

Chapter

Exploring the Potential of *Calotropis procera* in Pharmacological Approaches

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Abstract

Medicinal plants have been a source of treatments for many ailments for thousands of years. The WHO estimates that 80% of worldwide population use traditional medicines to treat common health issues. Plant derived bioactive substances constitute 50% of Western medications. The increase in incidents of emerging medical challenges, including post-COVID syndrome, rising multidrug-resistant (MDR), and many more, has raised annual fatalities. To address these issues, novel medications and strategic approaches are urgently required. Designing novel drugs relies on exploring medicinal plants, which have great scope in combating diseases. *Calotropis procera* is a medicinal plant belongs to Apocynaceae family and subfamily Asclepiadoideae that have been exploring for developing novel drugs. *C. procera* consists of numerous phytochemicals including flavonoids, terpenoids, cardenolides, steroids and oxypregnanes. Therefore, its phytoconstituents have been used to treat a variety of conditions including cancer, asthma, epilepsy and snake bite. *C. procera* is reported to have anti-inflammatory, anti-tumor, anthelmintic, antibacterial, antinociceptive and antimalarial properties. Roots, leaves and flower of *C. procera* have been used in wide range of ethnomedicinal and pharmacological actions including leukoderma, malaria and eczema. Recent ongoing techniques including computational tools using the phytoconstituents of *C. procera* against various diseases will open up avenues for developing novel drugs.

Keywords: *Calotropis procera*, anti-inflammatory, antibacterial, antimalarial, drugs

1. Introduction

For thousands of years, plants have been the only source of treatments to treat both human and animal illnesses [1]. Medicinal plants (MPs) are the primary source of basic healthcare in underdeveloped nations [2, 3]. According to World Health Organization (WHO), approximately 80% of the world's population relies on traditional medicines, primarily on MPs, for their everyday health problems. Also, 50% of Western medications contain bioactive substances derived from plants [4].

A dramatic increase in fungal diseases over the past few decades has caused the dispersion of fungal spores across the soil and the environment. As a result of excessive fungal spore exposure, numerous illnesses, such as sinusitis, lung infections, and skin infections, are reported to be increased in people with impaired immune systems [5]. Similar to fungal diseases, microbial diseases have historically been the leading cause of mortality [6]. Currently, multidrug-resistant (MDR) is solely to blame for about 230,000 of the 700,000 annual deaths caused by resistant infections. By 2050, drug-resistant illnesses will result in 10 million annual fatalities [6].

To address antibiotic resistance, new medications and alternative therapies (like traditional plant-based medicines, bacteriophage therapies, and combinational therapies) are urgently required [7, 8]. World Health Organization strongly emphasizes developing novel antibiotics to combat resistant diseases [9]. Since the dawn of civilization, phytochemicals such as alkaloids, terpenoids, tannins, steroids, coumarins, and flavonoids derived from medicinal plants have a great scope to combat diseases. Essential oils and phenolic acids from *Petroselinum crispum*, *Levisticum officinale* Koch, *Ocimum basilicum*, *Thymus vulgaris*, *Syzygium aromaticum* alter the physiology of bacteria such as *Bacillus cereus*, *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Escherichia coli*, and *Salmonella* by increasing cell permeability, altering the bacterial cell wall and membrane integrity, losing ATP, and inhibiting protein synthesis.

Compared to synthetic antimicrobials, medicinal plants are thought to have fewer side effects and exhibit varying degrees of efficacy against microbial infections [5, 10, 11]. Co-administration of antibiotics and non-antibiotic substances breaks down resistance and is a successful strategy for enhancing or restoring antibiotic efficacy [7]. This chapter describes the morphological description of *C. procera* and its phytochemical constituents or pharmacological properties described briefly.

2. *Calotropis procera*

The plants *Calotropis procera* referred to as “Raktha Arka”, in traditional Ayurvedic medicine. It serves a variety of functions. The plant fibers are used to make baskets, ropes, bags, and nets. The wood serves as both fuel and building material. The leaves of the plant serve as the animal’s food. The plant’s latex is a crucial component of many folk medicines. The common names [12] of the plant are summarized in **Table 1**. The taxonomic classification of *C. procera* is tabulated in **Table 2**.

Country	Names
India	Sanskrit- Arka, Ganarupa, Mandara, Vasuka, Svetapushpa, Sadapushpa, Alarka, Pratapass
	Hindi- Aak, Madar
	Kannada- Ekka
	Tamil and Malayalam- Erukku
	Telugu- Jilledi, Puvvu
Malaysia	Remiga, Rembega, Kemengu
Indonesia	Sundanese and Madurese- Bidhuri
	Javanese- Sidaguri
	Aceh- Rubik
Philippines	Tagalog- Kapal-kapal

Country	Names
Laos	Kok May, Dok Kap, Dok Hak
Thailand	Northern- Po Thuean, Paan Thuean
	Central- Rak
Vietnam	Bootng, Lashen, Nam Tit Bat
French	Faux arbre de soie, Mercure vegetal
English	Giant Indian milked weed, Madar and Sodom apple
Turkey	Ipekag
Arab	Oshar or Ushar
Persia	Kharak
Pushto	Spalmai

Table 1.
Vernacular names of C. procera.

Taxonomic classification
Kingdom: Plantae
Subkingdom: Tracheobionta
Super division: Spermatophyta
Division: Magnoliophyta
Class: Magnoliopsida
Order: Gentianales
Family: Asclepiadaceae
Genus: <i>Calotropis</i>
Species: <i>C. procera</i>

Table 2.
Taxonomic classification of C. procera.

3. Distribution

Calotropis procera is a perennial plant belonging to the family Apocynaceae. The plant is abundant in Asia, America, Africa, Afghanistan, Algeria, Burkina Faso, Cameroon, Chad, Cote d'Ivoire, the Democratic Republic of the Congo, Egypt, Eritrea, Ethiopia, Gambia, Ghana, Guinea-Bissau, Pakistan, and India. It thrives as a wild shrub across Punjab, especially on plain pastures and roads [13]. *Calotropis* grows wild up to 900 meters (msl) throughout the nation [14] and is tolerant to salt, and likes disturbed environments. It readily establishes as a weed along deteriorated roadways, lagoon edges, and overgrazed native grasslands and is propagated by seeds spread by wind and animals. It prefers abandoned agriculture sites and frequently predominates there, especially in places with disturbed sandy soils and little rainfall. It is believed to be a sign of overcrowding. It is the first vegetation to grow on arid soil and is tolerant of drought [15]. The xerophytic adaptations include the presence of latex, a profoundly branching root system, and thick leaves covered with wax.

The vegetative characteristics of plant are summarized in **Table 3** [16].

Vegetative characters	Description
Habit	Shrub or a small tree up to 2.5 m (max.6 m) height.
Roots	Simple, branched, woody at base and covered with a fissured; corky bark; branches somewhat succulent and densely white tomentose; early glabrescent. All parts of the plant exude white latex when cut or broken.
Leaves	Opposite-decussate, simple, sub sessile, extipulate; blade-oblong obovate to broadly obovate, 5–30 × 2.5–15.5 cm, apex abruptly and shortly acuminate to apiculate, base cordate, margins entire, succulent, white tomentose when young, later glabrescent and glaucous.
Flowers	Bracteate, complete, bisexual, actinomorphic, pentamerous, hypogynous, pedicellate, pedicel 1–3 cm long.
Floral characteristics	Inflorescence- A dense, multiflowered, umbellate, peduncled cymes, arising from the nodes and appearing axillary or terminal.
Calyx	Sepal five, Polysepalous, five lobed, shortly united at the base, glabrescent, quincuncial aestivation.
Corolla	Petals five, gamopetalous, five lobed, twisted aestivation.
Androecium	Stamens five, gynandrous, anther ditheous, coherent.
Gynoecium	Bicarpellary, apocarpus, styles are united at their apex, peltate stigma with five lateral stigmatic surfaces. Anthers adnate to the stigma forming a gynostegium.
Fruit	A simple, fleshy, inflated, subglobose to obliquely ovoid follicle up to 10 cm or more in diameter.
Seeds	Many, small, flat, obovate, 6 × 5 mm, compressed with silky white pappus, 3 cm or more long.

Table 3.
Vegetative characters of *C. procera*.

4. Phytochemistry of *C. procera*

C. procera contains cardenolide, triterpenoids, alkaloids, resins, anthocyanins, and other compounds. In addition to this it also contains hydrocarbons, saturated and unsaturated fatty acids. Different phytoconstituents isolated from different parts of *C. procera* were tabulated in **Table 4**.

Plant part	Compounds present	References
Leaves	a-amyrin	[17]
	a-amyrin-acetate	–
	β-sitosterol	–
	Urosolic acid	–
	Cardenolide	[18]
	Calotropin	[19]
	Calotropagenin	[20]

Plant part	Compounds present	References
Latex	Caoutchouc	[18]
	Calotoxin	[18]
	Calactin	[21]
	Uscharin	–
	Trypsin	[21]
	Voruscharin	–
	Uzarginin	–
	Syrioginin	[21]
	Proceroside	[22]
Flower	Queretin-3-ratioside	[22]
	Sterol	[23]
	D-arabinose	[22]
	Glucosamine	[23]
	L-rhamnose	[23]
Bark	Triterpenes	[24]
	Pentacyclic triterpinoides	[25]
	Calotropursenyl acetate	[26]
	Apundarol isovalerate	[24]
	Querecetin-3-rutinoside	[25]

Table 4.
Phytoconstituents of C. procera.

5. Traditional uses

Ancient Egyptians utilized *C. procera* as a medicinal plant throughout the Neolithic period in Egypt. The plant is a part of Greco-Arab medicine [27] and is traditionally used across 21 nations worldwide. The plant is also used in Ayurveda, Siddha, Unani, and Sudanese traditional systems of medicine. It is important to note that *C. procera* has been used more commonly to treat a variety of infectious disorders that may be generally divided into five categories:

1. Leprosy, boils, carbuncles, scabies, leishmaniasis, and infections of the skin, mouth, and teeth are examples of skin and dermal infections.
2. Respiratory infections include pneumonia, bronchitis, bronchial asthma, cough.
3. GIT infections include dysentery, diarrhea, cholera, gastritis, colitis, and worms.
4. GU infections include chronic renal failure and leucorrhea.
5. Systemic infections include malaria and both internal (oral) and external (topical) preparations have used *C. procera*.

Parts	Uses
Leaves	In leukoderma (skin disease); an antidote for rabies; prompt healing; applied for a poultice; treat migraine, fever, eczema, leprosy, elephantiasis, asthma, cough, and rheumatism).
Flower	Treat skin and gum infections; used in dysentery and antidote for scorpion bite.
Root	Used as a digestive; to treat body pain, malaria, eczema, leprosy elephantiasis, asthma, cough, and rheumatism.

Table 5.
Ethnomedicinal uses of C. procera.

However, given its increased usefulness in treating cutaneous infections, external or topical applications are more prevalent. Ethnomedicinal uses of *Calotropis procera* are summarized in **Table 5**.

6. Medicinal activity

This highly effective shrub is used in numerous widespread and traditional medicines to treat various illnesses like fever, leprosy, eczema, diarrhea, dysentery, and jaundice [28, 29]. The plant has reported anti-inflammatory, anti-tumor, anthelmintic, hepatoprotective, antioxidant, anticonvulsant, antibacterial, oestrogenic, antinociceptive, and antimalarial properties (**Figure 1**).

7. Antioxidant activity

The anti-inflammatory and anti-hyperglycemic effects of *Calotropis procera*'s dry latex (DL) were demonstrated in rats that had been given an alloxan-induced diabetes model. In daily oral treatment of DL at dosages of 100 and 400 mg/kg, a dose-dependent drop in blood sugar and an increase in hepatic glycogen content were seen. Additionally, DL slowed the loss of body weight in diabetic animals and decreased their daily water intake to levels comparable to those of rodents without diabetes. Additionally, in rats with alloxan-induced diabetes, DL reduced the levels of thiobarbituric acid-reactive substances (TBARS) while increasing the levels of endogenous antioxidants like catalase, glutathione, and superoxide dismutase (SOD). Comparable to glibenclamide, a popular anti-diabetic drug, DL proved effective as an antioxidant and an anti-diabetic agent [16].

The antioxidant activity (free radical scavenging capacity) of the methanolic extract of *C. procera* roots was evaluated by the *in-vitro* DPPH scavenging assays. The IC₅₀ value was found below 100 µg/ml, indicating the plant's potent antioxidant activity.

8. Antimicrobial activity

Calotropis procera seeds were extracted using chloroform and methanol and have been tested on a paper disc for possible *in vitro* antibacterial activity. The chloroform extract of the seeds showed superior antibacterial action [30]. The stems, fruit, leaves, and flowers of *C. procera*, as well as its n-hexane, ether, chloroform, and water fraction, were extracted with 70% methanol and water, and their antibacterial activity was investigated. The antibacterial and antifungal effects of the plant fractions were evaluated



Figure 1.
 Health benefits of *C. procera*.

using *Klebsiella pneumoniae* and *Aspergillus niger*, respectively. The test extracts with a concentration of 10 mg/mL were used in the study. On Muller Hinton agar for bacteria and Yeast Peptone Glucose (YPG) agar for fungi, which had previously been seeded with the microbial inocula of 0.5 MacFarland density, a volume of 10 L of each examined extract sample was detected. The inhibition zones on the inoculation plates were measured in mm after a 24-hour period of 37°C incubation. The plant's flower extract showed the greatest antibacterial activity in the n-hexane and ether fractions.

9. Anti-inflammatory activity

The anti-inflammatory impact of *C. procera* was tested using the various acute and chronic models of inflammation. Oral administration of dried latex of *C. procera* significantly inhibited edema formation induced by carrageenan and Freund's Adjuvant [31]. The plant also has potent anti-inflammatory effects against cotton pellets and carrageenan-induced granulomas in albino Wistar rats. The methanolic extracts

(180 mg/kg, p.o.) of the roots of *C. Procera* can reduce subacute inflammation by interrupting the metabolism of arachidonic acid in both the cotton pellet and paw edema models [32].

10. Antipyretic activity

Calotropis procera may become a more widely available and effective antipyretic medication, according to the study. In contrast to aspirin, *C. procera*'s ethanolic extract of the aerial parts, aqueous extract of the flower, and aqueous solution of the dry latex have all demonstrated potent antipyretic effects in animal models [33].

11. Anticancer activity

Cardenolide, a novel compound present in *C. procera*. According to Quaquebeke [34]. *C. procera* has strong anti-tumor properties in vitro and a high level of tolerance in vivo. Similar to this, di-(2-ethylhexyl) phthalate (DEHP) isolated from *C. procera* demonstrated anti-tumor activity, and copper nanoparticles synthesized using an aqueous extract of *C. procera* latex demonstrated cytotoxic [35] and cytostatic activity against tumor cells and cell lines [36].

12. Antimalarial activity

The alcoholic extract of *C. procera* flower extract exhibited a higher level of mosquito repellent activity against the female *Culex quinquefasciatus* mosquito as compared to the petroleum ether and chloroform extracts [37]. This study suggests the role of *C. procera* as a natural biocide for mosquito control. The aqueous extract of CG leaves at 125, 250, 500, and 1000 ppm exhibited larvicidal, mosquito-repellent, and ovicidal activity against *Culex gelidus* and *C. tritaeniorhynchus* mosquitoes. The extract showed dose-dependent larvicidal activity with a motility rate of $86 \pm 1.42\%$ ($LC_{50} = 137.90$) against *C. gelidus* and $94 \pm 1.31\%$ ($LC_{50} = 110.05$) against *C. tritaeniorhynchus*.

13. Anti-obesity activity (pancreatic lipase inhibitory activity)

The purified di-terpenoid fraction from the root extract of *C. procera* inhibits pancreatic lipase (PL) with an IC_{50} of 9.47 mg/mL. The purified di-terpenoid fraction was shown to have a considerably lower inhibition constant (K_i) than the positive control (Orlistat; IC_{50} : 0.15 μ M). The inhibition was determined to be competitive based on kinetic data. This explains the plant's antihyperlipidemic actions [38].

14. Antiviral activity

Globally, viral illnesses are regarded as one of the most significant hazards to people, animals, and plants. The outbreaks of deadly viral diseases like COVID-19, which pose a serious threat to human survival on a global scale, also call for the development of vaccines or other anti-toxin treatments. This is in addition to the

challenges brought on by the emergence of antiviral resistance and the negative side effects of currently available antiviral drugs [39]. Research has shown the potential role of medicinal plants and their bioactive compounds as antiviral agents [40, 41].

15. Toxicity

In addition to its well-documented traditional uses across many nations, *C. procera* is categorized as a weed, a toxic plant and a poisonous plant [42–44]. The herb was formerly employed as an abortifacient. The plant leaves also cause ocular toxicity if splashed/entered accidentally. It causes ocular Keratouveitis accompanied by inflammations, corneal edema, irreversible endothelial cell damage and vision deterioration [30, 45, 46]. Ruminants have experienced harmful effects after consuming *C. procera* leaves (CPL) [47].

The leading cause of the plant's toxicity is the presence of poisonous substances like toxic cardenolides in its latex. Similar to those of *Digitalis*, the cardiac glycosides of *C. procera* severely increase heartbeat and finally result in animal mortality. CPL's pH is 5.2, which is harmful to the animal's mucous membranes [45]. Additionally, *C. procera* thrives in various soils, including those contaminated with heavy metals and found along roadsides. As a result of the plant's remarkable capacity to absorb diverse chemical components, such as heavy metals, it bioaccumulates more significant levels of dangerous heavy metals like lead (Pb), chromium (Cr), nickel (Ni) and cadmium (Cd) as well as other environmental contaminants which increase the plant's toxicity [48].

16. Conclusion

The *C. procera* is one of the globally distributed medicinal plants. Despite of having pharmacological and traditional uses this is the plant that is forgotten as the time passes. But now many scientists have worked to evaluate its phytochemicals and pharmacological property. The pharmacology, traditional uses, toxicology and use of secondary metabolites has been discussed in this chapter. *C. procera* is the richest source of phytochemicals and screening its phytoconstituents will give a new avenue to investigate its therapeutic role. *In vivo* and *in vitro* study of *C. procera* was well documented in literature but human safety and efficacy yet to be done and clinical trials need to be done to confirm its standard dosage.

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