STM JOURNALS

Research & Reviews: Journal of
Botany

ISSN: 2278-2222
Volume 14, Issue 2, 2025
May–August
DOI (Journal): 10.37591/RRJoB

https://journals.stmjournals.com/rrjob

Review RRJoB

Calotropis: A Comprehensive Review of Its Phytochemistry, Pharmacology, and Therapeutic Potential

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Abstract

Calotropis gigantea is a genus in the family Apocynaceae that grows in tropical and semitropical climates. India is home to this plant's distribution. In Hindi, it is referred to as sweta arka. It is well known for its medicinal and ethnobotanical values. Calotropis gigantea, in particular, has a history of use in the treatment of many health-related issues, including disorders of the respiratory system, inflammation, and skin infections. Calotropis gigantea is a well-known and beneficial herb that is sometimes referred to as milkweed. The systematic position, colloquial names, vegetative characteristics, ecology and distribution, phytochemistry, and economic significance of Calotropis gigantea are all covered in this review paper. The plant is also known to possess diverse bioactive components, including Cardenolides, Flavonoids, Terpenoids, and Alkaloids, and possesses various ranges of pharmacological activities, such as anti-inflammatory, antimicrobial, anticancer, and antioxidant activities, among others. Recent research makes a case for therapeutics based on Calotropis, especially in relation to the management of chronic illness, notwithstanding the limitations of its toxicity and sustainable use.

Keywords: *Calotropis gigantea*, ethnobotanical, phytochemistry, pharmacological activity, milk weed

INTRODUCTION

Calotropis gigantea and *Calotropis procera* are referred to as "Sweta Arka" and "Raktha Arka" respectively, in traditional Ayurvedic treatment. Both frequently share similarities in their botanical characteristics and pharmacological effects. Throughout history, natural elements, such as plants and animals have played a crucial role in shaping human culture and civilization. From ancient times to the modern era, their influence can be seen across different regions of the world, including India. A kind of *Calotropis* known as "crown bloom" is said to be native to tropical Africa, China, Pakistan, Nepal, Somalia, Indonesia, Malaysia, the Philippines, Thailand, Sri Lanka, India, and Cambodia. Numerous insects and butterflies are attracted to this plant. In Hawaii, non-migratory ruler butterflies rely on this plant as their host. *Calotropis* (Figure 1), commonly known as Madar, has been an integral part of traditional medicine, including Unani, Ayurvedic, and Siddha practices, for centuries. Ayurvedic medicine is an indigenous practice that uses all parts of this plant for medicinal purposes. The common names for it are Crown flower weed and milkweed, respectively. *Lateriplastis gigantea* is a plant that produces latex, which is released following tissue damage. As a potential pesticidal source against insect pests, this milkweed plant has grown in significance recently. Proteins, gum, sugars, starch, tannins, alkaloids,

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Received Date: January 27, 2025
Accepted Date: February 12, 2025
Published Date: February 20. 2025

Citation: Gaurav P. Patil, Mansi A. Dhankani, S.P. Panwar, Ankit Kumar Dhankani. *Calotropis*: A Comprehensive Review of Its Phytochemistry, Pharmacology, and Therapeutic Potential. Research & Review: Journal of Botany. 2025; 14(2): 6–20p.

and resins can all be found in plant latex. Throughout history, this plant was frequently used, either directly for traditional medicines or indirectly for the manufacturing of modern pharmaceuticals. Indian pharmacological herbs describe the use of this plant in the treatment of several illnesses, including asthma, anorexia, colds, and coughs. Roasted leaves are beneficial for swollen or aching joints. Reports indicate that *Calotropis gigantea* possesses mosquito-controlling properties, specifically against *Culex gelidus* and *Culex tritaeniorhynchus*, which are known vectors of Japanese encephalitis. The *Calotropis gigantea* leaf aqueous extract showed notable homicidal, repellent, and larvicidal activity. This article aims to provide a comprehensive analysis of the plant's taxonomic rank, common names, origin, morphological and geographic distribution, propagation and planting, phytochemicals, medicinal properties and other uses [1, 2].

SCIENTIFIC CLASSIFICATION

- Kingdom
- Subkingdom
- Division
- Class
- Order
- Family
- Genus
- Species
- Plantae
- Tracheobionta
- Magnoliophyt
- Magnoliopsida
- Gentianales
- *Apocynaceae*
- *Calotropis*
- *C. gigantean*

Figure 1. *Calotropis*.

Vernacular Names

- English
- Hindi
- Kannada
- Manipuri
- Tamil
- Telungu
- Sanskrit
- Bowstring hemp, calotrope, crown flower, crown Plant, giant milkweed
- Safed aak
- Ekka
- Angkot
- Erukku
- Jilledi puvvu
- Svetarka

ORIGIN AND DISTRIBUTION

Calotropis gigantea originates from continental Asia and Southeast Asia but has spread to various regions, including the Pacific Islands, Australia, Central and northern South America, and Africa. It is commonly found as both a weed and an ornamental plant near settlements and temples. In Africa, it has been documented in Gabon, the Democratic Republic of Congo, Sudan, Kenya, Tanzania, Angola, and Mozambique, as well as in the Seychelles and Mauritius. However, its exact distribution remains uncertain, and it is likely present in additional countries. Native to Malaysia, China, and India, the plant has been introduced to many parts of the world. Within India, it is primarily found in regions, such as lower Bengal, the Himalayas, Punjab, Assam, Madras, and South India.

Common waste ground, roadsides, railway embankments, and an elevation of roughly 1000 meters in the Himalayas, spanning from Punjab to Assam [3, 4].

BOTANICAL DESCRIPTION

Macroscopic Features

The erect, heavily branched shrub *Calotropis gigantea* grows to a height of one to five meters. The roots are roughly 90 cm in length and 2.5–10 cm in diameter. They are tortuous, cylindrical, frequently branched, and have an exterior that is yellowish grey and white and an interior that is ceramic white. Short, curving, and rarely quilled, root bark has a distasteful, mucilaginous, bitter flavor. It is 2–5 mm thick and 3–5 cm broad. The leaves of the plant are simple, opposite-decussate, subsessile, and stipulate, with an oblong to broadly obovate shape, measuring between 5–30 × 2.5–15.5 cm. The flowers are complete, bisexual, bracteate, actinomorphic, pentamerous, hypogynous, and pedunculate. The corolla is gamopetalous, while the calyx consists of five sepals and a lobe, briefly fused at the base. The fruits are simple, fleshy, inflated, and range from subglobose to obliquely oval. The seeds, measuring approximately 6 × 5 mm, are flat, compact, and smooth with a white color. The plant produces two follicles per fruit, which are ovoid, boat-shaped, and inflated, measuring 6.5–10 cm × 3–5 cm, containing numerous seeds. Each oval seed is 5–6 mm long, with a 2–3 cm long coma at one end, attached to a dense white coma. The plant also spreads through suckering, where broken stems can take root and regenerate via crowns and roots. Pollination is primarily facilitated by insects, particularly bees and butterflies [5]. Different parts of *Calotropis* are depicted in Figure 2.

MICROSCOPIC FEATURES

The root's transverse cut reveals that cork makes up the outermost layer, composed of 15–20 layers of uniformly sized rectangular cells with no intercellular space in between. An abundance of starch granules is present in the cells in the cortical area. Lactiferous tubes and a calcium oxalate rosette are features of these cells, which are composed of parenchymatic cells with uneven shapes. An upper and lower single-

layered epidermis with thick striated cuticles covering the outer surface of the leaf, along with a small number of epidermal cells that have elongated to form 2–3 celled trichomes, are visible when a transverse section is made through the midrib of the leaf. Vessels and tracheids make up the majority of xylems. Vascular bundles and laticifers were likewise sporadically distributed in this area, and the central cells had an uneven shape [6].

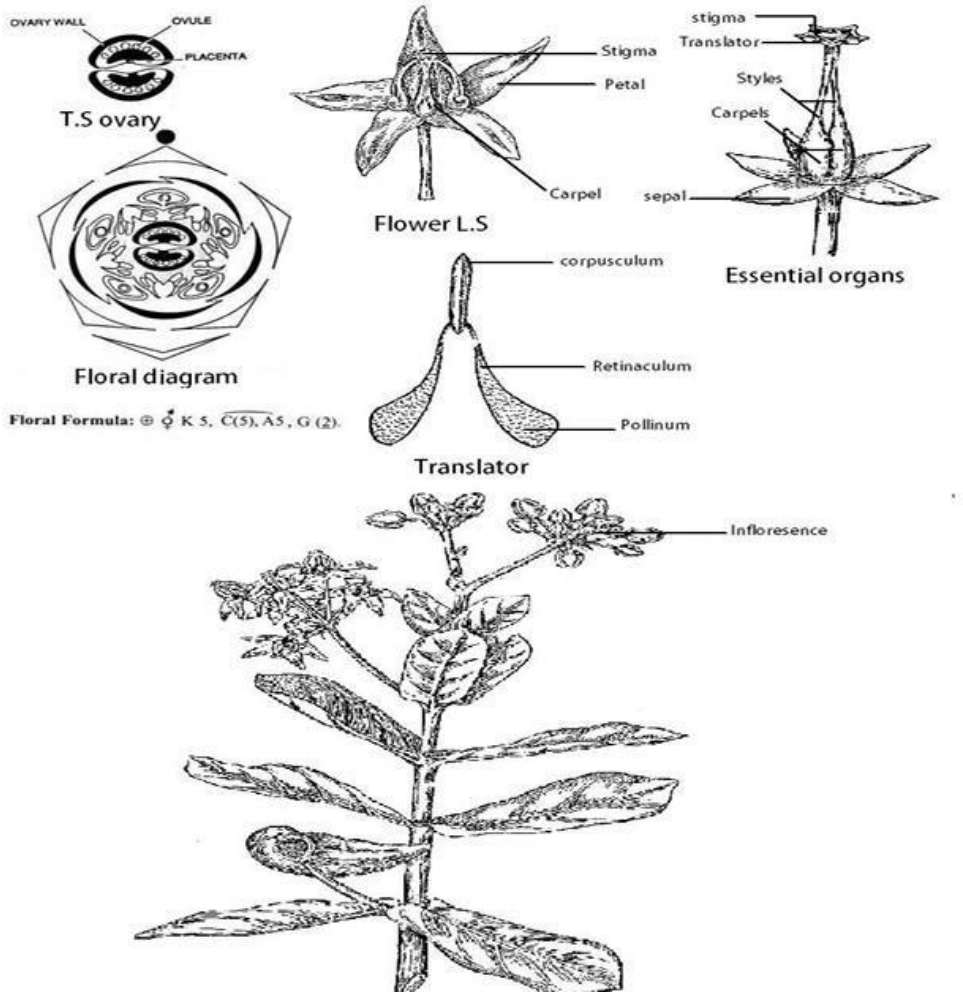

Figure 2. Part of *Calotropis*.

Calotropis is described botanically in the following sections:

- *Bark & Branches:* Thick, rough, and corky with a yellow-brown hue, the bark is covered in tomentum, which is a white, fur-like hair. Twigs are fleshy and green.
- *Leaves:* The leaves have a pale green hue and measure approximately 30x25 cm. The leaves are opposite-decussate, simple, and range from ovate to obovate in shape, with 4–6 pairs of subopposite veins prominently visible on the abaxial surface. They have a sessile, nearly decurrent base and a sharply pointed apex.
- *Inflorescences:* The inflorescences emerge from the leaf base in pedunculate cymes, approximately 7 cm long, containing 3 to 20 flowers.
- *Flowers:* Five small, dirty white triangular sepals enclose the flower, along with five thick, ovate petals (approximately 1 cm × 1 cm) that are white at the base and transition to purple at the tips. Surrounding the white, five-lobed stigma are five stamens with purple-tipped anthers.
- *Fruits:* Follicles, or ovoid, green fruits, can measure up to 15 cm in length and 10 cm in width. Their plumed, papery, light brown seeds with a pappus of up to 6 cm long white filaments on one side are released as they split open. March to October would be the principal blooming time.

- *Root:* The entire condition has the root. The diameter of the rootlets, which range in diameter from
- 0.2 to 0.5 cm, separates the bark from the wood by 0.5 to 2.0 cm. outwardly yellowish grey in hue, wrinkly when still fresh, and abundantly leaks whitish latex from bark wounds or cuts. Breakage is not complete.
- *Leaf:* The plant is simple, opposite, sub-sessile, slightly thick, meaty, and coriaceous. It is 10–15 cm long and 4.5–6.5 cm broad. Its base is auricled, and it is broadly cuneate, obovate or obovate oblong, slightly cordate, and has a tuft of short, simple hair on the upper side close to where it attaches to the petiole. The pubescence is ashy grey and covers the delicate leaves. When leaves are mature, they are pale green, almost smooth, or even glabrous.
- *Flowers:* Regular, bisexual, lavender or light rose in color, with a hint of greenish yellow or purple hue, and a slight scent. They are situated at the termini of laterally positioned or interpetiolar peduncles that emerge from different sides of the nodes in simple or sporadically compound corymbs. An involucre of many tiny, oblong-pointed, scaly, caducous bracts encircle each cluster of ovoid flower buds (Figure 3).
- *Calyx:* Five lobes broadly ovate with small fleshy teeth-like glands within the base.
- *Corolla:* Regular, gamopetalous, pale rose purple or lilac, subcordate to broadly sub-campanulate with A short tube and five broad, ovate, lanceolate, Valvate, spreading lobes.
- *Stamens:* Five are positioned at the enormous stamina column that is entirely adnate to but marginally shorter than the column formed by the union of filaments. Slightly shorter than the column, the appendages are meaty. The appendages have a pale hue and are squishy.
- *Root bark:* It is discovered that the tap roots have prominent crowns with spherical heads and spirally bent remaining portions. These tough roots have a greyish white hue and show sap evaporation where the bark has been broken. The elder roots have some cracks in their bark. The bark has a yellowish white inside and a yellowish grey outside. The inner bark portion is smooth and mucilaginous, whereas the upper cork portion is rough and spongy. The conspicuous tops with rounded heads and the remaining portion that is spirally curved have a bitter taste. These firm; grey-white roots, have sap oozing from the areas where the bark has been broken.

Figure 3. Flowers.

THERAPEUTIC EFFECT

The plant has purgative, anthelmintic, alexipharmic, leprosy, leukoderma, ulcers, tumors, piles, and disorders of the liver, spleen, and abdomen; its juice also has anthelmintic and leukoderma properties, and it treats tumors, ascites, and abdominal ailments. The leaves are applied to sore joints, swollen areas, and paralyzed areas to help cure wounds. For intermittent fevers 3, 4, the leaf tincture is used as an antiperiodic tumor, inflammations, rat bites, and ascites.

The milk has laxative, purgative, hot, and bitter properties that help with piles. The root bark has diuretic properties and treats syphilis and asthma. The flower has analgesic, astringent, bitter, anthelmintic, and healing properties [7].

ETHNOPHARMACOLOGICAL PROPERTIES

- *Leaf:* Treats skin ulcers, leprosy, and eye issues.
- *Flower:* Helps suppress bile, removes intestinal worms, and alleviates coughs, colds, and asthma.
- *Bark:* Acts as an analgesic, cures fever, neurodermatitis, and syphilis. The powdered bark is used for diarrhea, dysentery, elephantiasis, and leprosy. Stem bark is used as an expectorant and to treat dysentery, spleen disorders, convulsions, lumbago, scabies, ringworm, and pneumonia [8].
- *Fruit:* Helps treat piles, intestinal worms, eye problems, diabetes, and is abortive (fruit pulp).
- *Latex:* Used for dysentery, leprosy, elephantiasis, epilepsy, and asthma.
- *Bud:* Juice from young buds is used to treat earaches.
- *Seed:* Treats leprosy and intestinal worms [9, 10].

PROPAGATION AND MANAGEMENT

Natural regeneration occurs frequently, and the seeds fly around freely. For the large-scale reproduction of better genotypes, vegetative propagation using stem and root cuttings is highly helpful. To produce fibers at a spacing of one to one and a half meters, *Calotropis* has been grown in South America and the Caribbean Islands. Yields of up to 500 kg/ha are anticipated when cultivating. Single harvests are better than double or triple harvests every season since they save energy input on the field as well as in the processing plant. In dry or semi-arid areas without significant frost, it works well for intensive energy farming [11]. The plant flourishes in a wide range of soil and environmental conditions. It does not need specific cultivation practices. It is among the few plants that grazing animals do not consume [12–14]. It thrives in poor soil, especially in areas where overgrazing has reduced competition from native grasses. In some regions, this plant is the sole survivor, where no other plants grow. It is drought-tolerant and serves as pioneer vegetation in desert soil.

The plant has xerophytic adaptations, such as latex, a highly branched root system, and thick, wax-coated leaves. Therefore, it is found in tropical and subtropical regions globally, including throughout India. The plants reach their typical height, yielding fruits, seeds, or other products under non-destructive management systems. It can be cut back to the ground repeatedly and will resprout vigorously, supporting non-destructive management while maintaining soil organic carbon [13, 14].

DISEASE AND PESTS

Calotropis gigantea plants are pestized by the leaf hopper *Poecilocerus pictus*. The cardenolides used by the oleander aphid (*Aphis nerii*), the tiger butterfly (*Danaus chrysippus*), and the monarch butterfly (*Danaus plexippus*) caterpillars as a chemical defence mechanism as they feed on *Calotropis spp*. Although the leaf extract kills them, the nematodes *Meloidogyne incognita* and *Meloidogyne javanica* are detected on the roots of *Calotropis gigantea* in India. Aphis nerii is the carrier of a mosaic illness that is sap-transmissible in *Calotropis gigantean* (Figure 4) [15].

Figure 4. Disease and pests.

Lahore, Pakistan, saw an outbreak of leaf spot in September 2011 due to which grows in wasteland areas. In addition, a disease spot on leaves was seen in a halo of chlorotic yellow tissue zone. A yellow leaf eventually underwent abscission as the illness worsened, showing that disease spots were seen on the lower stem and older leaves. At the Institute of Plant Pathology, University of the Punjab, Lahore, Pakistan's First Fungal Culture Bank (FCBP), a voucher specimen (IR00027) has been deposited.

PRINCIPLE CONSTITUENTS OF *CALOTROPIS* GIGANTEAN

Heart glycosides, gigantin, calotoxin, uscharin, and calotropin are all present in *Calotropis gigantea* latex. The main components of the resinol portion are two novel alcohols, α and ß-ß-ß-calotropeols, which are present in almost equal proportions, along with trace amounts of ß-amyrin. *Calotropis gigantea* contains a combination of fatty acids, flavonoids, alkaloids, calotropain (a proteolytic enzyme), and trace amounts of sterols. It has been traditionally used to treat various ailments, including severe conditions. Researchers have conducted multiple in vitro and in vivo pharmacological studies to validate its traditional applications. These studies suggest that the plant holds promise as a natural medicinal resource.

The root bark of *Calotropis gigantea* contains seven oxypregnane-oligo glycosides, cardiac glycosides, and calotroposides A–G, along with β-amyrin, two isomeric crystalline alcohols, giganteol, isogiganteol, and cardenolides. It's latex, known as akundarin, comprises 0.45% uscharin, 0.15% calotoxin, and 0.15% capacity, as well as α-calatropeol, β-calotropeol, β-amyrin, and calcium oxalate. Additionally, it produces gigantin, a toxic compound that acts as a fish and heart poison containing sulphur and nitrogen. Trace amounts of glutathione and a papain-like proteolytic enzyme are also present in the latex. Alkaloids, Glycosides, and Mudarine in leaves. Stembark includes giganteol, β-Amyrin, and β-calotropeol. Flower: nα-calatropeol, β-Calotropeol, amyrin, asclepin, bitter resins (akundarin, calotropin), mudarine, and cardioactive glycosides [16]. The Structure of Calotropin is given in Figure 5.

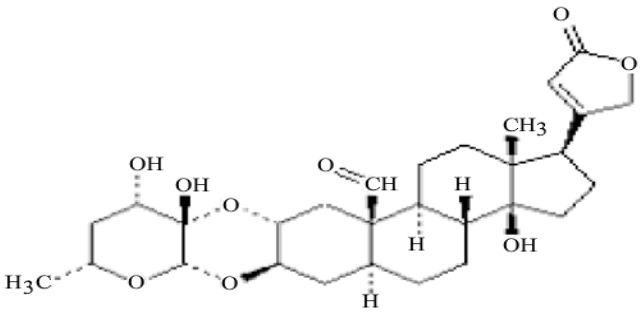

Figure 5. Structure of Calotropin.

CHEMICAL CONSTITUENTS

The plant, *Apocynaceae* family, bioactive compounds include cardenolides, flavonoids, terpenoids, and alkaloids, among others. The major chemical constituents are detailed below.

Cardiac Glycosides, or Cardenolides (E.g. Calotropin, Calotoxin, Uscharin, Gigantin, and Gigantein)

Properties

These cardiac glycosides are harmful to plants and very cardiotoxic. They have a conventional structure with sugar units joined to a steroidal core.

Applications

Cardenolides are used at low doses to treat heart-related conditions and have been investigated for their pharmacological properties, such as cardiac medications. However, when utilized in larger quantities, they become extremely poisonous.

Flavonoids

Examples: Include rutin, kaempferol, and quercetin

Properties

These are antioxidant-active polyphenolic chemicals. They prevent cellular damage by assisting in the removal of free radicals.

Applications

The anti-inflammatory, antioxidant, and perhaps anticancer properties of flavonoids derived from *C. gigantea* are presently being investigated.

Terpenoids

Example: Calotropin, calotropagenin, and sitosterol

Properties

Terpenoids are volatile substances with antibacterial and anti-inflammatory qualities that give plants their scent.

Applications

Calotropis gigantea terpenoids have been shown to be beneficial in anti-infective and wound-healing treatments [17].

Alkaloid

Example: Calotropis alkaloids, uscharin

Availability

Alkaloids are nitrogenous substances that have pharmacological action. These types of compounds exhibit poisonous features, still, those bad killers have good uses, like pain-relieving effects.

Application

Some of the alkaloids found in *C. gigantea* have analgesic and anti-inflammatory properties [18].

Oils and Fats

Examples: Linoleic acid, Oleic acid, Palmitic acid

Properties

They are used in easy metabolic functions, and most of these are found in seeds.

Uses

C. Genus oil, which is rich in fatty oil deposits, is used by some in ethnomedicine and for skin diseases and muscular inflammation.

Proteins and Amino Acids

Rather than, for instance, Calotropin, in most instances, it is a proteolytic enzyme.

C. gigantea, like some of its related latex-bearing plants, has proteins in the form of proteolytic activators.

Wound healing can be accomplished with the assistance of these proteins. In some folkloric medicine, they are taken as a drug that helps to digest food for healing.

Resins and Tannins

Traditionally utilized on irritated skin, they are also effective in the treatment of more serious abrasions accompanied by inflammation. Astringents, like tannins, have many negative applications.

The same applies to zein, a corn protein that may also be airbrushed to shorten the drying time. Generally, tannin/ resin totality is beneficial in their application for cutaneous as well as antibacterial purposes.

Many chemical constituents have been isolated from *Calotropis* species. These include cardenolides, flavonoids, alkaloids, proteolytic enzymes, and sterols. These compounds mediate numerous pharmacological activities (Figure 6) exhibited by the plant, including anti-inflammatory, antioxidant, antimicrobial, and analgesic activities. *Calotropis* shows incredible promise for therapeutic applications today, primarily in traditional medicine. However, on the other hand, the toxic components, especially the latex, call for precautionary measures in their usage. Most probably, further investigations on the pharmacodynamics and safe levels of *Calotropis* principles might facilitate its practical application in medicine today [19].

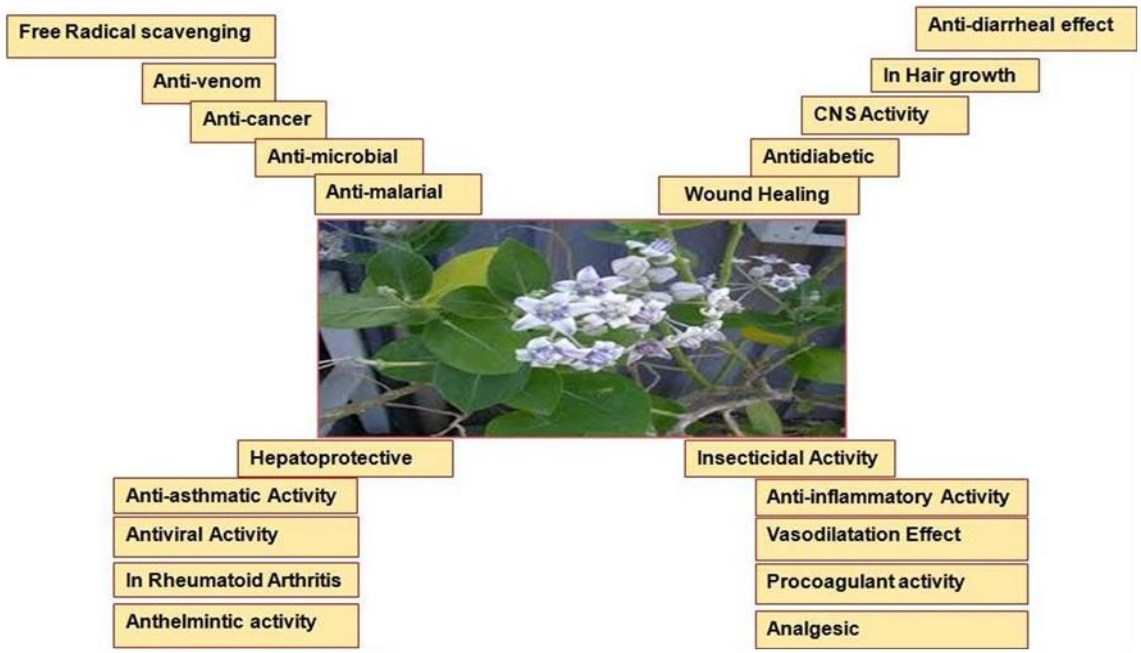

Figure 6. Pharmacological activities.

PHARMACOLOGICAL ACTIVITY

Anthelmintic, alexipharmic, heals leprosy, leukoderma, ulcers, tumors, piles, liver, abdominal illnesses; the juice is anthelmintic and treats leukoderma, tumors, ascites, and abdominal ailments. The leaves are used to treat wounds, swollen areas, painful joints, and paralyzed areas. In situations of intermittent fevers, the leaf tincture is utilized as an antiperiodic 3, 4. Tumors, inflammations, rat bites, and ascites are all good. It is a laxative, purgative, bitter milk that also cures piles. Syphilis and asthma are cured by diaphoretic root bark. Sweet, bitter, anthelmintic, analgesic, astringent, and curative is the flower. According to reports, roots have cytotoxic and antipyretic properties. Antibacterial action, insecticidal activity, wound healing activity, and central nervous system activity [20].

According to reports, the plant's latex has antibacterial, procoagulant, wound-healing, and purgative qualities. There have been reports of hepatoprotective properties of stem. The current review focuses on providing a general overview of the medicinal qualities and biomolecules of *C. gigantea*, as well as its potential for future scientific research aimed at developing potent medicinal compounds [21].

Antimicrobial Activity

Studies have shown that leaf extracts of *Calotropis gigantea* in aqueous, methanol, ethanol, and petroleum. Ether forms exhibit anti-*Candida* activity against clinical isolates of *Candida albicans,*

Candida parapsilosis, Candida tropicalis, and *Candida krusei*. Additionally, the aqueous extract of *C. gigantea* leaves has demonstrated antibacterial effects against *Staphylococcus aureus, Escherichia coli, Bacillus cereus, Pseudomonas aeruginosa, Micrococcus luteus*, and *Klebsiella pneumoniae*. Research indicates that the aqueous extract of *C. gigantea* latex significantly inhibits the growth of *S. aureus, B. cereus, E. coli,* and *C. krusei*. Furthermore, *C. gigantea* has been reported to possess antifungal properties against plant pathogenic fungi, including *Fusarium mangiferae,* which poses a serious threat to mango cultivation. The antibacterial activity of petroleum ether, chloroform, and ethyl acetate fractions derived from the methanol extract of *C. gigantea* root bark has also been documented. The methanol extract and its chloroform fraction were effective against *Sarcina lutea, Bacillus megaterium,* and *P. aeruginosa*, while the petroleum ether fraction showed activity against *P. aeruginosa* and *E. coli*. Meanwhile, the ethyl acetate fraction exhibited antibacterial effects against *Bacillus subtilis* and S*higella sonnei* [22, 23].

Analgesic Activity

The analgesic properties of the alcohol-based flower extract of *Calotropis gigantea* were evaluated in mice using both chemical and thermal models. The acetic acid-induced writhing test and the hot plate method were employed to assess its effectiveness. Administration of the ethanolic extract of *C. gigantea* flowers significantly reduced the number of writhes and prolonged the latency period for paw licking. Additionally, the analgesic potential of the alcoholic extract from the peeled roots of *C. gigantea* was tested in albino rats. Both Eddy's hot plate method and the acetic acid-induced writhing test confirmed its analgesic activity.

250 and 500 mg/kg of body weight of the extract taken orally caused a considerable delay. There were far fewer writhings and paw licking times [24].

Wound Healing Activity

The ability of *C. gigantea* root bark extract to treat wounds in Wistar albino rats was studied. For excision wound healing models, the extract was applied topically to the rats in the form of an ointment; for incision wound healing models, the extract was administered orally at doses of 100, 200, and 400 mg/kg. The findings suggest that rats' wound healing was sped up by extract treatment. 12 We assessed the ability of *C. gigantea* crude latex to heal wounds in albino rats using both incision and excision wound models. When given 200 mg/kg/day, *C. gigantea* latex demonstrated, compared to controls, who had a wound area of 76.22%, treated animals showed an 83.42% reduction in wound area, indicating a strong wound healing activity. In comparison to controls, wounds treated with extract are shown to epithelialize more quickly [25].

Cytotoxic Activity

Cardenolide glycosides extracted from the roots of *Calotropis gigantea* have demonstrated cytotoxic effects against various mice and human cell lines. The active compounds identified include calotropin, frugoside, and 4′–O-β-D-glucopyranosylfrugoside. Studies have shown that two specific compounds isolated from the ethanol extract of *C. gigantea* roots inhibit the growth of human gastric cancer (SGC-7901) and chronic myelogenous leukemia (K562) cell lines. Additionally, a crude ethyl acetate extract from *C. gigantea* flowers has been reported to suppress Ehrlich's ascites carcinoma in mice. Intraperitoneal administration of the extract at doses of 50, 100, or 200 mg/kg body weight significantly reduces viable tumor cell count, prevents excessive weight gain due to tumor burden, and prolongs survival. Furthermore, the extract helps restore altered biochemical and hematological markers, including blood urea, glucose, cholesterol, triglycerides, ALP, SGPT, and SGOT. The most effective activity has been observed at a dosage of 200 mg/kg body weight [26].

Anti-Diarrheal Activity

The hydroalcoholic (50:50) extract of the aerial parts of *Calotropis gigantea* was evaluated for its anti-diarrheal properties using a castor oil-induced diarrhea model in rats. At intraperitoneal doses of 200 and 400 mg/kg body weight, the extract significantly reduced fecal output and the frequency of droppings. Additionally, it effectively decreased both the weight and volume of intestinal contents [27].

Anti-Pyretic Activity

The antipyretic properties of the water-ethanol (50:50) extract of *Calotropis gigantea* roots were evaluated using yeast- and TAB (typhoid) vaccine-induced pyrexia models in Albino Swiss rats and rabbits. Intraperitoneal administration of the extract at doses of 200 and 400 mg/kg body weight significantly reduced fever and restored body temperature to normal levels [28].

Anti-Viral

(+)-pinoresinol 4-O-[60-O-Vanilloyl], a novel lignan glycoside that was extracted from *Calotropis gigantea* latex, A/PR/8/34 (H1N1) inhibitory activity was assessed using the cytopathic effect (CPE) inhibition assay on MDCK cells in combination with -b-D-glucopyranoside, two known phenolic compounds, 69-O-vanilloyltachioside and 69-O-vanilloylisotachioside, and one authentic compound, (+)-pinoresinol 4-O-b-D-glucopyranoside. Inhibitory efficacy against A/PR/8/34 (H1N1) was demonstrated by Compound 1. Using a panel of human and avian influenza viruses, this was further assessed for in vitro inhibitory activity using the CPE inhibition.

It had no effect on avian influenza viruses, but it demonstrated an inhibitory effect on human influenza viruses in both subtypes A and B. Its efficacy against subtype A human influenza viruses was also further validated using the plaque reduction assay. The assay's time course demonstrated that compound 1's antiviral action occurs early in the viral multiplication process.

According to a mechanistic investigation, compound 1 effectively and dose-dependently blocked the NF-KB pathway's activation caused by influenza viruses, but it had no effect on the Raf/MEK/ERK pathway's activation. Additional research revealed that 1, in addition to successfully inhibiting nuclear export of viral ribonucleoproteins, it also dramatically prevented nuclear translocation of transcription factor NF-kB generated by influenza viruses [29].

Anti-Cancer Activity

In India, *Calotropis gigantea* R.Br. (Asclepiadaceae), commonly known as milkweed or swallowwort, is a widespread weed found in wastelands. Over the past five years, 187 plant species from 102 genera and 61 families have been identified as active or potential sources of phytochemicals with anticancer properties, reflecting a 41% increase. Among these, some species demonstrate activity against cancer cell lines or show chemotherapeutic effects in tumor-bearing animals under experimental conditions. However, only 15 species, belonging to ten genera and nine families, have been utilized in clinical cancer chemotherapy. The most distributed bioactive compounds include phenylpropanoids (found in 18 families), terpenoids (14 families), and alkaloids (13 families).

The goal of the current investigation was to find possible phytosterols to support the prior assertions made by different researchers regarding their possible application in conventional medicine. Almost all HPV-positive malignancies exhibit the HPV E6 protein, one of the viral oncoproteins. E6 is therefore the primary target of anticancer treatment. Furthermore, the docking investigations of the phytosterols derived from *Calotropis gigantea* against the oncoprotein HPV 16 E6 are essentially nonexistent. Thus, the investigation was also done to evaluate the sterols isolated from *Calotropis gigantean* ability to prevent cervical cancer [30].

Antioxidant Activity

C. gigantea leaves have antioxidant properties, according to reports. The study evaluates the antioxidant properties of the hydroalcoholic extract of *Calotropis gigantea* leaves, focusing on DPPH radical scavenging, reducing power, and nitric oxide scavenging activities. The extract exhibited the highest DPPH radical scavenging activity, reaching 85.17% at a concentration of 400 µg/ml.

At 100 µg/ml concentration, the extract demonstrated 54.55% nitric oxide scavenging efficacy. The extract's reducing power increased as its concentration increased [31].

Hair Growing Activity

The study aimed to evaluate the effects of *Calotropis gigantea, Hibiscus rosa-sinensis* (HRSF), and a polyherbal formulation (HCF) on the initiation and promotion of hair growth in albino rats. The results and observations were compared with those of minoxidil to assess their efficacy. Potential hair growth activity was demonstrated by *Calotropis gigantea*, albeit it was less than that of other treatments [32].

Hypoglycemic Activity

The chloroform extracts of *Calotropis gigantea* leaves and flowers, administered at doses of 10, 20, and 50 mg/kg, were evaluated for their hypoglycemic effects in streptozotocin-induced diabetic rats and compared with glibenclamide. The extracts effectively lowered serum glucose levels in both diabetic and normal rats. The use of the test medication also resulted in an improvement in oral glucose tolerance [33].

Free Radical Activity

The ethanolic extracts of leaves and latex from *Calotropis procera* and *Calotropis gigantea* (Asclepiadaceae) were analyzed for their free radical scavenging potential using 1, 1-diphenyl-2-picrylhydrazyl (DPPH) radicals. While the leaf extract had modest free radical scavenging activity, the latex extracts of *C. gigeantea* and *C. procera* (10 mg/ml) demonstrated the highest capacity to scavenge DPPH radicals [34].

Anti-Inflammatory

Wistar albino rats' paw edema caused by carrageenan was shown to be alleviated by an ethanol extract of *C. gigantea*. Oral dosing of *C. gigantea* 400 mg/kg showed strong anti-inflammatory properties; the efficacy was greater than that of 100 mg/kg of ibuprofen [35].

Procoagulant Activity

Many highly basic proteins with potent proteolytic activity were present in the crude latex extract. In a dose-dependent manner, the crude extract hydrolyzes casein, human fibrinogen, and crude fibrin clot. IAA completely inhibited the hydrolysis activity, confirming that the enzymes belong to the cysteine protease superfamily. The crude extract effectively hydrolyzed the alpha, beta, and gamma subunits of fibrinogen.

The alpha subunit was the most likely to hydrolyze out of all the subunits, followed by the beta and gamma subunits. The gamma subunit is extremely resistant and hydrolyzes at greater protein concentrations or after longer incubation periods. In contrast to papain and trypsin, the crude extract hydrolyzes the crude fibrin clot very well.

Pharmacologically, the crude extract shortens the citrated plasma's coagulation time and causes cutaneous bleeding at >75 microns [36].

Hepatoprotective Activity

The hepatoprotective effects of the 50% ethanolic extract of *Calotropis gigantea* R. Br (*Asclepiadaceae*) stems were evaluated in male Wistar rats with liver damage induced by carbon tetrachloride (2 mL/kg, twice a week). The extract was administered at doses of 250 and 500 mg/kg to assess its protective potential. *C. gigantea* extract's defensive properties were contrasted. with silymarin, a common medication. Several biochemical indicators, including aspartate amino transferase (AST), glutathione (GSH), alanine amino transferase (ALT), lipid peroxide (LPO), and superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPx) were assessed [37].

Insecticidal Activity

The residual film toxicity, fumigant toxicity, and repelling impact of a methanol extract of *C. gigantea* root bark, as well as its chloroform and petroleum ether fractions, against several *Tribolium castaneum* larvae and adults were assessed. High insecticidal activity against *T. castaneum* was

demonstrated by the methanol extract, petroleum ether fraction, and chloroform fraction. No sample exhibited fumigant toxicity [38].

INDUSTRIAL USES

As biofuel: Calotropis has a high hydrocarbon content and contains compounds that decompose naturally, much like other agricultural crops that undergo fermentation. Tests and discovered that it works well as a biogas substrate. Synthesis and colleagues discovered that the oil composition of its seed's ranges between 19.7 and 24.0%, demonstrating its potential for applications, such as biodiesel, particularly in regions where people depend mostly on wood as a source of energy [39, 40].

As Biopesticides

Laticifer proteins (LP) from *Calotropis* were tested for their insecticidal effects on various crop pests to investigate the biological function of latex. Diets with 4% latex reduced weight gain (ED50 = 3.07%) and impacted survival (LD50 = 4.61%) in third instar larvae of Ceratitis capitata. Additionally, the crude flavonoid fraction (Cf), latex protein fraction (LP), and leaf methanolic extract displayed notable insecticidal activity [41].

- *Cheese-Making Agent:* In West Africa, a crude aqueous extract from *Calotropis* serves as a milk coagulating enzyme in the traditional process of cheese production. It demonstrated peak activity at a temperature of 75 °C, which is crucial for making cheese. The enzyme calotropain found in the plant is more potent than papain, chymosin, and bromelain. Moreover, it aids in milk coagulation and the digestion of meat, casein, and gelatin.

These findings support its traditional role as an agent in cheese production [42, 43].

- *As corrosion inhibitor:* Weight reduction, electrochemical, SEM, and UV methods were used to investigate the corrosion inhibition activity of *C. procera* extract. A significant corrosion inhibitory impact on mild steel in a sulfuric acid medium was noted, suggesting that it might be employed as a green corrosion inhibitor [44].

CONCLUSIONS

Calotropis species, including *Calotropis gigantea,* are plants of great economic value and have been utilized for various purposes, from medicine to agricultural and industrial, over the years. The remarkable pharmacological properties of these plants can be attributed to the presence of various bioactive compounds, including alkaloids, terpenoids, and flavonoids.

Other than its medicinal uses, *Calotropis* has an apparent potential in sustainable agriculture, through its applications as a natural pesticide and soil conditioner, as well as in industry, where the application of its fibers and latex is aimed at ecological materials. There is a need for further research in *Calotropis* systematics in pharmacology to include ethnobotanical studies, clinical trials, the improvement of Solvent Extraction techniques, and the use of other biological variants of *Calotropis* medicines. *Calotropis*, or the milkweed family, is one species of plant that can advance into several areas, although the use of the plant must be carefully assessed in terms of safety and efficacy.

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