Technical Data Report

for

GUACATONGA

(Casearia sylvestris)

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Guacatonga

Family: Flacourtiaceae

Genus: *Casearia*

Species: *sylvestris*

Synonyms: *Samyda parviflora* L., *Casearia parviflora* L., *Anavinga samyda* Gaertn. f.

Common Names: Burro-kaa, café-bravo, cafeiillo, café silvestre, congonhas-de-bugre, corta-lengua, crack-open, dondequiera, erva-de-bugre, erva de pontada, guayabillo, guacatonga, guassatonga, mahajo, papelite, pau de lagarto, piraquina, raton, sarnilla, ucho caspi, wild coffee

Parts Used: Bark, leaves, root

Guacatonga grows as a shrub or small tree usually 2 or 3 meters tall, but sometimes grows up to 10 meters in undisturbed areas of the Amazon. In the clay soils of the Amazon, the plant has adapted for absorption and support by forming extensive lateral roots that are white, stiff, and covered with a corky bark. The tree produces small white, cream, or greenish flowers, which smell like a mixture of honey and urine, crowded on short stalks on the leaf axils. After flowering it produces small fruits, 3–4 mm in diameter, which split open to reveal three brown seeds covered with a red-to-orange aril. Guacatonga grows wild throughout the tropics, adapting to both forests and plains. It is native to Cuba, Jamaica, Hispaniola, Puerto Rico, the Caribbean, Central America, and South America (including Brazil, Peru, Argentina, Uruguay, and Bolivia).

Guacatonga has a rich history in herbal medicine systems in nearly every tropical country where it grows. The Karajá Indians in Brazil prepare a bark maceration to treat diarrhea; the Shipibo-Conibo Indians of Peru use a decoction of the bark for diarrhea, chest colds and flu. Other Indian tribes in Brazil mash the roots or seeds of guacatonga to treat wounds and leprosy topically. Indigenous peoples throughout the Amazon rainforest have long used guacatonga as a snakebite remedy. A leaf decoction is brewed that is applied topically and also taken internally. The same jungle remedy is used topically for bee stings and other insect bites. This native use found its way out of the rainforest and into current herbal medicine practices in cities and villages in South America. It has been validated by scientists in the last several years who documented the leaf extract as capable of neutralizing several types of bee and snake venoms.[1–3]

Guacatonga has a long history of use in Brazilian herbal medicine, documented in early folk medicine books as an antiseptic and cicatrizant for skin diseases (in 1939), as a topical anesthetic (in 1941), and as an anti-ulcer drug (in 1958). It is currently used in Brazilian herbal medicine systems as a blood purifier, anti-inflammatory, and antiviral to treat rheumatism, syphilis, herpes, stomach and skin ulcers, edema, fevers of all kinds, diarrhea, and as an anesthetic and hemostatic for mucous and skin lesions. It is also employed topically for burns, wounds, rashes, and such skin disorders as eczema and vitiligo. The natural herbal remedy calls for 20 grams of dried leaves infused in 1 liter of water; quarter-cup amounts are taken orally 2–3 times daily.

The plant is also a popular herbal remedy employed in Bolivian herbal medicine, where it is considered to be analgesic, antacid, anti-inflammatory, antiulcerous, antimutagenic, antitumorous, vulnerary, and hemostatic. There it is used to treat skin diseases, cancer, stomach ulcers, snakebite and bee stings, herpes, and in dental antiseptic mouthwash products.

The chemical makeup of guacatonga is quite complex. Scientists conducting the antivenin research discovered that the leaves and twigs of the plant contain a phytochemical called *lapachol.*[3] This is the well known and studied anticancerous/antifungal compound from which another rainforest plant, pau d'arco (*Tabebuia impetiginosa*), gained much renown. (Pau d'arco is also featured in this book.) While other researchers have been studying the anticancerous and antitumorous properties of guacatonga, a completely different set of phytochemicals has fueled

their interest. These compounds, called *clerodane diterpenes,* are found abundantly in guacatonga. Clerodane diterpenes have been tested for a wide range of biological activities ranging from insect antifeedants, to antitumorous, anticancerous, and antibiotic agents, to HIV replication inhibitors. Some of the clerodane diterpenes documented in guacatonga are novel chemicals which scientists have named *casearins* (A thru S).

The research on guacatonga's anticancerous properties began in 1988 by Japanese researchers from the Tokyo College of Pharmacy and Pharmacognosy. They published one preliminary trial in 1988 on their discovery of these novel clerodane diterpenes and their cytotoxic and antitumorous activities. The study indicated that an ethanol extract of the leaf showed strong antitumorous activity in laboratory mice with sarcomas.[4] As soon as they made this discovery, they rushed to patent it, filing a Japanese patent for the casearin chemicals they'd discovered as new antitumorous agents.[5] They published a follow-up study in 1990, again reporting their results from injecting mice with sarcomas with an ethanol extract of guacatonga leaves (100 mg per gram of body weight) and confirming their previous findings.[6] They then tested individual casearins against various human cancer cell lines and published two more studies in 1991 and 1992.[7,8] These studies reported new casearin chemicals and their antitumorous and cytotoxic actions against cancerous tumors. Oddly, the Japanese researchers have not published any further studies and, since they had already filed patents, other research groups have not been forthcoming in funding research dollars on these patented antitumorous phytochemicals. In 2002, however, a well-known research group in North Carolina discovered three new casearins in the leaves and stems of guacatonga that the Japanese had not (and, obviously, hadn't patented). They named the new chemicals *casearvestrin A, B* and *C,* and published their first study in February, 2002, stating: "All three compounds displayed promising bioactivity, both in cytotoxicity assays against a panel of tumor cell lines and in antifungal assays . . ."[9] Their research tested the new plant chemicals against human lung, colon and ovarian tumor cells and indicated all three compounds had comparable IC_{50} values ranging from 0.2 and 0.8 µM. This research was supported by a grant from the National Cancer Institute, National Institutes of Health (NCI) and performed by a non-profit biotech company, a large pharmaceutical company and a major university. The NCI has also performed research in-house on clerodane diterpenoids found in another *Casearia* plant species documenting the antitumor properties of its novel diterpenoids[10] and another university research group has documented the cytotoxic properties of this class of chemicals in a *Casearia* plant from the Madagascar rainforest as well.[11] It will be interesting to see if this diversified group will actually develop these chemicals into new effective chemotherapeutic agents; their research is ongoing.

All other research on the chemicals and activities of guacatonga has been performed by Brazilian research groups over the years. The first published toxicity study with rats indicated no toxicity with an ethanol extract of the leaves at 1840 mg/kg.[12] This research group, at the University of Saõ Paulo, studied the antiulcerogenic properties of the plant (based on its long history of use as an effective herbal remedy for ulcers). They published two studies confirming these benefits. The first study, with rats (in 1990), showed that a crude leaf extract reduced the volume of gastric secretion by 42%, but had little effect on pH. The extract also prevented lab-induced acute gastric mucosal injury at 57.5 mg/kg, which was equivalent to the antiulcer drug cimetidine (Tagamet®).[12] Ten years later they published a second rat study, documenting that a crude leaf extract protected the stomach mucosa without changing gastric pH and sped healing of acetic acid-induced chronic ulcers and *H. pylori* ulcers.[13] Another Brazilian researcher documented that a bark-and-leaf infusion demonstrated analgesic and mild anti-inflammatory properties in mice.[14] A university researcher followed up on the anti-inflammatory research, publishing in her dissertation that a hydroalcoholic extract of the leaves was as effective against inflammation in mice as the NSAID drugs Prioxicam® and Meloxicam®.[15] Leaf extracts have also been shown by two research groups to be active against common food poisoning bacteria strains, *Bacillus cerus* and *B. subtilis,* but inactive against such other common bacteria as *Staphylococcus*, *Streptoccoccus,* and *E. coli*.[16,17]

It will be interesting to see what happens with guacatonga's ongoing cancer research. In the meantime, guacatonga is considered a safe plant and a natural herbal remedy for ulcers,

inflammations, and pain, and will continue to be used as a snakebite remedy throughout the Amazon jungles by the indigenous peoples.

Documented Properties and Actions: Analgesic, anesthetic, antacid, antifungal, anti-inflammatory, anti-ulcerogenic, antivenin, antiviral, antimutagenic, antitumorous, cicatrizant, cytotoxic, depurative, hemostatic, vulnerary

Main Phytochemicals: Caprionic acid, casearin A thru S, casearia clerodane I thru VI, casearvestrin A thru C, hesperitin, lapachol, vicenin

Traditional Remedy: Twenty grams of dried leaves are infused in a liter of water and quarter-cup amounts are taken 2–3 times daily. Since most of the chemicals are water soluble, powdered leaves in tablets or capsules (2–4 grams daily) can be substituted if desired.

Contraindications: None known.

Drug Interactions: None reported.

WORLDWIDE ETHNOBOTANICAL USES

Country	Uses
Bolivia	Analgesic, antacid, anti-inflammatory, antiulcer, antimutagenic, antitumorous, antiseptic (dental), cicatrizant, depurative, hemostatic, insect bite, skin diseases, snakebite
Brazil	Anti-inflammatory, depurative, diarrhea, chest and body pains, eczema, fevers, flu, herpes, leprosy, male sexual stimulant, rheumatism, sedative, skin diseases, snakebite, syphilis, tonic, wounds
Colombia	Skin diseases, snakebite, ulcers
India	Snakebite
Peru	Diarrhea
Elsewhere	Leprosy, snakebite, wound

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Ethnomedical Information on Guacatonga (Casearia sylvestris)

Plant Part / Location	Documented Ethnic Use	Type Extract / Route	Used By	Ref #
Bark Peru	Used for diarrhea.	H2O Ext / Oral	Human Adult	L04137
Dried Bark Brazil	Used for fevers. Used for diarrhea.	Decoction / Oral Maceration / Oral	Human Adult Human Adult	K07977 L04137
Dried Bark Brazil	Used as an anti-inflammatory and febrifuge.	Decoction / Oral	Human Adult	T15975
Dried Leaf Brazil	Used for fevers. Used to treat snakebite, herpes, and syphilis. Used as a sedative. Used as a male sexual stimulant. Used as a blood purifier, skin diseases, and syphilis. Used as a tonic, and anti-iflammatory; used to treat skin diseases and diarrhea.	Decoction / Oral Decoction / Oral Not stated / Oral Decoction / Oral Hot H20 Ext Not stated / Oral	Human Adult Human Adult Human Adult Human Adult Male Human Adult Human Adult	K07977 T15975 L05437 T15975 BB1003 L05437
Dried Leaf Brazil	Used as a febrifuge, depurative; used for fevers, rheumatism, ulcers, syphilis, and eczema. Used for skin diseases and fever.	Various / Oral Decoction / External	Human Adult Human Adult	BB1008 BB1008
Fresh Bark + Leaf Brazil	Used for snakebite.	Infusion / External	Human Adult	J12450
Leaf India	Used as an antivenin for snakebite.	Juice / Not given	Human Adult	K25892
Leaf + Stem Colombia	Used to treat ulcers and other skin afflictions.	Hot H20 Ext / External	Human Adult	A00709
Not Specified	Used to treat snakebite.	Not stated	Human Adult	K21146
Not Specified Bolivia	Used as an analgesic, antacid, anti-inflammatory, antiulcer, antimutagenic, antitumorous, antiseptic (dental), cicatrizant, depurative, hemostatic, used to treat insect bite, skin diseases, snakebite.	Not stated / Internal	Human Adult	BB1005
Dried Root Brazil	Used for chest and body pains. Used to treat wounds and leprosy.	Decoction / Oral Maceration / External	Human Adult Human Adult	T15975 L04137
Seed Oil Brazil	Used to treat leprosy.	Oil / External	Human Adult	L04137

Presence of Compounds in Guacatonga (Casearia sylvestris)

Compound	Type	Source	Origin	Amount	Ref #
Caprionic Acid		Leaf	Various	Not stated	BB1001
Casearin A	Diterpene	Leaf Leaf Leaf Leaf	Paraguay Not stated Paraguay Brazil	Not stated 00.01079% 00.58% 00.15%	M30433 K10958 H07106 H07106
Casearin B	Diterpene	Not stated Leaf Leaf	Not stated Paraguay Paraguay	00.10026% 00.71504% Not stated	K10958 H07106 M30433
Casearin C	Diterpene	Leaf Not stated Leaf	Paraguay not stated Paraguay	Not stated 00.03938% 00.76%	M30433 K10958 H07106
Casearin D	Diterpene	Leaf Leaf	Paraguay Paraguay	Not stated 00.32%	M30433 H07106
Casearin E	Diterpene	Leaf Leaf	Paraguay Paraguay	Not stated 00.08%	M30433 H07106
Casearin F	Diterpene	Leaf Leaf	Paraguay Paraguay	Not stated 00.6%	M30433 H07106
Casearin G	Diterpene	Leaf Leaf Leaf	Brazil Brazil Paraguay	Not stated 00.00025% Not stated	H06829 H23337 M30433
Casearin H	Diterpene	Leaf Leaf	Brazil Paraguay	Not stated Not stated	H06829 M30433
Casearin I	Diterpene	Leaf Leaf	Brazil Paraguay	Not stated Not stated	H06829 M30433
Casearin J	Diterpene	Leaf Leaf	Brazil Paraguay	Not stated Not stated	H06829 M30433
Casearin K	Diterpene	Leaf Leaf	Brazil Paraguay	Not stated Not stated	H06829 M30433

Compound	Type	Source	Origin	Amount	Ref #
Casearin L	Diterpene	Leaf Leaf	Brazil Paraguay	Not stated Not stated	H06829 M30433
Casearin M	Diterpene	Leaf Leaf	Brazil Paraguay	Not stated Not stated	H06829 M30433
Casearin N	Diterpene	Leaf Leaf	Brazil Paraguay	Not stated Not stated	H06829 M30433
Casearin O	Diterpene	Leaf Leaf	Brazil Paraguay	Not stated Not stated	H06829 M30433
Casearin P	Diterpene	Leaf Leaf	Brazil Paraguay	Not stated Not stated	H06829 M30433
Casearin Q	Diterpene	Leaf Leaf	Brazil Paraguay	Not stated Not stated	H06829 M30433
Casearin R	Diterpene	Leaf Leaf	Brazil Paraguay	Not stated Not stated	H06829 M30433
Casearin S	Diterpene	Leaf	Brazil	00.00014%	H23337
Casearia Clerodane I Casearia Clerodane II Casearia Clerodane III Casearia Clerodane IV Casearia Clerodane V Casearia Clerodane VI	Diterpene	Leaf	Paraguay	Not stated	H04119
Casearvestrin A	Diterpene	Leaf + Twigs	Ecuador	00.034%	H29066
Casearvestrin B	Diterpene	Leaf + Twigs	Ecuador	00.00214%	H29066
Casearvestrin C	Diterpene	Leaf + Twigs	Ecuador	00.043%	H29066
Hesperitin	Flavonoid	Leaf + Twigs	Brazil	Not stated	BB1004
Lapachol	Naphthoquinone	Leaf + Twigs	Brazil	Not stated	BB1004
Vicenin; 2	Flavonoid	Leaf + Twigs	Brazil	Not stated	BB1004

Biological Activities for Extracts of Guacatonga (Casearia sylvestris)

Plant Part - Origin	Activity Tested For	Type Extract	Test Model	Dosage	Result	Notes/Organism tested	Ref #
Dried Leaf Brazil	Toxicity Assessment (quantitative)	ETOH(75%)Ext	Intragastric Rat	LD50 >1840 mg/kg	Inactive	No toxicity noted.	M25176
Dried Leaf Brazil	Cytotoxic	ETOH(100%)Ext	Cell Culture	Not stated	Strong Activity	Several cancer cell lines.	H06829
Dried Leaf Paraguay	Antitumor Activity	ETOH(100%)Ext	Not stated Mouse	100 mg/kg	Strong Activity	Sarcoma 180 (ASC).	H04119
Dried Leaf Brazil	Antitumor Activity	ETOH Ext + Fractions	Cell Culture	Not stated	Active	Several cancer lines tested with isolated diterpenes from plant.	K10958
Leaf Paraguay	Antitumor Activity	ETOH(95%)Ext	IP Mouse	100 mg/kg	Active	Sarcoma 180 (ASC).	H07106
Dried Leaf Paraguay	Antitumor Activity	ETOH(100%)Ext	Cell Culture	Not stated	Active	Several cancer cell lines.	M30433
Leaf + Twig Ecuador	Antitumor Activity	MEOH(75%)Ext	Cell Culture	Not stated	Active	KB cell cytotoxicity against a panel of tumor cell lines including human lung, colon, and ovarian cancer.	H29066
Leaf + Twig Ecuador	Antitumor Activity	Fraction: Casearvestrin A	Cell Culture	IC50=.54 u/m IC50=.71 u/m IC50=.82 u/m	Active Active Active	Human lung cancer cells Human colon cancer cells Human ovarian cancer cells	H29066
Leaf + Twig Ecuador	Antitumor Activity	Fraction: Casearvestrin B	Cell Culture	IC50=.20 u/m IC50=.25 u/m IC50=.32 u/m	Active Active Active	Human lung cancer cells Human colon cancer cells Human ovarian cancer cells	H29066
Leaf + Twig Ecuador	Antitumor Activity	Fraction: Casearvestrin C	Cell Culture	IC50=.29 u/m IC50=.26 u/m IC50=.42 u/m	Active Active Active	Human lung cancer cells Human colon cancer cells Human ovarian cancer cells	H29066
Dried Leaf Brazil	Cytotoxic Activity	MEOH(75%)Ext	Cell Culture	1000 mcg/ml	Inactive	Cells-vero. (Healthy cells)	L05437
Dried Leaf Brazil	Antiviral Activity	ETOH(100%)Ext	Human Adult (3 patients)	Topical application	Active	*Herpes simplex 1.*	BB1007
Dried Leaf Brazil	Antiviral Activity	MEOH(75%)Ext	Cell Culture	500 mcg/ml	Inactive	*Virus Herpes simplex 1* and *Herpes simplex 2* in vero cells.	L05437
Bark + Leaf Brazil	Analgesic Activity	Infusion	Intragastric Mouse	1.0 gm/kg	Active	vs. acetic acid-induced writhing	J12450

Plant Part - Origin	Activity Tested For	Type Extract	Test Model	Dosage	Result	Notes/Organism tested	Ref #
Bark + Leaf Brazil	Anti-inflammatory Activity	Infusion	Intragastric Mouse	1.0 gm/kg	Weak activity	By dye diffusion assay	J12450
Dried Leaf Brazil	Antiulcer Activity	ETOH(70%)Ext	Intragastric Rat	57.5 mg/kg	Active	vs. stress-induced ulcers (water-immersion) & vs. stress-induced(restraint) ulcers	M25176
Dried Leaf Brazil	Antiulcer Activity	ETOH(75%)Ext	Intragastric Rat	57.5 mg/kg and 44.3 mg/kg	Active	vs. *H. pylorus* ligation-induced ulcers, vs. stress-induced ulcers(water-immersion), and vs. acetic acid-induced ulcers	L08768
Dried Leaf Brazil	Gastric Secretory Inhibition	ETOH(75%)Ext	Intragastric Rat	57.5 mg/kg	Active	vs. *H. pylorus* ligation-induced ulcers	M25176
Dried Leaf Brazil	Anti-inflammatory Activity	Hydroalcoholic	IP Mouse	300 mg/kg 100 mg/kg	Active Active	Inhibited induced inflammation at the same rate as the drugs Piroxicam and Meloxicam.	BB1002
Leaf + Twig Ecuador	Antifungal Activity	MEOH(75%)Ext Individual fractions	Disk diffusion	EC50= 0.34 to 1.4 mcg/ml	Active	*Aspergillus niger*	H29066
Dried Leaf Brazil	Antifungal Activity	CH2CL2:MEOH (1:1) Ext	TLC Plate	1 mg/.10 ml	Inactive	*Cladosporium sphaerospermum*	BB1006
Dried Leaf Brazil	Antibacterial Activity	CH2CL2:MEOH (1:1) Ext	Agar plate	5 mg/plate	Active	*Bacillus cerus*	BB1006
Not specified Brazil	Antibacterial Activity	Not stated	In vitro Disc	Not stated	Active Inactive Inactive Inactive	*Bacillus subtilis* *Escherichia coli* *Staphylococcus aureus* *Streptococcus faecalis*	T15630
Dried Leaf Brazil	Antbacterial Activity	CH2CL2:MEOH (1:1) Ext	Agar plate	5 mg/plate	Inactive	*Staphylococcus aureus* *Escherichia coli* *Pseudomonas aeruginosa*	BB1006
Dried Leaf Brazil	Phosholipase A2 Inhibition Activity / Antivenin Activity	ETOH Ext	Cell Culture	1:5 ratio	Active	Inhibited PLA 2 by 64% for *Bothrops jararacussu* venom and 48% for *Lachesis muta* venom.	BB1004

Plant Part - Origin	Activity Tested For	Type Extract	Test Model	Dosage	Result	Notes/Organism tested	Ref #
Dried Leaf Brazil	Antivenin Effect	H20 Ext	Not stated	Variable	Active	Extract neutralized the hemorrhagic, coagulant and proteolytic activity on casein or fibrinogen induced by five snake venoms and two bee venoms.	L19078
Dried Leaf Brazil	Antivenin Effect	H20 Ext	Mouse	Not stated	Active	vs. activity of venoms.	L16542
Dried Leaf Brazil	Phospholipase A2 Inhibition	H20 Ext	Not stated	Not stated	Active	vs. activity of venoms containing Class I, II, and II Pla2.	L16542
Dried Leaf Brazil	Collagen fibril (type I) reticulation stimulation	ETOH(75%)Ext	Intragastric Rat (male)	57.5 mg/kg & 44.3 mg/kg	Active	vs. acetic acid-induced ulcers	L08768
Dried Leaf Brazil	DNA Nicking Activity	MEOH:CH2CL2 (1:1) Ext	Not stated	Not stated	Active	vs. repair deficient mutant yeast RS 322YK.	H23337
Dried part not specified Brazil	Antimalarial Activity	ETOH(95%)Ext Hexane Ext	Intragastric Mouse	100 mg/kg 100 mg/kg	Inactive Inactive	vs. *Plasmodium berghei* (daily dosing for 4 days)	K07977
Dried part not specified Brazil	Antimycobacterial Activity Antiyeast Activity	Not stated	Disk diffusion	Not stated	Inactive Inactive	*Mycobacterium smegmatis* *Candida albicans*	T15630
Dried stem Brazil	Antimalarial Activity	CHCL3 Ext H2O Ext	SC Chicken Oral Chicken	580.0 mg/kg 4.88 gm/kg	Inactive Inactive	*Plasmodium gallinaceum*	A00785
Dried Leaf Belize	Antispasmodic Activity	Hot H2O Ext	Not stated Rat (Aorta)	300 ul	Inactive	vs. norepinephrine and carbachol induced contractions	L16245
Dried Leaf Brazil	Molluscicidal Activity	CH2CL2:MEOH (1:1) Ext	Agar plate	100 ppm	Inactive	*Artemia salina* & *B. glabra*	BB1006

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H04119	ANTITUMOR PRINCIPLES FROM CASEARIA SYLVESTRIS SW. (FLACOURTIACEAE), STRUCTURE ELUCIDATION OF NEW CLERODANE DITERPENES BY 2-D NMR SPECTROSCOPY. ITOKAWA,H: ET AL., CHEM PHARM BULL 36 4: 1585-1588 (1988) (TOKYO COLL PHARM TOKYO 192-03 JAPAN)
H06829	STRUCTURES AND CYTOTOXIC ACTIVITY RELATIONSHIP OF CASEARINS, NEW CLERODANE DITERPENES FROM CASEARIA SYLVESTRIS SW. MORITA,H., ET AL., CHEM PHARM BULL 39 3: 693-697 (1991) (DEPT PHARM TOKYO COLL PHARM TOKYO 19203 JAPAN)

H07106	NEW ANTITUMOR PRINCIPLES, CASEARINS A-F, FOR CASEARIA SYLVESTRIS SW.(FLACOURTIACEAE). ITOKAWA,H., ET AL., CHEM PHARM BULL 38 12: 3384-3388 (1990) (TOKYO COLL PHARM TOKYO 192-03 JAPAN)
H23337	ACETYLATED DNA-DAMAGING CLERODANE DITERPENES FROM CSEARIA SYLVESTRIS. DE CARVALHO,PRF: ET AL., PHYTOCHEMISTRY 49 6: 1659-1667 (1998) (INST QUIM UNIV ESTADUAL PAULISTA ARARAQUARA BRAZIL)
H29066	NOVEL BIOACTIVE CLERODANE DITERPENOIDS FROM THE LEAVES AND TWIGS OF CASEARIA SYLVESTRIS. OBERLIES,NH: ET AL., J NAT PROD 65 2: 95-99 (2002) (RESEARCH TRIANGLE INST RESEARCH TRIANGLE PARK NC 27709 USA)
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L16542	EFFECTS OF AQUEOUS EXTRACT OF CASEARIA SYLVESTRIS (FLACOURTIACEAE) ON ACTIONS OF SNAKE AND BEE VENOMS AND ON ACTIVITY OF PHOSPHOLIPASES A2. BORGES,MH: ET.AL., COMP BIOCHEM PHYSIOL SER B 127B 1: 21-30 (2000) (DEPT GENET BIOQUUIM UNIV FED UBERLANDIA UBERLANDIA BRAZIL)
L19078	NEUTRALIZATION OF PROTEASES FROM BOTHROPS SNAKE VENOMS BY THE AQUEOUS EXTRACT FROM CASEARIA SYLVESTRIS (FLACOURTIACEAE). BORGES,MH ET AL., TOXICON 39 12: 1863-1869 (2001)(DEPT GENETICA BIOQUIMICA UNIV FEDERAL UBERLANDIA UBERLANDIA BRAZIL)

M25176	PHARMACOLOGICAL ASSAY OF CASEARIA SYLVESTRIS. I. PREVENTIVE ANTI-ULCER ACTIVITY AND TOXICITY OF THE LEAF CRUDE EXTRACT. BASILE,AC. ET AL., J ETHNOPHARMACOL 30 2: 185-197 (1990) (DEPT PHARMACOL INST CIEN UNIV SAO PAULO SAO PAULO SP 05508 BRAZIL)
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J Nat Prod 2002 Feb;65(2):95-9

Novel bioactive clerodane diterpenoids from the leaves and twigs of Casearia sylvestris.

Oberlies, N.H. et al.

Fractionation of a methanol extract of the leaves and twigs of Casearia sylvestris, as directed by activity against KB cell cytotoxicity, led to the isolation of three novel clerodane diterpenoids, casearvestrins A-C (1-3). The structures of 1-3 were deduced from one- and two-dimensional NMR experiments, including relative stereochemical assignments based on ROESY correlations and COSY coupling constants. All three compounds displayed promising bioactivity, both in cytotoxicity assays against a panel of tumor cell lines and in antifungal assays via the growth inhibition of Aspergillus niger in a disk diffusion assay.

Phytochemistry 1998 Nov 20;49(6):1659-1662

Acetylated DNA-damaging clerodane diterpenes from Casearia sylvestris.

de Carvalho, P. R. et al.

In addition to the known diterpene casearin G (1), two new clerodane diterpene asearins type, casearin S (2) and casearin T (3), were isolated from an acetylated bioactive CH(2)Cl(2)/MeOH extract from leaves of Casearia sylvestris. The diterpenes 1-3 exhibited moderate but selective activity towards the DNA-repair deficient yeast Saccharomyces cerevisiae mutants RAD 52YK and RS 321. The structures of 1-3 were established on the basis of NMR spectroscopic experiments

Toxicon 2001 Dec;39(12):1863-9

Neutralization of proteases from Bothrops snake venoms by the aqueous extract from Casearia sylvestris (Flacourtiaceae).

Borges, M.H., et al.

Aqueous extract from Casearia sylvestris leaves, a typical plant from Brazilian open pastures, was able to neutralize the hemorrhagic activity caused by Bothrops asper, Bothrops jararacussu, Bothrops moojeni, Bothrops neuwiedi and Bothrops pirajai venoms. It also neutralized two hemorrhagic metalloproteinases from Bothrops asper venom. Proteolytic activity on casein induced by bothropic venoms and by isolated proteases, including Bn2 metalloproteinase from B. neuwiedi venom, was also inhibited by the C. sylvestris extract in different levels. The alpha- fibrinogen chain was partially protected against degradation caused by B. jararacussu venom, when this venom was incubated with C. sylvestris extract. We also observed that this extract partially increased the time of plasma coagulation caused by B. jararacussu, B. moojeni and B. neuwiedi venoms. C. sylvestris extract did not induce proteolysis in any substrate assayed.

Comp Biochem Physiol B 2000 Sep 1;127(1):21-30

Effects of aqueous extract of Casearia sylvestris (Flacourtiaceae) on actions of snake and bee venoms and on activity of phospholipases A(2).

Borges, M.H., et al.

The crude aqueous extract from the leaves of Casearia sylvestris, a plant found in Brazilian open pastures, was assayed for its ability to inhibit phospholipase A(2) (PLA(2)) activity and some biological activities of bee and several snake venoms, and of a number of isolated PLA(2)s. The extract induced partial inhibition of the PLA(2) activity of venoms containing class I, II and III PLA(2)s. When tested against the purified toxins, it showed the highest efficacy against class II PLA(2)s from viperid venoms, being relatively ineffective against the class I PLA(2) pseudexin. In addition, C. sylvestris extract significantly inhibited the myotoxic activity of four Bothrops crude venoms and nine purified myotoxic PLA(2)s, including Lys-49 and Asp-49 variants. The extract was able to inhibit the anticoagulant activity of several isolated PLA(2)s, with the exception of pseudexin. Moreover, it partially reduced the edema-inducing activity of B. moojeni and B. jararacussu venoms, as well as of myotoxins MjTX-II and BthTX-I. The extract also prolonged the survival time of mice injected with lethal doses of several snake venoms and neutralized the lethal effect induced by several purified PLA(2) myotoxins. It is concluded that C. sylvestris constitutes a rich source of PLA(2) inhibitors.

An Acad Bras Cienc 1999;71(2):181-7
Search for antifungal and anticancer compounds from native plant species of Cerrado and Atlantic Forest.
Bolzani, V., et al.
Bioactivity-guided fractionation of several bioactive extracts obtained from Cerrado and Atlantic Forest plant species led to the isolation of potent DNA-damaging piperidine 1-5 and guanidine alkaloids 6-9 from Cassia leptophylla and Pterogyne nitens respectively, two common Leguminosae from Atlantic Forest. By means of biotechnological approach on Maytenus aquifolium, a species from Cerrado, moderate DNA-damaging sesquiterpene pyridine alkaloid 10-11 was isolated. Bioassay-guided fractionation on Casearia sylvestris, a medicinal plant species found in Cerrado and Atlantic Forest, led to the isolation of clerodane diterpenes 12-13 which showed effect on DNA. In addition, we have reported several interesting potent antifungal iridoids: 1 beta-hydroxy-dihydrocornin (14), 1 alpha-hydroxy-dihydrocornin (15), alpha-gardiol (16), beta-gardiol (17), plumericin (18), isoplumericin (19), 11-O-trans-caffeoylteucrein (20); ester derivative: 2-methyl-4-hydroxy-butyl-caffeoate (21), amide N-[7-(3',4'-methylenedioxyphenyl)-2Z, 4Z-heptadienoyl] pyrrolidine (22) and triterpene viburgenin (23).

Chem Pharm Bull (Tokyo) 1991 Mar;39(3):693-7
Structures and cytotoxic activity relationship of casearins, new clerodane diterpenes from Casearia sylvestris Sw.
Morita, H., et al.
Casearins G-R, new cytotoxic clerodane diterpenes have been isolated from the leaves of Casearia sylvestris Sw. (Flacourtiaceae). Their structures have been elucidated by spectroscopic methods and chemical conversions, and their structure-activity relationships have been discussed.

Chem Pharm Bull (Tokyo) 1990 Dec;38(12):3384-8
New antitumor principles, casearins A-F, for Casearia sylvestris Sw. (Flacourtiaceae).
Itokawa, H., et al.
New antitumor clerodane diterpenes, named casearins A-F, have been isolated from the leaves of Casearia sylvestris Sw. (Flacourtiaceae). These structures have been completely elucidated by two dimensional nuclear magnetic resonance, circular dichroism spectroscopy, X-ray analysis, and chemical evidences.

Mem Inst Oswaldo Cruz 1991;86 Suppl 2:203-5
Pharmacological screening of plants recommended by folk medicine as anti-snake venom--I. Analgesic and anti-inflammatory activities.
Ruppelt, B.M., et al.
We have observed that several plants used popularly as anti-snake venom show anti-inflammatory activity. From the list prepared by Rizzini, Mors and Pereira some species have been selected and tested for analgesic activity (number of contortions) and anti-inflammatory activity (Evans blue dye diffusion--1% solution) according to Whittle's technique (intraperitoneal administration of 0.1 N-acetic acid 0.1 ml/10 g) in mice. Previous oral administration of a 10% infusion (dry plant) or 20% (fresh plant) corresponding to 1 or 2 g/kg of Apuleia leiocarpa, Casearia sylvestris, Brunfelsia uniflora, Chiococca brachiata, Cynara scolymus, Dorstenia brasiliensis, Elephantopus scaber, Marsypianthes chamaedrys, Mikania glomerata and Trianosperma tayuya demonstrated analgesic and/or anti-inflammatory activities of varied intensity.

J Ethnopharmacol 1990 Sep;30(2):185-97
Pharmacological assay of Casearia sylvestris. I: Preventive anti-ulcer activity and toxicity of the leaf crude extract.
Basile, A.C., et al.
An ethanol extract of the leaves of Brazilian Casearia sylvestris, given orally, inhibited gastric secretion in pylorus-ligated rats. At a prophylactic dose of 57.5 mg/kg, the extract showed a reduction of gastric juice more effective than misoprostol (500 micrograms/kg). In reducing hydrochloric acid output, the extract was less effective than misoprostol, cimetidine (32.0 mg/kg) and atropine (5.3 mg/kg). With the extract, the pH of the stomach contents was not significantly different from that of controls. Stress-induced lesions produced by restraint and water immersion were significantly prevented by the extract for all levels of severity when compared with the controls. The extract appeared more effective than misoprostol in suppressing light lesions, was equivalent to cimetidine and misoprostol for moderate lesions, and less effective than cimetidine and misoprostol for severe lesions. Toxicological experiments indicated a low acute toxicity, confirmed by subchronic daily testing. The oral LD50 value of greater than 1840 mg/kg was over 32 times higher than the antiulcerogenic ED50 (57.5 mg/kg).