



# INTERNATIONAL JOURNAL OF PHARMACEUTICAL AND HEALTHCARE INNOVATION

journal homepage: [www.ijphi.com](http://www.ijphi.com)



## Review Article

### Comprehensive Overview of *Calotropis gigantea* (L): Phytochemistry, Pharmacology and Therapeutic Potential

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#### Article Info

Article history:

Manuscript ID:

**IJPHI1102230207032026**

**Received:** 11-FEB-2026

**Revised :** 23-FEB-2026

**Accepted:** 07- MAR -2026

**Available online:**

MAR -2026

**DOI:** 10.62752/ijphi.v3i2.239

#### Abstract

*Calotropis gigantea* (L.), commonly known as giant milkweed or crown flower, is a medicinally important plant widely distributed in tropical and subtropical regions, particularly in India and Southeast Asia. For centuries, it has occupied an important place in traditional systems of medicine such as Ayurveda, Siddha, Unani, and folk healing practices, and almost every part of the plant, including leaves, flowers, latex, roots, and bark, has been used for therapeutic purposes. In recent years, *Calotropis gigantea* has attracted growing scientific interest due to its diverse phytochemical profile and broad spectrum of pharmacological activities. This review aims to present a comprehensive overview of the botanical description, traditional uses, phytochemistry, pharmacological properties, toxicological concerns, and future research potential of *Calotropis gigantea*.

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#### Keywords:

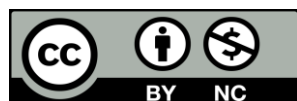
Itopride hydrochloride,

functional dyspepsia, gastric motility, prokinetic medication, and gastric emptying.

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0009-0003-0171-5809



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## 1. Introduction

Ayurveda, often known as the “science of life,” is one of the world’s oldest holistic healing systems, deeply rooted in the cultural and philosophical traditions of ancient India [1]. Developed more than 5,000 years ago, it offers a comprehensive approach to health that views the human body, mind, and spirit as interconnected aspects of overall well-being. Unlike modern medicine, which often focuses on treating symptoms, Ayurveda emphasizes balance, helping individuals maintain harmony among the body’s biological energies, known as *doshas* (Vata, Pitta, and Kapha) [2]. This system believes that health is not merely freedom from disease but a dynamic state of equilibrium that must be constantly nurtured through diet, lifestyle, herbal medicines, yoga, and meditation; Ayurveda has gained renewed global interest as people seek natural, personalized, and preventive approaches to healthcare [3]. Its principles offer valuable insights into sustainable wellness, disease prevention, and the integration of traditional wisdom with contemporary biomedical understanding. Exploring Ayurveda through a scientific lens allows us to bridge ancient knowledge and modern medicine, offering a holistic perspective on human health that resonates across cultures and generations [4]. Herbal medicines have been an integral part of healthcare since ancient times, forming the foundation of traditional healing systems across cultures. Derived from plants and herbs, these remedies offer a holistic approach to health by aiming not only to treat diseases but also to restore balance within the body [5]. In recent decades, increasing awareness of the side effects and limitations of synthetic drugs has renewed global interest in herbal therapies; people are turning to nature once again, seeking safer, more sustainable, and affordable options for managing various ailments, from chronic inflammatory disorders and metabolic diseases to mental health conditions [6]. Scientific advancements and modern analytical techniques have allowed researchers to unravel the pharmacological potential of herbal compounds, validating many age-old practices through evidence-based studies.

*Calotropis gigantea*, commonly known as the crown flower or giant milkweed, is a hardy, laticiferous shrub that has become part of the daily lives, traditional healing systems, and cultural practices of communities across tropical and subtropical regions of Asia and Africa [7]. Belonging to the family

Apocynaceae, this drought-tolerant species thrives in disturbed habitats such as roadside margins, wastelands, and overgrazed pastures, where its robust growth and striking clusters of waxy white to lavender flowers have made it ecologically prominent and visually distinctive for centuries. Different parts of the plant, particularly the roots, bark, leaves, and milky latex, have been used in Ayurveda and various folk traditions to manage a wide range of ailments, including respiratory disorders, skin diseases, digestive disturbances, inflammatory conditions, and painful states such as joint and muscle pain [8]. Modern phytochemical and pharmacological investigations increasingly support these ethnomedicinal claims, revealing a rich profile of bioactive constituents and documenting activities such as antimicrobial, anti-inflammatory, wound-healing, antioxidant, cytotoxic, and cardiogenic effects, which position *C. gigantea* as a promising source of novel therapeutic agents [9]. The potent latex and certain constituent compounds carry a well-recognized risk of toxicity, underscoring the need for careful standardization, dose optimization, and safety evaluation before transitioning from a traditional remedy to an evidence-based phytopharmaceutical. In the context of rising interest in plant-derived drugs, *Calotropis gigantea*, as both a resilient weed and a “multi-potential” medicinal resource, offers a compelling focus for integrative research, bringing together ethnobotany, phytochemistry, pharmacology, toxicology, and conservation biology to translate traditional knowledge into safe and effective clinical applications [10]. Herbal medicines promise tremendous therapeutic benefits; however, their use also raises important questions regarding standardization, safety, dosage, and potential interactions with conventional drugs [11]. As the boundaries between traditional knowledge and modern medicine continue to blur, exploring the current understanding, scientific validation, and challenges of herbal medicines becomes not only timely but also essential for integrating these natural remedies into mainstream healthcare responsibly and effectively.

## 2. Botanical Description

*Calotropis gigantea* belongs to the family Apocynaceae (subfamily Asclepiadoideae); it is an erect, evergreen shrub or small tree that typically grows up to 4–5 m in height. Plants are characterized by large, thick, opposite leaves with a grey-green

appearance and a waxy surface, and the flowers are attractive, waxy, and usually pale lavender to white in color, arranged in umbellate clusters. The fruit is a large, inflated follicle containing numerous seeds with silky white hairs that aid in wind dispersal [12].

### 2.1 Taxonomical Classification

Table 1 Taxonomical classification of *C. gigantea*

➤ Kingdom	Plantae
➤ Phylum	Tracheophytes
➤ Class	Cardiac Glycosides
➤ Order	Gentianales
➤ Family	Apocynaceae
➤ Sub-Family	Asclepiadaceae
➤ Genus	<i>Calotropis</i>
➤ Species	<i>C.gigantea</i>



Fig 1. Flower of *C. gigantea*

### 2.2 Vernacular names of *Calotropis gigantean*

*C. gigantea* is known for rich variety of vernacular names across different cultures, reflecting its long history of traditional use and familiarity to rural communities. In English, it is most often called giant milkweed, crown flower, bowstring hemp, giant calotrope, or milkweed, names that refer either to its milky latex. Across the Indian subcontinent, the plant is widely recognized as “aak” or “madar” in Hindi, “arka” in Sanskrit, “akondo” in Bengali, “aank” in Nepali, “ankado” in Gujarati, “rui” or “arka” in Marathi, “erukku” in Tamil, “jilledu” or “jilledi puvvu” in Telugu, “ekka” in Kannada, and “erikkam” in Malayalam. In other regional

languages, it continues to carry its own distinct identity; for example, “Angkot” in Manipuri [13].

### 2.3 Geographical Location

*C. gigantea* is widely distributed throughout India, Sri Lanka, Bangladesh, Myanmar, Thailand, Indonesia, and Africa. It thrives in dry, sandy, and saline soils and is commonly found along roadsides, wastelands, and in coastal regions, demonstrating remarkable adaptability to harsh environmental conditions [14].

### 2.4 Traditional and Ethno-medicinal Uses

*C. gigantea* used to treat a variety of ailments; leaves are commonly applied externally to relieve pain, inflammation, and swelling, particularly in joint disorders, rheumatism and used in skin infections, wounds, and eczema. The milky latex of the plant has been traditionally employed in small, controlled amounts for the treatment of warts, corns, and dental problems. In Ayurveda, the root bark is used as a purgative and is believed to help in digestive disorders, intestinal worms, and spleen enlargement; flowers are used in the management of cough, asthma, and bronchitis, while also being offered in religious rituals because of their symbolic significance [15].

### 3. Phytochemical Constituents

*C. gigantea* contains a wide range of bioactive compounds; latex is rich in complex chemicals like calotroposides A–G, which include oxy-pregnane oligo-glycosides and cardiac glycosides, it also has compounds such as giganteol, isogiganteol, cardenolides, and bioactive akundarin, along with small amounts of uscharin, calotoxin, and calactin. The latex further contains calatropeol, amyryl, calcium oxalate, and enzymes similar to papain, as well as nitrogen and sulfur compounds formed through interactions with fish. The leaves, stem bark, and flowers of the plant also contain various glycosides, alkaloids, and resins, such as asclepin and calotropin, many of which are known for their strong medicinal and toxic properties. Several key compounds have been identified, such as laurone, saccharose,  $\beta$ -amyryl, calotropone (A and B), cyanidin-3-rahmanoglucoside, taraxsterol isovalerate, giaganteol, calacitin, calotoxin, calotropins (DI and DII), gigantol, and uscharin, highlighting the plant’s rich and diverse chemical composition [16].

### 4. Pharmacological Activities

#### 4.1 Anti-inflammatory activity

Experimental studies using carrageenan- and kaolin-induced paw edema, cotton pellet granuloma, and adjuvant-induced arthritis models in rats have demonstrated that *Calotropis gigantea* extracts significantly inhibit both the acute and chronic phases of inflammation, with peak effects typically observed around 2 h after administration. Alkaloid-rich fractions, as well as chloroform, n-butanol-, and ethanolic extracts, often show activity comparable to or approaching that of standard nonsteroidal anti-inflammatory drugs, suggesting the involvement of prostaglandin and cytokine pathways [17]. *In-vitro* assays and *in-silico* docking have further indicated that leaf and whole-plant constituents can inhibit key inflammatory mediators, such as cyclooxygenase-2, inducible nitric oxide synthase, and pro-inflammatory cytokines, aligning with the observed reductions in edema and granuloma formation [18].

#### 4.2 Analgesic activity

The analgesic potential of *C. gigantea* has been validated in several nociceptive models, including acetic acid-induced writhing, phenylquinine-induced writhing, and hot plate tests in mice and rats. Oral administration of alcoholic flower and root extracts at doses of approximately 250–500 mg/kg significantly reduces the number of writhes and prolongs hot plate reaction time, with maximal analgesic effects appearing between 30 and 90 min after dosing. These findings imply both peripheral and central analgesic components, possibly mediated through suppression of inflammatory mediators in peripheral tissues and modulation of central pain perception, consistent with the broader neuropharmacological profile reported for the plant [19].

#### 4.3 Antimicrobial activity

*C. gigantea* has garnered significant attention for its potent antimicrobial properties demonstrate broad-spectrum activity against both Gram-positive and Gram-negative bacteria, as well as pathogenic fungi. For instance, leaf extracts effectively inhibit clinical isolates of *Staphylococcus aureus*, *Escherichia coli*, *Pseudomonas aeruginosa*, *Bacillus subtilis*, and *Klebsiella pneumoniae*, producing zones of inhibition up to 17–21 mm in disc diffusion assays, often rivaling standard antibiotics, such as ciprofloxacin. Latex extracts stand out for their strong antifungal effects, targeting *Candida* species such as *C. albicans*, *C. parapsilosis*, *C. tropicalis*, and

*C. krusei*, with minimum inhibitory concentrations (MICs) ranging from 1–8mg/mL, comparable to amphotericin B [20, 21].

#### 4.4 Antioxidant activity

*Calotropis gigantea* exhibits antioxidant activity primarily through its rich phytochemical profile, including flavonoids, phenolics, terpenoids, and alkaloids, extracted from leaves. Ethanolic leaf extracts demonstrate notable free radical scavenging in DPPH (67.90 mg TE/g) and ABTS (89.67 mg TE/g) assays, alongside strong reducing power in CUPRAC (207.29 mg TE/g) and FRAP (118.8 mg TE/g) tests, outperforming some standards, such as ascorbic acid, in certain models [22].

#### 4.5 Anticancer and Cytotoxic activity

*Calotropis gigantea*, a plant rich in cardiac glycosides such as calotropin and uscharin, shows strong potential in the fight against cancer through targeted cell death mechanisms. Extracts from its leaves, stems, roots, and flowers trigger cytotoxicity in various human cancer cell lines, including breast (MCF-7, MDA-MB-231), liver (HepG2), colon (HT-29, HCT-116), lung (A549), cervical, and leukemia cells, often at low concentrations comparable to those of standard drugs, such as paclitaxel or doxorubicin [23].

*In vitro* assays confirmed IC<sub>50</sub> values around 40 µg/mL for MCF-7 cells, with up to 57% apoptosis after 24 h of exposure, and animal models of liver cancer in rats and Ehrlich ascites carcinoma in mice revealed reduced tumor nodules, fibrosis, inflammation (via lower TNF- $\alpha$  and IL-6), and proliferation markers, such as Ki-67, when using stem bark extracts alone or in combination with chemotherapy [24, 25].

#### 5. Future prospects of review

*Calotropis gigantea* holds immense promise for advancing medicinal and material sciences, driven by its rich bioactive compounds, such as cardiac glycosides, flavonoids, and alkaloids, which exhibit potent anticancer, anti-inflammatory, and antimicrobial effects [26]. Future research should prioritize clinical trials to bridge the gap between promising *in vitro* and animal studies and human applications, particularly for wound healing, diabetes management, and tumor suppression through targeted therapies. Standardized extraction methods and nanoparticle formulations from the plant's latex and leaves could yield novel drugs with reduced toxicity and enhance treatments for chronic

conditions, such as arthritis and infections. Biotechnological advances, including tissue culture for higher yields and *in-silico* modeling to pinpoint molecular targets, offer pathways to safer and more scalable pharmaceuticals.

The unique hollow fibers of *C. gigantea* present opportunities in sustainable materials, such as oil-absorbing adsorbents, antibacterial textiles, and smart sensors for healthcare monitoring. Developing industrial-scale processing for these fibers could expand their uses into energy storage, insulation, and eco-friendly composites, thereby addressing current lab-to-market barriers.

## 6. Conclusion

*Calotropis gigantea* is a remarkable perennial shrub with profound medicinal value and economic promise, thriving across diverse soils and climates without cultivation, and boasting rich bioactive compounds, such as cardiac glycosides, flavonoids, and terpenoids, that underpin its wide-ranging pharmacological effects—from analgesic and anti-inflammatory actions to hepatoprotective, antimicrobial, and even anticancer potential. Traditional uses in treating leprosy, ulcers, tumors, piles, asthma, and wounds align seamlessly with modern studies validating its efficacy in models of fever, diarrhea, central nervous system disorders, and oxidative stress, highlighting how environmental factors, such as soil and climate, influence its phytochemical potency for standardized therapeutic applications. However, its latex harbors toxicity risks, including cardiac irritation and dermatitis, underscoring the need for cautious dosing and further research into purification, clinical trials, and novel hydrocarbon extraction from latex for energy applications. Overall, this versatile "milkweed" bridges ancient herbal wisdom and contemporary pharmacology, urging expanded global awareness, conservation, and innovative studies to unlock safer and more potent drugs for everyday health challenges.

## Submission Declaration:

The authors confirm that the work is original and have read and approved the final manuscript for submission. The authors confirm that the work is original and have read and approved the final manuscript for submission

## Conflict of Interest

The authors declare no competing financial interest.

## Acknowledgements

I would like to express my deepest appreciation to Prof. Rahul Prem Kumar Mishra and Prof. Shobha Singh (Seth Vishambhar Nath Institute of Pharmacy Barananki, Uttar Pradesh) to carry out my studies.

## Funding

The authors declare that no financial support was received for this study.

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