

Espinheira Santa

Monograph 3/1/04

Maytenus ilicifolia

Family: Celastraceae

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

Standard Common Name: Holy thorn - North American (Herbs of Commerce, 2nd edition)

Other Common Names: Espinheira santa (Herbs of Commerce, 2nd edition)

Additional Common Names: Cancerosa, cangorosa, congorosa, chuchuwasi, limaosinho, maiteno.

Overview

Botanical Description

Espinheira santa is a small, shrubby evergreen tree growing up to 5 m in height with leaves and berries that resemble holly. It is native to many parts of South America and is a popular garden plant because of its attractive, holly-like appearance.

Ethnobotanical Uses

The leaves, bark and root have traditionally been attributed by traditional herbal medicine practitioners to have the following properties and actions: antacid, antiasthmatic, antifertility, anticancerous, antiseptic, antitumorous, antiulcerogenic, astringent, cicatrizant, depurative, estrogenic, emmenagogue, stomachic and tonic.

The use of espinheira santa has been recorded in herbal medicine systems in the following countries:

Argentina,¹⁻⁴ Brazil,⁵⁻⁹ Paraguay^{10-18,4} and Uruguay.¹⁹

Summary of Traditional Uses of Espinheira Santa:²⁰

Entire Plant:	Abortifacient, acne, antiseptic, asthma, cancer, contraceptive, dyspepsia, emmenagogue, liver disorders, sialagogue, tumors, vulnerary.
Aerial Parts:	Acne, analgesic, anemia, cancer, cicatrizant, constipation, disinfectant, dyspepsia, gastritis, liver disorders, stomach disorders, tonic, ulcers.
Leaf:	Antiseptic, asthma, astringent, cholagogue, cholaretic, contraceptive, diarrhea, digestive, emmenagogue, gallbladder disorders, respiratory tract infections, sialagogue, spasms, urinary tract infections, vulnerary, wounds.
Branches:	Contraceptive.
Stembark:	Abortifacient, emmenagogue.
Rootbark:	Contraceptive.
Root:	Abortifacient, contraceptive.
Flowers:	Inflammation.

Primary Uses in Traditional Herbal Medicine Systems

Internal

Espinheira santa is widely sold in Brazilian stores and pharmacies today for ulcers and cancer. Several topical formulas for skin cancer are sold in Brazil with espinheira santa as the main active ingredient. It is also used for ulcers, as an antacid, as a laxative, as a colic remedy, to eliminate toxins through the kidneys and skin, to support kidney, adrenal gland, and digestive functions as well as an adjunctive therapy for cancer.^{3,4,7-9,20,21}

External

The leaf has been traditionally employed externally in some herbal medicine systems to heal wounds.¹⁹ It is considered by some herbal medicine practitioners to be antiseptic and vulnerary.^{1,5,19}

Chemistry

Espinheira santa is rich in terpenes, sesquiterpene alkaloids and flavonoids. Two alkaloids that have been the subject of attention are maytansine and mayteine. Other chemicals include: atropcangorosin A, dihydro-atropcangorosin A, 6'-7'-dihydro-atropcangorosin A, 6-benzoyl-6-deacetyl-mayteine, cangoaronin, cangorin A thru J, cangorinine E-1, cangorinine W-1, cangorinine W-II, cangorosin A, cangorosin B, celastrol, dispermol, dispermone, epigallocatechins, friedelan, friedelan acid derivatives, 22-hydroxytingenone, ilicifolin, ilicifolinoside A-C, kaempferol trisaccharides, kaempferol disaccharides, maitenine, maytanbutine, maytanprine, maytansine, maytenin, 20-alpha-hydroxy-maytenin, 22-beta-hydroxy-maytenin, maytenoic acid, maytenoquinone, phenoldienones, iso-pristimerin III, pristimerine, quercetin trisaccharides, salaspermic acid, oxo-tingenol, tingenone, iso-tingenone III, proanthocyanidins.²⁰

Various chemicals in espinheira santa have been documented with the following biological activities:

In vivo

Anticancerous Activity

Maytenin used topically in human adults showed activity against skin carcinoma and Kaposi's sarcomatosis.²²

Anti-inflammatory Activity

Celastrol suppressed adjuvant arthritis in rats.²³

Neurological Activity

In rats a celastrol fraction improved performance in memory, learning and psychomotor activity tests.²³

In vitro

Anticancerous Activity

Celastrol and pristimerin showed cytotoxic activity towards human colon adenocarcinoma (HT-29) cells.²⁴

Immunomodulatory and Anti-inflammatory Activity

Celastrol suppressed TNF-alpha and IL-1beta production by human monocytes and macrophages, and decreased induced nitric oxide production.²³ In addition it decreased the induced expression of class II MHC molecules.²³

Antioxidant

Celastrol had an antiperoxidative effect, being 15 times more effective than vitamin E, with an IC₅₀=7 mM.²⁵ It is able to prevent oxygen free radical damage to inner cell membranes by increasing the negative charge.²⁶

Antifertility Effect

The phytochemical celastrol inhibited sperm forward motility, capacitation, acrosome reaction and sperm penetration.²⁷

***In vivo and In vitro* Research and Pharmacological Actions**

Anticancerous Activity

Cytotoxic and Antitumor Activity

A rootbark methanol extract at 50 mcg/ml showed *in vitro* weak cytotoxic activity towards human oral epidermoid carcinoma (9KB); a 32% inhibition was seen.²⁸ A leaf and stem ethanol water extract had an ED₅₀<20 mcg/ml towards human oral epidermoid carcinoma (9KB) *in vitro*.²⁹ In another *in vitro* study cytotoxic activity was shown towards leuk-P388 (a predictor of antitumor activity), human oral epidermoid carcinoma (9KB) and chinese hamster lung V79 cell lines.³⁰ A hot water extract of the leaf at 0.1% showed activity in the artemia salina assay. The artemia assay system predicts antitumor activity.¹⁹

Antiulcer Activity

A leaf hot water extract administered intragastrically or intraperitoneally to rats at 136-340 mg/kg inhibited indomethacin-induced gastric ulcers.³¹ Eighty-five mg/kg given intraperitoneally to rats inhibited cold-restraint stress induced ulcers. At

125 mg/kg intragastrically both HCL- and ethanol-induced gastric ulcers were inhibited.³² Extracts given orally increased volume and pH of gastric secretions and reduced the ulceration index.^{31,33} This activity has been patented.³²

Central Nervous System Activity

A hot water leaf extract given intraperitoneally to mice at 680 mg/kg potentiated barbiturates.³⁴ No activity was seen when 1.36 gm/kg was given intragastrically.

A leaf water extract given intraperitoneally to mice at 170 mg/kg had a tranquilizing effect (Rotarod test).³⁴ No activity was seen at 1.2 and 1.36 mg/kg.

Contraceptive Effect

A water extract of leaf and twigs given intraperitoneally to female rats at 100 mg/kg had an anti-implantation effect and inhibited fertilization.³⁵ Chloroform and ether extracts had no effect.

A lyophilized hydroalcoholic extract of the leaf given orally to mice at 1000 mg/kg caused pre-implantation embryonic loss but had no effect on implantation or organogenesis.³⁶ A mild estrogenic effect was seen at this dose.³⁶ However water, ether and chloroform extracts between 25 and 100 mg/kg had no effect on the estrous cycle.³⁵

Patents Filed / Pending

A European patent has been filed on the anti-ulcerative effect of a methanol extract, aqueous component and chloroform component of espinheira santa on gastric mucosa lesions caused by ethanol.³²

Mechanism of Action

Antiulcer activity

Volume of gastric secretions and pH increased.^{32,33}

Central Nervous System Activity

Barbiturate-like activity seen.³⁴

Contraceptive Effect

In large doses espinheira santa may interrupt the estrous cycle.^{9,35,36}

Dosage

Internal

Crude Preparations, Leaves.

2-3 grams twice daily.

Decoction: 1 cup 2-3 times daily.

External

Leaf decoction applied externally as needed.

Duration of Administration

Duration of administration varies per complaint. No adverse effects have been reported with long-term ingestion.

Contraindications

Pregnancy and Lactation: May have an antifertility effect and may interrupt or enhance the estrous cycle.^{9,35,36} Traditionally the plant has been used to induce abortion and promote menstruation, therefore it should not be used during pregnancy. It is not known which chemicals are passed through breast milk, or their safety if ingested by an infant, therefore espinheira santa should not be used during lactation.

Drug Interactions

May potentiate barbiturates when injected (no effect seen when given orally).³⁴

Side Effects

None reported.

Safety Rating

Not rated.

In a toxicity assessment a benzene extract of the aerial parts of espinheira santa given IP to rats had an LD50 of 0.10 mg/kg. Given orally the LD50 was 1 gm/kg. A hot water extract given orally to rats was inactive, with an LD50>1 gm/kg. A methanol extract given IP to rats had an LD50 of 0.86 gm/kg. It was inactive when given orally, with an LD50>1 gm/kg.³⁷ In another study a water extract was given IG to mice at 1.09 gm/kg and 272 mg/kg; no toxicity was seen.³⁴

The chemical maytansine has shown embryotoxic and teratogenic activity in mice when given 0.36 μ moles/kg intraperitoneally on day 6, 7 or 8 of gestation.³⁸

No mutagenic activity was seen for a water extract at 100 mg/plate.⁶ The plant is considered to be antimutagenic.³⁹

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