

Guazuma Ulmifolia: A Review on its Traditional uses, Phytochemistry and Pharmacology

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ABSTRACT

Mutamba (*Guazuma ulmifolia* Lam.) is perhaps the most useful traditional medicinal plant in India. During the last five decades, apart from the chemistry of the mutamba compounds, considerable progress has been achieved regarding the biological activity and medicinal applications of mutamba. The extracts and metabolites of *Guazuma* particularly those from leaves and bark possess several useful bioactive compounds and recently additional data are available on exploitation of these compounds in the various biological activities including antibacterial, antiviral, antifungal, anti-inflammatory, antisecretory, antitumor, antioxidant and cytotoxicity. It is now considered as a valuable source of unique natural products for development of medicines against various diseases and also for the development of industrial products. This review gives a bird's eye view mainly on the biological activities of some of the mutamba compounds isolated, pharmacological actions of the mutamba extracts, clinical studies and plausible medicinal applications of mutamba along with their safety evaluation.

Keywords: *Guazuma ulmifolia*; Mutamba; Biological activity; Proanthocyanidins

INTRODUCTION

Medicinal plants are part and parcel of human society to combat diseases, from the dawn of civilization. Plants and plant-based medicaments are the basis of many of the modern pharmaceuticals we used today for our various ailments [1,2]. "Let food be your medicine and let medicine be your food" was advised by the father of medicine, Hippocrates, over two millennia ago. It's still true today that "you are what you eat." Folk medicine in different cultures has a long history of ancestors creating primitive medicines during their struggles against natural calamity and disease. *Guazuma* is one of the ancient medicinal herb used as folk medicine. *Guazuma ulmifolia* Lam. is well known in India for more than 2000 years as one of the most versatile medicinal plant having a wide spectrum of biological activity. The former is popularly known as "Bastard cedar" (in english), "mutamba" (in Portuguese) and Rudrakshi (in hindi). It is a member of Sterculiaceae family that grows in Ecuador, Panama and other Latin American countries from bush to tree size.

It is a favorite natural remedy among central and South American health practitioners and the indigenous peoples of the Amazon, often turned to first for upper respiratory infections as it can quiet coughs, reduce fever, as well as provide antiviral and antibacterial action [3]. The flowers and leaves of *Guazuma ulmifolia* are also used as a remedy for different conditions, such as kidney and

gastrointestinal diseases, fever and diabetes [4].

BOTANICAL DESCRIPTION

Guazuma ulmifolia grows to 30 m in height and 30-40 cm in diameter with a round-shaped crown. The alternate, ovate to lance-shaped leaves are 5-7 cm long and 2-5 cm wide, with finely saw-toothed margins. The flowers are brownish-yellow and form in clusters at the base of the leaves. The seeds are black, round to elliptic, 1.5-3 cm long, and hard. Seed capsules contain 5 cells which open at the apex and contain many seeds, 3-5 mm in diameter [5,6]. Young twigs are covered with rust-brown or light-gray star-shaped hairs. The bark is gray or gray-brown and becomes furrowed and rough or slightly shaggy.

Distribution

A very common tree of farmland, sometimes forming nearly pure stands in abandoned pasture. There are many along the road from Panama to Gamboa and quite a few in Gamboa. Fairly common inside secondary forest, and, remarkably, there are few individuals in the old forest on Barro Colorado Island. *Guazuma ulmifolia* is also found in the Caribbean, Mexico, Central America and Colombia, Ecuador, Peru, Bolivia, Paraguay, Argentina, and Brazil [7]. It has been cultivated in India for over 100 years. It has been

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introduced recently to Indonesia.

PHYTOCHEMISTRY

Although a large number of compounds have been isolated from various parts of mutamba, a few of them have been studied for biological activity as shown in Table 1. The structure of these bioactive compounds has been presented in Figure 1.

Table 1: Summary of traditional uses of Mutamba.

Part	Medicinal use
Bark	Alopecia, asthma, bronchitis, bruises, burns, childbirth, constipation, coughs, dermatosis, dermatitis, diarrhea, dysentery, elephantiasis, fevers, fractures, gastrointestinal pain, gonorrhoea, grippe, hemorrhage, hemorrhoids, hypertension, infections, influenza, kidney problems, leprosy, liver problems, malaria, nephritis, pneumonia, prostate problems, pulmonosis, skin conditions, stomach inflammation, stomachache, syphilis, ulcers, uterine pain, wounds.
Leaves	Alopecia, asthma, bruises, dermatitis, dysentery, erysipelas, fevers, inflammation, kidney diseases, liver diseases, skin eruptions, skin diseases, sores, ulcers, wounds.
Root	Childbirth.
Fruit	Diarrhea, hemorrhage, infection, uterine pain

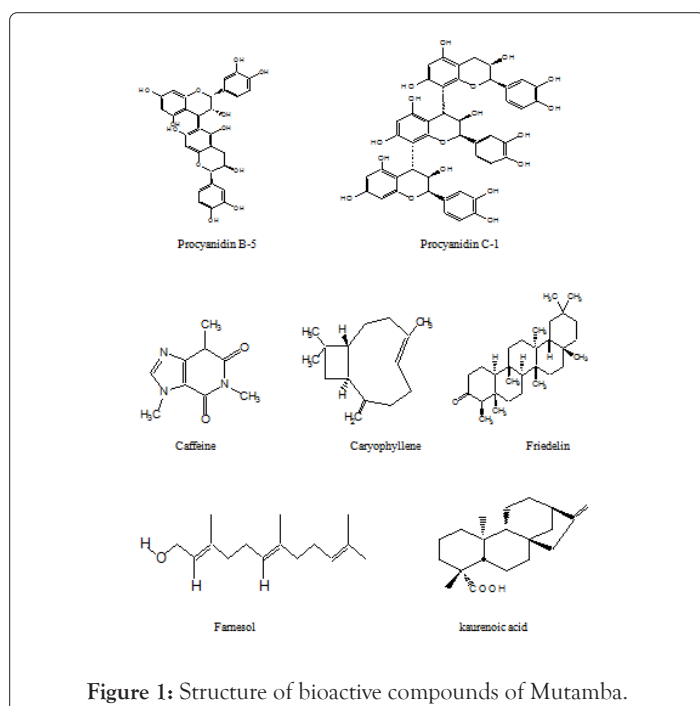


Figure 1: Structure of bioactive compounds of Mutamba.

Mutamba bark is rich in tannins and proanthocyanidins. Active constituent of the leaves is the alkaloid caffeine, which exhibits antioxidant properties. Beta-sitosterol, a phytosterol with anti-inflammatory and immunomodulator activity, is also present [8]. Furthermore, the essential oil in the leaf is rich in beta-caryophyllene (13.7%). This anti-inflammatory sesquiterpene has been proven to inhibit gastric mucosal lesions in rats when administered orally. Flavonoids such as quercetin, kaempferol and kaempferitrin, which possess anti-inflammatory, antiviral [9,10] and free radical-scavenging activity [11].

The main plant phytochemicals that have been found in various sections of the mutamba plant with their yield include: caffeine (alkaloid, quantity-0.14% from leaf), caryophyllene (sesquiterpene, quantity-13.7% from leaf), catechins (flavonoid, quantity-0.0673% from stem bark), epicatechins (flavonoid, quantity-0.00128%

from stem bark), farnesol (Sesquiterpene, quantity-06.6% from leaf), friedelin (triterpene, quantity-trace amount), kaurenoic acid (diterpene, quantity-trace, leaf), procyanidin B-2 (Flavonoid, quantity- 0.10769% from stembark), procyanidin B-5 (Flavonoid, quantity-0.00259% from stembark), procyanidin C-1 (Flavonoid, quantity- 0.0098% from stembark), sitosterol, kaempferol, quercetin, [7] etc.

TRADITIONAL AND MEDICINAL USES

In traditional medicine, the bark of *Guazuma ulmifolia* is used in the treatment of diarrhea, hemorrhages, fever, coughs, bronchitis, asthma, gastrointestinal pain and hypertension, and as stimulant for uterine contractions. Dried leaves are brewed into tea in some countries and used for kidney and gastrointestinal diseases, fever, dysentery and diabetes, and externally as an ailment for wounds, skin eruptions and even baldness. *Guazuma ulmifolia* leaves are also traditionally boiled as a treatment for diabetes and this method has been experimentally proven to decrease hyperglycaemia in rabbits. Currently, many countries with important biodiversity resources are developing and using non-toxic preparations from traditional medicinal plants for controlling various diseases, providing relief of symptoms comparable to that obtained from allopathic medicine. The Huastec Mayans of northeastern Mexico employ the fresh bark boiled in water to aid in childbirth, for gastrointestinal pain, asthma, diarrhea and dysentery, wounds, and fevers. Mayan healers in Guatemala boil the bark into a decoction to treat stomach inflammation and regular stomachaches. In the Amazon, indigenous people have long used mutamba for asthma, bronchitis, diarrhea, kidney problems, and syphilis. They use a bark decoction topically for baldness, leprosy, dermatosis and other skin conditions. Mutamba is a favorite natural remedy among Central and South American health practitioners and the indigenous peoples of the Amazon, often turned to first for upper respiratory infections as it can quiet coughs, reduce fever, as well as provide antiviral and antibacterial action. In Brazilian herbal medicine practices, a bark decoction is used to promote perspiration, cleanse and detoxify the blood, and to suppress coughs. There it is used for fevers, coughs, bronchitis, asthma, pneumonia, syphilis, and liver problems [3].

A bark decoction is also prepared and is used topically to promote hair growth, to combat parasites of the scalp, and to treat various skin conditions. Young leaves of this species are an occasional food of howling monkeys. The bark is used medicinally as a sudorific, against malaria, and a variety of other ailments. In Peru, the dried bark and/or dried leaves are made into tea (standard infusion) and used for kidney disease, liver disease, and dysentery. There the bark is also used topically for hair loss. In Guatemala, the dried leaves of the tree are brewed into a tea and drunk for fevers, kidney disease, and skin diseases, as well as used externally for wounds, sores, bruises, dermatitis, skin eruptions and irritations, and erysipelas. A beverage of crushed seeds soaked in water is used to treat diarrhea, dysentery, colds, coughs, contusions, and venereal disease. It is also used as a diuretic and astringent. The seeds are edible, fresh or cooked. The tough, fibrous bark and young stems are used to make rope and twine. Honey bees forage on the flowers [5]. The bark and leaves have traditionally been used for alopecia.

With a long history of effective uses in herbal medicine, researchers began studying mutamba's properties and activities in the laboratory beginning in 1968 and it has been the subject of numerous studies since. In the first study published, various water and alcohol Mutamba bark extracts demonstrated weak cardiac

depressant and cardiotoxic activity, as well as hypotensive, smooth muscle relaxant, and uterine stimulant activities in animal studies. Various leaf and bark extracts have clinically demonstrated *in vitro* antibacterial and antifungal activity against numerous pathogens in 5 different studies from 1987 to 1993. It also tested to have active properties against gonorrhoea *in vitro* [12-14]. A weak molluscicidal activity of the bark was documented in a 1974 study. Clinical and laboratory research has validated this traditional use [15-19].

PHARMACOLOGY

Although a large number of studies have been carried out on various biological activities of mutamba extracts and some of the isolated compounds in several animal models, a few reports are available on clinical studies with the extracts or the compounds and their medicinal applications. A number of studies have confirmed the antioxidant, antibacterial, antiviral, antisecretory, [17] and antihypertensive properties of *Guazuma ulmifolia* bark, mainly attributable to its content in polymeric proanthocyanidins, which consist of epicatechin units.

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

Antitumor activity

Procyanidin B-2 has shown *in vitro* antitumor activity [12,14]. In one study it showed activity towards melanoma cells PRMI-7951 with an ED₅₀ of 1.4 mcg/ml. No activity was seen towards lung carcinoma, ileocecal adenocarcinoma, epidermoid carcinoma of the nasopharynx and medulloblastoma.

Cardiovascular activity

Hypotensive activity may be due to the ability of bark extracts to inhibit the binding of angiotensin II to the AT₁ receptor. Binding has been inhibited by as much as 50%. This activity is thought to be due to the proanthocyanidins containing epicatechin units. In addition the compound procyanidin B-2 has been documented with blood pressure lowering activity through a decrease of sympathetic tone and direct vasodilatation [12]. In rats, intravenous procyanidin B-2 lowered blood pressure through a decrease of sympathetic tone and direct vasodilation [15]. An alcoholic and water extract of the bark had weak cardiac depressant activity on insect hearts and a water bark extract demonstrated hypotensive activity when given intravenously to cats. An alcoholic extract was inactive. Bark acetone extracts of 10 mcg/ml inhibited the binding of angiotensin II to receptor cells by more than 50% in an *in vitro* study.

Antimicrobial activity

Antifungal: In *in vitro* studies ethanol extracts of the fruit and bark, between 10-25 mcg, demonstrated activity against *Cladosporium cucumerinum* and *Penicillium oxalicum*.

Antibacterial: Leaf, bark and fruit extracts have demonstrated antibacterial activity at a range of concentrations, from 10 mcg-50 mg or 10 ml- 50 ml.

Antiviral: Procyanidin C-1 inhibited herpes simplex virus type 1 *in vitro* [19]. A methanol leaf extract at 100 mcg/ml demonstrated *in vitro* weak antiviral activity against the herpes simplex 1 virus.

Antioxidant activity

Procyanidin C-1 demonstrated antioxidant activity in lipid peroxidation and hydroxyl radical scavenging assays [19]. Mutamba

aqueous extracts demonstrated *in vitro* antioxidant activity, being able to scavenge DPPH and OH⁻ [20]. This activity may be due to its procyanidin content. Procyanidin C-1 has shown the highest antioxidant activity, inhibiting lipid peroxidation and hydroxyl radicals.

Hair growth promoting activity

The procyanidins in mutamba are thought to promote hair growth. This hair-growing activity of certain procyanidins is attributed to their ability to inhibit protein kinase C. Procyanidin B-2 and procyanidin C-1 are able to selectively inhibit protein kinase C. *In vitro* this results in hair epithelial cell proliferation, and anagen induction *in vivo*. *In vivo* studies in male humans using 1% procyanidin B-2 extract resulted in a 78.9% increase in hair diameter and in increase in the number of total hairs. In mice procyanidin B-2 promoted hair growth by 300%. Procyanidin C-1 in mice had a growth promoting effect of 220%. In other studies topical application of 1% procyanidin on shaven mice in the telogen phase led to hair regeneration-procyanidin B-2 increased regeneration by 69.6% and procyanidin C-1 by 78.3% [13]. Several *in vitro* studies have also demonstrated the hair growing effect of procyanidin B-2 and C-1. Procyanidin B-2 and C-1 down regulates protein kinase C isoenzymes (-alpha, -betaI, -betaII, -eta) in hair cells, promoting hair cell growth.

A US Patent was filed in 2003 on a hair growing agent containing a proanthocyanidin of one or more of the following: procyanidin B-1, procyanidin B-2, procyanidin B-3, procyanidin C-1 and procyanidin C-2. An *in vitro* study was cited in which procyanidin B-2 at 30 µmol/l had a relative cell growth rate of 310 on cultured mouse hair follicle cells (control 100).52

Antisecretory activity

The bark of mutamba has significant antisecretory activity in dysentery. It is able to completely inhibit cholera toxin-induced chloride secretion if delivered before administration of the cholera toxin. Mutamba directly interacts with the subunit of the cholera toxin, rendering it inactive. This activity is attributed to the procyanidins [17]. Ethanol extracts of the stem bark at 40 mcg/ml had an antisecretory effect in the rabbit colon, inhibiting cholera toxin-induced secretion.

Cytotoxic activity

In one *in vitro* study an ethanol extract of the leaf exhibited strong activity against human oral epidermoid carcinoma cells (Ca-9kb), inhibiting growth by 97.3% [16]. The cytotoxic activity of mutamba is attributed to the procyanidins, in particular procyanidin B-2 and procyanidin C-1 [14].

Anti-inflammatory activity

An ethanol bark extract demonstrated anti-inflammatory activity in the *in vitro* HET-CAM assay [20]. An ethanol-water leaf extract at 750 mcg/ml *in vitro* inhibited prostaglandin synthetase by 61.8%.

Antihyperglycemic activity

A decoction of the mutamba leaf given intragastrically to rabbits at 4 mg/kg reduced glucose-induced hyperglycemia; decreasing the hyperglycemic peak and the area under the glucose tolerance curve.

DOSAGE

Internal

Crude Preparations, Bark

1-2 grams of bark powder daily

Decoction-1 cup 2-3 times daily

Tincture: 2-3 ml twice daily of a 4:1 tincture

External

Crude Preparations, bark

Decoction applied topically 3-4 times weekly

CONTRAINDICATIONS

Mutamba bark has been documented with uterine stimulant activity in animal (rat) studies and should not be used during pregnancy [20]. It is not known if chemicals are passed through breast milk, or their effect, therefore it is advised that ingestion of mutamba be avoided during lactation.

Mutamba leaves contain a small amount (0.14%) of naturally-occurring caffeine. Those sensitive to or allergic to caffeine should not use mutamba leaves. Mutamba bark has been documented in an animal study to lower blood pressure. *In vitro* studies indicate that it can inhibit angiotensin II. People with low blood pressure should use with caution while monitoring their blood pressure accordingly.

CONCLUSION

Mutamba, the versatile medicinal plant is the unique source of various types of compounds having diverse chemical structure. Extensive literature survey revealed that *Guazuma ulmifolia* Lam., is an important medicinal plant with diverse pharmacological spectrum. Very little work has been done on the biological activity and plausible medicinal applications of these compounds and hence extensive investigation is needed to exploit their therapeutic utility to combat diseases. A drug-development programme should be undertaken to develop modern drugs with the compounds isolated from mutamba. Although mutamba have medicinal applications from time immemorial, modern drugs can be developed after extensive investigation of its bioactivity, mechanism of action, pharmacotherapeutics, toxicity and after proper standardization and clinical trials. As the global scenario is now changing towards the use of nontoxic plant products having traditional medicinal use, development of modern drugs from mutamba should be emphasized for the control of various diseases. In fact, time has come to make good use of centuries-old knowledge on mutamba through modern approaches of drug development. Quite a significant amount of research has already been carried out during the past few decades in exploring the chemistry of different parts of mutamba. Several therapeutically and industrially useful preparations and compounds have also been marketed, which generates enough encouragement among the scientists in exploring more information about this medicinal plant. An extensive research and development work should be undertaken on mutamba and its products for their better economic and therapeutic utilization for the welfare of the mankind.

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