

"CALOTROPIS GIGANTEA (L.) R. BR.: A COMPREHENSIVE REVIEW ON ITS PHYTOCHEMISTRY, TRADITIONAL USES, PHARMACOLOGICAL POTENTIAL, MECHANISM OF ACTION, AND TOXICOLOGICAL PROFILE"

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ABSTRACT

Calotropis gigantea (L.) R. Br., commonly known as "Arka," is a widely distributed medicinal shrub traditionally used in Ayurveda, Siddha, and folk medicine for treating a variety of ailments such as inflammation, skin diseases, respiratory disorders, and digestive issues. The plant is a rich source of diverse phytochemicals, including cardenolides, flavonoids, triterpenoids, alkaloids, and phenolic compounds, which are responsible for its broad spectrum of biological activities. Preclinical studies have demonstrated its anti-inflammatory, antimicrobial, anticancer, antidiabetic, hepatoprotective, and wound healing properties, mediated through mechanisms involving antioxidant effects, enzyme inhibition, and modulation of inflammatory and apoptotic pathways. While toxicological studies

suggest some dose-dependent adverse effects, the plant shows significant therapeutic promise. However, clinical evidence remains limited, necessitating further investigation to validate its efficacy and safety in humans. This review provides a comprehensive overview of the ethnomedicinal uses, phytochemistry, pharmacological actions, and toxicological profile of *Calotropis gigantea*, highlighting its potential as a valuable natural resource in drug development.

KEYWORDS: Calotropis gigantea, phytochemicals, pharmacology, toxicity, traditional medicine, drug development.

INTRODUCTION

Calotropis gigantea (L.) R. Br., commonly referred to as "Arka" in Hindi and "Erukku" in Tamil, is a hardy, xerophytic shrub extensively distributed across the Indian subcontinent and Southeast Asia. Traditionally recognized for its therapeutic applications in Ayurveda, Siddha, and folk medicine, the plant has been used for treating a wide range of ailments, including leprosy, fever, asthma, skin diseases, and gastrointestinal disorders. Various parts of the plant, leaves, flowers, roots, bark, and latex, are rich in pharmacologically active compounds such as cardenolides, flavonoids, triterpenoids, alkaloids, and glycosides. These bioactives exhibit diverse pharmacological properties, including anti-inflammatory, analgesic, antimicrobial, wound healing, antidiabetic, and cytotoxic activities. The plant's milky latex, although medicinally valuable, contains potent cardiac glycosides that demand caution due to potential toxicity. While traditional knowledge has long established its ethnomedicinal significance, recent pharmacological studies have begun to validate its bioactivities and propose its role as a promising lead in modern drug discovery. However, scientific standardization, clinical validation, and safety profiling are essential to translate its therapeutic potential into evidence-based pharmaceutical applications.^[1]



Calotropis gigantea(Giant milk-weed)

Botanical name: Calotropis gigantea Linn.

Family: Apocynaceae

Hindi : Ag, Akan Ark, Madar

Sanskrit: Arka, Aditya, Mandara

Marathi: Akand, Lal

Part used: Leaves, root, root bark, latex, stem bark, flowers.^[2]

Geographic Distribution

Calotropis gigantea, also known as Giant milkweed, is found in many tropical and subtropical regions around the world. It grows naturally in several Asian countries like India, Sri Lanka, Nepal, Bangladesh, Myanmar, Thailand, Indonesia, and China. It is also seen in parts of the Arabian Peninsula such as Saudi Arabia, Oman, and Yemen. In Africa, it grows in countries like Egypt, Ethiopia, and Sudan. The plant has been introduced to some areas in the Caribbean, Central America, and South America. In India, it is very common in dry and open places, especially in states like Tamil Nadu, Rajasthan, Maharashtra, Gujarat, Madhya Pradesh, Andhra Pradesh, and Odisha. It is usually found along roadsides, in wastelands, and near forest areas. *C. gigantea* grows well in sandy, salty, and alkaline soils, and it can survive in hot and dry climates. It is also seen growing up to 900 meters above sea level. Its wide presence shows how well it can adapt to different environments.^[3]

Botanical description

Calotropis gigantea (L.) R. Br. is a perennial, xerophytic shrub or small tree belonging to the family Apocynaceae, typically attaining a height of 2 to 4 meters and thriving in arid and semi-arid regions. It features an erect, pale grayish stem that exudes milky latex when damaged, and its leaves are large, oppositely arranged, ovate-oblong, and leathery, with a woolly, tomentose underside aiding in water retention. The plant produces star-shaped, waxy flowers in umbellate cymes, generally pale violet or white, with a unique crown-like corona at the center; the floral structure is highly specialized for insect pollination. Fruiting results in inflated paired follicles containing numerous flat, brown seeds equipped with silky hairs that facilitate wind dispersal. Its extensive, deep-penetrating root system enables survival in poor, dry soils. Commonly found in wastelands, roadside areas, and coastal belts, this hardy species showcases exceptional ecological resilience and is considered useful for land restoration and phytoremediation applications due to its robust growth in degraded environments.^[4]

Vernacular Names

Calotropis gigantea (L.) R.Br. is the scientific name of the plant. It belongs to the plant family Asclepiadaceae. In English, it is commonly known as Giant milkweed, sodom apple, calotrope, French cotton, and small crown flower. In Spanish, it is called algodón de seda, bomba, and cazuela. In French, names like cotton-france, arbre de soie, and bois canon are used. It is known as Calotropo in Italian, İpek ağacı in Turkish, and Wahre Mudarpflanze or Gomeiner in German.

In India, it is known by different names in local languages. In Tamil, it is called Vellerukku. In Hindi, names include Aaka, Aanka, and Ak. In Sanskrit, it is known as Arka, Alaka, and Ravi. These names vary by region, but all refer to the same important medicinal plant.^[5]

| Country | Local Name(s) |
|------------------------------------|--|
| India – Tamil Nadu | Vellerukku |
| India – Hindi Belt | Aak, Aaka, Ak, Madar |
| India – Kerala | Erukku, Erukam |
| India – Karnataka | Ekka gida, Ekkadagida |
| India – Andhra Pradesh / Telangana | Jilledu, Mandaram |
| India – Maharashtra | Rui, Arka |
| India – Gujarat | Akado, Ak |
| India – Punjab | Aak, Akk |
| India – West Bengal / Bangladesh | Akondo, Aakand |
| Pakistan | Aak, Madar |
| Nepal | Aank, Aak, Aaka |
| Sri Lanka | Erukku, Niyagala |
| Thailand | Rak, Yakrathong |
| Vietnam | Bông bông, Hoa đầu lân |
| Indonesia | Biduri |
| Malaysia | Tapak Dara |
| Philippines | Kapok-kapok, Loloan |
| Spain | Algodón de seda, Cazuela |
| Mexico / Latin America | Bomba, Algodón de seda |
| France | Cotton-france, Arbre de soie, Bois canon |
| Germany | Wahre Mudarpflanzer, Gomeiner |
| Italy | Calotrope |

Phytoconstituents in Various Parts of *Calotropis gigantea*

| | |
|------------------|--|
| Stem Bark | Contains giganteol, α - and β -calotropeol, and β -amyrin — all of which are triterpenoids known for their anti-inflammatory, hepatoprotective, and analgesic properties. ^[6] |
| Root | Rich in naphthalene derivatives (e.g., calotropnaphthalene) and various terpene derivatives like Calotropis sesterterpenol, calotropis sesterterpenol. These compounds exhibit antioxidant, antimicrobial, and possible cytotoxic properties. The root also contains calotropbenzofuranone (an aromatic compound) and sucrose, which may contribute to energy metabolism modulation or act as carriers. ^[7] |
| Seed Oil | Composed mainly of fatty acids such as palmitic, oleic, linoleic, and linolenic acids, which have nutritional and anti-inflammatory effects. The unsaponifiable fraction contains phytosterols (e.g., stigmasterol), melissyl alcohol, and laurane, known for their cholesterol-lowering, hormone-balancing, and antioxidant actions. ^[8] |
| Flowers | Contain esters of α - and β -calotropeols, contributing to aromatic and bioactive properties. Also reported are β -amyrin and stigmasterol, which are anti-inflammatory and anticancer agents. ^[9] |
| Leaves | Rich in sapogenins (precursors to steroidal drugs), holarrhetine (an alkaloid with probable neurological activity), cyanidin-3-rhamnoglucoside (an anthocyanin with antioxidant activity), and taraxasterol isovalerate (a triterpenoid). The leaves also contain mudarine and three cardenolide glycosides: calotropin, uscharin, and calotoxin — these are known for |

| | |
|------------------|---|
| | cardiotonic, cytotoxic, and anticancer effects. ^[10] |
| Latex | Composed mainly of water-soluble substances, caoutchouc (natural rubber), and resins. Latex contains proteolytic enzymes such as calotropains FI & FII, and other bioactives like calotoxin, uscharin, calactin, α - and β -calotropeols, and newly isolated triterpene esters (e.g., α -amyrin butanoate and Ψ -taraxasterol butanoate). These constituents contribute to antimicrobial, anti-inflammatory, wound-healing, and tumor-inhibitory properties. ^[11] |
| Root Bark | Includes β -amyrin, giganteol, and isogiganteol — triterpenoids with anti-ulcer, anti-inflammatory, and hepatoprotective activities. ^[12] |

Ethnomedicinal Uses

Calotropis gigantea has held a prominent place in traditional medicine across Asia, especially in systems like Ayurveda, Siddha, and Unani. The plant is known for its broad therapeutic applications, with nearly every part of the plant being used in traditional healing practices.

- Leaves are popularly used to treat inflammatory conditions, joint pains, and swelling. Warm leaves are externally applied to the chest for asthmatic relief and chronic coughs. In several rural regions, crushed leaf paste is applied to treat skin diseases, eczema, and fungal infections.
- Flowers are valued for their digestive and appetizer properties. They are often included in decoctions for treating indigestion, fever, and general weakness.
- Roots and root bark serve as natural purgatives and are used in the treatment of constipation, intestinal worms, and digestive blockages. External application of root paste is known to relieve lymph node swellings and scrofulous conditions.
- Latex, though toxic in its raw form, is carefully used in traditional remedies. It is applied topically on warts, corns, toothaches, and earaches. It is also a known treatment in rural medicine for snakebites and scorpion stings, though modern medicine recommends extreme caution.
- Stem bark is rarely used alone but is incorporated in polyherbal formulations for treating skin disorders, syphilis, and chronic infections.^[13]

Traditional Uses Of Calotropis Gigantea

Leaf



- Warm leaves placed on knees to reduce joint pain and swelling.
- Leaf paste is applied on the chest to give relief from asthma and wheezing.
- Leaf juice is given in small doses for indigestion and gastric problems.
- Leaf is applied externally to reduce inflammation in boils or abscesses.
- Used as a natural bandage over wounds in traditional medicine.
- Dried leaves are crushed and used in herbal tooth powder.

Roots

- Powdered root is used to treat asthma and chronic bronchitis.
- Decoction of roots is given during fever and body pain.
- Root paste applied on legs in elephantiasis (**reduces swelling**).
- Given as a remedy for constipation in some systems.
- Used in Siddha medicine for leprosy and skin diseases.



Flowers



- Dried flowers are used to make powder to treat cough and cold.
- Mixed with honey to improve appetite in children.
- Given in decoction form to people with chest congestion.
- Used for indigestion and loss of appetite.
- Boiled and taken during seasonal allergies.
- Also used in Ayurveda churnas (**herbal powders**).

Seeds



- Crushed seeds are used to stimulate bowel movement.
- The oil extracted is used for massage in arthritis and back pain.
- Oil is applied to ulcers and chronic skin wounds.
- Used in cracked lip healing (**mixed with beeswax**).
- Seeds are also used in traditional pest repellent powder.^[14]

Pharmacological Activity

1. Anti-inflammatory Activity

Calotropis gigantea possesses potent anti-inflammatory properties that have been validated in multiple experimental models. Leaf, flower, and latex extracts of the plant have demonstrated significant inhibition of inflammatory responses through suppression of key pro-inflammatory enzymes such as cyclooxygenase (COX) and lipoxygenase (LOX). These enzymes play a pivotal role in the synthesis of prostaglandins and leukotrienes, which are critical mediators of inflammation. Furthermore, the extracts downregulate the expression of cytokines including tumor necrosis factor- α (TNF- α), interleukin-6 (IL-6), and interleukin-1 β (IL-1 β), contributing to reduced inflammation and tissue damage. In animal models like carrageenan-induced paw edema and cotton pellet-induced granuloma, the anti-inflammatory effect of *C. gigantea* was found to be comparable to nonsteroidal anti-inflammatory drugs (NSAIDs) such as diclofenac and indomethacin.

2. Antioxidant Activity

The plant is an abundant source of natural antioxidants, mainly flavonoids, phenolic acids, and tannins, which endow it with excellent free radical-scavenging capacity. In vitro studies using assays like DPPH (2,2-diphenyl-1-picrylhydrazyl), ABTS (2,2'-azino-bis), and FRAP (ferric reducing antioxidant power) have confirmed the strong radical-neutralizing ability of *C. gigantea*. In vivo, the administration of extracts enhances levels of endogenous antioxidant enzymes such as superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPx). These enzymes combat oxidative stress and protect biomolecules like lipids, proteins, and DNA from oxidative degradation. The antioxidant effect contributes to the plant's protective role in managing chronic diseases linked to oxidative stress.

3. Anticancer / Cytotoxic Activity

Among the most compelling pharmacological properties of *Calotropis gigantea* is its significant anticancer and cytotoxic potential. Phytochemical-rich extracts from the latex, flowers, and roots have shown dose-dependent cytotoxic effects against a variety of human cancer cell lines, including MCF-7 (breast cancer), HeLa (cervical cancer), and HepG2 (liver cancer). The underlying mechanism primarily involves the induction of apoptosis through the intrinsic mitochondrial pathway. This process includes mitochondrial membrane depolarization, cytochrome c release, activation of caspases (especially caspase-3 and caspase-9), and upregulation of tumor suppressor gene p53. Cardiac glycosides such as

calotropin, uscharin, and calotoxin are identified as the primary active constituents responsible for antiproliferative effects. These compounds also inhibit angiogenesis and modulate key cell cycle regulatory proteins, positioning *C. gigantea* as a promising candidate for anticancer drug development.

4. Antimicrobial Activity

Calotropis gigantea demonstrates significant antimicrobial effects against a wide spectrum of bacterial and fungal pathogens. Extracts, particularly latex, have shown strong inhibitory action against gram-positive bacteria such as *Staphylococcus aureus* and *Bacillus subtilis*, as well as gram-negative strains like *Escherichia coli* and *Pseudomonas aeruginosa*. Furthermore, antifungal activity has been observed against species like *Candida albicans* and *Aspergillus niger*. The mechanism of antimicrobial action may involve disruption of microbial cell membranes, leakage of cellular contents, inhibition of protein synthesis, and interaction with microbial DNA. Bioactive compounds, including alkaloids, flavonoids, saponins, and terpenoids, are believed to contribute synergistically to the antimicrobial efficacy.

5. Antidiabetic Activity

Experimental studies using streptozotocin (STZ)-induced diabetic rats have demonstrated the hypoglycemic potential of *C. gigantea*. Both aqueous and ethanolic extracts significantly reduce blood glucose levels and enhance glucose tolerance. The antidiabetic effect is primarily attributed to the inhibition of key carbohydrate-digesting enzymes, namely α -amylase and α -glucosidase, thereby controlling postprandial hyperglycemia. Moreover, the extracts help preserve and regenerate pancreatic β -cells, increase insulin secretion, and improve insulin receptor sensitivity. These effects are likely mediated by the synergistic action of flavonoids, saponins, and phenolic acids present in the plant.

6. Hepatoprotective Activity

The hepatoprotective activity of *Calotropis gigantea* has been confirmed in several models of chemically induced liver damage, including exposure to carbon tetrachloride (CCl_4), paracetamol, and ethanol. Extract treatment restores elevated serum markers such as alanine aminotransferase (ALT), aspartate aminotransferase (AST), and alkaline phosphatase (ALP) to near-normal levels. Histological examination of liver tissue shows reduced necrosis, fatty degeneration, and inflammatory infiltration. The hepatoprotective mechanism is likely due to

the plant's strong antioxidant activity, membrane-stabilizing properties, and suppression of lipid peroxidation.

7. Analgesic Activity

Calotropis gigantea exhibits both peripheral and central analgesic effects. In experimental models like the hot plate and tail-flick test, the extracts increased reaction time, indicating central pain relief. The acetic acid-induced writhing test further supports its peripheral analgesic activity. The probable mechanism includes inhibition of prostaglandin synthesis and potential interaction with opioid receptors. Flavonoids and alkaloids in the plant are suggested to be the principal contributors to its pain-relieving action, which supports its traditional use in treating headaches, muscular pain, and joint stiffness.

8. Anthelmintic Activity

The anthelmintic potential of *C. gigantea* has been explored using *Pheretima posthuma* and *Ascaris lumbricoides* as model organisms. Extracts from the roots and flowers induce paralysis and subsequent death of worms. The mechanism may involve disruption of ATP generation, oxidative stress on worm tissue, and inhibition of essential metabolic enzymes. This property aligns with traditional uses of the plant in treating intestinal parasitic infections and promoting digestive health.

9. Immunomodulatory Activity

Extracts from *C. gigantea* have shown immunostimulatory effects in various animal studies. Latex and leaf extracts increased total white blood cell counts, enhanced antibody titers, and stimulated delayed-type hypersensitivity responses. The modulation of both innate and adaptive immune responses suggests its potential role in enhancing immunity during infections, and possibly in immunocompromised conditions. The activity is attributed to flavonoids, polysaccharides, and glycoproteins present in the plant.

10. Wound-Healing Activity

Topical application of *C. gigantea* latex and flower extract accelerates wound healing by promoting faster epithelialization, increased fibroblast proliferation, and enhanced collagen deposition. The antimicrobial and antioxidant properties further aid in wound protection and tissue repair. In excision and incision wound models, the extract-treated animals showed significantly reduced wound area and increased tensile strength, suggesting its effective role in wound management.^[15]

Preclinical and Clinical Studies

Preclinical Studies

Anti-inflammatory and Analgesic Activity

Animal models such as carrageenan-induced paw edema and acetic acid-induced writhing have confirmed the anti-inflammatory and analgesic properties of *C. gigantea* extracts. These effects are attributed to the inhibition of pro-inflammatory mediators like prostaglandins and cytokines.

Antioxidant Activity

Methanolic extracts of the leaves and flowers have shown strong free radical scavenging activity in DPPH and nitric oxide assays, indicating potent antioxidant potential. This may contribute to the plant's protective effects in oxidative stress-related diseases.

Anticancer and Cytotoxic Activity

Several in vitro studies have shown cytotoxic effects of latex and leaf extracts against human cancer cell lines such as HeLa (cervical cancer), MCF-7 (breast cancer), and A549 (lung carcinoma). The presence of cardenolides and other bioactive compounds likely contributes to these antiproliferative effects by inducing apoptosis and cell cycle arrest.

Antimicrobial and Antifungal Activity

Ethanollic and aqueous extracts have demonstrated significant inhibitory activity against pathogens like *Staphylococcus aureus*, *Escherichia coli*, *Pseudomonas aeruginosa*, and *Candida albicans*. These effects highlight the plant's potential in treating infectious diseases.

Hepatoprotective and Cardioprotective Effects

In animal models of CCl₄-induced hepatotoxicity, *C. gigantea* extracts restored liver enzyme levels and histopathological integrity. Latex extracts have also shown cardiotonic effects, but their toxic potential requires careful consideration.

Wound Healing Activity

Topical application of latex-based formulations accelerated wound contraction and epithelialization in excision and incision wound models, supporting its traditional use in treating skin injuries.^[16]

Clinical Studies

Dermatological Applications

A small-scale clinical evaluation investigated the use of a *C. gigantea*-based topical formulation for the treatment of chronic non-healing ulcers. Patients treated with the ointment experienced enhanced wound closure, reduced infection, and improved tissue regeneration. These findings, though promising, were not from large randomized controlled trials (RCTs).

Wart Removal and Skin Tags

Traditional application of *C. gigantea* latex for removing warts and skin lesions has been supported by anecdotal reports and minor case series. The latex appears to exert keratolytic effects, but its irritant nature and toxicity necessitate professional supervision.

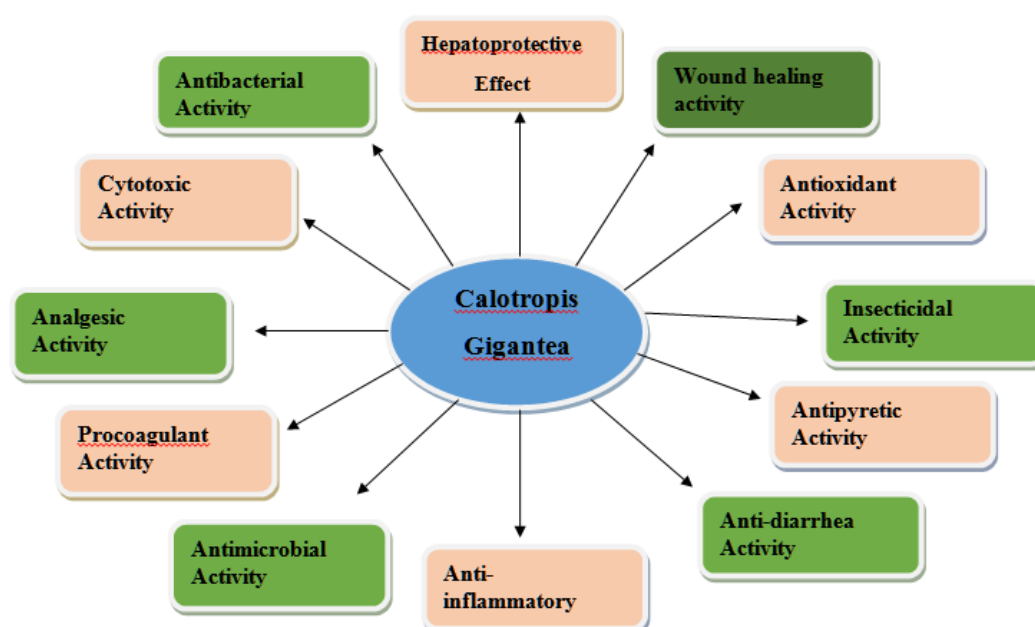
Anti-inflammatory and Pain Relief:

Some traditional healers have employed *Calotropis gigantea*-based poultices or decoctions for treating arthritic pain and joint inflammation. Limited clinical observations have shown temporary symptomatic relief, though no controlled trials have validated these uses.

Caution in Systemic Use

Due to the plant's known cardiotoxic glycosides and cytotoxic compounds, systemic administration without clinical evidence remains unsafe. No studies to date have evaluated its oral use in humans under controlled conditions.^[17]

Therapeutic Uses^[18]



Mechanism Of Action Of Calotropis Gigantea

Anti-inflammatory Action

- Plant extracts exhibit anti-inflammatory effects primarily by inhibiting the cyclooxygenase (COX) and lipoxygenase (LOX) enzymes, leading to reduced synthesis of inflammatory mediators like prostaglandins and leukotrienes.
- Suppression of nuclear factor-kappa B (NF- κ B) signaling minimizes the release of cytokines such as TNF- α , IL-1 β , and IL-6.
- Certain phytochemicals contribute to lysosomal membrane stabilization, by preventing the release of tissue-damaging enzymes.

Anticancer Activity

- The anticancer mechanism involves activation of apoptotic pathways, particularly via mitochondrial membrane permeabilization and release of cytochrome c.
- Upregulation of pro-apoptotic proteins (Bax) and downregulation of anti-apoptotic proteins (Bcl-2) initiate caspase activation, leading to programmed cell death.
- Compounds such as calotropin and uscharin trigger G2/M phase cell cycle arrest and enhance ROS production, contributing to cytotoxicity in cancer cells.

Antidiabetic Mechanism

- Antidiabetic effects are mediated by inhibition of carbohydrate-hydrolyzing enzymes like α -amylase and α -glucosidase, resulting in slower glucose absorption.
- Extracts also enhance insulin signaling and upregulate GLUT4 expression, facilitating glucose uptake by peripheral tissues.
- Antioxidants in the plant protect pancreatic β -cells from damage caused by oxidative stress.

Antimicrobial Effects

- Latex proteins and terpenoids exhibit antimicrobial action by disrupting the integrity of microbial cell walls and membranes, causing cell leakage and death.
- Some phytoconstituents interfere with bacterial quorum sensing and biofilm formation, weakening microbial defense mechanisms.

Analgesic and Antipyretic Mechanism

- The analgesic action involves a reduction in peripheral nociceptor sensitization, possibly through prostaglandin inhibition.

- Central antipyretic effects occur via modulation of the hypothalamic thermoregulatory center, likely influenced by suppression of PGE2 synthesis.

Antioxidant Defense

- The plant's antioxidant properties arise from the ability of its flavonoids and phenolics to neutralize reactive oxygen species (ROS).
- It enhances endogenous antioxidant enzyme activities such as superoxide dismutase (SOD), catalase, and glutathione peroxidase, thereby protecting cells from oxidative injury.

Immunomodulatory Pathway

- *C. gigantea* has been reported to modulate immune response by stimulating macrophage activity, enhancing lymphocyte proliferation, and regulating cytokine production.
- These effects may involve glycoproteins and latex-derived proteins that influence cell-mediated immunity.^[19]

Toxicological Profile Of *Calotropis Gigantea*^[20]

| Plant Part / Extract | Test Model | Dosage (mg/kg or %) | Observed Toxicity / Findings | LD ₅₀ (mg/kg) |
|----------------------------|------------------------------|---------------------|---|--------------------------|
| Latex (topical) | Human (topical use) | — | Skin irritation, blistering, dermatitis | — |
| Latex (ocular exposure) | Rabbit (eye irritation test) | — | Redness, conjunctivitis, temporary vision disturbance | — |
| Latex (oral) | Rat (acute oral) | 1000–3000 | Salivation, tremors, decreased motor activity | 2000–2500 |
| Root extract (aqueous) | Mice (oral) | 1000–3000 | Liver degeneration, behavioral toxicity at higher doses | 2500–3000 |
| Leaf extract (ethanolic) | Rat (oral, subacute) | 200–800 | No mortality, mild biochemical changes at 800 mg/kg | >3000 |
| Flower extract (ethanolic) | Rat (oral, subacute) | 100–400 | Well tolerated, no signs of toxicity or organ damage | >3000 |
| | | | | |
| Whole plant (powder) | Human (folk use) | — | Used externally with no reported toxicity in traditional practice | — |

CONCLUSION

Calotropis gigantea is more than just a traditional medicinal plant—it is a biological powerhouse that bridges ancient healing wisdom with modern scientific innovation. Every part of this hardy, resilient plant harbors potent bioactive compounds that demonstrate a wide spectrum of pharmacological actions, including anti-inflammatory, anticancer, antidiabetic,

antimicrobial, and wound-healing properties. These therapeutic potentials are backed by extensive preclinical studies, supported by traditional use, and increasingly being validated through modern pharmacological research. Beyond its role in health care, *C. gigantea* also shines in the industrial and agricultural sectors. Its bast fibers serve as sustainable alternatives in the textile and paper industries. Its latex, rich in cardenolides and enzymes, holds promise for the development of biopesticides, natural adhesives, and even biofuel. Its ability to thrive in arid, saline, and degraded soils makes it an ideal candidate for green manure, soil reclamation, and phytoremediation, contributing to sustainable agriculture and environmental restoration.

However, its toxic potential—especially due to cardiac glycosides—demands caution. There is an urgent need for standardized extraction methods, clinical validation, and safe dosage protocols to ensure responsible therapeutic use. With advancements in formulation science, biotechnology, and toxicological profiling, the full potential of *Calotropis gigantea* can be safely unlocked. In essence, *Calotropis gigantea* stands as a symbol of nature's duality—powerful yet perilous, healing yet hazardous. With proper scientific direction, it holds the promise to emerge as a cornerstone in phytopharmaceutical development, eco-friendly industries, and sustainable agriculture. This humble shrub, often found growing wild along roadsides, may well be a future green goldmine—waiting to be fully discovered, respected, and responsibly utilized.

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