Technical Data Report

for

ESPINHEIRA SANTA

Maytenus ilicifolia

Sage Press

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Espinheira Santa

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Family: Celastraceae

Genus: *Maytenus*

Species: *ilicifolia*

Synonyms: *Celastrus ilicinus, Gymnosporia ilicina, Maytenus ilicina*

Common Names: Espinheira santa, cancerosa, cangorosa, limaosinho, maiteno

Parts Used: Leaves, bark, roots

Espinheira santa is a small, shrubby evergreen tree growing to 5 m in height with leaves and berries that resemble holly. It is native to many parts of South America and southern Brazil and it is even found in city landscapes for its attractive, holly-like appearance. With over 200 species of Maytenus distributed in temperate and tropical regions throughout South America and the West Indies, there are many Maytenus species that are indigenous to the Amazon region which have been used medicinally by indigenous tribes.

This particular species, however, has not been used extensively by the indigenous peoples in the Amazon region. It has been used by some native groups in Paraguay, where women use the plant as a contraceptive and fertility regulator, and to induce menstruation and abortions. Espinheira santa has a much longer and better documented history of use in urban areas and in South American herbal medicine practices than in tribal areas, probably because of the types of illnesses that it treats. In Brazil, the leaves of the plant are brewed into a tea for the treatment of ulcers, indigestion, chronic gastritis, and dyspepsia (with a recorded history of use for these purposes dating back to the 1930s). The leaf tea is also applied topically to wounds and rashes and skin cancer. In other herbal medicine systems in South America espinheira santa for is used for anemia, stomach and gastric ulcers, cancer, constipation, gastritis, dyspepsia, and liver disorders and as a contraceptive. In Argentina herbal medicine the entire plant or leaves are infused or decocted for its antiseptic and wound healing properties and it is commonly used internally for asthma, respiratory and urinary tract infections, diarrhea and to induce menstruation.

Espinheira santa has been the subject of many clinical studies, fueled by its effectiveness in treating ulcers and even cancer, with research beginning as early as the mid-1960s. Toxicity studies in 1978 and 1991 showed no toxicity in rats and mice in dosages up to 1 gram per kilogram of body weight.[1,2] Due to its reported traditional use as a abortive aid and contraceptive, researchers studied those aspects specifically but were unable to clinically validate these uses. In one study, a water extract fed to pregnant mice daily did not induce abortion and did not cause any fetus change.[2] Another research group injecting pregnant rats with leaf extracts (up to 100 mg/kg) reported that it did not cause abortive effects or embryotoxic effects, but did interfere in fertilization and implantation in non-pregnant rats.[3] A recent study in 2002 confirmed these results again stating that a leaf extract had estrogenic actions which suggested the antifertility effect may be the interfence of uterine receptivity to the embryo and did not induce abortions or have any embyrotoxic effects.[4] It was also reported in 1998 by the same scientist that it had no effect in male mice on sperm production.[5]

Early research performed in Brazil in the early 1970s revealed that espinheira santa, as well as a few other species in the *Maytenus* family, contains chemical compounds that showed potent antitumor and antileukemic activities *in vivo* and *in vitro* at very low dosages.[6–9] Then in an 1976 plant screening program by the National Cancer Institute, an alcohol and water extract of the leaves was documented with cytotoxicity against cancer cells at very low dosages[10] and U.S. and European pharmaceutical companies began to show an interest in it. Two of the alkaloid chemicals, named *maytansine* and *mayteine*, were extracted and tested in cancer patients in the United States

and South America in the 1970s following the NCI research.[11–15] Although there were some significant regressions in ovarian carcinoma and some lymphomas with maytansine,[15] further research was not continued due to the toxicity at the dosages used.[16] Research with the compound mayteine revealed little to no toxicity[8,11,12] and validated its uses in traditional medicine for various types of skin cancers.[17,18] In the 1990s Japanese researchers discovered a different set of compounds (triterpene chemicals) in espinheira santa which they named *cangorins* (cangorin A through J). These new chemicals showed cytotoxic and/or inhibitory activity against various leukemia and cancer tumor cells and the researchers have published more than eight studies on their discovery and results.[19–26]

Although espinheira santa is still used in South American traditional medicine for various types of cancer, its most popular use has been for the treatment of ulcers and digestive complaints. Its potent antiulcerogenic abilities were demonstrated in a 1991 study which showed that a simple hot water extract of espinheira santa leaves was as effective as two of the leading antiulcer drugs, ranitidine (Zantac®) and cimetidine (Tagamet®). The same study showed that espinheira santa caused an increase in volume and pH of gastric juice.[27] In 1997 a Japanese research group filed a patent on the biologically active anti-ulcer compounds found in espinheira santa as a new anti-ulcer drug.[28]

With its popularity and beneficial results in South America, as well as its recent western research, espinheira santa is slowly becoming more popular and known to health practitioners in the United States. The leaf tea is currently being used for ulcers, as a laxative, as a colic remedy, to eliminate toxins through the kidneys and skin, to regulate hydrochloric acid production in the stomach, and to support kidney, adrenal gland, and digestive functions. While research may continue on espinheira santa's anticancer and antitumor properties, natural health practitioners around the world still have an important and highly effective natural remedy for many types of stomach and intestinal disorders at their disposal.

Documented Properties and Actions: Analgesic, antacid, antiasthmatic, antifertility, anticancerous, antileukemic, antiseptic, antitumorous, antiulcerogenic, astringent, cicatrizant, cytotoxic, depurative, estrogenic, diuretic, emmenogogue, laxative, stomachic, tonic

Main Phytochemicals: Atropcangorosin, cangoaronin, cangorins A thru J, cangorinine, cangorosin A & B, celastrol, dispermol, dispermone, friedelan, friedelin, friedelinol, friedoolean, friedooleanan, ilicifolin, ilicifolinoside A thru C, kaempferol trisaccharides, kaempferol disaccharides, maitenine, maytanbutine, maytanprine, maytansine, maytenin, maytenoic acid, maytenoquinone, pristimeriin, pristimerin, quercetin trisaccharides, quercitrin, salaspermic acid, tingenol, tingenone

Traditional Remedy: One-half cup leaf decoction 2–3 times daily or with meals. Three to 4 grams of leaf powder in tablets or capsules or stirred into juice or water 1–2 times daily can be substituted if desired.

Contraindications: While clinical studies have not demonstrated espinheira santa to be an abortive it should not be taken during pregnancy unless under the direction of a qualified health care practitioner.

Research suggests that water extracts of espinheira santa may be estrogenic and reduce fertility in females. Women seeking treatment for infertility, attempting to get pregnant, or those with estrogen positive cancers should not use this plant.

Drug Interactions: One study with mice injected (IP at 680 mg/kg) with a water extract of leaves recorded barbiturate potentiation activity.However the same study notes no potentiation activity when administered to mice intragastrically at 1.36 gm/kg.[1]

WORLDWIDE ETHNOBOTANICAL USES

Country	Uses
Argentina	Abortifacient, antiasthmatic, antiseptic, cancer, diarrhea, emmenogogue, respiratory tract infections, sialagogue, tea, urinary tract infections, vulnerary
Brazil	Analgesic, anti-inflammatory, antiseptic, aperitif, aphrodisiac asthma, astringent, cancer, cholagogue, choleretic, cicatrizant, intestine, sialogogue, stomachic, tea, tonic, ulcers, vulnerary
Paraguay	Abortifacient, antifertility, aphrodisiac, contraceptive, emmenogogue, sterilizant
Elsewhere	Antiarthritic, antirheumatic, antiseptic, antispasmodic, aphrodisiac, asthma, astringent, cancer, contraceptive, digestive, diuretic, tonic, tea, tumor, vulnerary

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Ethnomedical Information on Espinheira Santa (Maytenus ilicifolia)

Plant Part / Location	Documented Ethnic Use	Type Extract / Route	Used For	Ref #
Branches Paraguay	Used to prevent conception.	Hot H2O Ext / Oral	Human Female	X00002 X00005
Entire Plant Paraguay	Used for fertility regulation.	Hot H2O Ext / Oral	Human Female	A03499
Entire Plant Paraguay	Used as a long-term contraceptive.	Hot H2O Ext / Oral	Human Female	L02292
Entire Plant Argentina	Used as a vulnerary, sialagogue, anti-asthmatic and antiseptic.	Hot H2O Ext / Oral	Human Adult	T03492
Entire Plant Brazil	Used as an indigenous tumor remedy.	Hot H2O Ext/ Oral	Human Adult	T03492
Entire Plant Paraguay	Used as a menstrual inducer. An infusion is drunk at the time of anticipated menses, or shortly after the absence of it is noted.	Hot H2O Ext / Oral	Human Female	T03492
Entire Plant Paraguay	Used as a fertility-regulating agent.	Hot H2O Ext / Oral	Human Female	T03492
Flowers Brazil	Used as an anti-inflammatory.	Decoction / Oral	Human Adult	M28328
Leaf Argentina	Used as an antiseptic and vulnerary.	Not Stated / External	Human Adult	K03244
Leaf Argentina	Used as an anti-asthmatic and sialogogue.	Not Stated / Oral	Human Adult	K03244
Leaf Argentina	Used as an emmenagogue.	Hot H2O Ext / Oral	Human Female	T03717
Leaf Argentina	Used against diarrhea, to treat respiratory tract infections and urinary tract infections.	Decoction / Oral	Human Adult	K17523
Leaf Brazil	Used as a sialogogue, for asthma, as an antiseptic.	Infusion / Oral	Human Adult	H21342
Leaf Brazil	Used as a vulnerary.	Leaves / External	Human Adult	H21342
Leaf Brazil	Used as a cholagogue and choleretic.	Infusion / Oral	Human Adult	J12611
Leaf Uruguay	Used to improve digestion, as an antispasmodic, to treat asthma, and as a contraceptive.	Infusion / Oral	Human Adult	K18125
Leaf Uruguay	Used as an astringent, to heal wounds, and an antiseptic.	Not stated / External	Human Adult	K18125

Plant Part / Location	Documented Ethnic Use	Type Extract / Route	Used For	Ref #
Leaf + Root + Twig Paraguay	Said to be a sterilizant. Decoction drunk after delivery.	Hot H2O Ext / Oral	Human Female	A03500
Leaf + Twigs Paraguay	Used as a contraceptive.	Hot H2O Ext / Oral	Human Female	T02289
Not Stated Paraguay	Used as an abortifacient, emmenagogue, and as a sterilizant by the rural populace.	Not stated / Not stated	Human Female	J01423
Not Stated Paraguay	Used for sterility.	Hot H2O Ext / Oral	Human Female	T15375
Root Paraguay Stem Paraguay	Used to prevent conception.	Hot H2O Ext / Oral	Human Female	X00002 X00005
Rootbark Paraguay	Used as a fertility-regulating agent.	Decoction / Oral	Human Female	H12628
Stembark Argentina	Used as an emmenagogue. Used as an abortifacient - used with *Origanum vulgare*.	Hot H2O Ext / Oral	Human Female	T03717
Aerial Parts Brazil	Used as an analgesic, disinfectant, tonic and cicatrizant. Used for gastritis, ulcers and stomach disorders.	Hot H2O Ext / Oral	Human Adult	ZZ1013
Aerial Parts Brazil	Used for acne, anemia, cancer, constipation, dyspepsia, liver disorders.	Hot H2O Ext / Oral	Human Adult	ZZ1013 AD1002 ZZ1002

Presence of Compounds in Espinheira Santa (Maytenus ilicifolia)

Compound	Chemical Type	Plant Part	Plant Origin	Quantity	Ref #
Atropcangorosin A	Triterpene	Not Stated Rootbark	Not Stated Paraguay	Not Stated Not Stated	H07036 M30433
Atropcangorosin A,6'-7'-dihydro:	Triterpene	Not Stated	Not Stated	Not Stated	H07036
Atropcangorosin A,dihydro:	Triterpene	Rootbark	Paraguay	Not Stated	M30433
Cangoaronin	Triterpene	Rootbark	Paraguay	00.00070%	H07261
Cangorin A	Sesquiterpene	Rootbark	Paraguay	Not Stated	H12628
Cangorin B	Sesquiterpene	Rootbark	Paraguay	Not Stated	H12628
Cangorin C	Sesquiterpene	Rootbark	Paraguay	Not Stated	H12628
Cangorin D	Sesquiterpene	Rootbark	Paraguay	Not Stated	H12628
Cangorin E	Sesquiterpene	Rootbark	Paraguay	Not Stated	H12628
Cangorin F	Sesquiterpene	Rootbark	Brazil	00.00666%	H13581
Cangorin G	Sesquiterpene	Rootbark	Brazil	00.00140%	H13581
Cangorin H	Sesquiterpene	Rootbark	Brazil	00.00061%	H13581
Cangorin I	Sesquiterpene	Rootbark	Brazil	00.00070%	H13581
Cangorin J	Sesquiterpene	Rootbark	Brazil	00.00043%	H13581
Cangorinine E-1	Sesquiterpene Alkaloid	Rootbark	Paraguay	00.00263%	H13297
Cangorinine W-1	Sesquiterpene Alkaloid	Rootbark	Paraguay	00.00280%	H13297
Cangorinine W-II	Sesquiterpene Alkaloid	Rootbark	Paraguay	00.00114%	H13297

Compound	Chemical Type	Plant Part	Plant Origin	Quantity	Ref #
Cangorosin A	Triterpene	Not Stated Rootbark	Not Stated Paraguay	Not Stated Not Stated	H07036 M30433
Cangorosin B	Triterpene	Not Stated Rootbark	Not Stated Paraguay	Not Stated Not Stated	H07036 M30433
Celastrol	Triterpene	Rootbark	Brazil	Not Stated	L19743
Dispermol,(+)	Diterpene	Entire Plant	Brazil	Not Stated	J09329
Dispermone,(-):	Diterpene	Entire Plant	Brazil	Not Stated	J09329
Friedelan-3-alpha-ol	Triterpene	Leaf	Brazil	Not Stated	L17000
Friedelan-3-beta-ol	Triterpene	Leaf	Brazil	Not Stated	L11832
Friedelan-3-ol	Triterpene	Leaf	Brazil	Not Stated	K21227 L19361
Friedelin	Triterpene	Leaf Aerial Parts Leaf Leaf Leaf Leaf	Brazil Brazil Brazil Brazil Brazil Brazil	Not Stated Not Stated Not Stated Not Stated Not Stated 00.00362%	K21227 L15618 L19361 L11832 L17000 L08628
Friedelinol,epi	Triterpene	Leaf	Brazil	00.01718%	L08628
Friedoolean-24-al-3-en-3-ol-2-on-29 -Oic Acid,d:a:	Triterpene	Rootbark	Paraguay	Not Stated	M30433
Friedoolean-29-ol-3-one,d:a:	Triterpene	Rootbark	Paraguay	Not Stated	M30433
Friedoolean-5-en-3,beta-29-diol,d:b	Triterpene	Rootbark	Paraguay	Not Stated	H07261
Friedoolean-5-en-3-beta-29-diol,d:b	Triterpene	Rootbark	Paraguay	Not Stated	M30433
Friedooleanan-29-ol-3-one,d: A:	Triterpene	Rootbark	Paraguay	00.00263%	H07261
Ilicifolin	Triterpene	Rootbark	Paraguay	00.00131%	H07261

Compound	Chemical Type	Plant Part	Plant Origin	Quantity	Ref #
Ilicifolinoside A	Alkenol	Leaf	Brazil	00.031%	H21342
Ilicifolinoside B	Alkanol	Leaf	Brazil	00.014%	H21342
Ilicifolinoside C	Alkanol	Leaf	Brazil	00.008%	H21342
Kaempferol-3-O-alpha-L-rhamnopyranosyl (1-->6)-O-[alpha-L-arabinopyranosyl (1-->3)-O-alpha-L-rhamnopyranosyl (1-->2)]-O-beta-D-galactopyranoside	Flavonoid	Leaf	Brazil	Not Stated	AD1005
Kaempferol trisaccharides	Flavonoid	Leaf	Brazil	Not Stated	AD1005
Kaempferol disaccharides	Flavonoid	Leaf	Brazil	Not Stated	AD1005
Maitenine	Triterpene	Entire Plant	Brazil	Not Stated	J09329
Maytanbutine	Matansinoid	Leaf + Twigs Root + Stem	Paraguay Paraguay	Not Stated 00.00002%	T03492 T03492
Maytanprine	Matansinoid	Leaf + Twigs Root + Stem	Paraguay Paraguay	00.00002% 00.00002%	T03492 T03492
Maytansine	Matansinoid	Leaf + Twigs Root + Stem	Paraguay Paraguay	00.00002% 00.00002%	T03492 T03492
Maytenin	Triterpene	Rootbark	Brazil	Not Stated	L19743
Maytenin,20-alpha-hydroxy	Triterpene	Rootbark	Brazil	Not Stated	L19743
Maytenin,22-beta-hydroxy	Triterpene	Rootbark	Brazil	Not Stated	L19743
Maytenoic Acid	Triterpene	Rootbark Rootbark	Paraguay Paraguay	00.00307% Not Stated	H07261 M30433
Maytenoquinone,(+)	Diterpene	Entire Plant	Brazil	Not Stated	J09329
Pristimeriin III,iso:	Triterpene	Rootbark	Paraguay	Not Stated	M30433

Compound	Chemical Type	Plant Part	Plant Origin	Quantity	Ref #
Pristimerin	Triterpene	Rootbark	Paraguay	Not Stated	L19743
Pristimerin III,iso	Triterpene	Rootbark	Paraguay	00.00087%	H07261
Quercetin trisaccharides	Flavonoid	Leaf	Brazil	Not Stated	AD1005
Quercitrin,iso:	Flavonol	Not Stated Leaf	Paraguay Brazil	Not Stated Not Stated	K28456 L17000
Salaspermic Acid	Triterpene	Rootbark Rootbark	Paraguay Paraguay	00.00175% Not Stated	H07261 M30433
Tingenol,6-oxo	Triterpene	Rootbark	Paraguay	Not Stated	H15022
Tingenone	Triterpene	Bark	Brazil	Not Stated	T03177
Tingenone III,iso	Triterpene	Rootbark	Paraguay	00.00131% Not Stated	H07261 M30433

OTHER PHYTOCHEMICAL SCREENING:

ALKALOIDS ABSENT	**ENTIRE PLANT**	**A03499**
ALKALOIDS PRESENT	**FLOWERS**	**M28328**

Biological Activities for Extracts of Espinheira Santa (Maytenus ilicifolia)

Plant Part - Origin	Activity Tested For	Type Extract	Test Model	Dosage	Result	Notes/Organism tested	Ref #
Aerial Parts Paraguay	Toxicity Assessment (quantitative)	Benzene Ext	IP Rat	LD50 = 0.10 gm/kg			X00017
Aerial Parts Paraguay	Toxicity Assessment (quantitative)	Benzene Ext	Oral Rat	LD50 = 1 gm/kg			X00017
Aerial Parts Paraguay	Toxicity Assessment (quantitative)	Hot H2O Ext	Oral Rat	LD50 > 1 gm/kg	Inactive		X00017
Aerial Parts Paraguay	Toxicity Assessment (quantitative)	MEOH Ext	IP Rat	LD50 = 0.86 gm/kg			X00017
Aerial Parts Paraguay	Toxicity Assessment (quantitative)	MEOH Ext	Oral Rat	LD50 > 1 gm/kg	Inactive		X00017
Leaf Brazil	Toxic Effect (general)	H2O Ext	Intragastric Mice	1.09 gm/kg	Inactive	LD-50 was greater than given dose.	T16416
Leaf Brazil	Toxic Effect (general)	H2O Ext	Intragastric Mice	272.0 mg/kg	Inactive	Dose given daily for 8 weeks with no toxicity noted.	T16416
Flowers Brazil	Mutagenic Activity	Hot H2O Ext	Agar Plate	100.0 mg/plate	Inactive	*Salmonella typhimurium* Metabolic activation has no effect on the results.	M28328
Leaf Brazil	Mutagenic Activity	H2O Ext	Agar Plate	100.0 mg/plate	Inactive	*Salmonella typhimurium*	J12611
Leaf Brazil	Barbiturate Potentiation	Hot H2O Ext	Intragastric Mice	1.36 gm/kg	Inactive		T16416
Leaf Brazil	Barbiturate Potentiation	Hot H2O Ext	IP Mice	680 mg/kg	Active		T16416
Leaf Brail	Cytotoxic Activity Anleukemic Activity	Fraction: maytansine	IP Mice	Not stated	Active	P388 lymphocytic leukemia L1210 mouse leukemia Human Lewis lung carcinoma system and the human B-16 melanocarcinoma (Statistical data in report indicating significant results.)	AD1024
Rootbark Japan	Cytotoxic Activity	MEOH Ext	Cell Culture	50.0 mcg/ml	Weak Activity	CA-9KB (32% Inhibition)	K27314

GI = Gastric Intubation IG = Intragastric NG = Nasogastric IP = Intraperitoneally IV = Intravenously SC = Subcutaneously IM = Intramuscular

Plant Part - Origin	Activity Tested For	Type Extract	Test Model	Dosage	Result	Notes/Organism tested	Ref #
Rootbark Paraguay	Cytotoxic Activity	MEOH Ext	Cell Culture	Not stated	Active	LEUK-P388 CA-9KB Cells-hamster-chinese-V79	H07261
Leaf + Stem Uruguay	Cytotoxic Activity	ETOH-H2O(1:1) Ext	Cell Culture	ED50<20 mcg/ml	Active	CA-9KB	X00001
Leaf Uruguay	Anticrustacean Activity	Hot H2O Ext	Cell Culture	0.1%	Active	*Artemia salina* (Assay system is intended to predict for antitumor activity.)	K18125
Leaf Brazil	Antiulcer Activity	Hot H2O Ext	Intragastric Rat	136.0 mg/kg	Active	vs. indomethacin-induced ulcers.	T16484
Leaf Brazil	Antiulcer Activity	Hot H2O Ext	Intragastric Rat	340.0 mg/kg	Active	vs. indomethacin-induced ulcers.	T16484
Leaf Brazil	Antiulcer Activity	Hot H2O Ext	IP Rat	340.0 mg/kg	Active	vs. indomethacin-induced ulcers.	T16484
Leaf Brazil	Antiulcer Activity	Hot H2O Ext	IP Rat	85.0 mg/kg	Active	vs. cold-restraint stress induced ulcers.	T16484
Leaf Brazil	Gastric Secretory Stimulation	Hot H2O Ext	Intragastric Rat	85.0 mg/kg	Active	Volume and pH of gastric secretions were both increased.	T16484
Leaf Not Stated	Antiulcer Activity	Chromatographic Fraction	Intragastric Rat	125.0 mg/kg	Active	Biological activity reported has been patented. vs. HCL / ethanol-induced gastric ulcers.	L08628
Leaf Brazil	Miscellaneous Effects	Not stated	Cell Culture Blood	30 mg/ml	Active	Decreased uptake of radioactivity on the labeling of red blood cells.	L11341
Leaf Brazil	Tranquilizing Effect	H2O Ext	Intragastric Mice	1.2 gm/kg	Inactive	In Rotarod test.	T16416
Leaf Brazil	Tranquilizing Effect	H2O Ext	Intragastric Mice	1.36 gm/kg	Inactive		T16416
Leaf Brazil	Tranquilizing Effect	H2O Ext	IP Mice	170 mg/kg	Active		T16416
Leaf Brazil	Analgesic Activity	Hot H2O Ext	Intragastric mice	1.36 gm/kg	Inactive	In hot plate test and acetic acid-abdominal writhing test.	T16416

Plant Part - Origin	Activity Tested For	Type Extract	Test Model	Dosage	Result	Notes/Organism tested	Ref #
Leaf Brazil	Angiotensin-converting enzyme inhibition	Decoction	Rabbit	0.33 mg/ml	Equivocal	Lung	L11096
Leaf Brazil	Anticonvulsant Activity	Hot H2O Ext	Intragastric mice	1.36 gm/kg	Inactive	vs. transcorneal electroschock - induced convulsions.	T16416
Leaf Brazil	Anticonvulsant Activity	Hot H2O Ext	Intragastric mice	1.36 gm/kg	Inactive	vs. pentylenetetrazole-induced convulsions.	T16416
Leaf Argentina	Antibacterial Activity	Decoction	Agar Plate	Not stated	Inactive	*Pseudomonas aeruginosa*	K17523
Leaf Argentina	Antibacterial Activity	H2O Ext	Agar Plate	1.0 mg/ml	Inactive	*Salmonella typhi*	J11153
Leaf Argentina	Antibacterial Activity	H2O Ext	Agar Plate	62.5 mg/ml	Inactive	*Escherichia coli* *Staphylococcus aureus*	K14683
Leaf Argentina	Antifungal Activity	H2O Ext	Agar Plate	62.5 mg/ml	Inactive	*Aspergillus niger*	K14683
Leaf Brazil	Fertility Promotion Effect	Hot H2O Ext	Intragastric Mice (female)	544 mg/kg	Inactive	Dose given daily for 45 days preceding mating.	T16416
Leaf Brazil	Antispermatogenic Effect	ETOH(95%) Ext	Intragastric mice IP Mice	800 mg/kg 200 mg/kg	Inactive Inactive		J15847
Leaf Brazil	Teratogenic Activity	H2O Ext	Intragastric Mice	272.0 mg/kg	Inactive	Dose given daily during pregnancy.	T16416
Leaf + Twigs Paraguay	Abortifacient Effect	CHCL3 Ext	IP Rat (pregnant)	25.0 mg/kg	Inactive		T02289
Leaf + Twigs Paraguay	Abortifacient Effect	H2O Ext	IP Rat (pregnant)	100 mg/kg	Inactive		T02289
Leaf + Twigs Paraguay	Antiimplantation Effect	CHCL3 Ext	IP Rat (female)	25.0 mg/kg	Inactive		T02289
Leaf + Twigs Paraguay	Antiimplantation Effect	H2O Ext	IP Rat (female)	100.0 mg/kg	Active		T02289
Leaf + Twigs Paraguay	Antiimplantation Effect	Pet Ether Ext	IP Rat (female)	25.0 mg/kg	Inactive		T02289
Leaf + Twigs Paraguay	Embryotoxic Effect	CHCL3 Ext	IP Rat (pregnant)	25.0 mg/kg	Inactive		T02289
Leaf + Twigs Paraguay	Embryotoxic Effect	H2O Ext	IP Rat (pregnant)	100.0 mg/kg	Inactive		T02289

Plant Part - Origin	Activity Tested For	Type Extract	Test Model	Dosage	Result	Notes/Organism tested	Ref #
Leaf + Twigs Paraguay	Embryotoxic Effect	Pet Ether Ext	IP Rat (pregnant)	25.0 mg/kg	Inactive		T02289
Leaf + Twigs Paraguay	Estrous Cycle Disruption Effect	CHCL3 Ext Pet Ether Ext	IP Rat (female)	25.0 mg/kg	Inactive		T02289
Leaf + Twigs Paraguay	Estrous Cycle Disruption Effect	H2O Ext	IP Rat (female)	100.0 mg/kg	Inactive		T02289
Leaf + Twigs Paraguay	Fertilization Inhibition	CHCL3 Ext Pet Ether Ext	IP Rat (female)	25.0 mg/kg	Inactive		T02289
Leaf + Twigs Paraguay	Fertilization Inhibition	H2O Ext	IP Rat (female)	100.0 mg/kg	Active		T02289
Leaf + Twigs Paraguay	Ovulation Inhibition Effect	CHCL3 Ext Pet Ether Ext	IP Rat (female)	25.0 mg/kg	Inactive		T02289
Leaf + Twigs Paraguay	Ovulation Inhibition Effect	H2O Ext	IP Rat (female)	100.0 mg/kg	Inactive		T02289
Not Stated Brazil	Antioxidant Activity	Saline Ext	Agar Plate	5.0 mg/ml	Weak Activity	vs. stannous chloride oxidative damage	L17930
Fruit Paraguay	Contraceptive and/or Interceptive Effect	MEOH(85%) Ext	Not stated Hamster	Not stated	Inactive		L18021
Leaf Paraguay	Contraceptive and/or interceptive effect	MEOH(85%) Ext	Not stated Hamster	Not stated	Inactive		L18021
Root Paraguay	Contraceptive and/or Interceptive Effect	MEOH(85%) Ext	Not stated Hamster	Not stated	Inactive		L18021
Leaf Uruguay	Plant Root Growth Inhibition	Hot H2O Ext	On plant	5.0%	Active	Assayed in *Triticum aestivum*	K18125
Leaf Uruguay	Plant Root Growth Stimulant	Hot H2O Ext	On plant	0.5%	Weak Activity	Assayed in *Triticum aestivum*	K18125
Leaf Brazil	Antifertility Effect	Lyophilized Hydroalcoholic Ext	Oral Mice	1000 mg/kg		Extract caused pre-implantation embryonic loss but had no effect on implantation or organogenesis..	AD1004

Plant Part - Origin	Activity Tested For	Type Extract	Test Model	Dosage	Result	Notes/Organism tested	Ref #
Leaf Brazil	Embryotoxic Effect	Lyophilized Hydroalcoholic Ext	Mice Oral	1000 mg/kg	Inactive		AD1004
Leaf Brazil	Estrogenic Effect	Lyophilized Hydroalcoholic Ext	Mice Oral	1000 mg/kg	Active		AD1004

Biological Activities of Compounds found in Espinheira Santa

Compound Tested	Activity Tested For	Test Model	Dosage	Result	Notes/Organism tested	Ref #
Celastrol	Anti-inflammatory Activity	In vitro	Not Stated	Active	Suppressed pro-inflammatory cytokine production TNF-alpha and IL-1beta by human monocytes and macrophages. Decreased induced nitric oxide production.	AD1006
Celastrol	Anti-inflammatory Activity	Rat	Not Stated	Active	Suppressed adjuvant arthritis.	AD1006
Celastrol	Antineurodegenerative Effect	Rat	Not Stated	Active	Improved performance in memory, learning and psychomotor activity tests. Useful in neurodegenerative inflammatory diseases like Alzheimer's disease.	AD1006
Celastrol	Immunomodulator Activity	In vitro	Not Stated	Active	Decreased the induced expression of class II MHC molecules.	AD1006
Celastrol Pristimerin	Antimalarial Activity	In vitro	Not Stated	Active		AD1007
Celastrol Pristimerin	Cytotoxic Activity	Cell culture	Not Stated	Active	HT-29 cells	AD1007
Celastrol	Antispermatogenic Effect	Cell Culture	Not Stated	Active	Concentration dependent inhibition on sperm forward motility, capacitation, acrosome reaction and sperm penetration.	AD1008
Celastrol	Antiperoxidative Activity	In vitro	Not Stated	Active	Prevented oxygen free radical damage to the inner membrane by increasing its negative surface charge.	AD1009
Celastrol	Antiperoxidative Activity	Cell culture	IC50=7 mM	Active	Antiperoxidative effect 15 times more effective than vitamin E.	AD1010
Friedelin	Antifungal Activity	Agar Plate	Not Stated	Inactive		AD1011
Friedelin	Antibacterial Activity	Agar Plate	Not Stated	Active Inactive	Gram negative bacteria Vibrio parahaemolyticus	AD1011
Friedelin	Antibacterial Activity	Agar Plate	Not Stated	Active		AD1011
Friedelin	Antibacterial Activity	Agar Plate	Not Stated	Active	Concentration Dependent	AD1012
Friedelin	Cytotoxic Effect	Cell Culture	Not Stated	Weak activity	Reduced the cytotoxicity of cadmium on HepG2 cells.	AD1013

GI = Gastric Intubation IG = Intragastric NG = Nasogastric IP = Intraperitoneally IV = Intravenously SC = Subcutaneously IM = Intramuscular

Compound Tested	Activity Tested For	Test Model	Dosage	Result	Notes/Organism tested	Ref #
Maytanprine	Antimicrotubule Effect	Cell Culture	Not Stated	Active	Induced neurofibrillary tangles in cultured newborn mouse neurons.	AD1014
Maytenin	Antineoplastic Activity	Human Adult Topical	Not Stated	Active	Cellular carcinoma (skin) Kaposi's sarcomatosis	AD1015
Pristimerin	Immunomodulator Activity	Cell Culture	2 mg/ml	Weak Activity	Modulates the oxidative burst by macrophages	AD1016
Pristimerin	Insecticidal Activity	Codling moth	Not Stated	Active	Cydia pomonella, Lepidoptera: Tortricidae Antifeedant activity and molt suppression.	AD1017
Pristimerin	Anti-inflammatory Activity	In vitro	IC50=0.2-0.3 mM	Active	Reduced nitrite accumulation in LPS-stimulated macrophages. Reduced induction of nitric oxide synthase activity. Inhibited Nfkappa-B activation.	AD1018
Salaspermic acid	Antiviral activity	Cell Culture	Not Stated	Active	Inhibited HIV reverse transcriptase and HIV replication in H9 lymphocyte cells.	AD1022
Tingenone	Antitrypanosomal Activity	Agar Plate	30 mm	Active	Trypanosoma cruzi Crithidia fasciculata	AD1023

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L17000	EXTRACTS OF MAYTENUS ILICIFOLIA AS ANALGESIC ANTIINFLAMMATORY DRUG. NAKAMURA,M: NAKASUMI,T: YOSHIZAWA,T: MINAGAWA,Y: PATENT-EUR PAT APPL-776,666 : 16-. (1997) (NIPPON MEKTRON LTD JAPAN)
L17930	EFFECT OF THE CYMBOPOGON CITRATUS, MAYTENUS ILICIFOLIA AND BACCHARIS GENISTELLOIDES EXTRACTS AGAINST THE STANNOUS CHLORIDE OXIDATIVE DAMAGE IN ESCHERICHIA COLI. DE F MELO,S: SOARES,S: COSTA,RF: DA SILVA,CR: DE LIVEIRA,BN: BEZERRA,JAC: CALDEIRA DE ARAUJO,A: BERNARDO FILHO,M: MUTAT RES 496 1/2: 33-38 (2001) (DEPT BIOFISICA BIOMETRIA UNIV ESTADO RIO JANEIRO RIO JANEIRO BRAZIL)
L18021	PHYTOCHEMICAL SCREENING OF MEDICINAL PLANTS STUDIES OF FLAVONOIDS. MANDICH,L: BITTNER,M: SILVA,M: BARROS,C: REVLATINOAMER QUIM 15 2: 80-82 (1984) (LAB QUIMICA PRODUCTOS NATURLES UNVI CONCEPCION CHILE)
L19361	CHARACTERIZATION OF ADULTERATION OF "ESPINHEIRA SANTA" (MAYTENUS ILICIFOLIA AND MAYTENUS AQUIFOLIUM, CELASTRACEAE) HYDROALCHOLIC EXTRACTS WITH SOROCEA BOMPLANDII (MORACEAE) BY HIGH-PERFORMANCE THIN LAYER CHROMATOGRAPHY. VILEGAS,JHY: LANCAS,FM: WAUTERS,JN: ANGENOT,L: PHYTOCHEM ANAL 9 6: 263-266 (1998) (UNIV SA PAULO INST QUIM SA CARLOS SAO CARLOS BRAZIL)
L19743	QUANTITATIVE DETERMINATION OF CYTOTOXIC FRIEDO-NOR-OLEANANE DERIVATIVES FROM FIVE MORPHOLOGICAL TYPES OF MAYTENUS ILICIFOLIA (CELASTRACEAE) BY REVERSE-PHASE HIGH PERFORMANCE LIQUID CHROMATOGRAPHY. FILHO,WB: CORSINO,J: SILVA BOLZANI,V: FURLAN,M: PEREIRA,AMS: FRANCA,SC: PHYTOCHEM ANAL 13 2: 75-78 (2002) (NUCLEO BIOENSAIO INST QUIMICA UNIV ESTADUAL PAU ARARAQUARA SP BRAZIL)
M28328	SCREENING OF PLANTS USED IN SOUTH BRAZILIAN FOLK MEDICINE. ALICE,CB: VARGAS,VMF: SILVA,GAAB: DE SIQUEIRA,NCS: SCHAPOVAL,EES: GLEVE,J: HENRIQUES,JAP: HENRIQUES,AT: J ETHNOPHARMACOL 35 2: 165-171 (1991) (CURSO PAS GRADUACAO FAC FARM UNIV FED RIO GRANDE DO SUL PORTO ALGRE BRAZIL)
M30433	ANTITUMOR SUBSTANCES FROM SOUTH AMERICAN PLANTS. ITOKAWA,H: TAKEYA,K: WATANABE,K: MORITA,H: ICHIHARA,Y: TOTSUKA,N: SHIROTA,O: IZUMI,H: SATAKE,M: YASUDA,I: SANKAWA,U: MOTIDOME,M: FLORES,FA: J PHARMACOBIO DYN 15 1: S-2-. (1992) (TOKYO COLL PHARM TOKYO 192-03 JAPAN)
T02289	ANTIFERTILITY SCREENING OF SELECTED PLANTS IN FEMALE RATS. BINGEL,AS: FONG,HHS: FARNSWORTH,NR: LLOYDIA 39 6: 475C-. (1976) (COLL PHARM UNIV ILLINOIS MED CENT CHICAGO IL 60612 USA)
T03177	SPECTROSCOPIC EVIDENCE FOR THE INTERACTION OF TINGENONE WITH DNA. CAMPANELLI,AR: D'ALAGNI,M: MARINI-BETTOLO,GB: FEBS LETT 122 : 256-260 (1980) (FAC SCI MAT FIS NAT UNIV ROMA ROME I-00185 ITALY)

T03492	HIGH-PERFORMANCE LIQUID CHROMATOGRAPHIC SEPARATION AND QUANTITATION OF MAYTANSINOIDS IN MAYTENUS ILICIFOLIA. AHMED,MS: FONG,HHS: SOEJARTO,DD: DOBBERSTEIN,RH: WALLER,DP: MORENO,AR: J CHROMATOGR 213 : 340-344 (1981) (COLL PHARM UNIV ILLINOIS MED CENT CHICAGO IL 60612 USA)
T03717	FERTILITY-REGULATING PLANTS USED IN POPULAR MEDICINE IN NORTHEASTERN ARGENTINA. MARTINEZ-CROVETTO,R: PARODIANA 1 1: 97-117 (1981) (DEPARTAMENTO DE BOTANICA FAC AGRONOMIA Y VETERINARIA UNIV NACIONAL DEL NORDESTE CORRIENTES ARGENTINA)
T15375	A SURVEY OF PLANTS WITH ANTIFERTILITY PROPERTIES DESCRIBED IN THE SOUTH AMERICAN FOLK MEDICINE. GONZALEZ,F: SILVA,M: ABSTR PRINCESS CONGRESS I BANGKOK THAILAND 10-13 DECEMBER 1987 : 20PP-. (1987) (LAB QUIM PROD NAT UNIV CONCEPCION CONCEPCION CHILE)
T16416	PHARMACOLOGIC AND TOXICOLOGIC EFFECTS OF TWO MAYTENUS SPECIES IN LABORATORY ANIMALS. OLIVERIRA,MGM: MONTERIRO,MG: MACAUBAS,C: BARBOSA,VP: CARLINI,EA: J ETHNOPHARMACOL 34 1: 29-41 (1991) (DEPT PSYCH ESCOL PAULISTA MED SAO PAULO BRAZIL)
T16484	ANTIULCEROGENIC EFFECTS OF TWO MAYTENUS SPECIES IN LABORATORY ANIMALS. SOUZA-FORMIGONI,MLO: OLIVERIA,MGM: MONTEIRO,MG: DA SILVEIRA-FILHO,NG: BRAZ,S: CARLINI,EA: J ETHNOPHARMACOL 34 1: 21-27 (1991) (DEPT PSYCHOBIOL ESCOLA PAULISTA MED SAO PAULO BRAZIL)
W02705	REPRODUCTION, MATRIMONY AND FAMILY LIFE OF THE ABORIGENES IN PARAGUAY. MORENO,R: GINI,L: SUPL ANTROPOL 9 : 169-203 (1974) (INST CIENC BASICAS UNIV NACL ASUNCION ASUNCION PARAGUAY)
X00001	UNPUBLISHED DATA, NATIONAL CANCER INSTITUTE. ANON: NAT CANCER INST CENTRAL FILES : - (1976) (NO ADDRESS GIVEN)
X00002	PARAGUAYAN PLANTS USED AS ANTIFERTILITY AGENTS AS REPORTED BY ANTHROPOLOGISTS. ROSNER,J: PERSONAL COMMUNICATION THROUGH DR. NESTOR I. GERMANO,MAY 17,1977 : - (1977) (INST LATINOAMER FISIOL REPROD UNIV DEL SALVADOR SAN MIGUEL ARGENTINA)
X00005	PROGRESS REPORT ON PARAGUAYAN INDIGENOUS PLANTS FOR FERTILITY REGULATION TO WHO. MAY 20,1977. GERMINO,NI: PERSONAL COMMUNICATION : - (1977) (INST LATINOAMER FISIOL REPROD UNIV DEL SALVADOR BUENOS AIRES ARGENTINA)
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AD1025	INITIAL STUDIES ON MAYTANSINE-INDUCED METAPHASE ARREST IN L1210 MURINE LEUKEMIA CELLS. WOLPERT-DEFILIPPES MK; BONO VH JR; DION RL; JOHNS DG.; BIOCHEM PHARMACOL. 1975 SEP 15;24(18):1735-8.
AD1024	NOVEL NATURAL PRODUCTS WITH ANTITUMOR ACTIVITY. KUPCHAN SM; FED PROC. 1974 NOV;33(11):2288-95.

Clinical Abstracts

Contraception 2002 Feb;65(2):171-5
Effect of Maytenus ilicifolia Mart. on pregnant mice.
Montanari, T., et al.
Maytenus ilicifolia Mart. is used in Brazilian herbal medicine particularly for stomach disorders, but it is also used, as in other parts of South America, for fertility control. To verify its potential as an abortifacient, the lyophilized hydroalcoholic extract of its leaves was administered orally at a dose of 1000 mg/kg/day to mice between the first and third day of pregnancy (DOP), between the forth and sixth DOP, or between the seventh and ninth DOP. The extract caused a pre-implantation embryonic loss, but it did not have an effect on implantation or organogenesis. Morphological alterations of the reproductive system, not an embryotoxic effect, were not found. Estrogenic activity of the extract, exhibited by an uterotrophic effect, suggests that it may be interfering with the uterine receptivity to the embryo.

Contraception 1998 May;57(5):335-9
Effect of Maytenus ilicifolia Mart.ex. Reiss on spermatogenesis.
Montanari T., et al.
Published erratum appears in Contraception 1998 Aug;58(2):146
The effect of the ethanolic extract of Maytenus ilicifolia Mart.ex. Reiss leaves on spermatogenesis was studied in Swiss mice by evaluating morphological characteristics by light and electron microscopy. The extract was administered at a dose of 200 mg/kg/day intraperitoneally for 20 days, and at a dose of 800 mg/kg/day orally for 30 days. Structural analysis of the germ epithelium showed that treated animals were not noticeably different from control animals. The alterations included some exfoliated immature germ cells, occasional germ cell death (recognized as pyknotic nuclei) and a few vacuolized seminiferous tubules. Ultrastructurally, enlarged lipid droplets were found in Sertoli cells and swollen acrosomes occurred in early spermatids of animals treated with the higher dose. Sperm production indicated that the ethanolic extract of M. ilicifolia leaves did not contain substances sufficient to arrest spermatogenesis.

J Nat Prod 1994 Dec;57(12):1675-81
Cytotoxic aromatic triterpenes from Maytenus ilicifolia and Maytenus chuchuhuasca.
Shirota, O., et al.
The isolation and structure elucidation of four cytotoxic aromatic triterpenes [1-4] along with three known quinoid triterpenes [5-7] from the South American medicinal plants Maytenus ilicifolia and M. chuchuhuasca are described. The structures of these aromatic triterpenes contained aromatized A rings and C-6 oxygenated B rings, and were elucidated by 1H- and 13C-nmr spectroscopic studies and by X-ray crystallographic analysis of 3.

J Ethnopharmacol 1991 Aug;34(1):29-41
Pharmacologic and toxicologic effects of two Maytenus species in laboratory animals.
Oliveira, M.G., et al.
Leaves of Maytenus species are used in the popular medicine of Brazil for their reported antacid and antiulcerogenic activity. The present work examined the effects of a boiling water extract of equal parts of M. aquifolium and M. ilicifolia leaves on acute administration in rats and mice, in an attempt to detect any general depressant, hypnotic, anticonvulsant and analgesic effects. General depressant and hypnotic effects were seen only after intraperitoneal administration. After chronic administration, the overall behavior of animals did not change and they continued to gain weight at the same rate as controls. Several biochemical and hematological parameters as well as pathological examination of different organs did not show any significant alterations after 3 months of treatment. A search for the potential effects of the extract on the fertility of female and male rats and on the course of pregnancy as well as a search for potential teratogenic effects did not reveal any significant differences from controls. Taken together, the results indicate that these Maytenus species may be safe for human use and deserve further investigation.

J Ethnopharmacol 1991 Aug;34(1):21-7

Antiulcerogenic effects of two Maytenus species in laboratory animals.

Souza-Formigoni, M.L., et al.

Leaves of Maytenus species are commonly used in Brazil for the treatment of gastric ulcers, dyspepsias and other gastric problems. The present study evaluated the antiulcerogenic potential of a boiling water extract of equal parts of M. aquifolium and M. ilicifolia leaves against ulcer lesions induced by indomethacin and cold-restraint stress in rats. Ranitidine and cimetidine were used as reference drugs. The oral and intraperitoneal administration of the extract had a potent antiulcerogenic effect against both types of ulcers. The extract was shown to cause an increase in volume and pH of gastric juice of the animals with the pH effects comparable to those of cimetidine. The results tend to confirm the popular use of the plant.

Mutat Res 2001 Sep 20;496(1-2):33-8

Effect of the Cymbopogon citratus, Maytenus ilicifolia and Baccharis genistelloides extracts against the stannous chloride oxidative damage in Escherichia coli.

Melo, S. F., et al.

Stannous ion has been used in different sectors of human interest, such as in food industry and in health sciences. Much is known about stannous chloride (SnCl(2)) toxicity, although, there is no general agreement regarding its genotoxicity. Cymbopogon citratus, Maytenus ilicifolia and Baccharis genistelloides extracts have been used in popular medicine. We evaluated the influence of these crude extracts on the survival of the Escherichia coli wild type (AB 1157) strain submitted to SnCl(2) treatment. Reactive oxygen species (ROS) can be generated by a Fenton like reaction induced by SnCl(2). E. coli culture was treated simultaneously with SnCl(2) and a specific extract. Our results showed a reduction of the SnCl(2) effect on the survival of the cultures in presence of the crude extracts. The extract of M. ilicifolia showed the highest level of protection action against the SnCl(2) effect in comparison with the other extracts. This protector effect could due to the redox properties of these crude extracts. The compounds in the crude extracts could (i) chelate stannous ions, protecting them against the oxidation and avoiding the generation of ROS, (ii) be a scavenger of the ROS generated by the SnCl(2) oxidation and/or (iii) have oxidant compounds that could oxidise the stannous ions, abolishing or reducing the SnCl(2) effect.

J Ethnopharmacol 2001 Sep;77(1):41-7

Antiulcerogenic and analgesic effects of Maytenus aquifolium, Sorocea bomplandii and Zolernia ilicifolia.

Gonzalez F. G., et al.

Maytenus aquifolium (Celastraceae), Sorocea bomplandii (Moraceae) and Zolernia ilicifolia (Fabaceae) are native plants from the Tropical Atlantic Forest (Mata Atlantica, Brazil) known as "espinheira-santa". These plants are traditionally used as analgesic and antiulcerogenic medicine, with the same traditional uses of the true "espinheira-santa" (Maytenus ilicifolia, Celastraceae), an efficient antiulcerogenic agent. Pharmacological and toxicological studies with these plants have not been carried out. The purpose in this study was to evaluate the efficacy (analgesic and antiulcerogenic activities), safety (acute toxicity) and quality (phytochemical profile) of these three plants. The analgesic effect was analyzed by writhing and tail flick tests, while antiulcerogenic effect was performed through ulcer induction by ethanol and indomethacin/bethanecol assays. LD(50) and acute toxic effects, as well as phytochemical profiles of all plants also were carried. Surprisingly, the three plants showed analgesic and antiulcerogenic effects at dose of 1000 mg/kg, v.o. Maytenus aquifolium lowering all ulcerogenic parameters (ethanol test), but increased the ulcerogenic effects in the indomethacin/bethanecol test. Sorocea bomplandii produced antiulcerogenic effects in both experimental models used, while Zolernia ilicifolia showed significant effects only in indomethacin/bethanecol-induced gastric lesions. Pre-treatment with Zolernia ilicifolia induced someone toxic effects. A phytochemical profile for each plant species was determined and its main chemical classes of compounds were described.