Bulletin of Environment, Pharmacology and Life Sciences
Bull. Env. Pharmacol. Life Sci., Vol 4 [2] January 2015: 156-162

Online ISSN 2277-1808
Journal's URL:http://www.bepls.com
CODEN: BEPLAD
Global Impact Factor 0.533
Universal Impact Factor 0.9804

REVIEW ARTICLE

Pharmacognostical Aspects and Pharmacological activities of *Calotropis procera*

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ABSTRACT
Medicinal plants have remained the major sources of drugs; in fact many of the Currently available drugs were derived either directly or indirectly from them. The Approach to new drugs through natural products has proved to be the single most successful strategy for the discovery of new drugs. In the past decade, research has been focused on scientific evaluation of traditional drugs of plant origin for the treatment of various diseases. Arka (Calotropis procera) is small, erect and compact shrub, which is used in several traditional medicines to cure various diseases. This shrub has been known to possess analgesic, antitumor, antihelmintic, antioxidant, hepatoprotective, antidiarrhoeal, anticonvulsant, antimicrobial, oestrogenic, antinociceptive, and antimalarial activity. This review is a sincere attempt to summarize the information concerning pharmacognostical features of Calotropis procera shrubs.
Key words: Calotropis procera, medicinal plants.

Received 12.09.2014 **Revised 23.11.2014** **Accepted 21.12.2014**

INTRODUCTION

Arka (*Calotropis procera*) an important drug of Ayurveda is known in this country from the earliest time. It is mentioned by the earliest Hindu writers and the ancient name of the plant which occurs in the vedic literature was Arka alluding to the form of leaves, which was used in the sacrifical rites. There are two common species of Calotropis, viz. *Calotropis gigantea* (Linn.) and *Calotropis procera* (Ait.) described by the Sanskrit writers (1). Both the species are used as substitutes for one another and are said to have similar effects. In Dhanvantari Nigantu three varieties of Arka are mentioned viz. Rajarkah, Suklarkah and Sveta mandarah. It has 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 abortifacient, spasmogenic and carminative properties, antidysentric, antisyphilitic, antirheumatic, antifungal, mullusccide, diaphoretic and for the treatment of leprosy, bronchial asthma and skin infections Different parts of the plant have been reported to possess a number of biological activities such as proteolytic, antimicrobial, larvicidal, nematocidal, anticancer, anti-inflammatory (3). Its flowers possess digestive and tonic properties. On the contrary, the powdered root bark has been reported to give relief in diarrhoea and dysentery. The root of the plant is used as a carminative in the treatment of dyspepsia. The root bark and leaves of *Calotropis procera* are used by various tribes of central India as a curative agent for jaundice (4).

GEOGRAPHIC DISTRIBUTION

C. Procera is drought-resistant, salt-tolerant to a relatively high degree, and it disperses seeds through wind and animals. It quickly becomes established as a weed along degraded roadsides, lagoon edges and in overgrazed native pastures. It has a preference for and is often dominant in areas of abandoned cultivation especially sandy soils in areas of low rainfall; assumed to be an indicator of over-cultivation. C. Procera is native to India, Pakistan, Nepal, Afghanistan, Algeria, Iran, Iraq, Israel, Kenya, Kuwait, Niger, Nigeria, Oman, Saudi Arabia, United Arab Emirates, Vietnam, Yemen and Zimbabwe (7).

BOTANICAL DESCRIPTION OF Calotropis procera

Bark & Branches

The bark is thick, rough and corky and a yellow-brown colour; twigs are green and fleshy and may have a covering of tomentum (white fur like hairs).

Leaves

Leaves are opposite-decussate, simple, ovate to obovate with 4-6 pairs of subopposite nerves prominent on the abaxial surface, an acute apex, sessile (almost decurrent) base, a pale green colour, and quite large which is about 30x25
cm (8).

Inflorescences

Inflorescences arise from the base of the leaves in pedunculate (c.7cm) cymes of 3-20.

Flowers

Flowers consist of 5 small triangular dirty white sepals, 5 thick ovate petals (c1cm x 1cm) which are white at the base and purple at the tips and 5 purple tipped stamens, which surround a white 5 lobed stigma (9).

Fruits

Fruits consist of green, spongy ovoid fruits (follicles), up to 15cm long by 10cm wide. They split open to release plumed, papery light brown seeds with a pappus of white filaments up to 6cm long on one side. The main flowering period would be from March to October (10).

Macroscopical characteristics

Macroscopical characteristics of various parts of Calotropis procera are as follows:

Root

The root occurs in the entire condition. The bark is separated from the wood 0.5-2.0 cm. in diameter bearing rootlets with diameter varying from 0.2 to 0.5 cm. externally whitish grey in colour, wrinkled in the fresh condition, plenty of whitish latex exudes from cuts or wounds in the bark. Fracture is incomplete.

Leaf

Simple, opposite, sub-sessile, slightly thick, fleshy, coriacious,10-15 cm. long and 4.5 to 6.5 cm. broad, broadly cuneate, obovate or obovate oblong, slightly cordate and auricled at base with tuff of short simple hairs on the upper side near place of the attachment to the petiole. The tender leaves are covered with ashy gray pubescence. Mature leaves are nearly smooth or even glabrous and pale green
(11).

Flowers

Regular, bisexual, liliac or pale rose, purple or light greenish yellow and have a faint odour. They are arranged in simple or rarely compound cymose corymbs at the ends of laterally placed or interpetiolar peduncles arising from alternate sides of the nodes. Each cluster is surrounded by an involucre of several small oblong pointed scaly caducous bracts. Flower buds ovoid.

Calyx

Five lobes broadly ovate with small fleshy teeth like glands within the base.

Corolla

Regular, gamopetalous, pale rose purple or liliac, subcordate to broadly sub-campanulate with a short tube and five broad ovate, lanceolate, valvate, spreading lobes.

Stamens

Five, inserted at the base of the corolla. Filaments united to form a large staminal column provided with five conspicuous radiating coronal appendages that are completely adnate to, but slightly shorter than the column. The appendages are fleshy, pale purplish or yellowish white and laterally compressed with a circinnately recurved hollow corsal spur at base and two short obtuse obliquely divergent cuticles towards the top just below the apex. Anthers short, broad,
somewhat horny with broadly triangular membranous anther tips that are inflexed over the sides of the stigmatic hood.

Root bark

The tap roots are found to be having prominent tops with rounded head and rest of the portion spirally curved. These hard roots are grayish white in colour and exhibit sap exudations at the places where bark has been cut. The bark of the older roots is cracked at places. The bark is yellowish grey outside and yellowish white inside. The upper cork portion is spongy and rough while the inner portion of bark is smooth and mucilaginous. The dried bark is bitter to taste (12).

PHARMACOLOGICAL SCREENING

1. Pharmacological activities

The plant has attracted much attention due to following biological activities: The previous pharmacological studies include reports of anticancer, antifungal 13 and insecticidal activity of C.

procera. The flowers of the plant exhibit hepatoprotective activity 14, anti-diabetic, anti-inflammatory, antipyretic, analgesic, and antimicrobial effects and larvicidal activity (15, 16). The latex of the plant is reported to possess analgesic and wound healing activity (17, 18), as well as anti-inflammatory (19) and antimicrobial activity (20) while the roots are reported to have anti-fertility (21) and anti-ulcer effects (22).

2. 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 tan 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 (23). 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 forma l in in the 1s t and 2nd phases, respectively, and this effect was not reversed by pretreatment 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. (24).

3. 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 uterotropic activity was observed at a dose of 250 mg⁄kg (1⁄4 of LD50). No antiestrogenic activity was detected (25).

4. 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 based on apoptosis and cell cycle disruption (26).

5. 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 lessthan 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 (27).

6. 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 anti-diabetic agent was comparable with that of the standard antidiabetic drug, glibenclamide (28).

7. 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 (29).

8. 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 .

9. 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 (30).

10. 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), pentylenetetrazol (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 (31).

11. 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 for their possible in vitro antibacterial activities using the paper disc method (32).

12. 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 administration 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 (33).

13. 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 constituents. The results obtained support the ethnobotanical use of this plant (34).

14. Anti-diabetic Activity

Dry latex of C.procera was evaluate for its antioxidant and anti-hyperglycemic effects against alloxan-induced diabetes in rats. Daily oral administration of dry latex at 100 and 400mg/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 and increase in the hepatic levels of the endogenous antioxidants, namely superoxide dismutase (SOD), catalase and glutathione, while it brought down the levels of the thiobarbituric acid-reactive substance(TBARS) in alloxan-induced diabetic rats. The efficacy of dry latex as an antioxidant and as and anti-diabetic agent was found comparable to the standard anti diabetic drug, glibenclamide (35). In one study the various parts of the plant, viz.roots, aerial parts and latex have been evaluated for analgesic activity.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. The ethanolic extract of flowers of the pant found to possess a weak analgesic activity (36).

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 (37). Latex of Calotropis procera was studied for its inflammatory effects using pedal oedema and air pouch models of inflammation 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 inflammation in different models could be used to evaluate anti-inflammatory drugs (38).

ADVERSE EFFECTS

The adverse effects of Calotropis procera consumption are reported to cause blisters, lesions and eruptions when taken by patients for the treatment of joint pains and gastrointestinal problems. The preparations of *Calotropis procera* need to be used under the careful surveillance of a trained medical practitioner.

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 (39). 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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CITATION OF THIS ARTICLE

Maryam Rahimi. Pharmacognostical Aspects and Pharmacological activities of *Calotropis procera.* Bull. Env. Pharmacol. Life Sci., Vol 4 [2] January 2015: 156-162