Technical Data Report

for

CATUABA

Erythroxylum catuaba





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Catuaba

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Family: Erythroxylaceae

Genus: *Erythroxylum*

Species: catuaba

Other Species: *Trichilia catigua, Juniperus brasiliensis, Eriotheca candolleana, Anemopaegma mirandum*

Common Names: Catuaba, cataguá, chuchuhuasha, tatuaba, pau de reposta, caramuru, piratançara, angelim-rosa, catiguá

Part Used: Bark

Erythroxylum catuaba is a vigorous-growing, small tree that produces yellow and orange flowers and small, dark yellow, oval-shaped, inedible fruit. It grows in the northern part of Brazil, the Amazon, Para, Pernambuco, Bahia, Maranhao, and Alagoas. This catuaba tree belongs to the family Erythroxylaceae, whose principal genus, *Erythroxylon*, contains several species that are sources of cocaine. Catuaba, however, contains none of the active cocaine alkaloids.

A large amount of confusion exists regarding the actual species of tree that is harvested in Brazilian forests and sold around the world as catuaba. Experienced Brazilian harvesters will refer to two species: a "big catuaba" and a "small catuaba." The confusion thickens when relating these trees to approved botanical species names. "Small catuaba" is Erythroxylum catuaba (A. J. Silva ex. Raym.-Hamet —the name was accepted in 1936), which grows 2-4 m tall and sports yellow-toorange flowers and—in Brazil—is referred to as catuaba. "Big catuaba," in the mahogany family, is Trichilia catigua (A. Juss.), which grows 6-10 m tall, has cream-colored flowers and-in Brazil-is referred to as catiguá and angelim-rosa. Moreover, three other (unapproved) botanical names for catuaba are used incorrectly in herbal commerce today: Juniperus brasiliensis (which is thought to refer to "small catuaba"), and Anemopaegma mirandum and Eriotheca candolleana, which are completely different species altogether. Anemopaegma is a huge tree in the Bignonia family, growing to 40 m tall and called catuaba-verdadeira in Brazil. This species of tree is now harvested and exported out of Brazil (resulting in the incorporation in herbal products sold in the U.S. today) as just "catuaba." Erythroxylum catuaba and Trichilia catigua are the preferred Brazilian herbal medicine species, with the longest documented history of use as "big and little catuaba." Both types are used interchangeably in Brazilian herbal medicine systems for the same conditions.

Catuaba has a long history of use in herbal medicine as an aphrodisiac. The Tupi Indians in Brazil first discovered the aphrodisiac qualities of the plant; over centuries they have composed many songs praising its wonders and abilities. Indigenous and local peoples have used catuaba for generations. It is the most famous of all Brazilian aphrodisiac plants. In the Brazilian state of Minas there is a saying, "Until a father reaches 60, the son is his; after that, the son is catuaba's!"

In Brazilian herbal medicine today, catuaba is considered a central nervous system stimulant with aphrodisiac properties; a bark decoction is used for sexual impotency, agitation, nervousness, neurasthenia, poor memory or forgetfulness, and sexual weakness. According to Dr. Meira Penna, catuaba "functions as a stimulant of the nervous system, above all when one deals with functional impotence of the male genital organs . . . it is an innocent aphrodisiac, used without any ill effects at all."¹ In Brazil it is regarded as an aphrodisiac with "proven efficacy" and, in addition to treating impotence, it is employed for many types of nervous conditions including insomnia, hypochondria, and pain related to the central nervous system. In European herbal medicine catuaba is considered an aphrodisiac and a brain and nerve stimulant. A bark tea is used for sexual weakness, impotence, nervous debility, and exhaustion. Herbalists and health practitioners in the

United States use catuaba in much the same way: as a tonic for genital function, as a central nervous system stimulant, for sexual impotence, general exhaustion and fatigue, insomnia related to hypertension, agitation, and poor memory. According to Michael van Straten, noted British author and researcher of medicinal plants, catuaba is beneficial to men and women as an aphrodisiac, but "it is in the area of male impotence that the most striking results have been reported" and "there is no evidence of side effects, even after long-term use."²

The constituents found in catuaba include alkaloids, tannins, aromatic oils and fatty resins, phytosterols, cyclolignans, sequiterpenes, flavonoids, and steroids.^{3–6} One Brazilian researcher documented (in 1958) that catuaba contained the alkaloid yohimbine (but it was unclear which species of tree he was studying).³ A mixture of flavalignans, including cinchonains (also found in quinine bark), was isolated from the bark of *Trichilia catigua* and reported to have antibacterial and cytotoxic properties.^{6,7} To date, no toxicity studies have been done on catuaba—but its long history of use in Brazil has reported no toxicity or ill effects. In fact, according to Dr. Meira Penna, the only side-effects are beneficial—erotic dreams and increased sexual desire!

Clinical studies on catuaba also have shown results related to its antibacterial and antiviral properties. A 1992 study indicated that an extract of catuaba (*Erythoxlyum catuaba*) was effective in protecting mice from lethal infections of *Escherichia coli* and *Staphlococcus aureus*, in addition to inhibiting HIV significantly.⁸ The study found that the pathway of catuaba's anti-HIV activity stemmed (at least partially) from the inhibition of HIV absorption into cells, and suggested that catuaba had potential against opportunistic infections in HIV patients.⁸ A U.S. patent was granted (in 2002) to a group of Brazilian researchers for a catuaba bark extract (*Trichilia catigua*). Its patent refers to animal studies it conducted that reported a vasodilating, vasorelaxant, and analgesic effect in rats, rabbits and guinea pigs.⁹ A study published in 1997 reported that catuaba bark had significant analgesic activity *in vivo*.¹⁰

While no clinical research has validated the traditional use of catuaba as an aphrodisiac, it continues to be used widely for its ability to enhance sexual drive and increase libido in both men and women. In the last several years, its popularity has grown in the North American herbal market, with various products now available in health food stores. (The jury's still out as to which species is being sold, however!) Interested consumers should seek a reputable manufacturer and product—with a verified plant source and botanical species for the herbal ingredient being sold.

Documented Properties and Actions: Analgesic, antibacterial, antiviral, aphrodisiac, central nervous system stimulant, tonic, vasodilator, vasorelaxant

Main Phytochemicals: Alkaloids, tannins, aromatic oils, fatty resins, phytosterols, cyclolignans, sequiterpenes, flavonoids, steroids

Traditional Remedy: Generally in Brazil, a standard infusion (bark tea) and an alcohol tincture are employed. Recommended usage is reported to be 1–3 cups of an infusion daily, or 2–3 ml of a standard alcohol tincture twice daily.

Contraindications: None known.

Drug Interactions: None known.

WORLDWIDE ETHNOBOTANICAL USES

Region	Uses
Brazil	Aphrodisiac, central nervous system stimulant, exhaustion, fatigue, forgetfulness, frigidity, genitals, hypochondria, impotence, insomnia, nervousness, neurasthenia, pectoral, poor memory, sexual weakness, sleep, syphilis, tonic
Peru	Skin cancer
U.S.	Aphrodisiac, fatigue, impotency, insomnia, nervous exhaustion, nervous system, poor memory, sleep, tonic, weakness
Elsewhere	Brain, circulation, fatigue, genitals, impotence, low libido, nervous system

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The information contained herein is intended for education, research, and informational purposes only. This information is not intended to be used to diagnose, prescribe or replace proper medical care. The statements contained herein have not been evaluated by the Food and Drug Administration. The plant described herein is not intended to diagnose, treat, cure, mitigate, or prevent any disease.

Ethnomedical Information on Catuaba (Erythroxylum catuaba)

Part / Location	Documented Ethnic Use	Type Extract / Route	Used For	Ref #
Bark Amazonia	Functions as a male hormone stimulant and tonic for male organs; used for impotence; to stimulate the nervous system and enhance male libido. Used for disorders of general weakness and nervous exhaustion.	Infusion Oral	Human Adult	ZZ1016
Bark Amazonia	Said to be excellent for the male reproductive organs, to increase circulation andInfusion Orallibido. Stimulates the nervous system and brain and used for impotence.Infusion Oral			ZZ1015
Bark Brazil	Used as a brain and nerve stimulant and aphrodisiac for women. Used for sexual weakness, male impotence, nervous debility and exhaustion.	Infusion Oral	Human Adult	ZZ1011
Bark Brazil	Used to stimulate the nervous system, as a tonic for the genitals, for functional impotence, as an aphrodisiac and sexual stimulant. Said to increase sexual desire and cause exotic dreams.	Infusion Oral	Human Adult	ZZ1070
Bark Brazil	Used for sexual impotence, to fortify the nervous system, for neurasthenia, hypo- chondria, insomnia, nervous affections, as a stimulant and aphrodisiac.	Various Oral	Human Adult	ZZ1013
Bark Brazil	Used a tonic, as an energy stimulant of the nervous system, as an aphrodisiac for sexual impotence, for agitated sleep, nervousness, neurasthenia, forgetfulness, poor memory and sexual frigidity.	ETOH Ext Oral	Human Adult	ZZ1002
Bark Brazil	Used as a stimulant, pectoral, antisyphilitic and aphrodisiac.	H2O Ext Oral	Human Adult	ZZ1079
Root Brazil	Used as an aphrodisiac.	Hot H2O Ext Oral	Human Male	L02535
Root Brazil	Used as a stimulant.	Alcohol Ext Oral	Human Adult	K20642
Root Brazil	Used as an aphrodisiac.	Alcohol Ext Oral	Human Male	K20642
Not stated Peru	Used for skin cancer.	Not stated External	Human Adult	ZZ1047
Bark USA	Used as a tonic and fortifier of the nervous system, for general fatigue, restless sleep and insomnia from hypertension, for failing memories. Used as a tonic for the male organs, for male impotency and as a male aphrodisiac.	Infusion/Tincture Oral	Human Adult	ZZ1014
Bark USA	Used for male impotency, as a tonic for male organs and the nervous system and for extreme fatigue.	Tincture Oral	Human Adult	ZZ1067

Biological Activities of Catuaba (Erythroxylum catuaba)

Part – Origin	Activity Tested For	Type Extract	Test Model	Dosage	Result	Notes/Organism tested	Ref #
Bark Brazil	Cytotoxic Activity	EtOH (100%) Ext	Cell Culture	Not stated	Active	LEUK-11210.	L11339
Bark Brazil	Analgesic Activity	Hydro-alcoholic Ext	IG Mouse	200.0 mg/kg	Active	vs.acetic acid-induced writhing.	J13503
Bark Brazil	Analgesic Activity	Hydro-alcoholic Ext	IG Mouse	200.0 mg/kg	Active	vs.hot plate method.	J13503
Bark Brazil	Analgesic Activity	Hydro-alcoholic Ext	IG Mouse	200.0 mg/kg	Active	vs.tail flick response to radiant heat.	J13503
Bark Brazil	Analgesic Activity	Hydro-alcoholic Ext	IG Mouse	200.0 mg/kg	Active	vs.capsaicin-induced algesia.	J13503
Bark Brazil	Analgesic Activity	Hydro-alcoholic Ext	IG Mouse	200.0 mg/kg	Weak Activity	vs.formalin-induced algesia.	J13503
Not Stated	Antimicrobial Activity	Not stated	Not stated	Not stated	Active		AZ1003
Not Stated	Antibacterial Activity	Hot H2O Ext Alkaline Ext	Mice Mice	Not stated Not stated	Active Active	Protected from lethal infection of <i>E. coli and S. aureus</i> .	AZ1001
Not Stated	Antiviral Activity	Hot H2O Ext Alkaline Ext	Mice	IC50=21-263 mcg/ml	Active Active Active	Inhibited HIV-induced cytopathic effect. Inhibited expression of HIV antigen in HIV-1HTLV-IIIB or HIV- 2ROD infected human lymphotropic virus type 1 positive MT-4 cells. Inhibited HIV absorption to cells.	AZ1001
Not Stated	Hepatoprotective Activity	Cinchonain Ia Fraction	Cell Culture (mouse hepatocytes)	Not stated	Active	Inhibitory activity on TNF-alpha- induced cell death.	AZ1002

Presence of Compounds in Catuaba (Erythroxylum catuaba)

Compound	Chemical Type	Plant Part	Plant Origin	Quantity	Ref #
Calamenene, 7,14-dihydroxy	Sesquiterpene	Stem	Brazil	00.0008%	L03040
Calamenene, 14-nor: 7-hydroxy-1-oxo	Sesquiterpene	Stem	Brazil	00.002%	L03040
Cinchonain I-A	Flavonoid	Bark	Brazil	00.02919%	L11339
Cinchonain I-B	Flavonoid	Bark	Brazil	00.06649%	L11339
Daucosterol	Steroid	Stem	Brazil	00.002%	L03040
Yohimbine	Alkaloid	Not stated	Brazil	Not stated	AZ1004

Literature Cited – Catuaba (Erythroxylum catuaba)

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K20642	TRADITIONAL AMAZONIAN NERVE TONICS AS ANTIDEPRESSANT AGENTS: CHAUNOCHITON KAPPLERI: A CASE STUDY. ELISABETSKY,E: FIGUEIREDO,W: OLIVERIA,G: J HERBS SPICES MED PLANTS 1 1/2: 125-162 (1992) (DEPT FARMACOL UNIV FED RIO GRANDE DO SUL PORTO ALEGRE 90 0650 BRAZIL)
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L03040	SESQUITERPENES FROM TRICHILIA CATIGUA. GARCEZ,WS: GARCEZ,FR: RAMOS,L: CAMARGO,MJ: DAMASCENO JR,GA: FITOTERAPIA 68 1: 87-88 (1997) (DEPT QUIM CCET UNIV FED MATO GROSS SUL CAMPO GRANDE BRAZIL)
L11339	CYTOTOXIC CONSTITUENTS FROM ERYTHROXYLUM CATUABA ISOLATION AND CYTOTOXIC ACTIVITIES OF CINCHONAIN. SATOH,M: SATOH,Y: FUJIMOTO,Y: NATURAL MED 54 2: 97-100 (2000) (SHOWA PHARM UNIV TOKYO 194-8543 JAPAN)
AZ1001	EFFECTS OF CATUABA EXTRACTS ON MICROBIAL AND HIV INFECTION. MANABE, H: SAKAGAMI, H: ISHIZONE, H: KUSANO, H: FUJIMAKI, M: WADA, C: KOMATSU, N: NAKASHIMA, H: MURAKAMI, T: YAMAMOTO, N: IN VIVO. 6 2: 161-5 (1992) (HORIUCHI ITARO & CO. LTD, TOKYO, JAPAN)
AZ1002	HEPATOPROTECTIVE EFFECT OF APOCYNUM VENETUM AND ITS ACTIVE CONSTITUENTS. XIONG, Q: FAN, W: TEZUKA, Y: ADNYANA, IK: STAMPOULIS, P: HATTORI, M: NAMBA, T: KADOTA, S: PLANTA MED. 66 2: 127-33 (2000) (INSTITUTE OF NATURAL MEDICINE, TOYAMA MEDICAL AND PHARMACEUTICAL UNIVERSITY, JAPAN)
AZ1003	POLYMERS CONTAINING ANTIMICROBIAL AGENTS AND METHODS FOR MAKING AND USING SAME.' SEABROOK, JR, ET AL. MAGELLAN CO, INC. US PATENT #5,906,825 (1999)
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ZZ1047	THE PHYTOCHEMICAL DATABASE. BECKSTROM-STERNBERG, SM: DUKE, JA: ACEDB VERSION 4.3-DATA VERSION JULY 1994. NATIONAL GERMPLASM RESOURCES LABORATORY (NGRL), AGRICULTURAL RESEARCH SERVICE (ARS), US DEPARTMENT OF AGRICULTURE.
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ZZ1070	A POCKETBOOK OF BRAZILIAN HERBS. BERNARDES, ANTONIO. RIO DE JANEIRO: A SHOGUN EDITORA E ARTA LTDA. (1984)
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Clinical Abstracts

In Vivo 1992 Mar-Apr;6(2):161-5

Effects of Catuaba extracts on microbial and HIV infection.

Manabe H, Sakagami H, Ishizone H, Kusano H, Fujimaki M, Wada C, Komatsu N, Nakashima H, Murakami T, Yamamoto N.

Horiuchi Itaro & Co., Ltd., Tokyo, Japan.

Pretreatment of mice with hot water and alkaline extracts of Catuaba casca (Erythroxylum catuaba Arr. Cam.) effectively protected them from lethal infection of Escherichia coli and Staphylococcus aureus. The extracts significantly inhibited both the human immunodeficiency virus (HIV)-induced cytopathic effect and the expression of HIV antigen in HIV-1HTLV-IIIB or HIV-2ROD infected human lymphotropic virus type I (HTLV-1) positive MT-4 cells. The 50% effective concentrations of the active fractions (21-263 micrograms/ml) were 1/4 - 1/43 of their 50% cytotoxic concentrations. Their anti-HIV activity was shown to be induced, at least in part, via the inhibition of HIV adsorption to the cells. The data suggest a medicinal potential of Catuaba extracts against opportunistic infection in HIV patients.

Z Naturforsch [C] 2002 May-Jun;57(5-6):483-8

Two epimeric flavalignans from Trichilia catigua (Meliaceae) with antimicrobial activity.

Pizzolatti MG, Venson AF, Smania A Jr, Smania Ede F, Braz-Filho R.

Departamento de Quimica, Universidade Federal de Santa Catarina, Florianopolis-SC, Brazil. A mixture of flavalignan cinchonains la and lb was isolated from the bark of Trichilia catigua. The structures were established on the basis of spectroscopic data of the natural products and their methylated derivatives including 2D NMR experiments, and compared with data in the literature. These flavalignans exhibited antibacterial activity against Bacillus

Phytother Res 2001 Aug;15(5):416-21

The relaxation of isolated rabbit corpus cavernosum by the herbal medicine Catuama and its constituents.

Antunes E, Gordo WM, de Oliveira JF, Teixeira CE, Hyslop S, De Nucci G.

Department of Pharmacology, Faculty of Medical Sciences, UNICAMP, P.O. Box 6111, 13081-970, Campinas (SP), Brazil. eantunes@bestway.com.br

The effects of the Brazilian herbal medicine Catuama and each of its plant constituents (Paullinia cupana, Trichilia catigua, Zingiber officinalis and Ptychopetalum olacoides) were investigated on rabbit corpus cavernosum (RbCC) using a bioassay cascade. Catuama caused short-lived and dose-dependent relaxations (11% +/- 7%, 26% +/- 5% and 82% +/- 9%, at doses of 1, 3 and 10 mg, respectively). Neither the nitric oxide synthesis inhibitor N(omega)-nitro-L- arginine methyl ester (L-NAME; 10 microM) nor the soluble guanylate cyclase inhibitor ODQ (10 microM) significantly affected the Catuama-induced relaxations. Similarly, the selective ATP-dependent K(+) channel (K(ATP)) blocker glibenclamide (10 microM), the muscarinic receptor antagonist atropine (1 microM) and the voltage-dependent Na(+) channel blocker tetrodotoxin (1 microM) all failed to affect significantly the Catuama-induced relaxations. These results indicate that the relaxations induced by Catuama involve neither nitric oxide release nor K(ATP) channel activation. The extracts of P. cupana, Z. officinalis and P. olacoides caused short-lived and dose-dependent RbCC relaxations, whereas T. catigua evoked long-lasting relaxations which were occasionally preceded by a brief contractile effect. The extract of P. cupana was the most active in relaxing RbCC strips. The relaxations induced by all extracts were not significantly affected by L-NAME (10 microM). The infusion of ODQ (10 microM) had no significant effect on the P. cupana- and Z. officinalis-induced relaxations but reduced by >50% (p < 0.05) those evoked by P. olacoides and T. catigua. Incubations of RbCC with Catuama(10 mg/mL for 0.25 to 5 min) caused increases of cAMP levels (143% increase at 5 min of incubation). Incubations of RbCC with P. cupana extract (1 mg/mL) increased the cAMP levels by 200% whereas higher doses (10 and 100 mg/mL) caused smaller increases in the nucleotide levels (150% and 89%, respectively). The extracts of Z. officinalis and P. olacoides (same doses) caused smaller increases of the cAMP levels compared with the P. cupana extract, whereas T. catigua (1-100 mg) did not increase the levels of this nucleotide above the basal values. Our results show that of the four extracts assayed, P. cupana was the most effective, indicating that it is the main extract responsible for the relaxing effect of Catuama on rabbit cavernosal tissue.

FIELD OF THE INVENTION

The present invention refers to the use of vegetal material selected from Trichilia for the preparation of pharmaceutical compositions.

BACKGROUND OF THE INVENTION

Medicinal plants known as catuaba have recognized pharmaceutical use due to its aphrodisiac activities, as a tonic and in the treatment of physical and mental fatigues. Phytotherapic formulations prepared from such plants extracts are already known from the prior art, in which these specific extracts may used alone or in association with other medicinal plant extracts, such as the Brazilian shrub (Paullinia cupana). Several alternative formulations comprising extracts from other catuaba species have already been disclosed in the art, all of them being related to the tonic activity of this particular group of plants.

SUMMARY OF THE INVENTION

The present invention refers to the use of vegetal material selected from Trichilia for the preparation of pharmaceutical formulations showing vasodilating and analgesic activities. In another aspect the present inventions is directed to pharmaceutical compositions presenting vasodilating, analgesic or sexual stimulating activities comprising a vegetal material selected from Trichilia as the active ingredient. After detailed studies, the inventors found out that one particular plant of the group of catuaba, Trichilia sp., has surprising analgesic and vasodilating activities due to its vasorelaxant effect. It has been found that Trichilia catigua, for example, is able produce vasodilating effects in thoracic aorta and in pulmonary and mesenteric arteries of rodents. Although up to this moment there is no scientific corroboration of the exact mechanism which produces the above effect, evidences lead to the conclusion that the vasorelaxant activity of an Trichilia sp. extract depends upon the presence or absence of endothetium in blood and lymphatic vessels. In this event, the above mentioned effect would be associated to the release of nitric oxide (NO) or a NO-mediated substance in the endothelium. Tests carried out in rats' aortas, for example, showed that the vasorelaxation action of a Trichilia sp. extract was partially reduced when the vascular endothelium had been removed. In an additional experiment, the incubation of aorta, pulmonary and mesenteric arteries of rats, rabbits and guinea-pigs with the selective NO-synthase inhibitor L-NOARG, N-nitro-L-arginine, significantly antagonized the vasorelaxation effect caused by Trichilia extract. In a further assay, the inventors verified that the use of methylene blue which is an inhibitor of soluble guanylate cyclase activated by NO (Gruetter et al., 1981) partially affected the vasorelaxant action of Trichilia sp. in rings extracted from pulmonary arteries. Taken together, the results of the above cited studies show that the vasorelaxation actions of a vegetal material from Trichilia sp. is mediated both by endothelium-dependent and -independent mechanisms. Due to the unexpected vasorelaxant activity of Trichilia sp., the present inventors found out that extracts thereof also show an analgesic effect. Tests carried out in chemical models of pain stimulation in mice, for example, demonstrated a strong analgesic action of Trichilia extracts. Experimental results showed that this vegetal extract significantly inhibits the nociceptive effect induced by the chemical agent--acetic acid 0.6% v/v. The material extracted from Trichilia produced a significant and long lasting analgesic effect in the nociceptive condition in accordance with the previously mentioned model and such analgesic effect may last up to 6 hours. On the other hand, additional tests carried out with Trichilia extracts in association with other plant extractive products demonstrated that when the animals are previously treated (10 minutes before the main administration) with naloxone (a non-selective opioid antagonist), the analgesic action of morphine as well as of a Trichilia containing formulation has been reverted in the acute and inflammatory phases of pain induced by formalin at 2.5% w/v as the chemical agent. As occurs in its vasorelaxation action, the actual mechanism through which Trichilia provides an analgesic effect is not totally explained yet but it seems to involve, at least partially, an interaction with the opoid system. However, a deep analysis of the results obtained with the invention indicates that vegetal extracts of this particular catuaba species present excellent effects in the treatment of pain alleviation. An advantage of the present invention lays on the fact that, in contrast to what occurs, for example, with non-steroidal anti-inflammatory drugs, such as acetylsalicylic acid, Trichilia is effective in the initial (acute) phase of certain nociceptive conditions as it can be observed in nocicepptive conditions induced by formalin and capsaicin. Still another advantage of the present invention refers to the absence of toxic effects caused by the vegetal material extracted from Trichilia sp. Tests carried out in mice, for example, clearly showed the lack of toxicity in the administration of Trichilia sp. extracts, alone or in association with other plants extracts, even in high doses under acute or subcronic forms, in daily doses up to 1 g/kg. This observation could also be verified in human beings in dosages of 25 mL twice a day for four weeks.