Simarouba
Simarouba amara, glauca

Family: Simaroubaceae
Synonyms: Quassia simarouba, Zwingera amara, Picraena officinalis, Simarouba medicinalis
Other Common Names: Aceituno, bitterwood, bois blanc, bois amer, bois frene, bois negresse, caixeta, cajú-rana, cedro blanco daguilla, dysentery bark, gavilan, malacacheta, marubá, marupá, negrito, palo blanco, palo amargo, paradise tree, pitomba, robleceillo, simaba.

Overview

Botanical Description
Simarouba is indigenous to the Amazon rainforest and other tropical areas in Mexico, Cuba, Haiti, Jamaica and Central America. It grows up to 20 m high and has a trunk 50 to 80 cm in diameter. It produces bright green leaves 20 to 50 cm in length, small white flowers, and small red fruit.

Ethnobotanical Uses
In traditional herbal medicine systems the bark, wood and leaves of simarouba have been used for their amoebicide, analgesic, anthelmintic, antibacterial, antidysenteric, antimalarial, antimicrobial, astringent, febrifuge, stomachic, sudorific, tonic and vermifuge properties.

The traditional use of graviola has been recorded in herbal medicine systems in the following countries: Guiana, Belize, Brazil, Cuba, French Guyana, Haiti and Peru.

Summary of Traditional Uses of Simarouba:

Bark: Anemia, anorexia, bitter, diarrhea, dysentery, dyspepsia, emmenagogue, fever, hemorrhages, internal bleeding, intestinal worms, malaria, skin sores, sores, stomach and bowel disorders, tonic, wounds.

Leaf: Astringent, colitis, diarrhea, digestive, dysentery, emmenagogue, intestinal worms, malaria, skin affections.

Root: Diarrhea, dysentery, flatulence, intestinal worms, malaria, stomach pain, tonic.

Primary Uses

Internal
A bark tea is primarily used as the first line of defense for amebic dysentery and diarrhea. It’s also used for viruses.

External
The bark has been traditionally used in herbal medicine systems externally for wounds and skin sores.
Chemistry

The main active group of phytochemicals in simarouba are the quassinoids, which belong to the triterpene chemical family. Ailanthinone, glaucarubinone and holacanthone are considered some of the main active quassinoids in simarouba. Other chemicals include: benzoquinone, canthin, dehydroglaucarubinone, glaucarubine, glaucarubolone, melianone, simaroubidin, simarolide, simaroubin, simarubolide, sitosterol and tirucalla.12

Various chemicals in simarouba have been documented with the following biological activity:

Anticancerous Activity
Antitumor / Antileukemic Activity
The quassinoids glaucarubinone and alianthinone demonstrated in vitro antitumor activity.14 The quassinoids glaucarubinone and dehydroglaucarubinone have demonstrated activity in vitro towards murine leukemia and murine lymphocytic leukemia P388.15-17

Cytotoxic Activity
The cytotoxic activity has been attributed to the quassinoids, in particular glaucarubinone, alianthinone and holacanthone. Isolated from the bark these quassinoids have shown cytotoxic activity in numerous in vitro studies, in particular towards murine solid tumor cells, human solid tumor cells, human epidermoid carcinoma of the nasopharynx and multidrug resistant murine mammary tumor cells.14,15,18

In vivo and In vitro Research and Pharmacological Actions

Anticancerous Activity
Antitumor Activity
A methanol extract of the bark had an LD50= 7.38 ppm in the artemia salina assay system; a system that predicts antitumor activity.19

Cytotoxic Activity
An ethanol-water extract of simarouba root demonstrated cytotoxic activity towards human oral epidermoid carcinoma Ca-9KB at ED50<20 mcg/ml.20 A water extract of the seeds showed activity towards the same tumor cell line at ED50<20 mcg/ml.20 A water extract of the bark was cytotoxic at 10% towards human cervical adenocarcinoma (hela) cells.21

Antimicrobial & Antiprotozoal Activity
Antiviral
Bark water extracts are active in vitro towards the herpes virus, influenza virus, poliovirus and vaccinia virus.22

Antiamoebic
Hot water extracts of the bark given orally to humans with Entamoeba histolytica cured 3 out of 7 cases after 7 days of treatment.23 A water extract of the seed given orally to humans with Entamoeba histolytica was 91.8% effective.24 In vitro various extracts of the stem were active against Entamoeba histolytica at IC50=2.9 - 52.5 mcg/ml.25

Antibacterial
Water-ethanol bark extracts at 50 mcl/plate were active against Salmonella typhosa and Shigella flexneri.26

Antimalarial
Chloroform and water extracts of the wood, bark and twigs of simarouba demonstrated strong antimalarial activity when given orally or subcutaneously to chickens infected with Plasmodium gallinaceum. Active doses given...
ranged from 1.5 mg/kg - 500 mg/kg. A chloroform and methanol extract of the fruit was active against chloroquine resistant *Plasmodium falciparum*; the methanol extract was active at IC50=0.05 mcg/ml. In mice the methanol fruit extract given orally at 900 mg/kg was active towards *Plasmodium berghei*. In another study simarouba was active in both chloroquine-susceptible and resistant forms of *Plasmodium berghei* in mice.

**Skin Hydration Effect**
A water extract of the root bark at 10 mcg/ml increased cholesterol sulphate, cholesterol and ceramide content in keratinocyte cell cultures. At 25 mcg/ml transglutaminase activity was stimulated. Used externally in human female adults the extract (at 0.2%) had a skin moisturizing effect.  

### Patents Pending / Filed

There have been a number of patents filed on quassinoids and simarouba. In June 2003 a patent was filed on therapeutic quassinoid preparations with antineoplastic, antiviral and herbistic activity. In 1988 a patent was filed on quassinoids as novel anti-ulcer agents. A patent has also been filed on a simarouba extract as a cosmetic or pharmaceutical; simarouba is noted as having significant skin depigmentation activity with the ability to enhance the protective function of the skin (water barrier function) and keratinocyte differentiation.

### Mechanism of Action

**Anticancerous Activity**
Activity is attributed to the quassinoids.

**Antimicrobial & Antiprotozoal Activity**
Antimicrobial, antiamebic and antiprotozoal activity is attributed to the quassinoids. In malaria the quassinoids are able to inhibit protein synthesis and nucleic acid synthesis in human erythrocytes infected with *Plasmodium falciparum*.

**Skin Hydration Effect**
Extracts are able to increase cholesterol sulphate, cholesterol and ceramide content in keratinocyte cell cultures and stimulate transglutaminase activity. Transglutaminase isoenzymes are necessary for forming the horny layers of the skin, essentially acting as ‘super glue,’ cross-linking structural proteins and attaching lipids to the proteins. Abnormal transglutaminase activity is seen in skin conditions such as psoriasis and ichthyosis.

### Dosage

**Internal**
Crude Preparations, Bark
Decoction: 1 cup taken 2-3 times daily
Tincture: 5-10 mls twice daily

**External**
Bark Decoction: Apply topically as needed

### Duration of Administration

Duration of administration varies per complaint and individual. No adverse effects have been noted in the literature with long-term ingestion of simarouba.

Contraindications

Pregnancy and Lactation: No adverse effects during pregnancy and lactation are reported, however, simarouba is bitter and the effect of the quassinoids during pregnancy and lactation is not known. It is advised that this plant not be used during pregnancy and lactation.

Drug Interactions

None reported.

Side Effects

Side effects at high doses (approximately three times the traditional remedy) include increased perspiration and urination, nausea, and/or vomiting.\(^{37}\)

Safety Rating

Not rated.

References


35. Richard, Gabriele. Recent advances in molecular genetics of Ichthyosis. The Foundation for Ichthyosis and related skin types. www.scalyskin.org


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