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Review Article

An Overview of Calotropis Procera (Madar): A Versatile Medicinal Plant with Broad Therapeutic Potential

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ABSTRACT

Calotropis procera (Madar) is a resilient, long-lasting shrub that is found in tropical and subtropical areas around the globe. It has long been used in traditional medicine, and exhibits a number of medicinal properties possibly linked to its complex phytochemistry which consists of cardenolides, flavonoids, alkaloids, and saponins. Traditionally, it has been used for skin diseases, rheumatism, fever, asthma and diarrhoea, along with its use as a remedy for snake envenomation. Pharmacological studies have provided proof of a variety of these medicinal properties and pharmacological action including its anti-microbial, anti-inflammatory, anticancer, neuroprotective, and wound healing effects. Other studies have suggested that it may also possess antioxidant, hepatoprotective, and analgesic properties. This species' significance lies in its medicinal uses, the ecosystem services it provides, as well as its role in rural welfare. A consideration of the toxicological profile of this plant, and planning for further clinical trials appears necessary to explore and define its therapeutic potential and the role it can play in the modern medical community.

INTRODUCTION

For ages, herbal remedies have been beneficial component of the traditional medical system, providing all-natural solutions for preventing any illness. During this period, almost all formulations are basically based on the herbal preparations, as they are less likely to have any kind of adverse or side effects. This ethno pharmacology is an old way to understand how different cultures used the

plants and other natural substances for healing. Calotropis procera (Madar) is one such plant that has been practically gathered because of its distinctive therapeutic properties.^[1] The Latin term "procera" indicates a tall or raised structure, the Greek word "kalos" means beautiful (describing its blossoms), and the Greek word "tropis" denotes a boat-like structure. All of these words combine to form a gorgeous keel construction.^{[2][3]}

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Common names for this perennial shrub, which is a member of the Apocynaceae family, include Aak, the king's crown, Madar, Sodom apple, and Aak .^{[4][5]} Although it is widespread worldwide, this softwood, evergreen xerophytic plant is most common in dry and semi-arid tropical and subtropical regions of Asia and Africa ^[6]. In Ayurvedic practices, dried Calotrope procera leaves are traditionally utilized for managing migraines ^[9], relieving rheumatic joint pain and paralysis, and promoting the expulsion of phlegm ^{[7][8]}. Additionally, its powdered leaves have laxative, wound-healing, and indigestion-treating properties ^[5]. Traditional Saudi medicine uses a portion of C. Procera's aerial parts to cure constipation, fever, joint discomfort, and muscular

stiffness ^[10]. Furthermore, C. procera is useful for treating several skin conditions, diarrhea, and sinuses ^[11]. Ayurvedic texts like Raj Nighantu (Dravyaguna Grantha), Charaka Samhita, and Bhavaprakasha Nighantu (Bhavamishra) mention two varieties of Arka, Calotropis procera (Fig. no. 2) and Calotropis gigantea (Fig. no. 1), because of their distinct pharmacological properties. Despite having nearly the same traits, C. procera is regarded as slightly superior to C. gigantea because of its many more medicinal applications. This plant has been reported to have analgesic, anticancer, anti-helminthic, antioxidant, hepatoprotective, anti-diarrheal, anticonvulsant, antimicrobial, oestrogenic, neuroprotective, antinociceptive, and antimalarial properties ^[1].



Figure 1: C. Procera



Figure 2: C. Gigantea

Within C. gigantea, there are two varieties of plants that are often identified by the colour of their blossoms. These are mostly white (fig. no. 3)

and purple (fig. no. 4). Both have the same scientific name since, according to botany, colour variation does not result in a new plant variety.



Figure 3



Figure 4

2. Taxonomic Classification

1. Domain: Eukaryote
2. Kingdom: Plantae
3. Phylum: Spermatophyta
4. Subphylum: Angiospermae
5. Class: Dicotyledonae
6. Order: Gentianales
7. Family: Apocynaceae
8. Genus: Calotropis
9. Species: Calotropis procera

3. Other Names of Aak

The common name for Calotropis procera in India is:

1. **English name** – Sodom apple, Apple of Sodom, Kapok tree, Rubber bush, or Rubber tree.
2. **Hindi name** – Aak, Madar, Akvana
3. **Sanskrit name** – Arka, Toolaphala, Vikirana, Asfota, Alarka etc.
4. **Punjabi name** – Ak
5. **Telugu name** – Jilledu, Mandaram
6. **Bengali name** – Aaknad
7. **Arab name** – Ushar
8. **Persian name** – Kharak
9. **Malayalam name** – Neela Eukku [13]

4. Botanical Description:

The plant is a perennial herb that grows best in a variety of climates and is known to be stiff, woolly, and branched. It is also tolerant of drought and can grow as high as 900 meters. In its ordinary state, it measures up to 2-4 meters high, but it can reach much higher under perfect conditions. They are just seeds that are oblong to ovate in shape with a black surface appearance, and that have a white, shiny tuft of silk hair on the pointed end and are measured at about 2.5 to 3.2 cm [12]. The flowers up to the milky sap are 2-3 cm across and have about five lobes. The colour of the petals is usually light white, except for the purple scales and stamens that are dark. The racemose umbels are the clusters of flowers. The fruit is long, grey-green, and measures 8–12 cm in length. And are rounded at the bottom but point briefly at the tip. Each fruit contains hundreds of brown, weight 5.9–7 mg, flat seeds with a tuft of white hairs 2-3 cm long at one end.

5. Ecological Distribution

The Afro-Asian monsoon regions where Calotropis procera first appeared. It stretched from north-western Africa to the Indian subcontinent to the Arabian Peninsula, the Middle East, and beyond. It was brought to drier regions of Australia, the Mascarene Islands, subtropical

America, and most likely Southeast Asia. *Calotropis* grows on sandy soils in semi-arid environments with 150–1000 mm of annual rainfall from sea level to an elevation of 1300 m. *Calotropis procera* is found across many regions of the world, highlighting its significant value in traditional medicine. For generations, people in areas such as Africa, the Middle East, and South Asia have used this plant in folk remedies. Known for its healing properties, it has been commonly used to treat wounds, skin issues, asthma, digestive problems, and fevers, especially in countries like Ethiopia, Pakistan, and India. Different parts of the plant—such as its latex, leaves, flowers, and roots—are key ingredients in many herbal treatments. It also plays an important role in traditional healing systems like Ayurveda, Siddha, and Unani, offering both spiritual and therapeutic benefits. This widespread usage across both native and introduced regions reflects the strong ethnological connection between *Calotropis procera* and the traditional medicinal knowledge of diverse cultures, illustrating its role as a valuable resource in natural healing systems around the world. It can tolerate a variety of soil textures, though. It can withstand salt spray from the ocean and salinity in the soil. It can tolerate an annual rainfall of up to 2000 mm on soils that drain severely. It spreads swiftly in areas with minimal competition, such as overgrazed areas, deteriorated roadside edges, and lagoon borders in India, it is found from Punjab and Rajasthan to Assam and Kanyakumari up to an altitude of 1050 m. It grows abundantly in Rajasthan. It is found in wastelands and grows as a weed in cultivated areas.[14][50]

6. Traditional Uses:

The whole plant is used as a tonic, purgative, and for various ailments, including boils and sores. Specifically, the stem bark is used as an expectorant and diaphoretic, and it can help with

conditions including pneumonia, ringworm, scabies, convulsions, spleen enlargement, dysentery, and induce labor in pregnant women. *Calotropis procera* is a favored plant among traditional healers for its easy cultivation in the wild and drought tolerance area and is commonly used to treat snake bites, inflammation, pain, and infections in olden days. Though the plant has not originally been in most regions where it is implemented, the fact that it possesses healing properties has been recognized and trusted, and thus, it still remains an essential part of several traditional healing practices. Leprosy, dysentery, and elephantiasis are treated with powdered root [15]. the latex is used to treat rheumatoid arthritis, tumours, leprosy, ringworm, syphilis, toothaches, caries, and stings. purgative, vermifuge, antiseptic, and tism. Additionally, the blooms are used to treat asthma, ulcers, inflammation, and jaundice. The latex had digitalis-like behaviour. heart, as well as infanticide and abortive qualities [16]. the leaves are crushed, heated, and then placed on the rheumatic pains, burns, headaches, and in the form of tincture for fever. Infusion of even the flower is used to cure rheumatism. bouts of epilepsy and intestinal worms. Flower decoction is used to treat cough and asthma. When combined with cow's milk, powder can be used to treat rheumatism. Leprosy, ulcers, syphilis, diarrhoea, and dysentery.[12]

7. Phytochemistry

7.1 Chemical Composition *Calotropis procera* is recognized to be a good source of different types of secondary metabolites that provide a wide range of therapeutic effects.

7.2 Leaves

7.2.1 Flavonoids: The leaves, which are an example of flavonoid-rich plant sources, contain



quercetin and kaempferol, the compounds showing strong antioxidant activities [45].

7.2.2 Triterpenes: Among the numerous bioactive compounds present in the leaves, triterpenes like oleanolic acid, which can reduce inflammation, is the most significant. The other major components include calotropin and calotropogenin [48].

7.3 Bark

6.3.1 Cardenolides The most abundant in the bark of *Calotropis procera* are cardenolides, which cover many of the pharmacological properties, such as calotropin and uscharin. These compounds do display effects on the heart; however, they can be toxic eventually.

7.4. Roots

The root of the *Calotropis procera*, pentacyclic, triterpenes, alkaloids, cardenolides, phytosterols, triterpenoids, and saponins are present.

7.4.1. Saponins: The roots are known to contain saponins, which can enhance immune responses and exhibit cytotoxic properties against certain cancer cells.

7.4.2. Triterpenes: Similar to the bark, the roots also contain triterpenes that help in liver protection and inflammation reduction.

7.5. Flowers

7.5.1. Essential Oils: The flowers yield essential oils that may have antimicrobial properties. Such as hinesol, myristicin, linoleic acid, pentacosane.

7.5.2. Flavonoids: Similar to the leaves, they contain flavonoids that contribute to antioxidant effects.[18]

7.6. Latex

7.6.1. Cardenolides: The latex is particularly high in cardenolides, contributing to its use in traditional medicine for various ailments.

7.6.2. Proteins and Enzymes: The latex contains proteins and enzymes that may have therapeutic applications, though they require careful handling due to potential toxicity. *Calotropis procera* contain Calotropin, calotoxin, uscharin, uscharidin, glycoside calotropogenin, choline, o-protocatechuic acid, uzarigenin, and syriogenin in Their latex.[17]

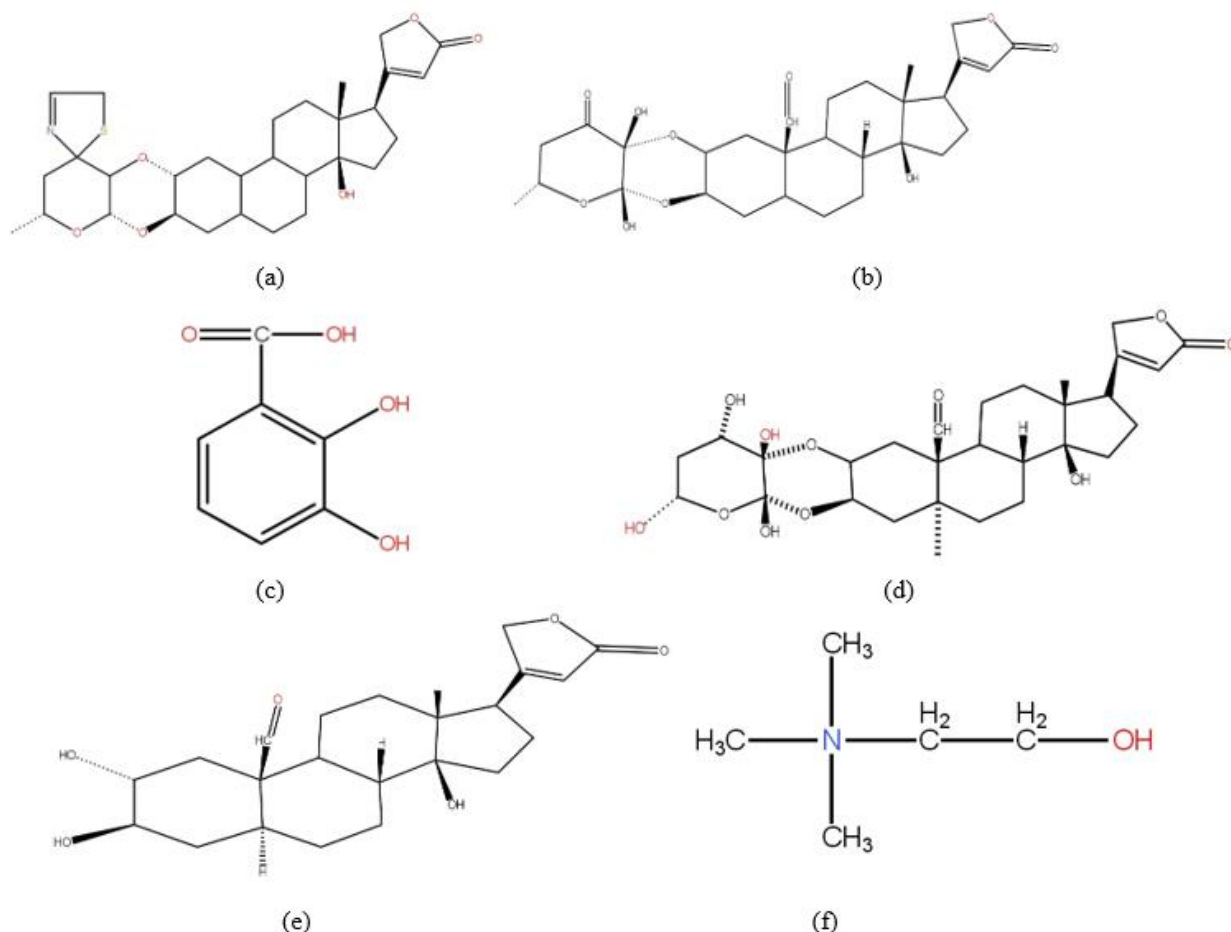


Table No 1: Major Chemical Constituents

a	Uscharin
b	Uscharidin
c	O-protocatechuic acid
d	Calotropin
e	Glycoside calotropigenin
f	Choline

8. Pharmacological Properties

8.1 Antimicrobial Effect

Both the Plant extracts and extracts of *C. procera* proteins exhibited antimicrobial action against bacteria, fungi, and a variety of bacteria, including gram-positive bacteria (*S. aureus* and *Bacillus subtilis*), gram-negative bacteria (*E. coli*, *Pseudomonas aeruginosa*), as well as some fungi, e.g., *Candida albicans* or other species. aqueous,

methanolic, and ethanolic extracts of latex showed strong antimicrobial activity, which produced considerable activity against serious pathogenic species. The antimicrobial activity was effective across a broad range of bacterial strains including both *E. coli* and *S. aureus* by compromising the stability of the cell walls of bacteria, resulting in the perforation of the membrane and loss of intracellular content which disrupted membrane functions and yielded death of the bacterial cell.^[38] These concentrations varied considerably, but the minimum inhibitory concentration was usually seen at low concentration (mg/mL) for the crude extracts, and $\mu\text{g/mL}$ for purified proteins/peptides.^{[20][21]}

8.2 Anticancer (Cytotoxic) Activity *Calotropis procera* has received a lot of interest for its anticancer attributes, with several studies

identifying its effectiveness for many different cancer types ^[49]. It was founded that both crude extracts and pure isolated compounds from the plant have induced cytotoxic effects, including mechanisms of action such as apoptosis, cell cycle arrest, and modification of multiple cellular signalling pathways.

8.2.1. Breast and Colon Cancer Cells: Ethanolic extracts of *C. procera* leaves caused dose-dependent cytotoxicity observed in an MCF-7 (breast cancer) cell line and an HCT-116 (colon cancer) cell line. The effects included inducing apoptosis and cell cycle arrest at distinct phases and both of which were mediated by the inhibition of the AKT/mTOR pathway and cyclin-dependent kinase level declines. ^[22]

8.2.2. Prostate Cancer Cells: Leaf extracts produced significant cytotoxicity against the PC-3 and 22Rv1 prostate cancer cell lines. The mechanism indicated regulation of autophagy pathways and the elevation/suppression of reactive oxygen species (ROS). Inducing cell death, decreased cell viability and proliferation were amongst the observed effects. ^[23]

8.2.3. Skin Melanoma Cells: Methanolic extracts were effective against the SK-MEL-2 melanoma cell line and induced apoptosis with a G2/M (cell cycle arrest) phase. This was inferred to have been caused by the high cardenolide content of the methanolic extracts. ^{[24][19]}

8.3. Neuroprotective effect

Alzheimer's disease (AD) a chronic neurodegenerative disease described as a long progressive disease characterized by continuous decline of cognitive function, including memory, language, comprehension, and orientation ability. Some studies have indicated that latex from *Calotropis procera* may have significant effects on the treatment of early symptoms of dementia.

Specifically, studies have reported that extracts of the latex of this plant may lessen beta-amyloid accumulation among experimental model organs (such as the rodent brain) and have significant antioxidant and protective qualities ^[47]. Furthermore, the aqueous extract, particularly extracted from the root bark, has been well noted for its neuroprotective effects, including the reduction in anxiety symptoms and memory loss. This extract may also stand against oxidative stress and reduce the toxicity of agents such as scopolamine exposure, This implies that incorporating *C. procera* extract into therapeutic uses can be beneficial in treating anxiety and protecting neural function in individuals susceptible to oxidative stress. ^[23]

8.4 Mercury Poisoning

Mercury chloride is a known neurotoxin that produces extensive brain damage characterized by marked changes to the cytoplasm and nuclei of brain cells. studies, with ethanol extracts from the air-dried powdered aerial parts of *Calotropis procera* (Apocynaceae), showed protective effects against mercury chloride-induced neurotoxicity in male and female Wistar albino rats. *C. procera* extracts protect neural cells by preserving nuclear integrity, which might have occurred even with mercury chloride exposure. The observed neuroprotection can likely be attributed to the high amount of antioxidant compounds present in *C. procera*, which developed as a metabolic adaptation to high-temperature stress exerted by the environment. The compounds are capable of crossing white blood cells, and the blood-brain barrier and protect useful neurotransmitters from the actions of mercury chloride, this daa support that *C. procera* may be therapeutically useful toward inflammatory conditions related to the brain. ^[24]

8.5. Wound-Healing Activity



The traditional usage of *Calotropis procera* for wounds, including latex and sap, and leaf powder on burns and injuries, has recently gathered scientific support. Preclinical studies conducted with the incision or excision wound model have demonstrated aqueous leaf extracts significantly increase all of the healing parameters measured. Some of these wound healing parameters measured were tensile strength, wound contraction, and the amount of time to achieve full epithelization, with all of these parameters significantly improved in the leaf extract treatment group, indicating accelerated tissue regeneration.^[25] The extract supported collagen deposition, a key element for wound remodelling and strength of scar tissue, which is compromised in diabetic models that generally show impaired wound healing^[26]. The topical application of *C. procera* latex-based ointment increases granulation tissue and re-epithelialization in dermal wound models. The extracts from the root bark have been identified to aid in the healing of wounds by increasing the strength of the tissue, especially in situations where the healing is not effective, for example, like in diabetic wounds.

8.6. Antimalarial (Antiplasmodial) Activity

The traditional use among many communities to treat febrile diseases, including malaria, had sparked scientific interest in investigating the antiplasmodial properties of *Calotropis procera*. Laboratory experiments have demonstrated that specific cardenolides isolated from *Calotropis procera* exhibit moderate inhibitory effects on both chloroquine-sensitive and chloroquine-resistant strains of *Plasmodium falciparum*. Two of the major extracted cardenolides calotropin and calactin were effective against *P. falciparum* at low micromolar concentrations^[42], suggesting these cardenolides could be considered bioactive leads. Although the mechanism by which these cardiac glycosides act is still uncertain, it is hypothesized

that cardiac glycosides could affect ion transporter systems or parasite-specific enzymes, which may interfere with membrane homeostasis or detoxification pathways essential to parasite survival, namely, detoxification of heme.^{[27][43]}

8.7. Anti-inflammatory and Analgesic Activity

Calotropis procera has been utilized in folk medicine for the management of issues regarding pain and inflammation. A considerable amount of experimental evidence accumulated over the last 20 years has supported many of these applications and found that different components of the plant (including its latex, leaves, and roots) have anti-inflammatory and analgesic activity.^[28] For example, in acute inflammation models (i.e., carrageenan paw edema in rats), latex extracts of *C. procera* produce significant decreases in swelling, which was associated with the decrease in common inflammatory agents such as prostaglandins and the cytokines TNF- α and IL-1 β .^{[28][29]} In chronic inflammation models, like the use of Freund's complete adjuvant (FCA), treatment with methanolic extracts of *Calotropis procera* produced a significant reduction in parameters of joint swelling and the inflammatory marker. Moreover, several pain models further demonstrated that the plant extract exhibited significant analgesic and anti-nociceptive effects. In the hot plate and tail flick tests, animals were shown to have a prolonged time to respond, while the acetic acid-induced writhing test showed a significant reduction in the number of writhes, supporting the pain decreasing aspects of the plant.^{[29][30]} The role of anti-inflammation is not restricted to latex. Extracts from the leaves and roots that were prepared in solvents - including, inter alia, water, petroleum ether, and ethyl acetate - exhibited significant activity in experimental models of inflammation^[33]. The activity may be due to the presence of phytochemicals (e.g., terpenoids, steroids, cardenolides) in non-latex



portions of the plant that may have biological activity. The mechanisms for *C. procera* appear to involve the down-regulation of inflammation pathways^{[31][32]} (e.g., inhibition of the synthesis of prostaglandins, production of nitric oxide, and release of cytokines). Some of the compounds in *C. procera* such as oleanolic acid and ursolic acid may certainly contribute to these effects given their established activity to modulate inflammation.^[33] The evidence provided by a series of reports points to the fact that *Calotropis procera* is one of the most effective plants for treating pain and inflammation^[39]. These results not only coincide with the traditional applications of the plant, which concerns the treatment of inflammatory conditions, but also strengthen them. The plant's effect on both types of inflammation, acute and chronic, allows it to be the subject of research and, if successful, a basis for the development of new treatments.

8.8. Antioxidant Potential

The antioxidant activity of *Calotropis procera* can be mainly explained due to the phenolic and flavonoid compounds found abundantly in the plant species. *Calotropis procera*'s extracts, particularly from the leaves as indicated by a systematic review, demonstrate free radical scavenging ability when conventionally assessed in vitro, acceptably with DPPH, ABTS, and FRAP tests. *C. procera* extracts exhibit reducing power, adding to their ability to quench oxidants.^{[34][35]} Phytochemical references report on bioactive compounds, for example, rutin, quercetin, catechin, and kaempferol, etc. associated with antioxidant activity, compounds that stabilize reactive oxygen species to deactivate oxidative stress in cells^[41]. The potential antioxidant activity is likely associated with the plant's traditional uses for wound healing, anti-inflammatory effects, and hepatoprotective functions. While most of the research relates to in vitro studies, there is a need

to consider *C. procera* as a natural source of antioxidants for future pharmacological studies. These activities have contributed to the traditional therapeutic properties attributed to the species, including but not limited to wound healing, anti-inflammatory responses, and hepatoprotective actions.^[35] Although the majority of findings to date are from in vitro evaluations, this work suggests that there is enough basis to evaluate *C. procera* as a natural source of antioxidants and support for future research within the pharmacological context.

8.9. Hematopoietic Effect

Evidence-based research revealed that *Calotropis procera* has significant hematopoietic and anti-anemic activity. In recent studies, it was pointed out that the oral administration of the leaf extract in rats at a dose of 500–1500 mg/kg for 60 days caused an observable increase in red blood cells.^{[36][37]}, haemoglobin and haematocrits levels, apart from being non-deleterious to the liver and kidneys, hence, targeted hematopoietic effects. Similarly, hydroalcoholic extracts of flowers were effective in recovering from anaemia in rats previously injected with phenylhydrazine. Additionally, it was found that the root bark ethanolic extract had immunomodulatory and myeloprotective effects in mice^{39][40]}, protected them against cyclophosphamide-induced marrow lethargy, and illustrated its supplemental hematopoietic effects.

9. Toxicity

Calotropis procera, while it still offers extensive medicinal applications, has harmful effects primarily because of the very strong cardiac glycosides found in the plant, mainly calotropin, uscharin, and calactin. The toxic principle is in the yellow milky latex of the plant and causes a variety of symptoms, such as vomiting, diarrhoea,



bradycardia, arrhythmias, dermatitis and even cardiac arrest with extreme exposure or ingestion. Toxicity studies conducted in animals indicate its hepatotoxic as well as nephrotoxic potential, with signs of oxidative stress and neurological effects, such as convulsions and respiratory depression. In spite of its toxicity, *Calotropis procera* has been used in traditional treatments of snakebites by rural people. The latices and root extracts are applied topically, or even dilute oral doses, alone or as a part of a polyherbal formulation. The antivenom activity is attributed to the presence of proteolytic enzymes and phytochemicals, which degrade the venom protein and its toxicity. Also, the anti-inflammatory and analgesic properties of the extracts of *C. procera* help to downregulate the local effects of snake envenomation. While several experimental models have indicated promise against cobra and viper venom using various dosing measures of *C. procera*, the inherently toxic properties make clinical translation difficult without careful doses and standardisation.^[51]

CONCLUSION

Calatropa procera is a plant species that has a great deal of ethnomedicinal, pharmacological, and economic potential. The constituents of the plant have various phytochemical profiles that support a variety of therapeutic applications today and historically, for example, antimicrobial, anticancer, neuroprotective, and wound healing properties. However, the plant's level of toxicity should inform caution for medicinal use. More research is needed to isolate active compounds, elucidate changes in the mechanism of action, and confirm safe therapeutical applications as well. *C. procera* also produces very high-quality fibres which can be used to make ropes, carpets, and fishing nets for industrial uses. The plant is very resilient and produces a large amount of high-quality biomass yearly for couching, or it is very useful for phytoremediation of toxic soils or for

improving soil health. The plant has also been explored for the synthesis of nanoparticles and as a renewable source for biotechnological applications^[44].

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