



Pau d'Arco

Scientific name: *Tecoma ocheracea*, *Tecoma ipe*, *Tabebuia cassinoide*, *Tabebuia avellanedae*.⁽¹⁾

Family: Bigniaceae (trumpet creepers).

The taxonomy division of the plants within the Bigniaceae family is confusing and the literature often interchanges the genera of *Tecoma* and *Tabebuia*. The four species of these genera have been identified and are sometimes referred as lapachol, which is the active ingredient of these plants.^(1,2)

Common names: Taheebo, LaPacho morado, Lapacho Colorado, ipe Roxo.⁽¹⁾

General description:

Tabebuia is a large genus of the tropical trees that grows worldwide. According to one source the correct name of the species is *T. impetiginosa*, however, the literature often refers to as *T. avellanedae*. The tree from which lapacho is obtained can grow up to 125 feet tall and has rose to violet colored flowers, which bloom before new leaves appear. There are about one hundred species of this evergreen tree native to the tropical America, which makes it hard to identify for the people who cultivate it. The active ingredient of this plant is derived from the inner bark. The outer bark does not have all the ingredients found within the inner bark. The tree grows widely throughout tropical South America and it is hard, durable and attractive with extreme resistance to insects and fungal growth.^(1,2,3)

Chemistry:

The heartwood of *Tabebuia avellanedae* contains chemical compounds called naphthoquinone such as lapachol, as well as significant amount of antioxidant quercetin.

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Lapacho was isolated from the heart of the wood of the species in 1882 and other related naphthoquinones have been found in the wood. The inner bark has a distinct group of furanonaphthoquinones not found in the wood and these compounds are more likely to be responsible for the bioactivity observed in Pau d' arco. The major components of the *T. avellanedae* are the 16 quinones containing both naphthoquinones and anthraquinones. Both groups of the quinines rarely occur in one plant and the lapachol content of the plant is approximately 2-7%. (4,6)

Mechanism of Action, Indications and Efficacy

Antitumor Activity:

Like camptothecin and topotecan beta lapachone inhibits DNA topoisomerase I. Topoisomerase inhibitors including beta-lapachone seem to be effective against several types of cancer including lung, breast, colon and prostate cancers and malignant melanoma. Lapachol is theorized to block pyrimidine biosynthesis through inhibition of dihydrofolate dehydrogenase. It is believed that the antitumor activity of lapachol to be due to interaction with nucleic acids. Also it is proposed that interaction of the naphthoquinone moiety between base pairs of the DNA helix occur with subsequent inhibition of DNA replication and RNA synthesis. However, since these compounds have high toxic side effects such as severe anemia and nausea their use in humans has been limited. On the other hand, researchers have found that a close relative compound, 3-allyl-beta-lapacho, to have lower toxicity in cell culture tests and therefore may be more useful than lapachol. (1,4,5)

Lapachol has also been extensively tested for antitumor activity in a variety of animal models. It has been found to have antitumor activity against Walker 256 carcinoma and sarcoma Yoshida, and no significant effect in other tumor models such as leukemia and adenocarcinoma. According to one study it was reported that lapachol analogs increased the life span of mice inoculated with leukemic cells by over 80% compared to the control group. However, this study has not been confirmed with other investigators. (7)

Antimicrobial and antifungal activity:

Lapachol like many naphthoquinones it interferes with the electron transport system and inhibits cell respiratory mechanism. In a study that was done in the 1940's, it was found that lapachol at 100mg/ml concentration to inhibit the uptake of oxygen in *Plasmodium Knowles* by 74% and the succinate oxidase system by 26%. These findings lead to the conclusion that lapachol exhibits antimalarial activity against *Plasmodium lapohuriae* via respiratory inhibition as a likely mechanism. However, the exact mechanism of action has been controversial. It is hypothesized that lapachol either inhibits the interaction between the cytochromes b and c or directly inhibits an unknown enzyme between the two cytochromes. (1,5)

In addition to its reported antitumor activities, Pau d' arco clearly has demonstrated broad clinical actions against a number of disease-causing organisms, which supports its wide uses in herbal medicine. Antimicrobial properties of many active phytochemicals were demonstrated in several trials, in which they exhibited strong in vitro activity against various gram-positive and gram-negative bacteria, fungi, and yeast (including

Candida albicans, *Candida tropicalis*, *cryptococcus neoformans*). Analog of lapachol (furanonaphthoquinone) extract from the tree bark was shown to significantly lower MIC against methicillin-resistant *Staphylococcus aureus* (MRSA) strain compared to methicillin-sensitive *Staphylococcus aureus* (MSSA). The finding was statistically significant with a p value of <0.01. Also it was found that lapachol has efficacy against *H.pylori*, *Staphylococcus*, *Streptococcus*, *Enterococcus*, *Bacillus* and *Clostridium* species with MIC ranging from 1.56 to 25mcg/ml. In addition it was reported that lapachol has a relevant effect against *Candida albicans*, *Candida tropicalis*, *cryptococcus neoformans*, etc, that was similar to Amphotericin B. The presumed antifungal activity of lapachol is believed to be due to its interaction with the cellular membrane. (8,9,10)

Nociceptive

In South American herbal medicine Pau d'arco has been used as an analgesic for a period of time. Its mechanism of action is not known but believed to be due to its effect on the adenosine system. Recently the inner bark aqueous extract was shown to have some antinociceptive effect in animal models. The aqueous extract was administered orally to study animals in three different concentrations namely 100, 200 and 400 mg/kg, which reduced the nociception produced by formalin by 49.9%, 63.7% and 43.8%, respectively, (the formalin model is the most used model to explain pain and analgesia mechanism, with better results than the ones using mechanical stimulation). (11)

Antiviral:

Lapachol has been stated to be active against certain viral strains including herpes virus types I and II. Naphthoquinones have been documented to show effectiveness against four strains of the flu, polio and vesicular stomatitis virus. The mechanism of action of these quinolones is supposed to be via DNA and RNA polymerase inhibition and retrovirus reverse transcriptase. Further Beta- lapachone is presumed to interfere with the replication of HIV-1 virus via transcriptase inhibition.(4,12)

Pau d'arco and its chemicals also have demonstrated in vitro antiviral properties against various viruses, including Herpes I and II, influenza, poliovirus, and vesicular stomatitis virus. It is reported that lapachol decreases the replication of viruses in human subjects however there is no available clinical data. (12)

Anti-inflammatory and antipsoriatic activity:

T.avellanadae is believed to have inhibitory effect on the histamine releasing cells, which leads to anti-inflammatory effects. According to one in vitro study lapachol and its analogs were shown to have antipsoriatic effect by inhibiting the growth of human keratinocyte cell line HaCaT and reducing inflammations. The authors of the study concluded that lapachol has similar antipsoriatic activity as anthralin in inducing damage to the cell membranes of the keratinocyte cells. However, the authors did not report the degree of similarity or difference between the two agents. (13)

Antiparasitic activity:

Lapachol has been used as a topical barrier to trematodes specifically *Shistosoma mansion*, which causes schistosomiasis. This parasite lives in water and enters the host by penetrating through the skin. This pathogen can cause a complicated disease, which can

sometimes be fatal. Also it is stated that oral lapachol formulation to be effective against skin penetration. In addition, lapachol is claimed to have some effect against *Trypanosoma cruzi*, which causes trypanosomiasis or Chaga's disease. This disease can present in acute or chronic forms and has no known cure to date. (1) However, there is no documented data available in either humans or animal models.

Dosage

Children: There are no known scientific reports on the pediatric use of Pau d'arco. Therefore this herb is not currently recommended for children.

Adults: the usual form of administration of lapachol is as a decoction. The standard dose is 1 cup of decocted bark two to eight times/day. The decoction is made by boiling 1 tsp of lapachol for each cup of water for 5-15 min. (1)

The more accurate dosage is based on lapachol content of 2-4% would be 15-20 g of bark boiled in 500 ml of water for 5- 15 min three times daily. (1)

Dosage of other forms should be based on lapachol content providing a daily lapachol intake of 1.5 – 2.0 g/day. (1)

Capsule in 500 mg – 2 caps. two to three times daily. (6)

Fluid Extract 1-2 ml per serving three times daily (inner bark extract) (6)

Tincture (1:5) solution made from herb and alcohol, or herb, alcohol and water, take 20 to 30 drops, two to three times a day. (6)

Drug and Disease Interaction

The only drug interaction that has been documented is with anticoagulation therapy. There is no documented contraindication of lapachol in any disease conditions even though it is supposed to undergo liver metabolism. (2)

Contraindications

There have been no reports in the literature of contraindications when a whole-bark decoction or tincture is used. However, at least one isolated phytochemical in Pau d'arco, lapachol, has demonstrated abortifacient properties in animal studies. As there are no studies confirming the safety of traditional bark decoctions used by pregnant women (nor is there indication in traditional medicine systems using this plant during pregnancy), the use of Pau d'arco during pregnancy is not recommended.

Also large single dose of Pau d'arco (decoctions of more than one cup) may cause gastrointestinal upset and/or diarrhea. It is recommended that high dose of Pau d'arco use is avoided. (3)

Toxicology:

The toxicology of lapachol was studied extensively and hemolytic anemia was found to be the main limiting toxicity in animal studies. Human toxicity was seen at doses of greater than 1.5g per day. (2)

Summary:

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The chemical ingredients and constituents of Pau d'arco have been well documented. In the 1960's it was researched for use in various types of cancer. The plant contains a large percentage of chemicals known as quinoids, and anthraquinones, benzoids and flavonoids. The quinoids have shown the most documented biological activity and are seen to be the center of the plant's efficacy as an herbal remedy. In the 1960's the extract of the heartwood demonstrated marked antitumor effect in animals, which drew the interest of the National Cancer Institute. (3)

Comments:

Pau d'arco is an important resource from the rainforest with many applications in herbal medicine. Unfortunately, its popularity and use have been controversial due to varying results obtained in with its use. For the most part, it could be due to lack of quality control and confusion to which part and which particular species of the genera and how to prepare it. Many species of the Tabebuia, as well as other completely unrelated tree species are exported today from S. America as Pau d'arco. Thus having few to none of the active constituents of the true medicinal part of the plant. The inner bark shaving commonly sold in the U.S. are actually by-products of the lumbar industries. In 1987, a chemical analysis of 12 commercially available Pau d'arco products revealed only one product containing lapachol and only in trace amounts. The typical lapachol concentration is 2-7% in true Pau d'arco, the authors of the study stated that the products were not truly Pau d'arco or that the processing and transportation had damaged them. Most of the studies in Pau d'arco are centered on the heartwood of the tree. However most of the commercially available products contain the inner and the outer bark of the tree. This may explain varying species of the Pau d'arco bark are being sold as herbal products and their diminished results in studies and use.(14)

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