possible to establish the LD50 (Chassot et al., 2011).

Santos et al. (2011) investigated whether maternal exposure to crude extract of *T. catigua* could interfere with the reproductive parameters of male offspring. Wistar rats received 400 mg/kg of crude extract from the first day of gestation to postnatal day 21. On the 90th postnatal day, male offspring preference and sexual behaviour, and sperm count in the testis and epididymis, were observed. The results do not show a significant difference when compared to the control. Thus, maternal exposure does not interfere with reproductive parameters of male offspring. The results suggest that the use of crude extract of *T. catigua* during pregnancy and lactation could be an alternative treatment for depression, but more studies are needed. Furthermore, in subsequent studies, the same group demonstrated that the maternal exposure to crude extract of *T. catigua* could interfere in initial phases of pregnancy, for example in implantation, or exert embryotoxicity or embryolethality (Santos et al., 2015).

The effect of maternal exposure to *T. catigua* crude extract on the production of antibodies (IgM, IgG1 and IgG2a) in the offspring of mice was evaluated by Silva et al. (2011). The authors administered 400 mg/kg of crude extract from the first day of pregnancy until 21 days after the birth of the puppies. The results indicate that maternal exposure to crude extract did not influence the production of antibodies in the offspring.

The cytotoxicity induced by hydrogen peroxide, sodium nitroprusside and nitropropionic acid was evaluated for hydroalcoholic extract of *T. catigua* barks. A neuroprotective effect was observed in which the extract showed the ability to prevent oxidative stress attenuation of cell death and the production of reactive oxygen species. Preliminary studies suggest that the protection offered by *T. catigua* may be related to their antioxidant capacity (Kamdem et al., 2012). The same group demonstrated the neuroprotection of hippocampal slices prior to treatment with *T. catigua*. So the data suggest a prevention of diseases as a consequence of oxidative stress (Kamdem et al., 2013).

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Analytical methods and pharmaceutical forms

Pharmacognostic analysis helps in quality control; after all, it characterizes the conditions of the plant drug as it does with the gross raw material for other processes.

Resende (2007) evaluated the quality of the vegetable raw material, *T. catigua*, using determination of moisture, particle size distribution, extractive content and total polyphenol content, just like Sereia et al. (2012), who also analyzed the total ashes and acid insoluble ashes. The results were relatively similar in both works, differing only in average particle diameter and extractive content. Meanwhile, Resende (2007) obtained an average diameter of 0.56 mm and 19.16% extractive content, while Sereia et al. (2012) obtained 0.149 and 25.99%, respectively. Braz et al. (2012) obtained 24.62% extractive content, and the authors also evaluated the moisture content and total ashes. These differences are probably related to variations in methodology (*e.g.* temperature, agitation, pH), equipment, solvents and reagents, and especially in plant material, such as: place of origin, soil composition, growing conditions, water and nutrient availability, intensity and amount of light incidence, seasonal, climate, genetic and circadian variations, age and development stage, content moisture, particle size and period and storage conditions (Mello, 1989; Mello and Petrovick, 2000; Audi et al., 2001; Delaporte et al., 2001; Cardoso, 2002; Silva, 2005; Lagos, 2006; Farias, 2007; Gobbo-Neto and Lopes, 2007; Resende, 2007; Sonaglio et al., 2007; Yunes and Cechinel-Filho, 2012).

Oliveira et al. (2011) performed obtained physico-chemical data of barks of *T. catigua* and suggested minimum specifications for quality control: total ash at maximum 6%, minimum aqueous extractives content of 19%, minimum foam index of 250, content of tannins between 10 and 12%, and saponins between 17 and 21%.

The bark extracts of *T. catigua* are rich in total polyphenols and total tannins. Crude extract acetone:water has about 36% and 27%, respectively. The preparation of a fraction rich in polyphenols and tannins has 81% and 55% of polyphenols and total tannins (Chassot et al., 2011).

The plant quality control is based on the chemical marker, which in general does not match the overall idea of the complexity of chemical composition that is the drug plant (Daolio et al., 2008). An analytical method of quality control is essential in assuring the drug plant quality, intermediate product and final product.

Taking into consideration several plants that have been commercialized, such as catuaba, Daolio et al. (2008) created a new analytical method aimed at determining the plants' identity at the same time as offering quick information on authenticity and/or tampering. The authors observed that the usage of NMR would be a possible way to determine a wide range of metabolites. This technique was associated with HPLC along with multivariate analysis for classification of commercial samples of catuaba. These samples were taken from some pharmacies and companies in São Paulo, Paraná and Mato Grosso do Sul states. The authors showed differences between the commercial samples and the standards (*T. catigua* and *A. arvense* barks and leaves). The differences were detected in the region referring to the chemical shifts of hydrogen, which correspond to carbohydrates and aromatics, as they have sugar and other components. They showed that the analysis of hydrogen NMR may be used in the future as the first step in screening to determine and characterize differences in the molecular composition of plant samples.

For the commercial extract with *T. catigua* and *P. olacoides*, an analytical method using UV spectrophotometry has been developed. The authors have established parameters of linearity, interval, specificity, limit of detection, limit of quantification, recovery, precision and accuracy, using rutin as an equivalent. By analysing the results, the authors came to a validated method for quantifying total flavonoids, equivalent in rutin, of commercial extract containing *T. catigua* and *P. olacoides* (Rolim et al., 2005).

Fourteen catuaba commercial samples, barks from the species *Anemopaegma*, *Erythroxylum* and *Trichilia*, have been examined in terms of identity and purity. Only a minority of the analyzed catuaba samples had crude extract on the label and more than half of the products had been adulterated with different extracts. Most of the samples contained barks from *T. catigua*. Fingerprinting by TLC has confirmed heterogeneity. Alkaloids in several concentrations have been detected in 50% of the samples. TLC and HPLC methods for separation and identification of alkaloids have been created. The structure of the two main alkaloids, catuabin D and its hydroxymethyl derivative, was elucidated (Kletter et al., 2004).

The TLC was used to assist in quality control of drugs and plants. The semi-purified extract of catuaba was evaluated with this approach, using a simple eluent system consisting of chloroform, acetic acid, methanol and water, vanillin perchloric chromogenic agent and the standard substance was cinchonain Ib. By revealing the TLC plate, the standard presented a yellow stain with R_f value of 0.58, and a corresponding spot was identified in the catuaba extract, confirming the presence of cinchonain Ib (Braz et al., 2012).

Beltrame et al. (2006) evaluated the hydroalcoholic extract of *T. catigua* by HPLC. Cinchonain Ib was isolated and used as external standard for the development and validation of the analytical method. As a resource for the isolation of cinchonain Ib the authors used counter-current chromatography.

Lagos (2006) obtained a chromatographic profile by HPLC of phenolic compounds from crude extracts of the bark and leaves of *T. catigua*. The author confirmed the data of retention times and UV spectra of catechin, chlorogenic acid and epicatechin with the standards previously injected. A chromatographic profile was also obtained by gas chromatography (GC) of crude extracts of the bark and leaves of the species, verifying the presence of stigmasterol and β-sitosterol.

The chromatographic profile of the ethyl-acetate fraction was also developed and validated by our research group, quantifying procyanidin B2 and epicatechin. The stability of the working solution was evaluated, and this was stable for three days, after which time the colour changed from light yellow to orange and new peaks appeared in the chromatogram. However, monitoring of antioxidant activity for 49 days of a stability study showed no significant difference. The formation of new compounds has been suggested, which may be quinones, as also suggested by Martinelli (2010). *T. catigua* contains many substances with reactive groups such as hydroxyl and carbonyl of which atoms can make hydrogen bonds break links or other interactions. These results are consistent with the high reactivity of the compounds present in the extract, and their easy and rapid oxidation to give new compounds (Longhini et al., 2013). Castañeda-Ovando et al. (2009) proposed a free radical mechanism for stabilizing the semiquinone formed oxidation of cyanidin (anthocyanidin), and Longhini et al. (2013) suggested that the same mechanism could occur with chinchonains, due to their structural similarity. They also pointed to another plausible explanation that the instability of analytes, including cinchonains Ia and Ib, is due to the presence of the hydroxyl group in position 3 of the C ring. The elimination of the hydroxyl group as water gives rise to a double bond between C2 and C3, leading to conjugation with the oxygen in position 1, resulting in a more stable compound.

Grosso et al. (2015) studied the herbal teas of *T. catigua*, *A. muricata*, *C. grandiflorus* and *H. officinalis* and their binary mixtures by HPLC-DAD. In *T. catigua* four phenolic compounds were identified (catechin, epicatechin, epicatechin-3-O-gallate and 5-caffeoylquinic acid), and the extract has about 85 mg/g of phenolic content.

With regard to technological studies, variations in extraction solvents have been reported.

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To study the effects of different solvents (water, acetone, methanol and ethanol) and their mixtures on yield, the total polyphenol content and antioxidant activity of barks of *T. catigua*, Lonni et al. (2012a) used a statistical design. The authors demonstrated through experimental results and response surface models that the quaternary mixtures containing equal proportions of all solvents provided higher yields, polyphenol content and antioxidant activity followed by the ternary mixtures. This system results in eighteen peaks in the fingerprint of the chromatography, and an incorrect choice of extraction solvent hinders the detection of a maximum number of peaks and produces a poor chromatographic fingerprint (Lonni et al., 2011).

Martinelli (2010) also optimized the preparation of extracts, but varied the alcohol ratio, water mixture at different temperatures, extraction time and drug-solvent ratio, to obtain a higher proportion of cinchonains Ia and Ib. Thus, it was established that the best condition for extraction of cinchonains was drug: solvent proportion 10%, 50% ethanol solution and reflux for one hour at 60 °C. Also, the chromatographic profile was developed and validated by HPLC for quantification of cinchonains Ia and Ib.

Other techniques have been tested as alternatives to HPLC, for example capillary electrophoresis. This method is a more economical technique because it involves smaller spent solvents and is often faster, especially in relation to the number of theoretical plates involved (Baker, 1995). Sereia and Mello (2012) and Sereia (2013) applied capillary zone electrophoresis, a methodology developed for identifying a polyphenol fraction of semipurified barks of *T. catigua*. During development, the wavelength, voltage, concentration and borate buffer pH, type and concentration of cyclodextrins are evaluated. The method using voltage gradient and the chiral selector 2-hydroxypropyl-β-cyclodextrin afforded the electropherogram with a resolution suitable for identifying nine substances, catechin, epicatechin, procyanidins B1 and B2, cinchonains Ia, Ib, IIa and IIb, and chlorogenic acid, in a relatively short time analysis (15 min).

Some research groups have developed semi-solid pharmaceutical forms and analytical methods to quantify the active substance content and/or marker to evaluate the quality.

Among them we should mention the papers of Baby et al. (2006), who developed and validated a method using UV spectrophotometry to quantify total biflavonoids, an O/W emulsion containing standardized extract of *T. catigua* and *P. olacoides*. The method presented is linear for reference chemical rutin, with the concentration ranging from 5 to 15 μg/ml with specificity for total biflavonoids (expressed in rutin) to 361 nm with the absence of interfering complex matrix.

The same group evaluated the accelerated chemical stability of the O/W emulsion developed. Stability was determined based on the total flavonoids, expressed as rutin, containing the same standardized extract of *T. catigua* and *P. olacoides*. The samples were evaluated for 90 days and stored at 5 ± 0.5 °C, 24 ± 2 °C and 40 ± 0.5 °C. According to the results, the O/W emulsion showed acceptable chemical stability during the 90 days of the experiment when stored at 5 ± 0.5 °C and 24 ± 2 °C. In temperature conditions of 40 ± 0.5 °C it was shown accelerate the degradation process of the total flavonoids (Baby et al., 2007).

The same research group also evaluated the quantification of the flavonoids in O/W emulsion with Brazilian plant extracts. Rolim et al. (2006) used the method of derivative spectrophotometry to quantify the total flavonoids. The formulation also contains plant extracts of *T. catigua* and *P. olacoides* as in the formulation of Baby et al. (2006), differentiating the wavelength of the analysis as being 388 nm and had linearity for the concentration of rutin of 10–60 μg/ml.

Compared to pharmaceutical development, Velasco et al. (2008) developed cosmetic emulsions containing 5% of the commercial extract of *T. catigua* and *P. olacoides*. Fourteen test formulations were prepared and evaluated by macroscopic stability, apparent viscosity, pH compatibility with the skin and proper organoleptic characteristics, by means of preliminary tests and accelerated stability. The formulations are grouped into two groups: fluid emulsions and more viscous emulsions. After analysis, eight test formulations were considered suitable for submission to a preliminary stability test. Of these, five test formulations were selected for the accelerated stability test. Assays were conducted on storage conditions, light and temperature extremes. At the end of the study, only two test formulations showed the most stable profiles, both being fluid emulsions consisting of self-emulsifying waxes, and 0.3% (w/w) of a natural polymer, and one of them also added 2% soybean lecithin.

The multiple emulsion W/O/W containing *T. catigua* extract was prepared by the emulsification phase inversion method, with vegetable oil, such as andiroba, buriti and canola. The best formulation was obtained with canola oil and showed non-Newtonian flow and pseudoplastic behaviour. The release profile *in vitro* of these systems demonstrated that emulsions containing 1 to 0.5% of extract of *T. catigua* can release phenolic compounds in a controlled manner over a period of 16 and 23 h, respectively. Accelerated stability tests were carried out after 90 days, and the pH, conductivity, size of droplets, rheological properties and polyphenol contents of these systems were evaluated. High temperatures and humidity accelerated the process of degradation of the total polyphenols, and resulted in phase separation (Lonni, 2012; Lonni et al., 2015; Lonni et al., 2012b).

Challenges

The set of data presented allows us to foresee the development of high-performance cosmetic products, such as products for the treatment of cellulite, products with fatty regulator activity due to the high content of tannins as well as for the treatment of acne-prone skin. Furthermore, the development of formulations that are appropriate qualitatively and quantitatively based on the protection of various cutaneous cellular compartments may delay the onset of signs of senescence, as well as improving the appearance of skin.

In view of the antioxidant capacity of bioactive compounds present in plants, extracts and fractions, particularly in the barks of catuaba, the antioxidant potential of *T. catigua* shown in previous studies (Albrecht et al., 2006; Bruyne et al., 1999) for both the pharmaceutical field and the cosmetic area is emphasized.

The standardized extract or fractions derived from this species, associated or not with other available drugs, may represent a potential alternative for the treatment of degenerative diseases triggered by free radicals (Brighente et al., 2007; Resende, 2007), inflammatory processes (Barbosa et al., 2004) and neurological disorders (Campos et al., 2005; Chassot et al., 2011) where the classical treatment is not effective.

The constituents of *T. catigua* for which the chemical compounds and the pharmacological properties have been well characterized are excellent candidates for further investigation, which may result in clinical and/or cosmetic use. Some of these components with well-defined chemical structures may turn out to be excellent phytomedicines and/or phytocosmetics. However, although they have shown therapeutic potential in animal models, the challenge is to unravel the mechanism of action for the activities reported here and safety for use in humans.

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General conclusion

Through the studies conducted to date with the *T. catigua* species, considering that its commercial availability is greater than the other species also known as "catuaba", and considering their relevance in pharmaceutical and cosmetological areas, it is believed that the investment in new studies related to the pharmacological activity, pharmacokinetics, quality control as well as pre-clinical and clinical trials will take extracts and substances to be used both in therapeutics and cosmetology as improving the quality of life of the users since studies have demonstrating promising results associated with *T. catigua* species.

Authors' contributions

RL, AASGL, ALS (Ph.D. student), LMK (M.Sc.), GCL wrote and revised the article. JCPM was responsible for the project concept and supervision of the study, as well as the writing and review of the manuscript.

Conflicts of interest

The authors declare no conflicts of interest.

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