A VALUABLE PLANT CALOTROPIS PROCERA LINN IN INDIAN SYSTEM OF MEDICINE: AYURVEDA

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ABSTRACT

Herbal medicines have been used from the earliest times to the present day. The ethnobotanical pharmacology is as old as man himself. Herbal medicines exhibit a remarkable therapeutic diversity. *Calotropis procera* Linn. is an Ayurvedic plant which is used in several traditional medicines to treat a variety of diseases. The extracts from different parts of the plant have significant therapeutic value. The whole plant when dried exhibits good tonic, antihelmintic and expectorant activities. The roots also have similar activities and also act as an effective laxative. Traditionally, the powdered rot is used to treat bronchitis, asthma, leprosy, eczema, elephantiasis while the latex s used to, treat vertigo, baldness, hair loss, toothache, intermittent fevers, rheumatoid/joint swellings, and paralysis. The leaves are usedto treat joint pain, and reduce swelling. Besides its Ayurvedic use, *Calotropis* is also used as a Homoeopathic medicine. In ancient Ayurvedic medicine the plant Calotropis procera was known as “Rakt- arka”. The pungent latex extracted from the leaves and flowers of Calotropis procera is processed and used in the commercial preparation of eye tonics.

KEYWORDS: Pharmacological activity, Calotropis procera, Ayurveda.

INTRODUCTION

*Calotropis procera* Linn. Family Asclepiadaceae is an Ayurvedic plant with important medicinal properties. It is known by various vernacular names like Swallow wort in English, madar in Hindi, and Alarka in Sanskrit. It is found in most parts of the world with a warm climate in dry, sandy and alkaline soils. *Calotropis* is primarily harvested because of its distinctive medicinal properties. It is commonly referred to as ark, swallow-wart or milkweed and it occurs frequently in Indonesia, Malaysia, China, and the Indian subcontinent as wasteland weed. The ark plant with white flowers is a superior variety and is referred to as *Calotropis procera*. In India, it is found from the Punjab and Rajasthan to Assam and Kanyakumari up to an altitude of 1050 m. It grows abundantly in Rajasthan. It is found in waste lands and grows as a weed in cultivated areas. It also grows well on rubbish heaps, waste and fallow land, by the roadside and in sand dunes[1].

The inner bark of *Calotropis* is used to make strong fibers called madar which are used in the manufacture of weave carpets, ropes, sewing thread and fishing nets. *Calotropis procera* Linn is an erect, tall, large, highly branched and perennial shrub or small tree that grows to a height of 5.4 m, with milky
latex throughout. The bark is soft and corky, the branches are stout, terete with fine appressed cottony pubescence (especially on young). The leaves are sub-sessile, opposite, decussate, broadly ovateoblong, elliptic or obovate, acute, thick, glaucous, green, covered with fine cottony pubescent hair on young but glabrous later and base cordate. Flowers in umbellate-cymes and tomentose on young, Calyx glabrous, ovate and acute. The corolla is glabrous, the lobes erect, ovate, acute, with coronal scales 5-6, latterly compressed and equally of exceeding the staminal column. Follicles are sub-globose or ellipsoid or ovoid. Seeds broadly ovate, acute, flattened, minutely tomentose, brown coloured and silky coma is 3.2 cm long. The bark of the plant contains Madar-alban, Madar-fluavil, black acid resin, and yellow bitter resin\textsuperscript{[2]}. The present review summarizes the information concerning the Ayurvedic use, ethnopharmacology, phytochemistry, biological activity and toxicity of Calotropis procera Linn. It should be of interest students and scientists who are interested in ayurvedic research.

**SYNONYMS**\textsuperscript{[3]}

1. Sanskrit : Ravi, Bhïnú, Tapanä
2. Assamese : Akand, Akan
3. Bengali : Akanda, Akone
4. English : Madar Tree
5. Gujarati : Aakado
6. Hindi : Aak, Madar, Akavana
7. Kannada : Ekka, Ekkadagida, Ekkegida
8. Kashmiri : Acka
9. Malayalam : Erikku
10. Marathi : Rui
11. Oriya : Arakha
12. Punjabi : Ak
13. Tamil : Vellerukku, Erukku
14. Telugu : Jilledu
15. Urdu : Madar, Aak

**DESCRIPTION**\textsuperscript{[4]}

**Macroscopic:**

Root-rough, fissured longitudinally, corky and soft, externally yellowish-grey while internally white, central core cream coloured, bark easily separated from xylem, odour, characteristic: taste, bitter and acrid. Leaf- Sub-sessile, 6-15 cm by 4.5-8 cm, broadly ovate, ovate-oblong, elliptic or obovate acute, pubescent when young and glabrous on both sides on maturity.
Microscopic:

Root- Transverse section of root shows outer most cork tissue consisting of 4-8 rows of tangentially elongated and radially arranged cells followed by 3-6 rows of moderately thick-walled, irregular cells of secondary cortex devoid of calcium oxalate crystals and starch grains, cortex composed of large polyhedral parenchymatous cells containing abundant rounded starch grains, some cortical cells contain rosette crystals of calcium oxalate, scattered laticifer cells with brown contents, phloem consists of sieve elements and phloem parenchyma, sieve tubes thick-walled, cells more prominent towards inner region of phloem traversed by uni to tetraseriate medullary rays, phloem cells contain crystals of calcium oxalate, starch grains and laticifers similar to these found in cortex: cambium present just within the phloem consisting of 2-5 rows of thin-walled, tangentially elongated cells xylem forms the central part of root composed of vessels. tracheids, fibres and xylem parenchyma, vessels present throughout xylem region and arranged radially in groups of 2-7, sometime single vessels also occur, usually cylindrical having bordered pits on their walls, xylem fibres long, lignified with wide lumen, tapering on ends and have simple pits on walls, medullary rays 1-4 seriate and triseriate in outer region and uni or biseriate in inner region: cells of medullary rays radially elongated, filled with starch similar to those present in cortical cells.

Leaf- transverse section through midrib shows an upper and lower single layered epidermis externally covered with thick, striated cuticle, few epidermal cells on both surfaces of leaf elongated to form uni-seriate, 2-3 celled trichomes, epidermal cells cubical and radially elongated, epidermis followed by 3-8 layered collenchyma on both lower and upper surfaces, parenchymatous cells thin-walled, isodiametric to circular with intercellular spaces present in ground tissue, stele crescent shaped composed of bicollateral and open vascular bundle, xylem consists mostly of vessels and tracheids, a strip of cambium present between xylem and phloem tissues, laticifers also present in the phloem and parenchymatous zone.

Lamina-dorsiventral with mesophyll differentiated into a palisade and spongy tissue, upper and lower epidermis covered externally with a thick, striated cuticle, below upper epidermis three rows of elongated, closely arranged palisade parenchyma present, spongy parenchyma tissues almost radially elongated with intercellular spaces, central cells irregular in shape, laticifers and vascular bundles also present scattered in this region

**PROPERTIES AND ACTION**[5]

- **Rasa**: Katu, Tikta
- **Guna**: Laghu
- **Virya**: Ushna
- **Vipaka**: Katu
Karma: Dipana, Kaphavatahar, Bhedana, Krumighna, Vranahara, Vishaghna, Kushathghna

IMPORTANT FORMULATIONS

Mahavishagarbha Tail
Dhanvantara ghrta
Arkalavana

DOSE - 1-3 g of the drug for decoction and 250-750 mg of the drug in powder form.

PHYTOCHEMISTRY:
The plants contain the cardenolide, proceragenin, while the root bark contains benzoylinesolone and benzoylisolinelone. The leaves and stalk contain calotropin, and calotropagenin while the flower contains calotropenyl acetate, and multiflavenol and the latex contains uzarigenin, and terpenol ester.

Chemical investigation of this plant has shown the presence of triterpenoids, calotropurseny acetate and calopfriedenyl, a norditerpenol ester, calotropenyl ester oleanene triterpenes like calotropoleanyl ester, proceroleanol A and B and cardiac glycosidescalotropogenin, calotropin, uscharin, calotoxin and calactin. The plant also has been investigated for the presence of cardenolides and anthocyanins. Phytochemical investigation of the roots of Calotropis procera Linn yields two new phytoconstituents, procerursenyl acetate and proceranol, together with the known compounds N-dotriacont-6-ene, glyceryl mono-oleoyl-2- phosphate, methyl myristate, methyl behenate and glyceryl-1, 2-dicapriate-3-phosphate. The structures of the new compounds have been identified as urs-18 alpha-II-12, 20 (30)-diene-3 beta-yl acetate and n-triactan-10 beta-ol on the basis of spectral data analysis and chemical reactions. The root bark has also been found to possess alpha-amyrin, beta-amyrin, lupeol, beta-sitosterol and flavanols like quercetin-3-rutinoside. In the leaves, mudarine is the principal active constituent as well as a bitter yellow acid, resin and 3 toxic glycosides calotropin, uscharin and calotoxin. The latex contains a powerful bacteriolytic enzyme, a very toxic glycoside calactin (the concentration of which is increased following insect or grasshopper attack as a defense mechanism), calotropin D I, calotropin D II, calotropin F I, calotropin F II and a non toxic proteolytic enzyme calotropin (2 % - 3 %). This calotropin is more proteolytic than papain, and bromelain coagulates milk, digests meat, gelatin and casein. The whole plant contains a- and b-amyrin, b-amyrin, teraxasterol, gigantin, giganteol, isogiganteol, b-sitosterol and a wax.

AYURVEDIC USES
The parts of the plant used in Ayurvedic medicine are the leaves, fresh or dried, the roots and root bark, and the flowers. The powdered leaves are used for the fast healing of wounds, as a purgative and to treat indigestion. They are also used to treat skin disorders and liver problems. The dried leaves are used to promote sexual health including penile dysfunction and are reputed to be an aphrodisiac. Hot
poultices are made from the leaves and applied to the stomach to relieve pain, and stop headaches and also applied to sprains to ease the swelling and pain. The flowers are used as a milk drink to treat a variety of complaints including coughs and catarrh, asthma and indigestion, as well as cholera. They are collected from September to February and are also used to treat piles when prepared in the form of a paste.

The plant is also known for its use in folk medicines. Traditionally, the plant has been used as an antifungal[18], antipyretic[19] and analgesic agent[20]. The dried leaves used as an expectorant, and anti-inflammatory[21], for the treatment of paralysis and rheumatic pains[22]. The dried latex and dried root are used as an antidote for snake poisoning. It is also used as an abortifacient[23], for the treatment of piles[24] and intestinal worms[25]. The tender leaves of the plant are also used to treat migraine. The capsulated root bark powder is effective against diarrhoea and asthma[26].

PHARMACOLOGICAL PROFILE OF CALOTROPIS PROCERA

The plant has attracted much attention due to following biological activities: The previous pharmacological studies include reports of anticancer, antifungal[27] and insecticidal activity of C. procera. The flowers of the plant exhibit hepatoprotective activity[28], anti-inflammatory, antipyretic, analgesic, and antimicrobial effects and larvicidal activity[29, 30]. The latex of the plant is reported to possess analgesic and wound healing activity[31, 32], as well as anti-inflammatory[33] and antimicrobial activity[34] while the roots are reported to have anti-fertility[35] and anti-ulcer effects[36].

Analgesic activity:

A single oral dose of dry latex ranging from 165 to 830 mg/kg produces a significant dose-dependent analgesic effect against acetic acid-induced writhing. The effect of dry latex at a dose of 415 mg/kg is more pronounced than a 100 mg/kg oral dose of aspirin. In addition, dry latex (830 mg/kg) produces marginal analgesia in a tail-flick model which is similar to that of aspirin. The analgesic effect of dry latex is delayed 1 h by naloxone at a dose of 0.5 mg/kg, which completely blocks the analgesic effect of morphine (10 mg/kg). However, the effect of aspirin was not blocked by naloxone. An 830 mg/kg oral dose of dry latex did not produce any toxic effects in mice and the LD50 was found to be 3000 mg/kg[37].

Antinociceptive effect of proteins from Calotropis procera (Asclepiadaceae) latex using three different experimental models of nociception in mice. The latex protein fraction administered intraperitoneally to male mice at doses of 12.5, 25 and 50 mg/kg showed a dose-dependent antinociceptive effect compared with the respective controls in all assays. Inhibition of the acetic acid-induced abdominal constrictions was observed at doses of 12.5 (67.9 %), 25 (85 %) and 50 (99.5 %) mg/kg compared with controls. Latex protein at doses of 25 (39.8 %; 42 %) and 50 mg/kg (66.6 %; 99.3 %) reduced the nociception produced by formalin in the 1st and 2nd phases, respectively, and this effect was not reversed by pre-
treatment with naloxone (1 mg/kg). In the hot plate test, an increase in the reaction time was observed only at 60 min after treatment with latex at doses of 25 (79.5 %) and 50 (76.9 %) mg/kg, compared with controls and naloxone was unable to reverse this effect. It was concluded that the protein fraction derived from the whole latex of *Calotropis procera* possesses antinociceptive activity, which is independent of the opioid system[38].

**Antifertility activity:**
The effect of an ethanolic extract of the roots of *Calotropis procera* has been studied in albino rats to explore its antifertility and hormonal activities. Strong anti-implantation (inhibition 100 %) and uterotrophic activity was observed at a dose of 250 mg/kg (1/4 of LD50). No antiestrogenic activity was detected[39].

**Anti-tumor studies:**
The anti-tumor potential of the root extracts of *Calotropis procera* Linn., was investigated using the methanolic (CM), hexane (CH), aqueous (CW) and ethyl acetate extract (CE) and its possible mechanism against Hep2 cancer cells was studied. Cellular proliferation activities were assayed by tetrazolium bromide (MTT) colorimetry. Morphological changes in cancer cells were observed under an inverted microscope and the cell cycle parameters were determined by flow cytometry following propidium iodide staining. Treatment with the extracts at different doses of 1, 5, 10 and 25 μg/ml revealed that CM, CH and CE possessed cytotoxicity, whereas CW had no cytotoxic effect. CE (10 μg/ml) showed strongest cytotoxic effect (96.3 %) on Hep2 at 48 hr following treatment, whereas CM and CH exhibited cytotoxicity of 72.7 and 60.5 %, respectively. The extract-treated cells exhibited typical morphological changes of apoptosis. The results of flow cytometric analysis clearly demonstrated that the root extracts produced apoptosis of Hep2 cells through cell cycle arrest at the S phase, thus preventing cells from entering the G2/M phase. The results of this study indicate that the root extracts of *C. procera* inhibit the proliferation of Hep2 cells via mechanisms base don apoptosis and cell cycle disruption[40].

**Anthelmintic activity:**
The anthelmintic activity of *Calotropis procera* Linn. Flowers, in comparison with levamisole, was evaluated in a series of in vitro and in vivo studies. The in vitro studies demonstrated the anthelmintic effects (*P*<0.05) of crude aqueous (CAE) and crude methanolic extracts (CME) of *Calotropis procera* flowers on live *Haemonchus* (*H.*) *contortus* as shown by mortality or temporary paralysis. For the in vivo studies, *Calotropis procera* flowers were administered as a crude powder (CP), CAE and CME to sheep naturally infected with a mixed sample of gastrointestinal nematodes. The percentage reduction in egg count (ECR) was recorded as 88.4 and 77.8 % in sheep treated with CAE and CP at 3000 mg/kg body weight on day 7 and 10 post-treatment (PT), respectively. CME was the least effective producing only a 20.9 % reduction in ECR on day 7 PT. It was found that *Calotropis procera* flowers possess
good anthelmintic activity against nematodes, although this was less than that exhibited by levamisole (97.8–100 %). It is suggested that further research be carried out on a larger scale involving a greater number of animals, doses higher than those used in the current study, together with identification of active principles, and standardization of the dose and toxicity studies for drug development [41].

**Anti-hyperglycemic effect:**
The dry latex (DL) of *Calotropis procera* possessing potent anti-inflammatory activity was evaluated for its antioxidant and antihyperglycemic effects in rats with alloxan-induced diabetes. Daily oral administration of dry latex at 100 and 400 mg/kg produced a dose-dependent decrease in blood glucose and an increase in hepatic glycogen. Dry latex also prevented the body weight loss in diabetic rats and reduced the daily water consumption to values comparable with those of normal rats. Dry latex also produced an increase in the hepatic levels of endogenous antioxidants, namely superoxide dismutase (SOD), catalase and glutathione, while it reduced the levels of thiobarbituric acid-reactive substances (TBARS) in alloxan-induced diabetic rats. The efficacy of dry latex as an antioxidant and as an antidiabetic agent was comparable with that of the standard antidiabetic drug, glibenclamide [42].

**Hepatoprotective activity:**
The plant is a rich source of phytoconstituents but there is no scientific basis or reports in recent literature regarding the usefulness of the root bark as a hepatoprotective agent and this prompted us to evaluate the root bark of the plant for possible hepatoprotective activity. An aqueous ethanolic extract (70 %) of *Calotropis procera* flowers was prepared and tested for its hepatoprotective effect against paracetamol-induced hepatitis in rats. Changes in the levels of biochemical markers of hepatic damage, like SGPT, SGOT, ALP, bilirubin, cholesterol, HDL and tissue GSH, were investigated in both treated and untreated groups. Paracetamol (2000 mg/kg) has been reported to enhance SGPT, SGOT, ALP, bilirubin and cholesterol levels and reduce serum levels of HDL and the tissue level of GSH while treatment with an aqueous ethanolic extract of *C. procera* flowers (200 mg/kg and 400 mg/kg) restored the altered levels of biochemical markers to almost normal levels in a dose-dependent manner [43].

**Inflammatory activity:**
Latex of *Calotropis procera* was studied for its inflammatory reactions using pedal oedema and air pouch models of inflammation in rats. Subcutaneous injection of aqueous solution (0.1 ml of 1%) of dry latex (DL) into the plantar surface of paw produced significant inflammation. Maximum inflammatory response was obtained 1 h after the injection and was maintained for a further 1 h. The inflammatory response was accompanied by an increase in vascular permeability that reached its maximum within 15 min. Inflammation was also induced in the 6-day-old rat air pouch by injecting a 2.5 % solution of DL. The latter model was characterized for the exudates volume and its protein concentration, and wet and dry weights of granuloma. A time-course study indicated that both the exudates volume and
the weight of granuloma were at maximum on day 5 after DL injection while the protein concentration peaked on the third day. Further, the two models were also studied for the anti-inflammatory effect of various drugs. It was observed that in the pedal oedema model, phenylbutazone was more effective than prednisolone while almost complete inhibition was produced by mepyramine and cyproheptadine. On the other hand, in the air pouch model, prednisolone was more effective than phenylbutazone in inhibiting the inflammation. Thus, the DL-induced inflammation in different models could be used to evaluate anti-inflammatory drugs[44].

Anti-diarrhoeal activity:
The dry latex (DL) of *Calotropis procera*, a potent anti-inflammatory agent, was evaluated for its anti-diarrhoeal activity. Like atropine and phenylbutazone (PBZ), a single oral dose of DL (500 mg/kg) produced a significant decrease in the frequency of defecation and the severity of diarrhea as well as protecting from diarrhoea in 80 % rats treated with castor oil. To understand the mechanism of its anti-diarrhoeal activity, we evaluated its effect on intestinal transit, castor oil-induced intestinal fluid accumulation (enteropooling) and electrolyte concentration in intestinal fluid. Dry latex produced a decrease in intestinal transit (27 %–37 %) compared with both normal and castor oil-treated animals. Unlike atropine, dry latex significantly inhibited castor oil induced enteropooling. However, it did not alter the electrolyte concentration in the intestinal fluid compared with castor oil-treated rats[45].

Anticonvulsant effects:
The anticonvulsant activity of different root extracts of *Calotropis procera* was studied in rats in order to evaluate the traditional use of this plant. The anticonvulsant activity of different extracts of Calotropis procera roots was studied using seizures induced by maximal electroshock seizures (MES), pentylentetrazol (PTZ), lithium-pilocarpine and electrical kindling seizures. In the MES test, the chloroform extract of Calotropis procera roots showed the most significant (*P*<0.01) anticonvulsant effect by decreasing the duration of hind limb extension (extensor phase), clonus and also the duration of the stupor phase, compared with the controls. In the PTZ test, the chloroform extract exhibited a highly significant (*P*<0.001) effect, and the aqueous extract had the most significant (*P*<0.01) effect compared with the controls by delaying the onset of convulsions. The extracts also inhibited convulsions induced by lithium-pilocarpine and electrical kindling. The results of this study indicate that the chloroform extract and aqueous extract of Calotropis procera roots may be beneficial in absence (petit mal) and tonic clonic (grand mal) types of seizures[46].

Antimicrobial activity:
We studied the antimicrobial activities of chloroform and methanol extracts of seeds of Calotropis procera obtained from plants located in the forest area of Ghaziabad, India. The chloroform extract of Calotropis procera seeds exhibited better antimicrobial activity while the extracts obtained from *Calotropis procera* seeds were evaluated. The chloroform extract showed significant antimicrobial activity against all the tested bacterial and fungal strains, while the methanol extract showed moderate activity. The results indicate that the chloroform extract of Calotropis procera seeds may be beneficial in the treatment of infections caused by the tested microorganisms[47].
ropis procera seeds were evaluated for their possible in vitro antibacterial activities using the paper
disc method\[47\].

**Oestrogenic functionality:**
The effects of ethanolic and aqueous extracts of Calotropis procera roots were studied on the oestrous
cycle and on some parameters of oestrogenic functionality in rats. Both extracts were found to interrupt
the normal oestrous cycle in 60 % and 80 % of rats treated. The rats exhibited a prolonged dioestrous
stage of the oestrous cycle with consequent temporary inhibition of ovulation. The contemporary ad-
ministration of a commercial oestro-progestinic preparation exhibited the same effects in 100 % of rats
treated. However, the extracts had no oestrogenic activity when tested in immature female bilaterally
ovariectomized rats\[48\].

**Antimalarial activity:**
The ethanolic extracts of the different parts of Calotropis procera showed IC50 values ranging from
0.11 to 0.47 mg/ml against P. falciparum MRC20_CQ-sensitive. and from 0.52 to 1.22 mg/ml against
MRC76_CQ-resistant strains, flower and bud extracts being the most active. Although 220-440 times
less effective than CQ, these extracts deserve further study aimed at identification of the active constit-
uents. The results obtained support the ethnobotanical use of this plant\[49\].

**Toxicity:**
The plant is toxic and is one of the few plants not eaten by grazing animals. Due to its toxicity, the latex
extracted from the stem has traditionally been used to make poison arrows. The latex is highly toxic to
human eyes and produces sudden painless dimness of vision with photophobia\[50\]. Latex of Calotropis
procera was studied for its inflammatory effects using pedal oedema and air pouch models of inflam-
mation in rats. Subcutaneous injection of an aqueous solution (0.1 ml of 1 %) of dry latex (DL) into the
plantar surface of the paw produced significant inflammation. It was observed that, in the pedal oedema
model, phenylbutazone was more effective than prednisolone while almost complete inhibition was
produced by mepyramine and cyproheptadine. On the other hand, in the air pouch model, prednisolone
was more effective than phenylbutazone in inhibiting inflammation. Thus, dry latex -induced inflam-
mation in different models could be used to evaluate anti-inflammatory drugs\[51\].

**Adverse effects:**
The adverse effects of Calotropis procera consumption are reported to cause blisters, lesions and erup-
tions when taken by patients for the treatment of joint pains and gastrointestinal problems. The prepara-
tions of Calotropis procera need to be used under the careful surveillance of a trained medical practi-
tioner.

**CONCLUSION**
The World Health Organization has estimated more than 80% of the world’s population in developing countries depends primarily on herbal medicines for their basic healthcare needs. In recent years, ethno-botanical and traditional uses of natural compounds, especially those of plant origin, have received much attention as they are well known for their efficacy and are generally believed to be safe for human use. It is best to use the classical approach in the search for new molecules to manage a variety of diseases. A thorough review of the published literature on *Calotropis procera* shows that it is a popular remedy in a variety of ethnic groups, as well as Ayurvedic and traditional practitioners for the treatment of a range of ailments. Researchers are exploring the therapeutic potential of this plant as it is likely to have more therapeutic properties than are currently known.

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