

Review on Pharmacological Properties of Aaka (*Calotropis procera*)

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e-mail: amoo.ap@gmail.com**Article History**Article ID: IJEP0261
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Calotropis procera belongs to the family Asclepiadaceae. It is commonly known as Madar and well known for its medicinal value. Its medicinal properties are explain in Unani medicinal system and regarded as a useful tribal shrub. India has a huge diversity of rural and tribal community still depends upon medicinal plants. The genus contained a large group of chemical compounds that exert many pharmacological effects. The plant parts have significant therapeutic value even in fresh or in dry form and exhibits valuable activity against diarrheal, malaria, diabetes, inflammation, helminthic, sterility, spasmodic, hepatic, carcinogenic and skin diseases. The present article is an attempt to provide collective information on phytochemical and pharmacological of shrub.

Keywords: Calotropis, pharmacological effect, medicinal, diarrheal, inflammation, phytochemical, helminthic, spasmodic

1. Introduction

Calotropis procera is a native plant of North Africa referred as a tropical plant growing of about 1050 meters. Particularly it prefers the warm climate so it's distributed is maximum in Rajasthan (Dwivedi et al., 2010). *Calotropis procera* properly grows in dry and open habitat found along road-side, dry land of rural and urban region where soil is excessively drained and xerophytic conditions are available. It established very rapidly because it tolerates a high degree of abiotic stresses such as drought, salinity, temperature etc and dominating the arid zones where annual precipitation is very low (Kumar et al., 2013). The number of ethnomedicinal uses of calotropis are mentioned in Ayurveda and popularly known as Raktha Arka. Traditionally it was used as an excellent substitute for ipecac, to treat cholera, elephantiasis diarrhea dysentery indigestion and used in extracting guinea worms (Moronkola et al., 2011).

Calotropis procera contained many biological active chemical groups including, cardenolides, steroids, tannins, glycosides, phenols, terpenoids, sugars, flavonoids, alkaloids and saponins. It exerted many pharmacological effects such as antimicrobial, anthelmintic, anti-inflammatory, analgesic and antipyretic, anticancer activities. Traditionally it was used to treat cholera, extracting guinea worms and indigestion (Pusapati et al., 2012).

2. Botanical Classification

Kingdom: Plantae

Subkingdom: Tracheobionta
Super division: Spermatophyta
Division: Magnoliophyta
Class: Magnoliopsida
Subclass: Asteridae
Order: Gentianales
Family: Asclepiadaceae
Subfamily: Asclepiadoideae
Genus: Calotropis
Species: *Calotropis procera*

3. Synonyms

Sanskrit name - Arka
Hindi - Aaka
Vernacular name- Giant Indian Milkweed, Sodom Apple, Small Crown Flower, Rooster tree
English name - French Cotton
Malaysia- Remiga
Laos- Dok Hak
Philippines- Kapal-kapal
French- Pomme de Sodome
Indonesia- Rubik
German- Mudarpflanzer
Spanish- Algodon Extranjero
Turkish- Ipekag
Oshar- Arabic
Italian- Calotropo



Table 1: Medicinal activities associated with different plant parts

Sl. No.	Part used	Effects
1.	Root	Analgesic, antinociceptive, antipyretic, antiangiogenesis, antifertility
2.	Flower	Hepatoprotective, hemorrhagic, septicemia, Antibacterial, antiparasitic, antimicrobial, anticoccidal, antifertility
3.	Latex	Antiathritis, monoarticular arthritis, antihelminthic, anticancer and in vitro cytotoxicity hepatocellular carcinoma, skin melanoma, antitumor, anticonvulsant, Antidiabetic, diabetic wound, diabetic nephropath, neuropathy, antidiarrheal, antiedematogenic, antifertility, anti-oxidant and free-radical scavenging, antiproliferative, cardiotoxic, anticogulant, bullous eruption, cognition enhancer, muscle stimulation, enzymatic activity, oral mucositis, gastric ulcer, gastric mucosal protective activity, anti-helicobacter, urease inhibition, histamine, hyperalgesis, hypotensive, interleukin-1 beta inducer, myocardial, myocardial infection,
4.	Root barks	Antitumour, apoptosis, antitumorous, estrogenic functionality
5.	Whole plant	Antieczima, dermatophytic activity, molluscicidal activity, antifungal, antilithic, antimycoplasmal, spasmodic activity
6.	Leaf	Purgative, wound healing, Hypoglycemic, lipolytic, lipoxigenase activities, Antifilarial, antihyperbilirubinemic, anti-implantation, antiplasmodial, antitussive.

4. Botanical Description

4.1. Vegetative characteristics

C. procera is erect, tall, evergreen, perennial shrub attains a maximum height 5.5 m. The soft-wooded twigs and barks are thick, rough, corky and soft with terminal sub-sessile leaves (Meena et al 2010). Leaves are simple, slight leathery arranged opposite-decussate, pale green colour 4-6 pairs about 30x25

cm² and 4-6 pairs.

4.2. Reproductive characteristics

The plant possesses regular bearing bisexual aromatic flowers arranged in simple or rarely compound cymose corymbs inflorescence.

Flowering period - March to October (Table 2).

Table 2: Different types of chemical constituents in different parts of plants

Roots: It contains triterpenes, a new norditerpenyl ester, named Calotropterpenyl ester, mundarol isovalerate and quercetin -3-rutinoside. pentacyclic triterpinoids such as Calotropurseny acetate and calotropfriedelenyl acetate, akundarol isovalerate.

Flower: It contains quercetin-3-rutinoside, sterol, calactin, calotoxin, calotropagenin, calotropin, polysaccharides with D-arabinose, glucose, glucosamine, L-rhamnose, lupeol, proceragenin (cardenolide), syriogenin, taraxast-20(30)-en-3-(4-methyl-3-pentenoate), 3-thiazoline cardenolide, gigantol, giganteol, isogiganteol, uscharidin, uzarigenin, voruscharin, a-calotropeol, 3-epimoretenol, alactuceryl-acetate and a-lactuceryl isovalerate, uscharin, proceroside.

Latex: In latex the main components present such as: caoutchouc, calotropin, calotoxin 0.15%, calactin 0.15%, uscharin 0.45%, trypsin, voruscharin, uzarigenin, syriogenin and proceroside, calactin, calotropagenin, calotropin, calotoxin, L-lactuceryl, proceroid, syriogenin, tetraxasterol, uscharin, uscharidin, uzarigenin, voruscharin, β -amyryn, calotropeol, 3-epimoretenol, lupeol, trypsin, active labenzyme and a heart poison traces of orthohydroxy phenol, 2,6-dimethyl tetra-1,5-decaene and 3,7,11-Trimethyl-2,6,10,12-pentadecatrien-1-ol.

Leaves: The leaves contain mainly the amyryn, amyryn acetate, β -sitosterol, urosolic acid, cardenolides, calotropin, calotropagenin.

5. Pharmacological Activities in *Calotropis procera*

- Analgesic Activity
- Antifertility activity
- Anti-tumor studies
- Anthelmintic activity
- Anti-hyperglycemic effect
- Hepatoprotective activity

- Inflammatory activity
- Anti-diarrhoeal activity
- Anti-convulsant effects
- Anti-microbial activity
- Anti-malarial activity
- Antipyretic Activity
- Antiulcer Activity
- Wound Healing Activity



- Cardiovascular Effect
- Neuroprotective Activity

5.1. Analgesic activity

Dry latex (DL) of *Calotropis procera* having analgesic activity observed by Kumar et al (2000). A single oral dose of DL ranging from 165 to 830 mg kg⁻¹ produced a significant effect against acetic acid induced writhing. The dose of 830 mg/ml DL produced marginal analgesic effect. The effect of DL was delayed by 1 hour by naloxone at dose of 0.5 mg kg⁻¹, i.e., which completely blocked the analgesic effect of morphine (10 mg kg⁻¹). However, the effect of aspirin was not blocked by naloxone. In mice, the similar dose of DL did not produced toxic effects and the LD50 was found to 3 g kg⁻¹ (Quazi et al., 2013).

5.2. Antifertility activity

The roots of *Calotropis procera* having the high amount of ethanolic content have been studied in albino rats. To investigate its antifertility and hormonal activities. The dose level of 250 mg kg⁻¹ (1/4 of LD50) strong antiimplantation (inhibition 100%) and uterotrophic activity was observed at the dose level of 250 mg kg⁻¹ (1/4 of LD50). While no antiestrogenic activity could be detected in root extract (Kumar et al., 2011).

5.3. Anti-tumour activity

The extract of flowers of *Calotropis procera* showing scavenging activity, cytotoxic activity and polyphenolic content of methanolic. Free radical scavenging activity was like 1,1,-diphenyl-2- picryl hydrazyl (DPPH), hydroxyl radical, hydrogen peroxide radical, reducing power and ferric thiocyanate was estimated (Samar et al., 2009). Better scavenging activity was found in methanol extract of *C. procera* by ferric thiocyanate method (83.63%) with the lowest IC50 of 100 µg ml⁻¹ followed by hydrogen peroxide, hydroxyl radical scavenging and least activity was found to be present in DPPH assay (50.82%). The extract had 100% cytotoxicity on Hep2 cell lines (Ahmad et al., 2011).

5.4. Antihelminthic activity

The antihelminthic activity of *Calotropis procera* flowers in comparison with levamisole was observed through *in vitro* and *in vivo* studies by Iqbal et al., (2005). *In vitro* studies revealed anthelmintic effects ($p < 0.05$) of crude aqueous and crude methanolic extracts of *Calotropis procera* flowers on live *Haemonchus contortus* as evident from their mortality or temporary paralysis. For *in vivo* studies, *Calotropis procera* flowers were administered as crude powder to sheep naturally infected with mixed species of gastrointestinal nematodes. The ethanolic extract of *Calotropis procera* (Ait.) R. Br. leaves were separated into n-butanol and water fractions. The n-butanol fraction was subjected to column chromatography. Ethanolic extract, n-butanol, and water fractions as well as n-hexane, chloroform, chloroform: methanol (9:1); chromatographic elutes of n-butanol fraction were evaluated for *in-vitro* anthelmintic activity using Indian earthworm

Pheretima posthuma as a experimental models. The results revealed that ethanolic extract, water fraction, n-hexane, and chloroform elute showed better activity as compared to n-butanol fraction and chloroform: methanol (9:1) elutes of *Calotropis procera* leaves (Dahiru et al., 2013).

5.5. Anti-hyperglycemic effect

In the present study, dry latex (DL) of *Calotropis procera* possessing potent anti-inflammatory activity was evaluated for its antioxidant and anti hyperglycemic effects against alloxen induced diabetes in rats by Kumar et al. (2005). Daily oral administration of DL at 100 and 400 mg kg⁻¹ doses produced a dose- dependent decrease in the blood glucose and increase in hepatic glycogen content. The efficacy of DL as an antioxidant and as anti-diabetic agents was comparable to the standard anti-diabetic drug, glibenclamide.

5.6. Hepatoprotective activity

Hydro-ethanolic extract (70%) of flowers was prepared and tested for its hepatoprotective effect against paracetamol-induced hepatitis in rats by Setty et al. (2007). Alteration in the levels of biochemical markers of hepatic damage like SGPT, SGOT, ALP, bilirubin, cholesterol, HDL, tissue GSH were tested in both treated and untreated groups. Paracetamol (2.0 g kg⁻¹) has enhanced the SGPT, SGOT, ALP, bilirubin and cholesterol levels and reduced the serum level of GSH. Treatment with hydro-ethanolic extract of *Calotropis procera* flowers (200 mg kg⁻¹ and 400 mg kg⁻¹) has brought back the altered levels of biochemical markers to the near normal levels in the dose dependent manner (Khaimar et al., 2012).

5.7. Anti-inflammatory activity

The anti-inflammatory property of the *Calotropis procera* was studied on carrageen in and formalin induced rat paw edema model by Kumar et al. (1994). A single dose of the aqueous suspension of the dried latex was effective to a significant level against the acute inflammatory response (Suresh and Karki, 2011).

5.8. Anti-diarrhoeal activity

The dry latex (DL) of *Calotropis procera* (Asclepiadaceae), a potent anti-inflammatory agent has been evaluated for anti-diarrhoeal activity by Kumar et al. (2001). Like atropine and phenyl butazone, a single dose of DL (500 mg kg⁻¹) produced a significant decrease in frequency of defecation, severity of diarrhea and afforded protection from diarrhea in 80% rats treated with castor oil induced intestinal fluid accumulation and electrolyte concentration in intestinal fluid. DL produced a decrease in intestinal transit (27–37%) as compared to both normal and castor oil treated animals. Unlike atropine, DL significantly inhibited castor oil induced enteropooling.

5.9. Anticonvulsant activity

Alcoholic extract of the roots of *Calotropis procera* was evaluated for various pharmacological parameters like acute toxicity, anticonvulsant, analgesic, anti-inflammatory and



hypnotic activities by Kamath et al. (2003). The extract at the dose level of 125 mg kg⁻¹ and 250 mg kg⁻¹ potentiated the hypnotic effect of pentobarbitone sodium and was found to possess significant analgesic and anti-inflammatory activities. However the extract failed to exhibit anticonvulsant activity both in leptazole and electroshock induced convulsion in rats.

5.10. Antimicrobial activity

The antimicrobial effect of ethanol, aqueous and chloroform extracts of leaf and latex of *Calotropis procera* on six bacteria, three fungi, one yeast *Candida albicans* were determined using agar well diffusion and paper disk methods (Kareem et al., 2008). The results revealed that ethanol was the best extractive solvent for antimicrobial properties of leaf and latex of *C. procera* followed in order by Chloroform and aqueous ($p < 0.05$). The ethanolic extracts of *C. procera* latex gave the widest zone of inhibition (14.1 mm) against E-coli using agar well diffusion while 9.0 mm was recorded for the same organism in the disc plate method. The growth of six bacterial isolates was inhibited by the three extracts except *P. aeruginosa* and *S. pyogenes* that were not inhibited by the aqueous extracts of both leaf and latex of *C. procera*. Similarly, the growth of four test fungi were inhibited by ethanol and chloroform extracts while the aqueous extract was the least effective on the test fungi. The best antifungal activity was recorded in ethanol extract of *C. procera* latex against *Candida albicans*.

5.11. Antimalarial activity

From an ethnobotanical approach, the ethanolic extracts of *Calotropis procera* leaves, stems, roots, flowers and buds have been screened *in vitro* for anti malarial activity against chloroquine sensitive and chloroquine resistant *Plasmodium falciparum* strains (Gupta et al., 2012) (Figure 1 to 3).

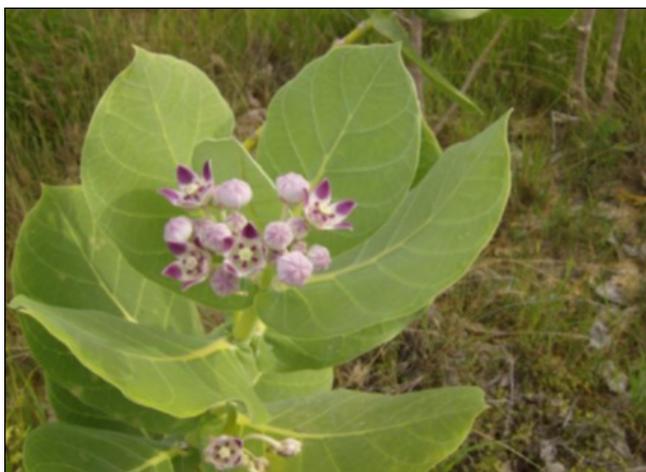


Figure 1: Parts of *Calotropis procera* (stem, inflorescence, buds, leaves)

5.12. Antipyretic activity

The ethanolic extract of the aerial parts, aqueous extract of flowers and aqueous solution of dry latex of *Calotropis procera*



Figure 2: Inflorescence and leaves of *Calotropis procera*



Figure 3: Stem, leaves and capsules of *Calotropis procera*

showed significant antipyretic activity in animal models that was comparable to aspirin (Vasconcelos, 2005).

5.13. Antiulcer activity

Basu, A., Chaudhary, A.K., 1991. Evaluated the antiulcer activity of chloroform fraction of *Calotropis procera* root extract using different *in vivo* ulcer models. The results of the study revealed that it significantly inhibited aspirin, reserpine, absolute alcohol and serotonin induced gastric ulcerations in rats and also protecting the gastric mucosa from aspirin-induced ulceration in pyloric-ligated rats and significant protection was observed in histamine-induced duodenal ulcers in guinea-pigs.

5.14. Wound healing activity

Based on its traditional use the *Calotropis procera* was evaluated for its wound healing potential. For this purpose

four full thickness excisional wounds of 8.0 mm diameter were inflicted on the back of guinea pigs. Topical application of 20 μ l of 1.0% sterile solution of the latex of *Calotropis procera* twice daily was followed for 7 days. The latex significantly augmented the healing process by markedly increasing collagen, DNA and protein synthesis and epithelisation leading to reduction in wound area thus the study provided a scientific rationale for the traditional use of this plant in the management of wound healing (Samy and Chow, 2012).

5.15. Cardiovascular effect

Latex of *Calotropis procera* was evaluated for protection against isoproterenol (20 mg 100 g⁻¹) induced myocardial infarction in albino rats. The pretreatment with an ethanolic latex extract of *Calotropis procera* at a dose of 300 mg/kg body weight orally three times a day for 30 days, reduced significantly ($p < 0.01$) the elevated markers enzyme levels in serum and heart homogenates in isoproterenol induced myocardial infarction (Sharma et al., 2011).

5.16. Neuroprotective activity

Alzheimer's disease (AD) commonly known as dementia is an organic, progressive, chronic brain disorders characterized by multiple cortical functions, including memory, orientation, comprehension and language ability and learning. Powder latex can be used to treat the early symptoms of dementia of Alzheimer type. Powder latex, had decreased the deposition of beta amyloid in mouse brain, and showed a protector and antioxidant activity in this organ.

6. Adverse Effects and Toxicity of Calotropis Plant

Aqueous extract did not produce any significant changes in the behavioral or neurological responses up-to 2500 g/kg. Acute toxicity studies revealed the non-toxic nature of the petroleum ether, methanol and aqueous extracts of the roots of *C. procera*.

The safety evaluation studies revealed that the use of extract in single high doses (up to 3 g kg⁻¹) didn't produce any visible toxic symptoms or mortality. However, prolong treatment (90 days) causes significantly higher mortality as compared to control group.

An 830 mg kg⁻¹ oral dose of dry latex did not produce any toxic effects in mice and the LD50 was found to be 3000 mg kg⁻¹. LD50 of chloroform extract of *Calotropis procera* in rats was 993 mg kg⁻¹ in rats (Lima et al., 2011). The plant is toxic and is one of the few plants not given to grazing animals due to its toxicity; the latex extracted from the stem was used traditionally to make poison arrows. The latex is highly toxic to human eyes and produces sudden painless dimness of vision with photophobia. The toxic effects of *Calotropis procera* latex were studied in rats and *C. procera* leaves in sheep. Male rats were subjected to an intra-peritoneal injection of fresh *C. procera* latex (without carrier solvent) at 1.0, 0.6, 0.3 or 0.1 ml of latex kg⁻¹ of

body weight. None of the rats died. The histological lesions were restricted to rats dosed with 1.0 ml of latex kg⁻¹ body weight and included multi-focal coagulation necrosis of cardiac fibers and vacuolized hepatocytes (Manivannan et al 2011). Sheep were treated with a single dose of 30 g kg⁻¹, a single dose of 60 g kg⁻¹ or 60 g kg⁻¹ day⁻¹ for 10 consecutive days. Exposure to the *C. procera* leaves caused tachycardia and transitory cardiac arrhythmias in sheep of all groups. Gross pathological analysis of sheep dosed with 60 g/kg per day for 10 days revealed mild ascites, exudates on the trachea, pulmonary edema, mild hemorrhage in the liver, hydropericardium, flaccid heart, ulcers on the abomasum and kidneys presenting pale juxtamedullary cortex. The histological findings of the rat and sheep studies were similar and included multi-focal coagulation necrosis of cardiac fibers and vacuolized hepatocytes. These findings indicate that *C. procera* is a cardiotoxic and hepatotoxic plant (Verma et al., 2012).

The toxic effects of ethanolic leave extract of *C. procera* on the liver were evaluated in adult male rabbits. Group A served as the control, which received distilled water only. Rabbits were treated with ethanolic extracts of *C. procera* at 250 and 500 mg kg⁻¹ body weight respectively for two weeks (14 days). Histological observations of the liver showed that ethanolic leave extract of *C. procera* caused damage to the liver tissues of male rabbits at a high dose as evident in necrotic tissue seen in treated groups.

7. Conclusion

Calotropis procera is a popular remedy in Ayurvedic and traditional time for the treatment of a range of ailments. The phytochemicals of this plant needs to be standardized to explore its medicinal values with the help of various methods. Further research is necessary to elucidate the phytochemical and pharmacological aspects of this plant. The presence of a number of phytoconstituents and pharmacological actions of *Calotropis procera* is a potential source for the development of new drugs to pharmaceutical industry.

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