A review on *Calotropis procera* Linn and its Ethnobotany, Phytochemical, Pharmacological profile

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**ABSTRACT**

*Calotropis procera* Linn is small, erect and compact shrubs, which is used in several traditional medicines to cure various diseases. This shrub has been known to possess Analgesic, Antitumor, Antihelmintic, Antioxidant, Hepatoprotective, Inflammatory, Antidiarrhoeal, Anticonvulsant, Antimicrobial, Oestrogenic, Antinociceptive, and Antimarial activity. A wide range of chemical compounds including- Benzoyllineolone, benzoylisolinelone and ß-amyrin. The root bark contains the calotropoleanyl ester, proceroleanenol A and proceroleanenol B. The latex contains the calactin, calotropin, uscharin, sitosterol, and calotoxin. The presented review summarizes the information concerning the ethnobotany, pharmacological, phytochemistry, biological activity and toxicity of the *calotropis procera* shrubs.

**Keywords:** *Calotropis procera* Linn, Phytochemistry, Bioactivity, Toxicity.

1. INTRODUCTION

**OCCURRENCE,BOTANICAL DESCRIPTION AND ETHNO-PHARMACOLOGY**

*Calotropis procera* Linn. Is often found as a weed throughout India in more or less warm dry places, predominantly in Sub-Himalayan tracts, Deccan to Kanya- Kumari. *Calotropis procera* Linn is an erect, tall, large, much branched and perennial shrubs or small trees that grow to a height of 5.4 m., with milky latex throughout. Bark is soft and corky. Branches stout, terete with fine appressed cottony pubescence (especially on young). Leaves sub-sessile, opposite, de-cussate, broadly ovate-oblong, 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. Corolla glabrous, lobes erect, ovate, acute, 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.¹

*Calotropis procera* Linn have been widely used in the Sudanese, Unani, Arabic and Indian traditional medicinal system for the treatment of various diseases namely leprosy, ulcers, piles and diseases of the spleen, liver and abdomen.² The latex is used as an abortifacient³, spasmodic and carminative properties⁴, antidysentric, antisyphilitic, antirheumatic, antifungal, mullusccide, diaphoretic and for the treatment of leprosy, bronchial asthma and skin affliction⁵.⁶

Different parts of the plant have been reported to possess a number of biological activities such as proteolytic⁷, antimicrobial⁸, larvicidal⁹, nematocidal¹⁰, antitumor¹¹,¹², antinflammatory¹³. Its flowers possess digestive and tonic properties. On the contrary, the powdered root bark has been reported to give relief in diarrhoea and dysentery.¹⁴
The root of the plant is used as a carminative in the treatment of
dyspepsia\textsuperscript{15}. The root bark and leaves of \textit{Calotropis procera} are
used by various tribes of central India as a curative agent for jaundice
\textsuperscript{16}.

\section*{2. PHYTOCHEMISTRY}

Phytochemical studies on \textit{Calotropis procera} have afforded
several types of compounds such as Cardenolide, triterpinoids, alka-
loids, resins, anthocyanins and proteolytic enzymes in latex, flav-
nonoids, tannins, sterol, saponins, cardiac glycosides\textsuperscript{17-19}. Flowers
contain - terpenes, multiflorenol, and cyclisadol\textsuperscript{20}.

\subsection*{2.1. Leaves}

The leaves contain mainly the a-amyrin\textsuperscript{21} (fig 1), a-amyrin ac-
etate\textsuperscript{22} (fig. 2), \textbeta-\textit{sitosterol}\textsuperscript{F1-24} (fig. 3), urosolic acid\textsuperscript{25-26} (fig. 4),
cardenolides, calotropin\textsuperscript{1} (fig. 5), calotropagenin\textsuperscript{27} (fig. 6).

\subsection*{2.2. Latex}

The latex contains caoutchouc, calotropin, calotoxin 0.15% (fig. 7), calactin 0.15% (fig. 8), uscharin 0.45% (fig. 9), trypsin, voruscharin (fig. 10), uzarigenin, syriogenin and proceroside\textsuperscript{28-31}.

\subsection*{2.3. Flower}

The flower contains the flavonoids, quertin- 3- ratinoside, sterol\textsuperscript{32}, calactin, calotoxin, calotropagenin, calotropin, polysaccharides with D-arabinose, glucose, glucosamine and L-rhamnose. Flow-
ers also contain enzymes 3-proteinase and calotropain (protease).

Other chemical constituents of \textit{C. procera} flowers are lupeol, uscharin, proceroside, proceragenin (cardenolide), syriogenin, taraxast-20(30)-en-3-(4-methyl-3- pentenoate), 3-thiazoline cardenolide, gigantin, giganteol, isogiganteol, uscharidin, uzarigenin voruscharin a-calotropeol, 3-epimoretenol, a- lactuceryl acetate and a-lactuceryl isovalerate\textsuperscript{33}.

\subsection*{2.4. Bark}

Root bark of \textit{Calotropis procera} contains triterpenes\textsuperscript{34}. A new
norditerpenyl ester, named Calotropterpenyl ester, and two unknown
pentacyclic triterpinoids, namely calotropsenyl acetate and
calotropfriedelenyl acetate\textsuperscript{35}, akundarol isovalerate, mundarol
isovalerate and quercetin -3- rutinoside\textsuperscript{36}.

\section*{3. BIOACTIVITY}

\textit{Calotropis procera} is regarded as useful medicinal plant and
used in folk medicines\textsuperscript{37-39}, such as –

\subsection*{3.1. Analgesic}

In this study we have evaluated the analgesic activity of dry
latex (DL) of \textit{Calotropis procera}. A single oral dose of DL ranging
from 165 to 830 mg/kg produced a significant dose dependent analge-
sic effect against acetic acid induced writhing. The effect of DL at a
dose of 415 mg/kg was more pronounced as compared to a 100 mg/kg
oral dose of aspirin. On the other hand DL (830 mg/kg) produced
marginal analgesia in a tail-flick model which was comparable to aspi-
rin. The analgesic effect of DL was delayed by 1 h by naloxone at a
dose of 0. 5 mg/kg, which completely blocked the analgesic effect of
morphine (10 mg/kg). However, the effect of aspirin was not blocked
by naloxone. The 830 mg/kg oral dose of DL did not produce toxic
effects in mice and the LD50 was found to be 3 g/kg\textsuperscript{40}.

\subsection*{3.2. Antifertility activity}

The effect of ethanolic extract of the roots of \textit{Calotropis pro-
era} has been studied in albino rats to explore its Antifertility and
hormonal activities. A strong anti implantation (inhibition 100%). and
uterotrophic activity was observed at the dose level of 250 mg / kg (1/
4 of LD50). No antiestrogenic activity could be detected.

3.3. Anti-tumor studies

Anti-tumor potential of root extracts of *Calotropis procera* Linn. methanolic extract (CM), hexane extract (CH), aqueous extract (CW) and ethyl acetate extract (CE) and its possible mechanism against Hep2 cancer cells has been investigated. Cellular proliferation activities were assayed by tetrazolium bromide (MTT) colorimetry. Morphological changes of cancer cells were observed under inverted microscope and cell cycle parameters were determined by flow cytometry following propidium iodide staining. Treatment with the extracts at various doses of 1, 5, 10 and 25 µg/ml revealed that CM, CH and CE possessed cytotoxicity, whereas CW did not have cytotoxic effect. CE (10 µg/ml) showed strongest cytotoxic effect (96.3%) on Hep2 at 48 hr following treatment, whereas CM and CH showed cytotoxicity of 72.7 and 60.5%, respectively.

Extract-treated cells exhibited typical morphological changes of apoptosis. Results of flow cytometric analysis clearly demonstrated that root extracts initiated apoptosis of Hep2 cells through cell cycle arrest at S phase, thus preventing cells from entering G2/M phase. Results of the study indicate that the root extracts of *C. procera* inhibit the proliferation of Hep2 cells via apoptotic and cell cycle disruption based mechanisms.

3.4. Anthelmintic activity

The Anthelmintic activity of *Calotropis procera* Linn. flowers in comparison with levamisole was evaluated through in vitro and in vivo studies. In vitro studies revealed anthelmintic effects (*P* < 0.05) of crude aqueous (CAE) and crude methanolic extracts (CME) of *Calotropis procera* flowers on live *Haemonchus (H.) contortus* as evident from their mortality or temporary paralysis. For in vivo studies, *Calotropis procera* flowers were administered as crude powder (CP), CAE and CME to sheep naturally infected with mixed species of gastrointestinal Nematodes. Egg count percent reduction (ECR) was recorded as 88.4 and 77.8% in sheep treated with CAE and CP at 3 g kg-1 body weight on day 7 and 10 post-treatment (PT), respectively. CME was least effective resulting in 20.9% reduction in ECR on day 7 PT. It was found that *Calotropis procera* flowers possess good anthelmintic activity against nematodes, yet it was lower than that exhibited by levamisole (97.8–100%). It is suggested that further research on large scale be carried out involving a large number of animals, doses higher than those used in the current study, identification of active principles, and standardization of dose and toxicity studies for drug development.

3.5. Antioxidant effect

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

3.6. Hepatoprotective activity

Hydro-ethanolic extract (70%) of *Calotropis procera* flowers was prepared and tested for its hepatoprotective effect against paracetamol-induced hepatitis in rats. Alteration in the levels of biochemical markers of hepatic damage like SGPT, SGOT, ALP, bilirubin, cholesterol, HDL and tissue GSH were tested in both treated and untreated groups. Paracetamol (2 g/kg) has enhanced the SGPT, SGOT, ALP, bilirubin and cholesterol levels and reduced the serum levels of HDL and tissue level of GSH. Treatment with hydro-ethanolic extract of *C. procera* flowers (200 mg/kg and 400 mg/kg) has brought back the altered levels of biochemical markers to the near normal levels in the dose dependent manner.
3.7. 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 46.

3.8. Anti-diarrhoeal activity

The dry latex (DL) of Calotropis procera, a potent anti-inflammatory agent has been evaluated for anti-diarrhoeal activity. Like atropine and phenylbutazone (PBZ), a single oral dose of DL (500 mg/kg) produced a significant decrease in frequency of defecation, severity of diarrhoea and afforded protection from diarrhoea in 80% rats treated with castor oil. To understand the mechanism of its anti-diarrhoeal activity, we further evaluated its effect on intestinal transit, castor oil induced intestinal fluid accumulation (enteropooling) and electrolyte concentration in the 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. However, it did not alter the electrolyte concentration in the intestinal fluid as compared to castor oil treated rats 47.

3.9. Anticonvulsant effects

The anticonvulsant activity of different root extracts of Calotropis procera in rats in order to evaluate the traditional use of this plant. The anticonvulsant activity of different extracts of Calotropis procera roots was studied against 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 stupor phase, as compared to control. In the PTZ test, the chloroform extract showed a highly significant (p < 0.001) effect, whereas the aqueous extract showed the most significant (p < 0.01) effect as compared to control 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 the absence (petitmal) and tonicclonic (grand mal) type of seizures 48.

3.10. Antimicrobial activity

Antimicrobial activities of chloroform and methanol extracts of seeds of Calotropis procera located in the forest area of Ghaziabad, India. Chloroforms extract of Calotropis procera seeds exhibited better antimicrobial activity. On the other hand, the extracts obtained Calotropis procera seeds tested have been evaluated for their possible in vitro antibacterial activities based on paper disc method 49.

3.11. OTHER ACTIVITY

3.11.1 Oestrogenic functionality

Effects of ethanolic and aqueous extracts of Calotropis procera roots have been studied on oestrous cycle and on some parameters of oestrogenic functionality in rats. Both extracts have been shown to interrupt the normal oestrous cycle in 60 and 80%, respectively, of rats treated. The rats exhibited prolonged dioestrous stage of the oestrous cycle with consequent temporary inhibition of ovulation.
The contemporary administration of commercial oestro-progestinic preparation exhibited the same effects in 100% of rats treated. However, the extracts have not demonstrated to possess oestrogenic activity when tested in immature female bilaterally ovariectomized rats.

3.11.2 Antinociceptive activity

Antinociceptive effect of proteins from the *Calotropis procera* latex using three different experimental models of nociception in mice. The latex protein fraction administered intraperitoneally in male mice at the doses of 12.5, 25 and 50 mg/kg showed the antinociceptive effect in a dose dependent manner compared to the respective controls in all assays. Inhibitions of the acetic acid-induced abdominal constrictions were observed at the doses of 12.5 (67.9%), 25 (85%) and 50 (99.5%) mg/kg compared to controls. Latex protein at the 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 pretreatment with naloxone (1 mg/kg). In the hot plate test, an increase of the reaction time was observed only at 60 min after the treatment with latex at the doses of 25 (79.5%) and 50 (76.9%) mg/kg, compared to controls and naloxone was ineffective to reverse the 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.

3.11.3 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 MRC 76 _CQ-resistant strains, flower and bud extracts being the most active. Though 220, 440 times less effective than CQ, these extracts deserve further studies aimed at the identification of the active constituents. In the meantime, the obtained results provide a support for the ethnobotanical use of the plant.

4. TOXICOLOGICAL STUDY

*Calotropis procera* (giant milkweed) has been reported to have numerous medicinal arid economic importance but was observed to be potentially injurious to the body especially after prolonged or chronic use.

Calotropin which is found in latex cause slowing of heart beat and gastroenteritis if injected into the lymph sac of frog. It is supposed to cause death if it is given more than 0.12 mg/k.g. Latex is irritant to the skin and mucous membrane and said to cause blindness. Approximately 4-5 ml of latex may cause death. It may rupture the muscle of intestine and colon and death may occur. The plant may cause sever bullous dermatitis, slowed but stronger heart beat, labored respiration, increased blood pressure, convulsions and death. Latex is highly toxic to human eyes presented with sudden painless dimness of vision with photophobia.

According to Dunean the root bark is said to be similar to Ipecacuanha because of the presence of madaralban which shows emetic effects.

5. CONCLUSION

The above collected information regarding the use of *Calotropis procera* in world is matched with available literature. The use of this plant suggests that the conservation of the plant in question. Furthermore, the uses of this plant which is not known by the human should be widely disseminated in the world under study so that they can exploit its uses for their well being in daily life.

*Calotropis procera* is one of the potential candidates for petrofarming. The latex obtained from *Calotropis procera* may be hydrocracked to obtain hydrocarbons. There is need to more research work on *calotropis procera* to obtain petroleum products.

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