Review Article

Calotropis gigantea Linn.: Phytochemical Composition, Traditional Uses and Pharmacological Applications

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ABSTRACT

Ayurvedic and traditional treatment systems make extensive use of *Calotropis gigantea* (L.) R.Br., a persistent herb of the family Asclepiadaceae. It is a plant, which prized for its medicinal adaptability, grows widely in a variety of ecological settings without the need for cultivation. Its round, light green leaves and smooth stem are among its physical characteristics. Its diverse pharmacological profile is attributed to the presence of resins, tannins, alkaloids, terpenoids, flavonoids and cardiac glycosides according to phytochemical tests. C. gigantea widely used in formulations of Ayurveda to treat conditions like leprosy, ulcers, tumours, piles, fever, asthma, and skin conditions. Its traditional use is further supported by contemporary pharmacological research that reports antioxidant, antibacterial, antimalarial, cytotoxic, analgesic, anti-inflammatory, antipyretic, wound-healing, anti-diarrheal, antitussive, and insecticidal properties. This review shows the plant's potential as a valuable medicinal and Economic resource by summarizing its morphological and phytochemical characteristics, investigating its therapeutic uses, and highlighting its significance in Ayurvedic formulations.

Keywords: *Calotropis gigantea*, Milkweed, Sweta, Arka, Giant Milkweed, Potential herb, Crown flower.

INTRODUCTION

Calotropis, also referred to as milkweed or Aak, is a genus in the Apocynaceae family with substantial therapeutic value. The characteristic that gives these plants their common name, "milkweed".

Figure 1: *Calotropis gigantea* [plant and flower]

In ancient Ayurveda, it is a well-known and well-documented herb. This gives any research or product development a solid, well-established base. Parts Used: Traditional remedies for various illnesses make use of almost every part of the plant, including the root bark, leaves, flowers, and even the milky latex. The two main species *Calotropis procera* [Rakta Arka] and *Calotropis gigantea* [Sweta Arka] both of which are significant in Ayurvedic toxicology and medicine. *C. sussuela* and *C. Acia* are two other species in the genus. Medicinal plants are generally defined as those that have therapeutic qualities or provide positive physiological impact on the biological systems of animals or humans. Alkaloids, glycosides, tannins, volatile oils, minerals, and nutrients are among the secondary metabolites that these plants biosynthesize and accumulate, which add to their therapeutic and restorative value.

Calotropis gigantea is called Sweta Arka in traditional Ayurvedic literature, but Calotropis procera is called Raktha Arka. Many colloquial names, such as Akada, Aak, Mandar, and Aakh, are extensively used to identify it. [1]

Figure 2: *Calotropis gigantea* [leaf and fruit]

Geographical Distribution:

Calotropis gigantea is a widespread plant that grows in dry, sandy, alkaline soil in warm climates. It grows up to 900 meters above sea level in the plains and lower hills of India, including the Andaman Islands. For *C. gigantea*, a broad habitat with little competition is ideal. This type of plant can be found in arid environments where rainfall is limited to 150 to 1000 mm and in regions with overly drained soil where annual precipitation can reach up to 2000 mm.

Additionally, it can be found in common settings including seaside dunes, roadside sand dunes, and densely populated urban areas. *C. gigantea* can also be found at elevations reaching 1000 meters above sea level. The plant is sometimes planted as an ornamental in dry or coastal areas since it is easy to handle, reproduces, and may do well in xerophytic environments. It is cultivated in Eastern Asia, Africa, and South East Africa. It is indigenous to China, Malaysia, Indonesia, India, Sri Lanka, Iran, and Africa-Asia. [3]

Systematic Taxonomy of *Calotropis gigantea*, *Calotropis procera* and *Calotropis Acia*:

Table 1: Systemic Taxonomy of Calotropis [2]

Classification	*Calotropis gigantean*	*Calotropis procera*	*Calotropis acai*
Kingdom	Plantae-Plants	Plantae-Plants	Plantae-Plants
Sub kingdom	Trophobiont-Vascular plant	Trophobiont-Vascular plant	Trophobiont-Vascular plant
Super division	Spermatophyta-Seed plant	Spermatophyta-Seed plant	Spermatophyta-Seed plant
Division	Spermatophyta-flowering plants	Spermatophyta-flowering plants	Spermatophyta-flowering plants
Class	Magnoliopsida-Dicotyledons	Magnoliopsida-Dicotyledons	Magnoliopsida-Dicotyledons
Sub class	Asteroidea	Asteroidea	Asteroidea
Order	Gelatinases	Gelatinases	Gelatinases
Family	Apocynacea	Apocynacea	Apocynacea
Sub family	Asclepiadoideae	Asclepiadoideae	Asclepiadoideae
Tribus	Asclepiadean	Asclepiadean	Asclepiadean
Sub tribus	Asclepiadean	Asclepiadean	Asclepiadean
Genus	CalotropisR.Br-Calotropis	CalotropisR.Br-Calotropis	Calotropis
Species	*Calotropis gigantea*	*Calotropis procera* (Aiton).W. T. Aiton-rooster tree	Acacia

Microscopic Features:

Table 2: Systemic Taxonomy of Calotropis [2]

Roots	The roots are cylindrical, tortuous and often branched, externally yellowish grey while internally ceramic white and about 90cm in length and 2.5-10cm in diameter
Roots Bark	Is short, curved and is more rarely quilled pieces, 2-5 mm thick and 3-5cm broad and has distinctly mucilaginous, bitter taste.
Leaves	The leaves are broadly elliptical to oblong-obovate in shape, with the size of 9-20cm x 6-12.5cm but sub sessile.
Habit	Shrub or a small tree up to 2.5m (max.6m) height.
Flowers	Bracteate, complete, bisexual, actinomorphic, pentamerous, hypogynous, pedicellate, pedicel 1-3cm long.
Fruits	A simple, fleshy, inflated, sub globose to obliquely ovoid follicle up to 10cm or more in diameter.
Seeds	Numerous, 6 by 5mm, broadly ovate, flattened narrowly margined, minutely tomentose, brown coma 2.5-3.2cm long
Cymas	Are 5-12.5cm in diameter
Calyx	Has five sepals and lobe, shortly united at the base
Corolla	Petals five, gamopetalous, five lobed, twisted aestivations.

Propagation constituents:

Gigantea and planting:

The technique of creating new plants from different plant parts is known as plant propagation. Cuttings from the stem or seeds are used to propagate *Calotropis gigantea*. Water, wind, or wasps, bees, and butterflies typically pollinate the seeds.

Additionally, it was multiplied using the plant tissue culture approach. Natural regeneration occurs frequently. Vegetative propagation, which involves cutting roots and stems, is a particularly useful method for multiplying better genotypes on a wide scale.[5]

Chemical Constituents:

It consists of cardenolides, oxypregnane–oligoglycosides, triterpenoids, terpenes, terpenes esters, flavonoids, sterols, proteinases, cardiac glycosides, aromatic product, carbohydrate, resin, fatty acids and nonprotein amino acids etc. Chemical components: Kadiyala et [2013] have reported the presence of phytoconstituents such as 19-nor-10-hydrocalactinic acid methyl ester, uzarigenin, calactin

acid methyl ester, 19-carboxyl- calactinic acid methyl ester, 18,20-epoxycalotropin, calactin, calotropin, 15β-hydroxycitric- pin, 2α,15β-dihydroxy-19-oxo-uzarigenin, 19-nor-2α,10,15β-trihydroxy uzarigenin, 19-nor-10-hydroperoxy-2α, 15β-dihydroxy uzarigenin, 15β-hydroxycalactinic acid, 16α-hydroxylian- tinic acid methyl ester, 16α-hydroxycalotropagenin, calactinic acid, 12β-hydroxycoroglauci- genin, calotropagenin, frugoside, 6'-O-(E-4-hydroxycinnamoyl)desglucouzarin, coroglauci-genin, calotoxin, 16α-hydroxycalotropin, 9,12,13-trihydroxy octadeca-10(E),15(Z)-dienoic acid, R-(-)-mevalonolactone, calotroposide A, calotroposide B, calotroposide C, calotroposide D, calotroposide E, calotroposide F, calotroposide G, calotropisesquiterpenol, calotro pisesterter- penol, γ-taraxasteryl acetate, giganticine, calotropbenzofuranone and calotropnaphthalene. Other reported chemical constituents from *C. gigantea*. [4]

Materials and methods

C. gigantea sampling:

Fresh leaves were collected by carefully chopping and packaging them. For the following procedure, the samples were transported to the lab. [5]

1. Extraction process:

For seven days, the leaf samples of *C. gigantea* were dried in an area shielded from the sun. The leaves are ground into a powder known as simplisia once they have dried. Set up three containers, weigh *C. gigantea* simplisia powder about 200 grams in each, after that use 2000 ml of ethanol, ethyl acetate, and n-hexane solvents to extract (macerate) powder for 72 hours, or three days. Following the maceration procedure, filter paper and a Buchner funnel were used to filter the extract. To filter the extract, there was a rotary evaporator was employed which producing a concentrated extract that was then utilized for phytochemical screening.

Extraction yield [%] calculated by using the formula:

$$\% \text{ Extraction Yield} = \frac{\text{mass of extract mass of dried}}{\text{mass of dried}} \times 100\%$$

1. Maceration:

This extraction technique involves adding a solvent to coarsely crushed plant material, such as leaves, until the plant material is completely submerged. Seal the jar containing the extract and store it for a minimum of three days. The mixture is kept in a jar after being periodically mixed. It should be occasionally shaken for the full extraction. After extraction, marc and micelle are separated by decantation or by filtration. After that, the micelle is extracted from the menstruum by evaporating it in an oven or water bath.

2. Decoction:

Before putting the plant material in a sanitized container, this extraction method entails drying, grinding, and powdering it. Before heating it, a suitable solvent is added and constantly agitated for a few minutes. The process usually takes 20 minutes. Usually, a solvent to crude drug ratio of 4:1 or 16:1 is used. Plant material that is soluble in both water and heat is extracted using this technique. This technique works well for removing plant material that is heat-stable and readily soluble phytochemicals. [6]

3. Phytochemical screening

Phytochemical testing is used to determine a plant's secondary metabolite content qualitatively. In this case, there are several tests such as – phenolic test, tannins, terpenoids, steroids, saponins, flavonoids, and alkaloids tests —were used to perform phytochemical screening on the three extracts of *C. gigantea*.

1. Alkaloids test:

Three test tubes were filled with certain extracts. When Mayer's reagent was added to the first test tube, a white, creamy precipitate showed that alkaloid compounds were present. Wagner's reagent is added to the second test tube; the presence of alkaloid compounds is indicated by a reddish - brown precipitate. When Dragendroff's reagent is added to the third test tube, a crimson precipitate forms, signifying the presence of alkaloid compounds.

2. Flavonoids test:

Lead acetate solution was put into a test tube containing a few extracts. The flavonoid compound's presence is indicated by the formed yellow colour.

3. Saponins test:

Fill a test tube with 50 mg of extract, dilute it in about 20ml of distilled water, and mix it for the five minutes. When a lot of foam forms, saponin chemicals are present.

4. tests for steroids and terpenoids:

Liberman Burchard reagent was added to a test tube containing a few extracts. Steroid chemicals are indicated by the creation of a green colour, while terpenoid compounds are indicated by the formation of a purplish red colour.

5 Tannins test:

To a test tube containing a few extracts, a 1% gelatine solution containing sodium chloride was added. Tannin compounds are present when a white precipitate forms.

6 Phenolic tests:

When ferric chloride solution is added to certain extracts in a test tube, the creation of a bluish -black colour indicates the presence of phenol compound. [7]

Toxicity

C. gigantea finds its widespread distribution over many regions of the globe. What makes its phytochemistry interesting is the exudation of milky and toxic latex from all the plant parts. The latex is referred to as vegetable mercury as it shows mercury like effects on human body. Every part of this plant is toxic, but stem (latex) and roots are more poisonous than leaves. The leaves of this plant have three toxic glycosides calotropin, calotoxin and uscharin, whereas

its latex contains calotropin, calotoxin and calactin, which are caustic and considered poisonous in nature. In addition, the plant is not eaten by cattle or other grazing animals because the quantity of calactin, a toxic glycoside, increases as a defence mechanism upon encountering grasshopper or insect attack. In addition, plants are protected from phytopathogens by osmotic, a laticifer protein extracted from latex. Its milk has anticholinergic, neurotoxic, and irritating properties that lead to intoxication and potentially lethal consequences. Salivation, stomatitis, vomiting, diarrhoea, dilated pupils, titanic convulsions, collapse, and death are all brought on by the bitter taste and scorching agony of madar juice and latex. Between 30 and 8 hours can pass before someone dies. Latex can induce keratoconjunctivitis, corneal edema, and painless dimness of vision if it gets into the eye. After three weeks, endothelial cell injury was visible in certain cases. Gigantea was discovered to be harmful to chick embryos at a level of 100 mg kg-1. Its toxicity resulted in underdeveloped lungs, kidneys, sinusoids, central vein dilatation, cerebral congestion, and hepatocellular degeneration in the liver. Therefore, more research should be done to clarify the toxicity and safe use of *C. gigantea* in light of the harmful effects of certain extracts and glycosides.[10]

Detoxification process of *C. gigantea*:

However, based on general principles and documented methods for similar toxic plants in Ayurveda, the detoxification typically involves processes like:

- Boiling/Steaming with Specific Liquids: A common method for purifying certain poisonous herbs involves boiling or steaming them in liquids like milk, buttermilk, cow's urine, or decoctions of other herbs for a specified duration. This process is intended to leach out or neutralize the toxic components.
- Soaking: Soaking the plant parts in a medium like water, rice gruel, or specific herbal decoctions for a set time, followed by drying.
- Washing/Drying Cycles: Repeated washing and drying to reduce harmful substances. [8]

Traditional Use of *Calotropis gigantea*:

1. In Ayurveda: -

For the treatment of fevers, swellings, and paralysis the leaves of plant *C.gigantea* are used. And for the treatment of fever, inflammation, helminthic infections, anorexia, asthma, and catarrh flowers can be used. Ascites, intestinal worms, helminth infections, and skin infections are all treated with the plant's root bark.

2. In Siddha: -

Intestinal worms, ulcers, periodic fever, vatha diseases, and poisonous snake bites are all treated with *C. gigantea* leaves. The roots of this plant are applied by vigorously rubbing over the bite area after being completely crushed. The latex from this plant can be used to treat rheumatic conditions, gonococcal arthritis, swellings, dental problems, and rat bites. using flowers to treat bronchial asthma.

3. In Unani: -

In Unani: In the Unani system, root bark powder has long been used to treat dysentery and diarrhoea. The plant's root helps with indigestion and is a carminative. [9]

4. Pharmacological Aspects:

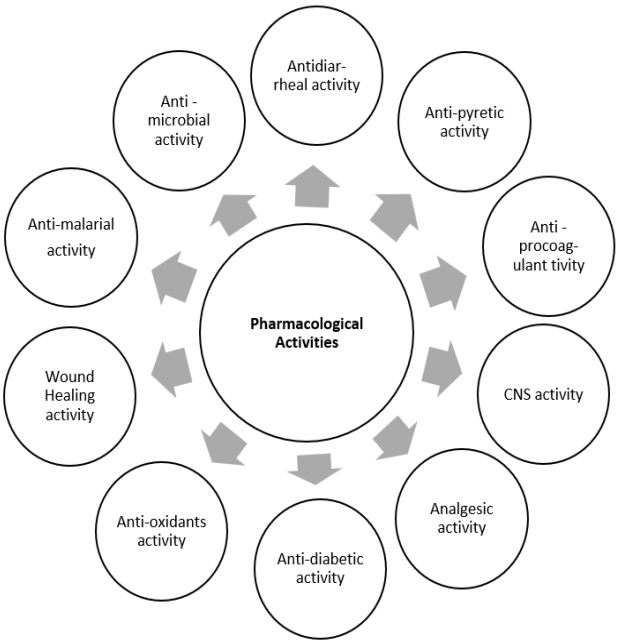

Figure 3: Pharmacological activity.

1. Antidiarrheal Activity:

Rats with castor oil-induced diarrhoea were used to test the anti-diarrheal effects of a hydroalcoholic (50:50) extract of the aerial portion of *Calotropis gigantea*. The percentage of the largest distance the charcoal travelled divided by the entire length of the small intestine was used to calculate the gastrointestinal transit rate. Using the enter pooling method, the weight and volume of intestinal content caused by castor oil were examined.

2. Antipyretic Activity:

In Indian traditional medicine, the roots of *Calotropis gigantea* have been used to treat leprosy, dermatitis, syphilis, elephantiasis, ulceration, and cough. The current study describes pyrexia in rats and rabbits caused by the TAB (typhoid) vaccine. When 200 and 400 mg/kg doses were administered, the fever was considerably reduced and the body temperature returned to normal in both yeast-induced and TAB vaccine-induced fevers

3. Procoagulant Activity:

Numerous highly basic proteins with significant proteolytic activity were found in the crude latex extract. Casein, human fibrinogen, and crude fibrin clot are all hydrolysed by the crude extract in a dose-dependent fashion. IAA totally stopped the hydrolysing activity, suggesting that they are members of the super family of cysteine proteases.

Fibrinogen's alpha, beta, and gamma subunits are hydrolysed by crude extract.

4. CNS Activity:

Alcoholic extract of peeled roots of *Calotropis gigantea* R.Br. (Asclepiadaceae) was tested orally in albino rats at the dose level of 250 and 500 mg/kg bodyweight for CNS activity. Prominent analgesic activity was observed in Eddy's hot plate method and acetic acid- induced writhing's. The paw licking time was delayed, and the numbers of writings were greatly reduced. Significant anticonvulsant activity was seen as there was a delay in the onset of pentylenetetrazol-induced convulsions as well as a decrease in its severity. The extract treated rats spent more time in the open arm of EPM showing its antianxiety activity. There was a decrease in the locomotor activity. The fall off time (motor coordination) was also decreased. A potentiation in the pentobarbitone-induced sleep due to the sedative effect of the extract was observed. No mortality was seen up to the dose of 1 g/kg. These results show the analgesic, anticonvulsant, anxiolytic and sedative effect of the extract. The locomotor activity decreased. Additionally, there was a reduction in fall off time (motor coordination). Because of the extract's sedative properties, pentobarbitone-induced sleep was found to be amplified. Up to a dose of 1 g/kg, no mortality was observed. These findings demonstrate the extract's sedative, analgesic, anticonvulsant, and anxiolytic properties.

5. Analgesic activity:

The analgesic effects of an alcoholic extract of *Calotropis gigantea* flowers were investigated in mice using thermal and chemical models. The number of writhes in the acetic acid-induced writhing test was inhibited by 20.97% and 43.0%, respectively, at dosages of 250 and 500 mg/kg. The paw licking period was postponed in the hot plate procedure. The analgesic effect began to manifest 30 minutes after the dose was administered and peaked after 90 minutes.

6. Antidiabetic activity:

According to several research, *Calotropis gigantea* exhibits antidiabetic efficacy by lowering high blood glucose levels. *Calotropis gigantea* plant extracts have a hypoglycaemic impact. When diabetes mellitus is present, *Calotropis gigantea* prevents weight loss. In the pancreatic islet, *Calotropis gigantea* increases the number of granulated cells and normal beta cells. According to reports, the plant extract effectively lowers increased serum glucose levels in experimental animals. [10]

7. Antioxidant activity:

All extremely reactive oxygen-bearing molecules, including free radicals, are classified as reactive oxygen species (ROS). Examples of free radicals include singlet oxygen, nitric oxide radical, super oxide anion radical, hypochlorite radical, hydrogen peroxide, and other lipid peroxides that are constantly produced in the body as a natural result of fundamental metabolic activities and that disrupt regular cellular mechanisms.

All of these ROS interact with proteins, nucleic acids, membrane phospholipids, and other cellular constituents, potentially causing additional cellular damage. ROS is a major factor in the complications of many diseases. The presence of free radicals increases oxidative stress in Type-II diabetes mellitus. Elevated blood sugar levels harm different tissues and also cause the production of reactive oxygen species that are harmful to tissues. *Calotropis gigantea* has been shown to lessen oxidative stress brought on by free radicals in Type-II diabetes.

8. Wound Healing:

Granulation, collagenization, collagen maturation, scar formation, and other processes are all part of the intricate process of wound healing. These are independent of one another and distinct continuous processes in wound healing. According to reports, *Calotropis gigantea* has prohealing properties. *Calotropis gigantea* promotes wound healing by accelerating the epithelization process and increasing the concentration of collagen. *Calotropis gigantea* raises hydroxyproline levels, which aid in collagen formation. *Calotropis gigantea* latex exhibits remarkable wound healing activity.

9. Anticancer:

It has been stated that *Calotropis gigantea* is an anticancer shrub. The plant contains cardiac glycosides that are cytotoxic. By causing damage to the DNA of leukaemia cells in breast cancer, cardiac glycosides (calactin) typically cause growth suppression in neoplastic cells. Cardinolides and calotroposides A exhibit anticancer properties. Anhydrosophoradiol-3-acetate, one of the active ingredients in *Calotropis gigantea* flowers, has been shown to improve cancer-related problems (in vivo).

10. Anti-malarial:

Malaria is lethal parasitic disease leads to mortality. *Calotropis gigantea* exhibited antimalarial activity against plasmodium falciparum and plasmodium berghei. *Calotropis gigantea* shows excellent antiplasmodial activity result against chloroquine sensitive plasmodium falciparum.

11. Antimicrobial:

There are various types of pathogenic microorganisms that become are resistant to most of antibiotic. Microorganism becomes sensitive and resistant due to the unsystematic use of antimicrobial drugs. This may lead to various clinical issues in treatment of infectious diseases. Antibiotics are used in treatment of infectious disease having associated adverse effect including allergic reaction, hypersensitivity, and immunosuppression. Plants having some active constituents, which are naturally toxic to fungi and bacteria. *Calotropis gigantea* reported as antimicrobial, antibacterial and cytotoxic effect. [11]

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