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Review of the Ethnobotany, Phytochemistry and Pharmacological Characteristics of *Calotropis procera* Linn

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ABSTRACT

Medicinal plants are used from the ancient time as the major sources of drugs. The fact is that we can obtain many of the presently available drugs, either directly in the extract form or in the modified synthetic form. Naturally, plants have the ability to synthesize products beneficial for us namely as phytoconstituents that are used to perform biological functions, which also protect us against predators such as virus fungi and other microorganisms. The phytoconstituents obtained from the natural products are one of the most successful strategies for the discovery of new drugs. Calotropis procera is a plant which is used in several traditional medicine and folklore systems to cure various ailments as reported in the Hindu literature. It is widely used in the Indian traditional medicinal system as well as in Arabic, Unani, and Sudanese systems. C. procera is also used by various tribes of the world as a curative agent for ailments such as skin disease and elephantiasis. Different parts of the plant have been reported to possess various phytochemicals containing cardiotonic agents such as calotropin, calotropagenin, calotoxin, calotropagenin and voruscharine, steroids, di and triterpenes such as stigmasterol, β-sitosterol, flavonoids, polyphenolic compounds, and various newer reported hydrocarbons and proteins. This shrub is known to possess a wide range of pharmacological activities such as anticancer, acaricidal, schizonticidal, antimicrobial, anthelmintic, insecticidal, anti-inflammatory, antidiarrheal, anticancerous, and larvicidal activities with other beneficial properties. C. procera is small, erect shrub, which is used in several herbal and empirical medicines to cure simple and deadly diseases and disorders. It is also reported widely in various folklore preparations and ethnomedicines. This review is a profound attempt to stack the information concerning pharmacognostical, phytochemical, and pharmacological features of C. procera shrubs. The knowledge on the ethnobotany, pharmacology, phytochemistry, biological activity, and toxicity of the shrubs called Calotropis procera is summarised in the review that is being presented.

Keywords*: Calotropis procera, pharmacology, phytochemistry, biological activity, Toxicity.*

INTRODUCTION

Botanical Description, Occurrence, and Ethno Pharmacology

Calotropis is a tiny genus with three recognized species that belongs to the Asclepiadaceae subfamily Apocynaceae. They are *Calotropis gigantea* (L.) Dryand, *Calotropis procera* (Aiton) Dryand, and *Calotropis acia*, all synonyms for *Asclepias gigantea*. Ham. Buch (syn.

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Asclepias herbacea and Madoriusacia). These species are multi-stemmed, 3–4 m tall shrubs or small trees that yield an abundance of milky latex. The underside of the opposite, thick, fleshy, broad leaves is hairy. Flowers are white with five fleshy lobes, and the terminals of *C. gigantea's* flowers are pale lilac and those of *C. procera's* flowers are purple violet (Figure 1). The seeds are ovoid with an apical tuft of white silky hairs, while the fruits are a fleshy aggregate with a pointy tip. Both of the plants grow quickly and bloom all year long. While *C. acia* is limited to India, Bangladesh, and Nepal in South Asia, both *C. gigantea* and *C. procera* occur natively from Africa to South and Southeast Asia, including southern China [1].

Figure 1. Flowers of Calotropis gigantea (left) andCalotropis procera (right)

In more or less warm, arid regions all over India, mainly in Sub-Himalayan tracts, from Deccan to Kanya- Kumari, Linn's Calotropis procera is widely found as a weed. Calotropis proceraLinnis is a 5.4 m tall, erect, tall, broad, many-branched, perennial shrub or small tree with milky latex all over. The bark is flexible and corky. Strong, terete branches with repressed, fine, cottony pubescence (especially on young). The leaves are opposite, cordate at the base, decussate, broadly ovate-oblong, elliptic, or obovate, thick, glaucous, green, and covered with fine cottony pubescent hair when young. Young plants have umbellate cymes with tomentose flowers. Glabrous, elliptical, and sharp describe the calyx.Corolla glabrous, with lobes that are upright, ovate, and sharp, and coronal scales that are 5 to 6 and that are equally longer than the staminal column. Follicles can be oval, ellipsoid, or subglobose. Seeds are 3.2 cm long, roughly oval, sharp, flattened, minutely tomentose, brown in colour, and silky.[1]

Procera Calotropis Leprosy, ulcers, piles, and ailments of the spleen, liver, and abdomen are among the many illnesses that are treated with linn in the Sudanese, Unani, Arabic, and Indian traditional medical systems[2]. The latex is used to treat leprosy[3], bronchial asthma, skin affiction [4], spasmogenic diarrhoea, antidysentric, antisyphilitic, antirheumatic, antifungal, mullusccide[5,6], and diaphoretic conditions. Numerous biological actions, including proteolytic[7], antibacterial[8], larvicidal[9], nematocidal[10], anticancer[11,12], and anti-inflammatory[13], have been linked to various components of the plant. Digestive and tonic characteristics can be found in its flowers. On the other hand, it has been claimed that the powdered root bark can treat diarrhoea and dysentery[14].

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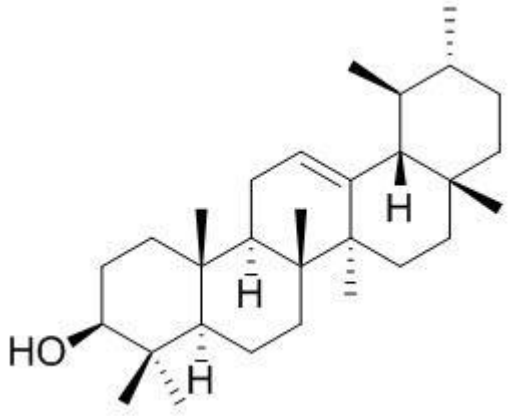

Fig.2. α-Amyrin

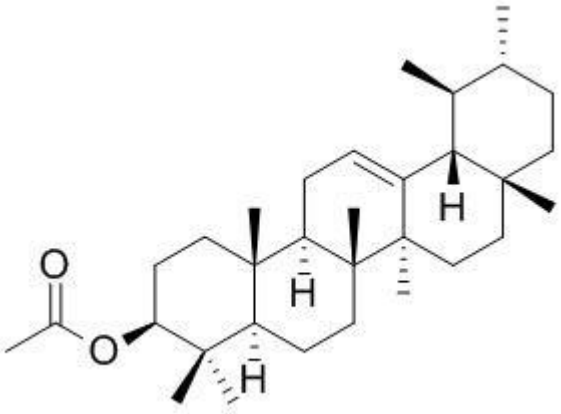

Fig.3. α-Amrin acetate

In order to alleviate dyspepsia, the plant's root is utilized as a carminative. [15]. Several tribes in central India employ the roots, bark, and leaves of *Calotropis procera* as a treatment for jaundice [16].

Phytochemistry

Numerous types of substances, including Cardenolide, triterpinoids, alkaloids, resins, anthocyanins, and proteolytic enzymes in latex, as well as flavonoids, tannins, sterol, saponins, and cardiac glycosides, have been discovered through phytochemical studies on the plant Calotropis procera.[17- 19].Terpenes, multiflorenol, and cyclisadol are all found in flowers [20].

Leaves

The primary compounds found in the leaves are a-amyrin [21] (Figure 2), a-amyrin ac-etate22 (Figure 3), ß-sitosterol [23–24] (Figure 4), urosolic acid [25–26] (Figure 5), cardenolides, calotropin1 (Figure 6), and calotropagenin [27].

Latex

The latex contains the following substances: caoutchouc, calotropin, calotoxin (0.15 percent) (fig. 8), calactin (0.15 percent) (fig. 9), uscharin (0.45 percent) (fig. 10), trypsin, voruscharin (fig. 11), uzarigenin, syriogenin, and proceroside[28-31].

Flower

The flower includes flavonoids, sterol [32], calactin, calotoxin, calotropagenin, calotropin, polysaccha-rides containing D-arabinose, glucose, glucosamine, and L-rhamnose, as well as queretin-3-ratinoside, calactin, and calotoxin. The enzymes 3-proteinase and calotropain are also found in flowers (protease).

Other chemical components of C. procera flowers include gigantin, giganteol, isogiganteol, uscharidin, uzarigenin voruscharin, proceroside, proceragenin (cardenolide), syriogenin taraxast-20(30)-en-3-(4-methyl-3- pentenoate), 3-thiazoline cardenolide, a- lactuceryl acetate, and alactuceryl isovalerate [33].

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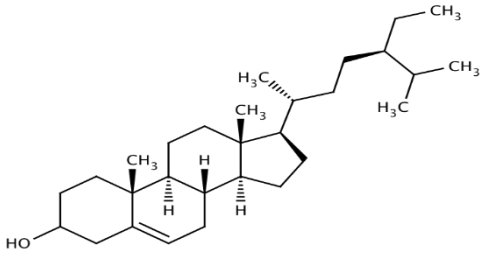

Fig. 4. ß- Sitosterol

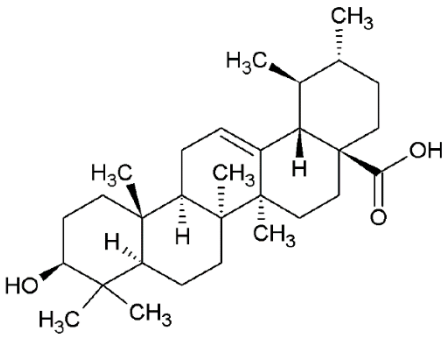

Fig. 5. Urosolic acid

Bark

Triterpenes, a newly discovered norditerpenyl ester called calotropterpenyl ester, two unidentified pentacyclic triterpinoids [34], namely calotropursenyl acetate and calotropfriedelenyl acetate [35], akundarol isovalerate, mundarol isovalerate, and quercetin - 3- rutinoside[36] are all present in the root bark of Calotropis procera .

Bioactivity

Calotropis procera is regarded as a valuable medicinal plant and is utilised in a variety of traditional cures [37-39], including

A. Analgesic

In this study, we assessed the analgesic efficacy of Calotropis proceradrylatex (DL). The analgesic efficacy of DL against acetic acid-induced writhing was significantly dosage-dependent and was produced by a single oral dose ranging from 165 to 830 mg/kg. In comparison to a 100 mg/kg oral dosage of aspirin, the impact of DL at a dose of 415 mg/kg was stronger. However, in a tail-flick model, DL (830 mg/kg) only moderately reduced pain, which was comparable to aspirin's effects. Naloxone at a level of 0.5% mg/kg totally prevented the analgesic action of morphine (10 mg/kg), delaying the analgesic impact of DL by 1 hour. Naloxone did not, however, prevent the effects of aspirin from occurring. Mice did not experience harmful effects from the 830 mg/kg oral dose of DL, and the LD50 was discovered to be 3 g/kg [40].

B. Preventing Infertility

In order to investigate the hormonal and antifertility effects of an ethanolic extract of the roots of Calotropis procera, albino rats were used in the study. At a dosage of 250 mg/kg (1/4 of LD50), a potent anti implantation (inhibition 100%) and uterotropic activity was seen. There was no evidence of antiestrogenic activity [41].

C. Anti-tumor Research

The anti-tumor activity of Calotropis procera Linn. root extracts in methanolic, hexane, aqueous, and ethyl acetate extracts (CM, CH, CW, and CE) as well as their probable mechanisms against Hep2 cancer cells have been studied. Tetrazolium bromide (MTT) colorimetry was used to measure cellular growth activities. Under an inverted microscope, cancer cells' morphological alterations were examined, and after being stained with propidium iodide, cell cycle parameters were calculated using flow cytometry. It was discovered after treatment with the extracts at varied concentrations of 1, 5, 10, and 25 g/ml that CM, CH, and CE possessed cytotoxicity, however CW did not. At 48 hours after treatment, CE (10 g/ml) had the highest cytotoxic impact (96.3%) against Hep2, whereas CM

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and CH had cytotoxicities of 72.7 and 60.5%, respectively. The root extracts of Calotropis procera Linn have anti-tumor potential. Cells treated with the extracts showed typical morphological alterations associated with apoptosis. The results of flow cytometric analysis clearly showed that root extracts caused Hep2 cells to undergo apoptosis by causing a cell cycle arrest at the S phase, preventing the cells from progressing to the G2/M phase.
According to study findings, C. procera root extracts prevent Hep2 cells from proliferating by cell cycle disruption and apoptosis mechanisms [42].

D. Antineoplastic Action

Through in vitro and in vivo investigations, the antihelmintic activity of Calotropis procera Linn. flowers in contrast to levamisole was assessed. Calotropis procera flower crude aqueous and crude methanolic extracts had anthelmintic effects on live Haemonchus (H.) contortus, as shown by their mortality or temporary paralysis, according to in vitro tests (P 0.05). For in vivo research, sheep naturally infected with mixed types of gastrointestinal nematodes were given Calotropis procera flowers as crude powder (CP), CAE, and CME.On days 7 and 10 post-treatment (PT), respectively, sheep treated with CAE and CP at 3 g kg-1 body weight showed egg count percent reductions (ECR) of 88.4 and 77.8%. CME had the least impact, which led to a 20.9% decrease in ECR on day 7PT. Calotropis procera flowers were found to have good anthelmintic efficacy against nematodes, however it was less than levamisole's (97.8-100%). It is advised that more extensive research be done, including the use of many more animals, doses that are greater than those used in the current study, the discovery of active ingredients, and the standardisation of dose and toxicity tests for the development of new drugs [4].

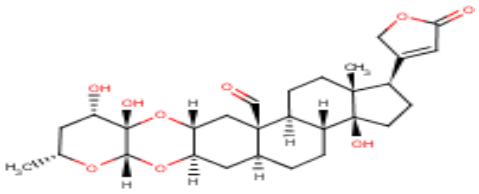

Fig. 6. Calotropin

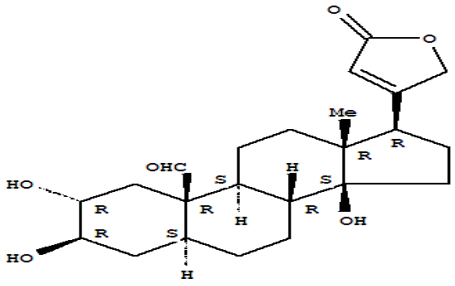

Fig. 7. Calotropagenin

E. Antioxidant Effect

Calotropis procera's dry latex, which has strong anti-inflammatory properties, was tested for its antioxidant and anti-hyperglycemic properties against rats with alloxan-induced diabetes. An increase in hepatic glycogen content and a dose-dependent decrease in blood glucose were the results of daily oral treatment of DL at dosages of 100 and 400 mg/kg. Additionally, DL stopped diabetic animals from losing weight and reduced their daily water intake to levels equivalent to normal rats.Superoxide dismutase (SOD), catalase, and glutathione levels in the liver were also increased by DL, and it decreased levels of thiobarbituric acid-reactive compounds (TBARS) in rats with alloxan-induced diabetes. Comparable to the conventional anti-diabetic medication, glibenclamide[44], DL was effective both as an antioxidant and an anti-diabetic agent.

F. Liver-Protective Behaviour

Rats were used to assess the hepatoprotective potential of a 70% hydro-ethanolic extract of *Calotropis procera* flowers against paracetamol-induced hepatitis. Both treated and untreated groups were examined for changes in the levels of biochemical indicators of liver damage

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such as SGPT, SGOT, ALP, bilirubin, cholesterol, HDL, and tissue GSH. The serum levels of HDL and tissue levels of GSH were decreased while the levels of SGPT, SGOT, ALP, bilirubin, and cholesterol were increased by paracetamol (2 g/kg). Treatment with C. procera flower hydro-ethanolic extract (200 mg/kg and 400 mg/kg) reduced the altered levels of biochemical markers to levels that were close to normal in a dose-dependent manner [45].

G. Anti-inflammatory Behaviour

Rat oedema pedal and air pouch models of inflammation were used to examine the inflammatory responses of Calotropis procera latex. The plantar surface of the paw was injected subcutaneously with 0.1 ml of dry latex (DL) in an aqueous solution to cause substantial irritation. After the injection, the inflammatory response reached its peak and persisted for another hour. Vascular permeability increased along with the inflammatory response and peaked after 15 minutes. By injecting a 2.5% solution of DL, inflammation was also elicited in the 6-day-old rat air pouch. The exudates volume, protein content, and wet and dry granuloma weights of the latter model were used to describe it. According to a time-course research, the protein content peaked on the third day after DL injection, whereas the exudates volume and granuloma weight reached their maximums on day five. The effects of different medications on the two models' ability to reduce inflammation were also investigated. Prednisolone was found to be less effective than phenylbutazone in the pedal oedema model, but mepyramine and cyproheptadine achieved practically full suppression. Prednisolone, on the other hand, was superior to phenylbutazone at reducing inflammation in the air pouch model. Thus, the inflammation caused by DL in various animals could be utilised to assess anti-inflammatory medications [46].

H. Anti-diarrheal Properties

The anti-diarrheal properties of the dry latex (DL) of Calotropis procera, a strong anti-inflammatory agent, have been studied. A single oral dose of DL (500 mg/kg) had similar effects to atropine and phenylbutazone (PBZ) in terms of reducing the frequency and severity of diarrhoea and providing protection against it in 80 percent of castor oil-treated rats. We also assessed its impact on intestinal transit, castor oil-induced intestinal fluid accumulation (enteropooling), and electrolyte content in the intestinal fluid to further understand the mechanism of its anti-diarrheal effects.

Intestinal transit was reduced by DL (by 27–37%) compared to control and castor oil-treated rats. In contrast to atropine, DL dramatically reduced enteropooling caused by castor oil. In contrast to rats given castor oil treatment, it did not change the electrolyte concentration in the intestinal fluid [47].

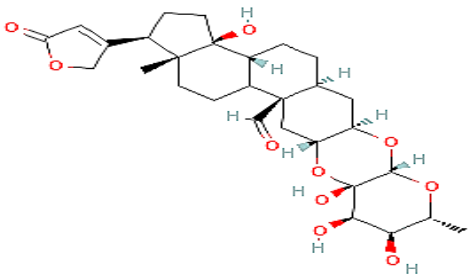

Fig. 8. Calotoxin

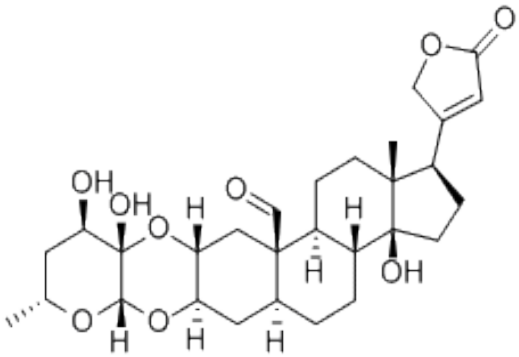

Fig. 9. Calactin

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I. Effect of Anticonvulsants

The anticonvulsant effect of various *Calotropis procera* root extracts in rats to assess the plant's traditional use. Different *Calotropis procera* root extracts were tested for their ability to prevent convulsions brought on by maximal electroshock seizures (MES), pentylenetetrazol (PTZ), lithium-pilocarpine, and electrical kindling seizures. The chloroform extract of *Calotropis procera* roots had the most notable (p 0.01) anticonvulsant effect in the MES test by reducing the duration of clonus, extendor phase, and stupor phase, as compared to control. In the PTZ test, the aqueous extract had the greatest effect (p 0.01) by delaying the beginning of convulsions, whereas the chloroform extract had a highly significant (p 0.001) effect. Additionally, the extracts prevented electrical kindling and lithium-pilocarpine-induced convulsions. The outcomes of this investigation suggest that the roots of Calotropis procera may be helpful in the absence (petitmal) and tonic-clonic (grand mal) types of seizures [48].

J. Anti-microbiological Action

Calotropis procera seeds were extracted using chloroform and methanol and were found in the forests of Ghaziabad, India. *Calotropis procera* seed extract in chloroform showed superior antibacterial action. On the other hand, the paper disc method was used to examine the extracts from *Calotropis procera* seeds for potential in vitro antibacterial properties [49].

Other Activity

Oestrogenic Properties

On the rat oestrous cycle and several parameters of oestrogenic functioning, the effects of ethanolic and aqueous extracts of *Calotropis procera* roots have been investigated. In 60 and 80% of the rats that were given each extract, the regular oestrous cycle was demonstrated to be disrupted. The rats' oestrous cycle's prolonged dioestrous stage resulted in a transient suppression of ovulation. In 100% of the treated rats, the modern administration of a commercial oestrogen-progestin preparation produced the same results. However, tests on immature female bilaterally ovariectomized rats did not show the extracts to have oestrogenic action [50].

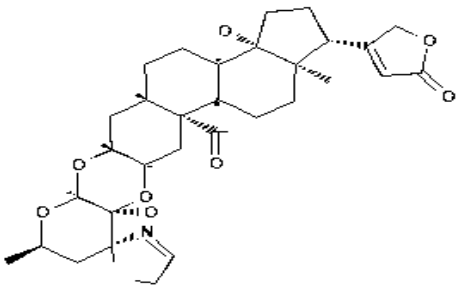

Fig. 10. Uschari

Antinociceptive Activity

Using three separate experimental models of mouse nociception, researchers examined the antinociceptive effects of proteins from the latex of *Calotropis procera*. Male mice were given the latex protein fraction intraperitoneally at doses of 12.5, 25 and 50 mg/kg, and all assays demonstrated a dose-dependent antinociceptive effect in comparison to the corresponding controls. At dosages of 12.5, 25, and 50 mg/kg in comparison to controls,

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there were inhibitions of the acetic acid-induced abdominal constrictions. In the first and second phases, respectively, latex protein at dosages of 25 (39.8%; 42%) and 50 (66.6%; 99.3%) mg/kg reduced the nociception caused by formalin, and this effect was not reversed by pretreatment with naloxone (1 mg/kg). In the hot plate test, latex at doses of 25 (79.5%) and 50 (76.9%) mg/kg increased the reaction time just 60 minutes after treatment, compared to controls, while naloxone had no effect in undoing the effect. It was determined that *Calotropis procera's* entire latex's protein fraction exhibits antinociceptive activity that is not dependent on the opioid system [51].

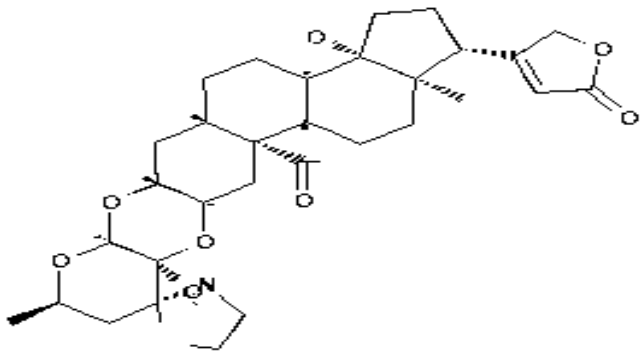

Fig. 11 Voruscharin

Antimalarial Activity

The IC50 values for the various *Calotropis procera* components against MRC20 _CQ-sensitive P. falciparum ranged from 0.11 to 0.47 mg/ml. and against MRC 76 _CQ-resistant strains from 0.52 to 1.22 mg/ml, with flower and bud extracts being the most effective. Although these extracts are 220, 440 times less effective than CQ, further research should be done to identify the key ingredients. While waiting for those results, the plant's ethnobotanical use is supported by the findings. [52].

Toxicological Study

Giant milkweed, *Calotropis procera*, has been noted to be potentially harmful to the body, particularly after prolonged or chronic use [53,54,55], according to reports on its medical and economic value in [56, 57, and 58]. If given to a frog's lymph node, the latex compound calotropin causes gastroenteritis and slows down heartbeats [59]. If more than 0.12 mg/kg is administered, it is intended to result in death. Latex is reported to cause blindness and irritate mucous membranes and the skin. A fatal dose of 4-5 ml of latex is possible. It could cause death if the gut and colon muscles burst. The plant may result in fatal convulsions, severe bullous dermatitis, a slower but stronger heartbeat, difficult breathing, elevated blood pressure, and other symptoms [60,61]. Latex is extremely harmful to human eyes, causing abrupt, painless vision loss or photophobia[62]. According to Dunean [62], the presence of madaralban, which has an emetic effect, makes the root bark comparable to Ipecacuanha.

CONCLUSION

The aforementioned data on the global use of *Calotropis procera* is compared to the literature that is currently available. The utilization of this plant implies that it should be preserved. Additionally, the human uses for this plant should be extensively publicized in the area of

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study so that people can take advantage of such purposes for their everyday well-being. One of the probable possibilities for petrofarming is *Calotropis procera*. *Calotropis procera* latex can be hydrocracked to produce hydrocarbons. *Calotropis procera* has to be the subject of further study if petroleum products are to be obtained.

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