A REVIEW ON MEDICINAL UTILITY OF CALOTROPIS PROCERA

Preeti Chaudhary1*, Shamim Ahamad1, Najam Ali Khan2

1Department of Pharmacy, Translam Institute of Pharmaceutical Education and Research, Meerut, Uttar Pradesh, India.
2Department of Pharmacy, I.F.T.M University Moradabad, Uttar Pradesh, India.

*Corresponding Author: Preeti Chaudhary
Department of Pharmacy, Translam Institute of Pharmaceutical Education and Research, Meerut, Uttar Pradesh, India.

ABSTRACT
Calotropis procera is a wild growing plant of family Asclepiadaceae. It is well known for its medicinal properties. The present paper enumerates the medicinal utility of different parts of Calotropis procera for the treatment of various human ailments. Different parts of this plant have been reported to exhibit anti-inflammatory, analgesic, antitumor, antihelmintic, hepatoprotective, antiarrhoegal, anticonvulsant, antimicrobial, oestrogenic, antinociceptive, antimalarial and antioxidant properties. Calotropis procera contains various phytoconstituents such as alkaloids, flavonoids, sterol, saponins, triterpinoids, tannins, resins, anthocyanins, proteolytic enzymes in latex, cardenolide, cardiac glycosides which are responsible for different pharmacological activities. Calotropis procera is a well known plant and has been traditionally used for diarrhoea, stomatic, sinus fistula, and skin disease and the leaf part is used to treat jaundice. It also has been used as a purgative, digestive, emetic, expectorant, sedative, blood purifier, an antidote for snake poisoning.3.

KEYWORDS: Calotropis procera, Medicinal utility, Phytoconstituents, Hepatoprotective, Flavonoids.

1. INTRODUCTION
Calotropis procera of family Asclepiadaceae is a tropical plant growing wild in warm climate up to an altitude of about 1050 meters. It is a native plant of North Africa. This plant is well distributed throughout India, particularly it is abundantly found in Rajasthan. It also found in Pakistan, Africa, Mexico, Australia, Egypt, Central and South America and Caribbean islands,1,2 From pre-historic times to the modern era in many parts of the world and India, plants, animals and other natural objects have profound influence on culture and civilization of man. Since the beginning civilization, human beings have worshiped plants and such plants are conserved as a genetic resource and used as food, fodder, fiber, fertilizer, fuel, and febrifuge in every other way, Calotropis procera is one such plant.3

In ancient Ayurvedic medicine the plant Calotropis procera is popularly known as “Raktha Arka” and Caotropis gigantea as “Sweta Arka”. Both of them are often similar in their botanical aspects and also have similar pharmacological effects.4,5 Common names for the plant include apple of Sodom, Sodom apple, Stabrgh, Kapok tree, King's crown, Rubber bush or Rubber tree.

A number of ethnomedicinal uses of the drug are reported. Whole plant was used either alone or with other herbs for the treatment of common diseases such as fever, rheumatism, indigestion, cold, eczema and diarrhoea.4,5,6 paste of root bark was locally applied in the treatment of elephantiasis and Root bark powder was used to treat diarrhea and dysentery and it is an excellent substitute for ipecac. Traditionally it was used to treat cholera, extracting guinea worms and indigestion.6

Scientific Classification
Kingdom : Plantae
Subkingdom : Tracheobionta
Super division : Spermatophyta
Division : Magnoliophyta
Class : Magnoliopsida
Subclass : Astereae
Order : Gentianales
Family : Asclepiadaceae
Subfamily : Asclepiadoideae
Genus : Calotropis
Species : Calotropis procera7

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trafterpenoids, calotropursenyl acetate and calopfriedelenyl, a norditerpenyl ester, calotropternyl ester oleane triterpenes like calotropoleanly ester, procerleanol A and B and cardiac glycosides calotropogenin, calotropin, uscharin, calotoxin and calactin. The plant also has been investigated for the presence of cardenolides and anthocyanins (Table 1).[10]

2.1. Leaves The leaves contain mainly a-amyrin, a-amyrin acetate, β-sitostero, uscharin, calotoxin, calotropin, calotropagenin.[11]

2.2. Latex The latex contains caoutchouc, calotropin, calotoxin 0.15%, calactin 0.15% uscharin 0.45%, trypsin, voruscharin, uscharidin, uscharin and proceroside.[12]

2.3. Flower The flower contains the flavonoids, quereitin-3-rutinoside, sterol, calactin, calatoxin, calotropagenin, calotropin, polysaccharides with D-glucose, glucosamine and L-rhamnose. Flowers also contain enzymes 3-proteinase and calotropin (protease). Other chemical constituents of Calotropis procera flowers are lupeol, uscharin, proceroside, procerogenin (cardenolide), syriogenin, taraxast-20(30)-en-3-(4-methyl-3-pentenoate), 3-thiazoline cardenolide, gigantin, giganteol, isogiganteol, uscharidin, uscharigenin voruscharin a-calotropeol, 3-epimorenol, a-lactuceryl acetate and a-lactuceryl isovalerate.[13]

2.4. Bark Root bark of Calotropis procera contains triterpenes, A new norditerpenyl ester, named Calotropternyl ester, and two unknown pentacyclic triterpinoids, namely calotropursenyl acetate and calopfriedelenyl acetate35, akundarol isovalerate, mundarol isovalerate and quercetin-3-rutinoside.[14]

Table 1: Phytochemical Screening of Calotropis procera.

<table>
<thead>
<tr>
<th>Sl. No</th>
<th>Class of Compounds</th>
<th>Leaves</th>
<th>Flower</th>
<th>Root</th>
<th>Bud</th>
<th>Tests performed</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Alkaloids</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>Dragendorff’s test, Mayers test</td>
</tr>
<tr>
<td>2</td>
<td>Carbohydrates</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>Molish test, Fehling test</td>
</tr>
<tr>
<td>3</td>
<td>Glycosides</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>Keller killiani test</td>
</tr>
<tr>
<td>4</td>
<td>Phenolic compounds/tannins</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>Ferric chloride test, Lead acetate test, Dilute Iodine solution</td>
</tr>
<tr>
<td>5</td>
<td>Proteins and amino acids</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>Xantho protein test, Ninhdyrin test, Biuret test</td>
</tr>
<tr>
<td>6</td>
<td>Flavanoids</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>Ammonia test, Shinoda test, Lead acetate test</td>
</tr>
<tr>
<td>7</td>
<td>Saponins</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>With water With Na2CO3, Foam test</td>
</tr>
<tr>
<td>8</td>
<td>Sterols</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>Liebermann-Burchard test, Salkowski test, Hesse’s test.</td>
</tr>
<tr>
<td>9</td>
<td>Acid compounds</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>With Na2CO3, With litmus paper</td>
</tr>
<tr>
<td>10</td>
<td>Resins</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>With double distilled water, With acetone and conc. HCl</td>
</tr>
<tr>
<td>11</td>
<td>Peroxides</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>Potassium Iodide test</td>
</tr>
<tr>
<td>12</td>
<td>Polyuronoids</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>Haemotoxylin test</td>
</tr>
</tbody>
</table>

Note: ‘+’ sign indicates presence and ‘−’ sign indicates absence.

Figure 1: Calotropis procera (Leaves & Flowers)
3. MEDICINAL UTILITY OF CALOTROPIS PROCERA

*Calotropis procera* is small, erect and compact shrub, which is used in several traditional medicines to cure various diseases. This plant has been known to possess its analgesic, antitumor, antihelmintic, antioxidant, hepatoprotective, antidiarrhoeal, anticonvulsant, antimicrobial, oestrogenic, antinociceptive and antimalarial activity (Table 2). [10]

Table 2: Medicinal utility of *Calotropis procera*.

<table>
<thead>
<tr>
<th>S/No</th>
<th>Part Used</th>
<th>Medicinal Utility</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Whole Plant</td>
<td>To treat common diseases such as fever, rheumatism, indigestion, cold, eczema and diarrhea. In boils and also to remove thorn from body for the treatment of jaundice. [15]</td>
</tr>
<tr>
<td>2.</td>
<td>Root</td>
<td>Eczema, leprosy, elephantiasis, asthma, cough and rheumatism. In the treatment of Diarrhoea and dysentery. In case of diarrhoea it changes the faecal matter into a semisolid mass with in the first day of treatment. [16]</td>
</tr>
<tr>
<td>3.</td>
<td>Stem</td>
<td>For the treatment of skin diseases, enlargements of abdominal viscera, intestinal worms, leprosy and in Leucoderma.</td>
</tr>
<tr>
<td>4.</td>
<td>Leaves</td>
<td>To prompt healing, used for joints and waist pain, for asthma. To cure malarial fever. Eczema, leprosy, elephantiasis, asthma, cough and rheumatism. In rheumatism, gout and to relieve pains. [9]</td>
</tr>
</tbody>
</table>

4. PHARMACOLOGICAL ACTIVITIES

4.1 Hepatoprotective Activity

An aqueous ethanolic extract (70 %) of *Calotropis procera* flowers was prepared and tested for its hepatoprotective effect against paracetamol-induced hepatitis in albino 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. [17]

4.2 Antioxidant Activity

The antioxidant components were extracted using 80% aqueous methanol, 80% aqueous ethanol and 80% aqueous acetone solvents. The antioxidant yield from leaves and flowers of *Calotropis procera* ranged from 8.48 to 14.07 g/100 g dry weight. The total phenolic and flavonoid content were considerable with total phenolic yields (expressed as gallic acid equivalents) reported in the range 0.11 to 0.32 g/100 g dry weight, and total flavonoid content (expressed as catechin equivalents) reported in the range 0.01 to 0.10 g/100 g dry weight. *C. procera* extracts exhibited a reasonable DPPH radical scavenging activity (IC50 8.81 to 37.30 mg/ml) and inhibition of linoleic acid peroxidation (13.63 to 41.53 %). [18]

4.3 Antipyretic Activity

The ethanolic extract of the aerial parts, aqueous extract of flowers and aqueous solution of dry latex of *Calotropis procera* showed significant antipyretic activity in animal models that was comparable to aspirin. [19]

4.4 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.\(^\text{[20]}\)

4.5 Anti-inflammatory Activity
The crude dry latex of Calotropis procera possesses a potent anti-inflammatory activity. The anti-inflammatory activity of petroleum ether, acetone, methanol and aqueous extracts of dry latex of Calotropis procera was tested in carrageenan induced rat paw oedema model. All the fractions exhibited anti-inflammatory activity but inhibition of edema was found to be greatest with the acetone and aqueous extracts.\(^\text{[21]}\)

The anti-inflammatory property of the latex of Calotropis procera was studied on carrageenin and formalin induced rat paw oedema model. A single dose of the aqueous suspension of the dried latex was effective to a significant level against the acute inflammatory response.\(^\text{[22]}\) A chloroform soluble fraction from Calotropis procera root showed significant dose related anti-inflammatory activity in rats using the pharmacologic models of carrageenan induced pedal oedema, cotton pellet granuloma and formaldehyde induced arthritis.\(^\text{[23]}\)

4.6 Anti-diarrhoeal Activity
The dry latex of Calotropis procera has been evaluated for anti-diarrhoeal activity. Like atropine and phenylbutazone, single oral dose of dry latex 500 mg/kg produced a significant decrease in frequency of defecation, severity of diarrhea and afforded protection from diarrhea in 80% rats treated with castor oil. Dry latex of Calotropis procera produced a decrease in intestinal transit (27-37%) as compared to 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 as compared to castor oil treated rats.\(^\text{[24]}\)

4.7 Spasmolytic Activity
The aqueous extract of Calotropis procera was evaluated for its spasmytic activity using in vitro trachea smooth muscle chain of guinea pigs. The extract (50, 100 & 200 µg/ml) showed a dose dependent relaxant activity probably exhibited through the direct relaxant action on the smooth muscles.\(^\text{[25]}\) Kumar and Shivkar reported the effect of dried latex on smooth muscles of gastrointestinal tract. Oral administration of dried latex to rats (50–1000 mg/kg) produced a dose-dependent decrease in intestinal transit along with a decrease in intestinal content as compared to control group. At lower doses dried latex produced dose-dependent contractions of gastrointestinal smooth muscles in vitro (rabbit ileum and fundus of rat stomach) that was followed by desensitization at higher doses.\(^\text{[26]}\)

4.8 Antidiabetic Activity
Dry latex of Calotropis procera was evaluated for its antioxidant and anti-diabetic activity against alloxan induced diabetes in rats. Daily oral administration of dry latex at 100 and 400 mg/kg doses produced a dose dependent decrease in the blood glucose and increase in the hepatic glycogen content. Dry latex also prevented the loss of body weight in diabetic rats and brought down the daily water consumption to values comparable to normal rats. Dry latex also produced an increase in the hepatic levels of the endogenous antioxidants, namely superoxide dismutase (SOD), catalase and glutathione while it decrease the levels of the thiobarbituric acid reactive substance (TBARS) in alloxan induced diabetic rats.\(^\text{[27]}\)

4.9 Antiulcer Activity
Basu A 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.\(^\text{[28]}\)

4.10 Anti-Fertility Activity
The effect of Ethanolic extract of the roots of Calotropis procera in albino rats was evaluated to explore its anti-fertility 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).\(^\text{[29]}\)

4.11 Analgesic Activity
The analgesic activity of various parts of Calotropis procera viz. roots, aerial parts and latex have been evaluated by Basu A. The ethanol extract of aerial parts, chloroform extracts of roots and the aqueous solution of dried latex were tested in acetic acid induced writhing model and exhibited significant analgesic activity.\(^\text{[30]}\)

4.12 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 µl 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 rational for the traditional use of this plant in the management of wound healing.\(^\text{[30]}\)
4.13 Antimicrobial Activity
The antimicrobial activity of aqueous and ethanolic extract of roots and leaves of *Calotropis procera* against *Staphylococcus aureus*, *Streptococcus pyogenes*, *Escherichia coli* and *Pseudomonas aeruginosa* was studied on disc method. Both ethanolic and aqueous extracts of *Calotropis procera* had inhibitory effect on the growth of isolates. The effect exhibited by ethanolic extract of leaves and roots was significantly greater than that of the aqueous extract of leaves and roots.[31]

4.14 Antinociceptive Activity
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 constricrions 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 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.[32]

4.15 Anticonvulsant Activity
Jalalpure reported the anticonvulsant activity of different root extracts of *Calotropis procera* which 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), pentylenetetrazol (PTZ), lithium-pilocarpine and electrical kindling seizures. In the 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.[33]

4.16 Antiarthritic Activity
The methanol extract (ML) of dry latex was showed protection against inflammation and oxidative stress in monoarthritis induced by Freund’s complete adjuvant (FCA) in rats. Daily treatment of rats with methanolic extract (50 and 500 mg/kg) and standard anti-inflammatory drug rofecoxib (20 and 100 mg/kg), produced a significant attenuation in the inflammatory response and ameliorated the arthritic changes in the joint. The protection afforded by methanolic extract and rofecoxib was more pronounced than that of phenylbutazone and was associated with normalization of the levels of inflammatory mediators and biochemical parameters of oxidative stress. However, the overall protection afforded by rofecoxib was better than that of methanolic extract.[34]

4.17 Antimalarial Activity
The traditional use of latex is given in malarial and low hectic fevers.[35] Sharma and Sharma screened the ethanolic extracts of *C. procera* leaves, stems, roots, flowers and flower buds, for their *in vitro* antimalarial activity against a chloroquine (CQ) sensitive strain, MRC 20 and a chloroquine resistant strain, MRC 76 of *Plasmodium falciparum* using the Desjardins method and the effectiveness of its fractions were compared with the CQ sensitive strain than the CQ resistant strain.[36, 37] In further investigation, *in vitro* hemolysis of human erythrocytes has been studied with above extracts. The putative anti-plasmodium activity of these extracts was correlated to their cytotoxicity as represented by the *in vitro* rate of hemolysis.[38]

4.18 Cardiovascular Effect
Latex of *Calotropis procera* was evaluated for protection against isoproterenol (20 mg/100g) 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.[39]

4.19 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.[40]

4.20 Antitumor Activity
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 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.[41, 42]

CONCLUSION

Calotropis procera is a potential plant with many curative principles and economic values. It is used as a traditional medicinal plant with unique properties. This review shows that it is a popular remedy in Ayurvedic and traditional practitioners for the treatment of a range of ailments. Though Calotropis procera has various medicinal applications, but still 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, its wide variety of pharmacological actions Calotropis procera is a potential source for the development of new drugs to pharmaceutical industry.

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