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Pharmacological insights into *Calotropis gigantea*: A literature review

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Abstract
People have cherished plants since the dawn of civilization, and they have been genetically preserved. Fuel, food, fiber, fertilizer, and febrifuge are just a few of the uses for this resource. *Calotropis gigantea* is one of these plants. The study examines *Calotropis gigantea's* systematic position, common names, vegetative characteristics, ecology, and distribution, as well as its photochemistry and economical benefits.
Calotropis gigantea, a perennial herb belonging to the Asclepiadaceae family, has long been utilized in folk medicine. This plant has produced numerous chemical substances, including cardiac glycosides, flavonoids, terpenoids, alkaloids, tannins, and resins. The herb has been used to treat a wide range of maladies, including piles, tumors, ulcers and leprosy. The observed pharmacological activity include analgesic, antipyretic, pregnancy prevention, central nervous system, anti-inflammatory, procoagulant, anti-diarrheal, free radical scavenging, antimicrobial, anti-tumor, antifungal, antitussive and antifeedant characteristics.

Keywords: *Calotropis gigantea*, medicinal plant, pharmacological activity, phytochemistry

Introduction
Plants with therapeutic properties or positive pharmacological effects on the animal body are commonly referred to as "Medicinal Plants". Plants that create and accumulate specific secondary metabolites, such as alkaloids, glycosides, tannins, volatile oils, minerals, and nutrients, have been demonstrated to have medicinal properties [1]. Nature, including animals and plants, has had a significant impact on human culture and civilization throughout history, notably in India. Since the beginning of civilization, people have cherished plants, which are maintained as genetic resources and used for fuel, food, fiber, fodder, fertilizer, febrifuge, and other functions [2].
In traditional Ayurvedic medicine, Calotropis gigantea is known as "Sweta Arka" and Caotropis procera as "Raktha Arka" [2]. *Calotropis gigantea* is the focus of our inquiry. *Calotropis gigantea* Linn belongs to the Asclepidaceae family of flowering plants. It is also known as Akada, Aak, Mandar, and Aakh [3].
Calotropis gigantea, sometimes known as giant milkweed, is a common weed in desert areas. This plant is native to several countries, including India, Bangladesh, Burma, China, Indonesia, Malaysia, Pakistan, the Philippines, Thailand, and Sri Lanka. The plant has clusters of white or lavender waxy flowers, a milky stem, and oval, light green leaves [4]. In India, *C. gigantea* is abundantly available and used in traditional medicine for a variety of therapeutic purposes. Scientists have lately documented many of *C. gigantea's* medicinal characteristics. According to accounts, the blooms possess cytotoxic, antimicrobial, and analgesic effects. The leaves and aerial parts of the plant have been shown to have antidiarrheal, antibacterial, anti-candida, and antioxidant effects Antipyretic, cytotoxic, antibacterial, insecticidal, wound-healing, central nervous system, and load-blocking characteristics have all been documented for the roots. It has been observed that plant latex possesses antibacterial, procoagulant, wound-healing, and laxative qualities. Stem has been shown to have hepatotoxic properties.

A broad overview of *Calotropis gigantea* medicinal and biomolecular characteristics is the main emphasis of this review, along with the potential for future scientific investigation to produce potent therapeutic molecules [5].

Table 1: Taxonomical classification of *Calotropis gigantea* Linn

Kingdom	Plantae
Order	Gentianales
Family	Apocynaceae
Subfamily	Asclepiadaceae
Genus	*Calotropis*
Species	*C.gigantea*

Vernacular Names [6]

Table 2: Vernacular names of *Calotropis gigantea* Linn

Common names	Giant Milkweed, Crown Flower, Swallow Wort.
Hindi	Safed aak, Aak, Alarkh, Madar, Sveta Arka, Akanda, Bara Akand.
Gujarati	Aakando
English	Crown flower, giant Indian milkweed. Bowstring hemp, crownplant, madarMalaysia: Remiga, rembega, kemengu
Indonesia	Bidhuri (Sundanese, Madurese), sidaguri (Javanese), rubik (Aceh).
Philippines	Kapal-kapal (Tagalog).
Thailand	Po thuean, paan thuean (northern), rak(central)
French	Faux arbre de soie, mercure vegetal

Fig 1: *Calotropis gigantea*

Microscopic characters of *Calotropis gigantea*

The upper and lower surfaces of the leaves' midrib are covered in a single layer of epidermis and have thick, striated cuticle on the outside. Uniseriate, two to three celled trichomes are formed by the elongation of a few epidermal cells on both surfaces [6]. The tracheid and vessels comprise the majority of the xylem [10]. The cork, the outermost layer of the root's transverse section, is made up of 15-20 layers of properly aligned, rectangular cells with no intercellular space. The cells that comprise the cortical area are packed with starch granules. These cells were composed of a calcium oxalate rosette, laticiferous tubes, and parenchymatic cells with irregular morphologies [7].

Propagation and planting

The process of growing new plants from different plant parts is called plant propagation.

Calotropis gigantea is accomplished through seed or stem cutting. Water, wind, or wasps, bees, and butterflies are the usual pollinators of the seeds.

It also multiplied using the technique of plant tissue culture. Natural regeneration occurs frequently. Vegetative propagation, which involves cutting roots and stems, is a particularly useful method for multiplying better genotypes on a wide scale [8].

Across the country, *Calotropis* grows wild up to 900 meters (msl) and is somewhat tolerant of salt and drought. It prefers sandy, disturbed soils with 300-400 mm of mean annual rainfall [9]. Because its seeds are dispersed by wind and animals, it quickly becomes a weed along damaged roads, lagoon shores, and on native grasslands that have been overgrazed. In areas with disturbed sandy soils and low rainfall, it often predominates and prefers abandoned agricultural lands. It is thought to indicate over cultivation [10]. For *C. gigantea*, a broad habitat with little competition is ideal. This species' plants grow in arid environments with rainfall limited to 150-1000 mm per year and in regions with overly drained soil where annual precipitation can reach up to 2000 mm. Additionally, it can be found in common settings such as densely populated urban areas, seaside dunes, and roadside sand dunes. *C. gigantea* can also be found at elevations of up to 1,000 meters above sea level. Because it is easy to handle, reproduces, and may even flourish in xerophytic environments, the plant is sometimes planted as an ornamental in arid or coastal areas [11-12].

In addition to Madagascar, the Arabian Peninsula, West Africa, North and East Africa, Macaronesia, and South Asia, *C. gigantea* is indigenous to Southern Asia and Indo-China. The plant is a natural species in Australia, Central America, North America, South America, and the West Indies. Many countries now tolerate and grow the plant, including those in Mexico, Central and South America, the Pacific Islands, Australia, and the Caribbean [13].

Main features of plant

The plant may thrive in a variety of soil types and climates and doesn't require any special gardening techniques. This is one of the few plants that grazing animals will not consume [14]. Because of this, it can be found in tropical and subtropical areas of the world, including all of India [15], particularly in areas where native grasses are no longer in competition due to overgrazing [16].

Thereupatic use

The plant is purgative, anthelmintic, alexipharmic, and heals leprosy, leucoderma, ulcers, tumors, piles and disorders of the spleen, liver, and abdomen. Its juice also acts as an anthelmintic and treats leucoderma, tumors, ascites, and gastrointestinal issues. The leaves are used to treat swellings, painful joints, paralysis, and sores. A tincture made from the leaves is used as an antiperiodic to treat intermittent fevers [17, 18]. Inflammation, rat bites, tumors, and helpful in ascites. In addition to treating piles, milk has laxative, purgative, and bitter qualities. The root bark has diaphoretic properties and can be used to treat asthma and syphilis. The flower's properties include being sweet, bitter, anthelmintic, analgesic, astringent, and therapeutic [19].

- **In Ayurveda:** The *Calotropis gigantea* plant's leaves are used to treat swelling, intermittent fevers, and paralysis. Flowers can be used to treat fever, inflammation, helminthiasis, anorexia, asthma, and catarrh. The plant's root bark is used to treat skin conditions, intestinal parasites, helminth infections, and ascites.

- **In siddha:** *Calotropis gigantea* leaves are used to treat ulcers, intestinal parasites, vatha illnesses, periodic fever, and potentially dangerous snake bites. After crushing the plant roots, they are vigorously massaged over the bite area. This plant's latex is used to treat gonococcal arthritis, swellings, dental problems, rat bites, and other rheumatic conditions. Using flowers to treat bronchial asthma.
- **In Unani:** In the Unani system, root bark powder has long been used to treat dysentery and diarrhea. The plant's root treats dyspepsia and has carminative qualities.

Chemical Component

Calotropis latex includes several compounds, including cardenolide, triterpinoids, alkaloids, resins, anthocyanins, and proteolytic enzymes.

Multiflorenol, cyclisadol and terpenes are found in flowers [20].

The main substances included in leaves are amyrin, amyrin acetate, ß-sitosterol, urosolic acid, cardenolides, calotropin, and calotropagenin.

Latex

(Figure 1, *C. gigantea* leaves) in levels ranging from 0.15 to 0.45%, the latex contains caoutchouc, calotropin, calotoxin, calactin, uscharin, trypsin, voruscharin, uzarigenin, syriogenin, and proceroside [21]. Flower: The flower has flavonoids, queretin-3-ratinoside, sterol, calactin, calotoxin, calotropagenin, and calotropin in addition to polysaccharides that include D-arabinose, glucose, glucosamine, and L-rhamnose. Flowers also contain the enzymes 3-proteinase and calotropain (protease). Giantin, giganteol, isogiganteol, uscharidin, uzarigeninvoruscharin, proceroside, proceragenin (cardenolide), syriogenin, taraxast-20(30)-en-3-(4-methyl-3-pentenoate), 3-thiazoline cardenolide, a-calotropeol, and 3-epimoreteno [22] are further chemical components of *C. gigantea* flowers.

Bark: The root bark of *Calotropis* contains triterpenes, akundarol isovalerate, mundarol isovalerate, quercetin-3-rutinoside, two unidentified pentacyclic triterpinoids called calotropursenyl acetate and calotropfriedelenyl acetate, and a novel norditerpenyl ester called Calotropterpenyl ester [23-24].

Toxic Effect

Grazing animals steer clear of the plant since it has been determined to be dangerous. The latex from the plant was used by the natives to construct poison arrows for hunting. Because latex causes ocular toxicity, which results in vision loss and photophobia, it is very harmful to human eyes. The anti-inflammatory properties of *C. gigantea* latex were examined using rat pedal edoema and air pouch models of inflammation, which may be used to assess anti-inflammatory drugs. Inappropriate usage of latex in the eye can result in keratitis, corneal endothelial cytotoxicity, keratoconjunctivitis, and toxic iridocyclitis.

DL, flowers, and ethanolic extracts of *C. procera* were introduced to MCF-7 and HeLa cell line cultures in order to ascertain the test compounds' inhibitory effects on cell development *in vitro*. In contrast to the common medication tamoxifen, which lowers breast cancer (MCF-7) cells by 60.46 percent, DL and floral ethanolic extract demonstrated cytotoxic activities against both MCF-7 and HeLa cells in a dose-dependent mannequin experiment [25-27]. It is believed that *Calotropis gigantea* is more toxic than cobra venom. These two plants exhibit comparable chemical and physiological responses and are members of the Asclepiadaceae family [28].

Calactin, calotropin, calotropage, calotoxin and uscharin are among the toxic principles. Milk can be dangerous and present in a number of deadly ways due to its irritating, neurotoxic, and anticholinergic properties. Giantin, an incredibly dangerous toxin, is present in serum at 3% concentrations [29].

Madar juice and latex have a nasty, bitter taste and produce burning pain in the mouth, throat, and stomach when consumed in large quantities. The next symptoms include tetanic convulsion, collapse, vomiting, diarrhea, stomatitis, dilated pupils, and death. Sometimes delirium can happen. It is unknown what the fatal dose is. The lethal window is between 30 and 8 hours [30].

Pharmalogogical Report

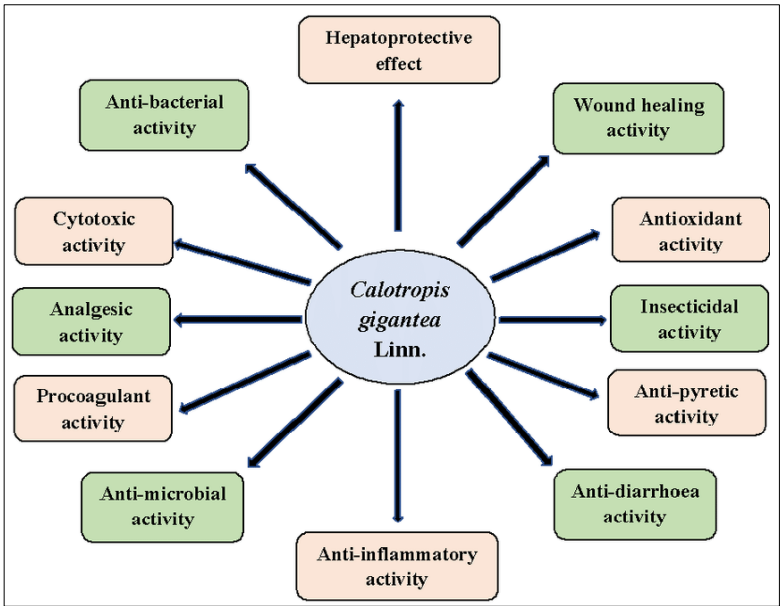

Fig 2: Showing pharmological effect of *Calotropis gigantea*

Anhydrosophoradiol-3-acetate (A3A), an isolated chemical found in *Calotropis gigantea* flowers, inhibits the growth of body weight and kills viable tumor cells. A3A's ability to inhibit EAC growth and reduce cancer-related consequences has been studied in vivo [31].

Anti-inflammatory activity

The anti-inflammatory qualities of *Calotropis gigantea* were evaluated in a number of experimental animal models. The anti-inflammatory qualities of *Calotropis gigantea* leaf extracts in ethanol, distilled water, chloroform, and n-butanol were evaluated. This activity was compared to that of the widely used drug paracetamol using the carrageenan-induced rat paw oedema method [32].

However, a model of carrageenin-induced kaolin-induced rat paw oedema for acute inflammation and adjuvant-induced arthritis for chronic inflammation are used to evaluate the anti-inflammatory effect [33].

Furthermore, the anti-inflammatory qualities were shown to be superior to the albumin denaturation method [34].

Wound healing property

Animal models are used in several studies on the activities of wound healing. Albino rats are initially treated with *Calotropis gigantea* latex by means of an excision and incision wound method. When compared to the control, which had a wound area of 76.22%, the latex-treated animal's wound area decreased by 83.42% using framycetin sulphate cream (1%) as a reference [35].

In the second, rats with diabetes caused by streptozocin (50 mg/kg) were anesthetized and given a 2 cm excision wound. Next, as part of the treatment, a 2 percent ointment of *Calotropis gigantea* latex extract was applied for 14 days. Rats given the test medication exhibited a significant (p<0.05) reduction in the epithelization duration and an increase in the rate of wound concentration. Furthermore, arteries' length density, collagen fibers' volume density, and fibroblasts' numerical density all increased significantly (p<0.05). The aforementioned study claims that *Calotropis gigantea* enhances histological factors and promotes collagen formation, all of which are critical for diabetics to heal wounds as best they can [36].

Antivenom property

The plant extract *Calotropis gigantea* possesses antivenomous qualities against the venom of viper Russell snakes. *Calotropis gigantea*'s methanolic extract has beneficial properties that counteract the venom's many impacts, including mortality, oedema-forming, necrotizing, and hemorrhagic effects [37].

Oral administration of extract at 200 and 400 mg/kg effectively reduced the lethal effects of 2LD50 and 3LD50 venom in mice. The plant extract efficiently neutralized the 2LD50 and 3LD50 of venom at 100, 200, and 400 mg/kg, according to in vitro testing. Viper venom methanolic extract effectively reduces oedema after 60, 120, 180, and 240 minutes [38].

Vasodilation property

In *Rana hexadaetyla* (green frog), the vasodilator effect of *Calotropis gigantea* latex extract was examined. A percentage increase in cardiac output was the outcome of diluting the crude extract with distilled water at concentrations of 1:10 and 1:100. A 1:10 ratio resulted in 50% cardiac output, while a larger dilution factor increased cardiac output by 66%. This indicates that at a certain diose content, the latex has a vasodilatory action [39].

Hypoglycaemic effect

In one study, glibenclamide was compared to *Calotropis gigantea* flower and leaf chloroform extracts at 10, 20, and 50 mg/kg in Streptozotocin-induced diabetic rats. Consequently, *Calotropis gigantea* flower and leaf extracts effectively reduce serum glucose levels in rats in good condition. Additionally, oral glucose tolerance was improved by treatment with the test drug. When Streptozotocin-induced diabetic rats were given flower and leaf extracts, their serum glucose levels significantly decreased [40].

Antitussive property

Calotropis gigantea leaf extract has antitussive effects due to its alkaloid and glycoside content [41].

Hepatoprotective property

Using carbon tetrachloride (2 ml kg-1), the ethanolic action of *Calotropis gigantea* stem at dosages of 250 and 500 mg kg-1 was evaluated for hepatoprotective efficacy in male wistar rats with liver injury [42].

On the other hand, the methanolic extract of *Calotropis gigantea* leaf in a dose-dependent manner has good hepatoprotective efficacy against CCL4 induced hepatotoxicity in rats [43].

Free radical scavenging property

In streptozotocin-induced diabetic rats, the lipid profile and free radical scavenging properties of a chloroform extract of *Calotropis gigantea* leaves and flowers were examined [44].

However, using 1, 1 Diphenyl Picryl hydrazyl radicals, the ethanolic extracts of *Calotropis* procera and *Calotropis gigantea*'s leaves and latex were tested for their ability to scavenge free radicals. The latex extract (10 mg/ml) of *Calotropis* procera and *Calotropis gigantea* shows a greater capacity to scavenge DPPH radicals, while the leaf extract demonstrates a moderate level of free radical scavenging activity [45].

Hair growing activity

A polyherbal formulation (HCF) and *Calotropis gigantea* with *Hibiscus Rosa sinensis* (HRSF) were used to see how they affected the commencement and promotion of hair development in albino rats. The study's findings and observations were contrasted with those of Minoxidil. *Calotropis gigantea* demonstrated some promise for hair growth, but not as much as other treatments [46].

Analgesic activity

Alcoholic extract from *Calotropis gigantea* flowers has shown mild analgesic effects in a number of preclinical investigations. An oral dose of alcoholic extract significantly reduces the frequency of paw licking time and writhing reflexes. The acetic hot plate method and the acid writhing model are used to study the activity [47].

CNS activity

Calotropis gigantea extract contains the flavonoids chrysin and apigenin, which have analgesic, antidepressant, and antianxiety actions in addition to sedative and hypnotic

effects. By boosting axonal and dendritic numbers, lengths, and branching orders, the *Calotropis gigantea* extract enhances collateral branching even in this kind of activity [42].

Anti-malarial property

The growth of Plasmodium falciparum and Plasmodium berghei is inhibited by *Calotropis gigantea* extract. Because it contains antiplasmodial activity against Plasmodium falciparum, which is susceptible to chloroquine, this plant has great anti-malarial action [46].

Pregnancy interceptive properties

In rats, several root extracts from *Calotropis gigantea* have pregnancy-interceptive properties. Diverse botanicals display pregnancy-interceptive action at varied dosages. For instance, the extract reacts 100% at 100 mg/kg.

When given on the days of the 1-5 and 1-7 postcoitum regimens, the other side extract produces a 100% response at a dose of 12.5 mg/kg [47].

Conclusion and Future Prospective

Calotropis gigantea is a potentially beneficial plant with a range of therapeutic or restorative properties in addition to its commercial value. In India, it is widely used as an auxiliary plant, fiber, fuel, ornamental, traditional medicine, mosquito control, and other purposes. The root, leaves, root bark, milk, and flower are among the parts of this plant that are utilized ethno medically to treat a variety of human ailments.

Despite the fact that *Calotropis gigantea* has many medicinal uses, the presence of phytochemicals and other unidentified compounds in this plant calls for the development of new drug therapy classes as well as the standardization and characterization of powerful molecules that suppress a range of pathological conditions.

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