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Review Article

To Comparatively Study of Calotropis Gigantea Drug Used as Various Pharmacological Properties

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ABSTRACT

Calotropis gigantea (commonly known as Madar or Crown Flower) is an important medicinal plant widely used in traditional Ayurvedic and folk medicine. It contains several bioactive compounds such as flavonoids, alkaloids, terpenoids, and glycosides, which are responsible for its diverse pharmacological activities. This review aims to comparatively study the various pharmacological properties of Calotropis gigantea, including its anti-inflammatory, analgesic, antimicrobial, antioxidant, antidiabetic, wound-healing, and anticancer effects. The paper also discusses its phytochemical composition, mechanism of action, and therapeutic potential compared with other medicinal plants. The findings reveal that Calotropis gigantea exhibits strong pharmacological efficacy and can serve as a valuable natural source for developing new herbal formulations and modern drugs. Further studies are required to validate its safety, dosage, and clinical effectiveness.

INTRODUCTION

Plants have likely been utilized medicinally for as long as humanity. Every traditional practice incorporates the use of plants' therapeutic qualities. Since prehistoric times, people on every continent have utilized hundreds of native plants to treat a variety of illnesses. Evidence points to the existence of Neanderthals 60,000 years ago. Worldwide, ethnomedicine continues to make extensive use of these herbs.

It is frequently said that traditional and folklore healers acquired their knowledge from animal observation. Sick animals have been seen to favor bitter herbs that they would often avoid. They tend to forage plants rich in secondary metabolites such as tannins and alkaloids which are commonly connected with medicinal characteristics like antiviral, antibacterial and antifungal capabilities. To put it another way, animals use self-medication in the wild.

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Due to the lack of antibiotics and analgesics, herbal medicine was the mainstay of the healthcare system in the early 20th century. Herbal medicine, which relied on the quick therapeutic effects of synthetic medications, rapidly lost favor with the emergence of the allopathic medical system. The limitations of the allopathic medical system have been observed for nearly a century. Herbal medicine has gained popularity recently, as evidenced by the fact that some herbal medicines have reached levels comparable to those of synthetic medications. Both industrialized and developing nations make extensive use of herbal remedies. Other European nations have also seen an increase in the usage of plant-based health products. According to export-import bank data, the global commerce in plant-derived and plant-originated goods is estimated to be worth US \$60 billion (growing at a rate of 7% annually), of which India owns US \$1 billion. By the end of 2015, this amount is projected to reach US \$3 trillion.

India is a tropical nation endowed with abundant natural resources and traditional wisdom that can be used wisely. However, these treatments must be evaluated scientifically to determine their active principles and comprehend their mechanism of action in order for modern medicine to embrace them. [4] A new avenue for the study and investigation of medicinal plants has been made possible by the recent recognition of the therapeutic potential of a number of traditionally utilized plants.

The variety of secondary metabolites found in plants is bewildering. Since ancient times, they have served as the foundation for the treatment of illnesses in indigenous societies. This study focuses on verifying the therapeutic and chemical characteristics of a particular plant that is widely used to cure a number of illnesses, including

bronchitis, asthma, leprosy, eczema, toothaches, and sporadic fevers. elephantiasis, diarrhea, rheumatoid arthritis, joint swellings, etc. The current study aimed to identify the biologically active components and investigate the antidiabetic potential of *Calotropis gigantea* flowers.

In July and August, flowers of *Calotropis gigantea* were gathered from Neemuch, Madhya Pradesh, India, and verified by a botanist. Petroleum ether, chloroform, and 90% ethanol were used to extract the flowers after they had been dried in the shade. The extracts were then concentrated and dried. Several phytochemical tests were used to assess the extracts' phytoconstituents. The qualitative characteristics established by the phytochemical studies can be a valuable source of data for additional research.

We subsequently assessed the chloroform extract of *Calotropis gigantea* for in-vivo antidiabetic activity in light of the findings of in-vitro antidiabetic and antioxidant studies. Prior to conducting the in-vivo antidiabetic investigations, the extract was assessed for acute toxicity, which demonstrated the non-toxic character of *Calotropis gigantea* chloroform extract because no adverse responses or lethality were observed at any of the chosen doses.

DRUG PROFILE

Drug:

Botanical identity and biological source [6]

Calotropis gigantea (L.) Dryand is the scientific name.

Asclepias gigantea L. is a synonym.

Family: Apocynaceae (formerly Asclepiadaceae/Asclepiadoideae).



Morphology and Habit: A perennial, upright shrub with several branches that is usually between one and five meters tall. Every part of it has a milky latex. Opposite, sessile or subsessile, thick, elliptic-oblong to obovate, with a bluish-green top and a tomentose (hairy) underside.

Flowers: White to purple-lilac, with five sepals and five petals in umbellate cymes; a characteristic "crown" in the center of the flower.

Fruit / Seed: Boat-shaped follicles approx. 8–10 cm; when dry, they dehisce to release many seeds with silky hairs.



Figure: Asclepias gigantea L.

Sensory or organoleptic characters [7]

These are the sensory and macroscopic characteristics that are helpful in pharmacognosy:

Stem/Latex: When cut, a white, milky latex is released. Thick, slightly leathery leaves with a cottony feel due to their hairy underside (**tomentose**).

Flowers: White to lilac/purple, with a waxy (or "cerous") feel.

Root bark: Mucilaginous and bitter, according to pharmacognostic descriptions.

Microscopic (anatomical/microscopical) characteristics [8]

Crucial microanatomical characteristics (for pharmacognostic identification):

Anatomy of leaves (transverse section): [13]

A thick cuticle covers the single-layered upper and lower epidermis.

Mesophyll underwent differentiation into spongy parenchyma with wide intercellular gaps and palisade (three rows of elongated parenchyma cells).

Vascular bundles in ground tissue are bicollateral and open, meaning that both xylem and phloem are present on both sides.

Stomata: paracytic type, meaning that subsidiary cells run parallel to guard cells on each side of each stoma.

Powder microscopy:[9]

In contrast to unicellular trichomes in *C. procera*, multicellular trichomes (hairs) are visible in *C. gigantea* leaf powder. [12]

Parts of arteries, sclerenchyma cells, and epidermal cells are also present.

Anatomy of flowers: Five gamopetalous petals, five gamosepalous sepals, and an ovary with ovules are seen in cross-section. [10]

Chemical Components: Different portions of *C. gigantea* have been reported to contain a wide range of phytochemicals. Important classes and a few example compounds: [11]

Plant Part	Major Chemical Constituents
Leaves / Aerial parts	Flavonoid glycosides (e.g., isorhamnetin-3-O-rutinoside, isorhamnetin-3-O-glucopyranoside) cardenolides (19-nor and 18,20-epoxy, e.g., 15 β -hydroxycardenolide, hydroxycalactinic acid methyl ester) terpenoids, steroids other: alkaloids, phenolic compounds, saponins, quinones per extract studies.
Latex	Cardenolide / cardiac glycosides: e.g., calotropin, calotoxin, calactin, uscharin, voruscharin. Resins, caoutchouc (rubber), proteolytic enzymes (calotropains FI & FII)
Roots / Root bark	β -amyrin, α - and β -calotropeol, giganteol, isogiganteol. Other terpenes; aromatic derivatives (e.g., calotropis-sesquiterpenol, calotropbenzofuranone)
Flowers	Triterpenoids: e.g., di-(2-ethylhexyl) phthalate, anhydrosophoradiol-3-acetate flavonoids; sterols; glycosides; polysaccharides (e.g., with D-arabinose, glucose, glucosamine, L-rhamnose)
Seeds / Seed oil	Fatty acids: palmitic, oleic, linoleic, linolenic acid; unsaponifiable fraction contains stigmasterol, phytosterols, lauryl alcohol, etc.
Essential oil (leaf)	From GC-MS: ~42 components; major ones include phytol (~17.9%), phenylacetaldehyde, benzyl alcohol, 4-methyl-1-heptanol, 4-vinyl guaiacol, phenethyl alcohol.

PHARMACOLOGICAL ACTIVITY

Pharmacological Activity of *Calotropis Procera* and *Calotropis gigantea*

Since ancient times, the medicinal qualities of *Calotropis procera* and *gigantea* have been used to cure a wide range of illnesses. Here, some of the most important pharmacological activities are covered in great depth.

1. Analgesic Activity

The dry latex (DL) of *Calotropis procera* has been shown to have analgesic qualities [15]. A dose of 415 mg/kg of DL was more effective in suppressing writhing brought on by acetic acid than an oral dosage of aspirin (100). The alcoholic extract of *Calotropis gigantea* flowers has analgesic properties. An oral intake of this extract generated a notable result. The activity was conducted using the hot plate technique and the writhing test caused by acetic acid.

The effects of an alcoholic peeling extract of *Calotropis gigantea* roots (at oral dosages of 250

and 500 mg/kg body weight) on the central nervous system (CNS) of albino rats were investigated. Both the writhings caused by acetic acid and Eddy's hot plate approach demonstrated significant analgesic advantages.[16]

2. Wound Healing Activity

There have been reports of the wound-healing properties of aqueous latex extract [17,18], ethanolic bark extracts [19], and aqueous leaf extracts [20] of *Calotropis procera*. For seven days, the guinea pig's wound was treated twice a day using a sterile latex preparation. The animal's treated area had higher levels of protein, DNA, and collagen fibers. It was investigated whether *Calotropis gigantea* root bark extract might heal wounds in Wistar albino rats. The extract was used topically to rats as an ointment to mimic the healing of excision wounds;

For models of incision wound healing, oral dosages of 100, 200, and 400 mg/kg of the extract were utilized. The results indicate that extract therapy accelerated the healing of rats' wounds [14]. Assessed the wound-healing properties of



employing both excision and incision wound models, *Calotropis gigantea* crude latex was administered to albino rats. Treated animals showed an 83.42% decrease in wound zone compared to controls, who had a wound area of 76.22%. This suggests that *Calotropis gigantea* latex, at a dosage of 200 mg/kg/day showed significant wound-healing efficacy. It has been shown that extract-treated wounds epithelize more quickly than controls [21].

3. Antifertility activity

Ethanollic preparations of the roots and leaves of *Calotropis procera* have been shown to exhibit antifertility properties [22, 23]. The ethanolic extract of *Calotropis procera* roots has been used to investigate the hormonal and antifertility effects of those roots in albino rats. Significant antiimplantation (100% inhibition) and uterotrophic effect were seen at a dose of 250 mg/kg. Certain phytochemicals, such as tannins, psoralen, gigantein, stigmasterol, and saponins, have also been connected to *Calotropis gigantea*'s antifertility characteristics [24].

4. Anti-diarrhoeal activity

Diarrhea, which results in an excessive loss of fluid in the stools, is caused by an imbalance between the secretory and absorptive processes of the digestive tract combined with hurry. The bark [25], latex [26], leaves, stems, roots, flowers, and buds [27] of *Calotropis procera* have all been shown to have anti-diarrheal qualities. *Calotropis procera*'s DL has been evaluated for its anti-diarrheal qualities. A single 500 mg/kg dose of DL significantly decreased the frequency of defecation, much like atropine and phenyl butazone. Eighty percent of rats fed castor oil suffered diarrhea due to the electrolyte content in intestinal fluid, which also induced intestinal fluid accumulation and protection.

Compared to animals that did not get castor oil treatment, intestinal transit decreased (by 27–37%) in DL animals. Using a model of castor oil-induced diarrhea in rats, the anti-diarrheal effects of the hydroalcoholic (50:50) extract of the aerial component of *Calotropis gigantea* were examined. At intraperitoneal dosages of 200 and 400 mg/kg body weight, the extract showed significant reductions in both the frequency of droppings and the production of feces. The extract was also shown to significantly reduce intestinal content volume and weight [28].

5. Antiulcer Activity

The hydroalcoholic and chloroform extract of the stem bark, the ethanolic extract of the leaves, and the root chloroform extract are among the *Calotropis procera* components that show antiulcer efficacy [29, 30]. *Calotropis procera* stem bark extract was dissolved in hydroalcohol and chloroform because it can prevent ulcers and reduce inflammation. In order to investigate anti-ulcer efficacy, albino rats using ulcers were used, and the carragennan-generated paw oedema model was used for anti-inflammatory effectiveness. The extract shown significant activity when compared to traditional drugs. Using pylorus ligation and indomethacin-induced ulcer models, the effects of a 100% alcohol extract of *Calotropis gigantea* flower were investigated in experimental Wistar albino rats. When the alcoholic extract of *Calotropis gigantea* was given at dose rates of 500 mg/kg and 1000 mg/kg, the ulcer index and ulcer intensity score in both models shown a significant ($P < 0.01$) suppression when compared to the control. At a dosage rate of 500 mg/kg, the extract showed the biggest reduction in ulcer index in animals with pylorus ligated ulcers [31].

6. Antifungal and anti-bacterial activity



The aqueous [32], methanol, acetone, and ethanol extracts of the leaves [33, 34], root bark [34, 35], and latex of *Calotropis procra* [35] have all been reported to exhibit antifungal activity. The antimicrobial effects of ethanol, aqueous, and chloroform extracts of *Calotropis procera*'s leaves and latex were examined on five bacteria (*S. pyogenes*, *E. coli*, *S. aureus*, *S. albus*, and *S. pneumoniae*), three fungi (*Aspergillus niger* and *flavus*, and *Microsporum bouliardii*), and one yeast (*C. albicans*) using agar well diffusion and paper disc methods [36]. The results demonstrated that ethanol was the most efficient extractive solvent for the antibacterial properties of the latex and leaves of *Calotropis procera*, with water and chloroform ranking second and third, respectively.

Calotropis gigantea has been found to have antifungal activity against dangerous plant fungi including *Fusarium mangiferae*, which poses a serious risk to mango production [37]. *Pseudomonas aeruginosa*, *E. coli*, *Klebsella pneumonia*, *Bacillus cereus*, and *S. aureus* have all been found to be effectively combatted by the aqueous extract of *Calotropis gigantea* leaves [38]. It has been demonstrated that the aqueous extract of *Calotropis gigantea*'s latex significantly inhibits *C. krusei*, *S. aureus*, *B. cereus*, and *E. coli* [39]. *Calotropis gigantea* has been found to have antifungal properties against plant pathogenic fungi including *Fusarium mangiferae*, which pose a serious threat to mango farming [37].

7. Antipyretic Activity

Calotropis procera's ethanolic floral extract [16] and dry latex aqueous extract have been shown to have antipyretic properties. There have been reports of antipyretic effects from a 50:50 ethanol and water extract of *gigantea* roots. Anti-pyretic activity was assessed in a rabbit and an Albino Swiss rat that had been given the TAB (typhoid) vaccination or yeast. At dosages of 200 and 400

mg/kg body weight, it was discovered that the extract significantly reduced fever and restored body temperature [42].

8. Anti-Inflammatory Activity

Dry latex [43], hydro-alcoholic and chloroform extracts of stem bark [30], ethyl acetate, C_6H_{14} , CH_2Cl_2 , *n*-butanol, and water-based extracts of latex [44], leaves [45], flowers [41], and the ethanolic and ethanolic extracts of *Calotropis procera*'s root bark [46] have all been reported to have anti-inflammatory qualities. The anti-inflammatory qualities of DL's aqueous and methanolic extracts were superior to those of phenylbutazone (PBZ) when it came to carrageenan, but they were comparable to those of chlorpheniramine and PBZ when it came to histamine and prostaglandin E₂, respectively.

The ethanolic extract of *Calotropis gigantea* leaves had a more potent anti-inflammatory activity than other solvent extracts. In Wistar albino rats with carrageenan-induced paw edoema, the anti-inflammatory qualities of *Calotropis gigantea* ethanol extract were found to be effective. Oral administration of 400 mg/kg of *Calotropis gigantea* was found to significantly reduce inflammation; this potency was found to be greater than that of 100 mg/kg of Ibuprofen [47].

9. Anti-cancer activity

There have been reports of anticancer activity in aqueous extracts of dry latex [48], hexane, dichloromethane, ethyl acetate, acetone, and methanol extract of the stem [49,50] of *Calotropis procera*. The DL of *Calotropis procera* was found to offer complete protection against the formation of hepatocarcinogenesis when tested in a transgenic hepatocellular cancer model in mice. While Huh-7 and COS-1 cells had severe cell death and a marked drop in serum vascular



endothelial growth factor levels, AML12 cells were found to be alive.

Calotropis gigantea's cardiac glycosides have the ability to stop the growth of cancer and tumor cells. In vitro, p53 and Bcl-2 gene expression in breast cancer CF-7 can be influenced by cardiac glycosides as calactin, calotropin, asceplin, and cymarin. Bcl-2 modulation, which disrupts antiapoptotic activity, is more likely to have caused tumor suppression actions on the mediated test sample than p53, which promotes apoptosis [51].

10. Immunomodulatory activity

By altering a number of immunological markers, the ethanolic extract of Calotropis procera root bark can be utilized in alternative medicine to treat immunodeficiency illnesses [52]. Immunomodulatory efficacy was evaluated in mice at three dose levels using immunological tests, including peritoneal macrophage count, humoral mediated antibody titer, delayed-type hypersensitivity, vascular permeability, and haematological profile. The water-soluble latex and entire aqueous extract of Calotropis gigantea are undeniably immunomodulatory [53].

11. Antioxidant Activity

Antioxidant activity has been reported in methanolic and aqueous leaf extracts [54], methanolic and aqueous root extracts [55], methanolic flower and fruit extracts [54–56], and Calotropis procera bark extracts in ethanol [19]. The hydroalcoholic leaf extract of Calotropis gigantea has shown antioxidant activity through reducing power, nitric oxide scavenging, and DPPH radical scavenging. The extract showed a maximum scavenging activity of 85% for DPPH radicals at 400 µg/mL concentration, 54% for nitric oxides at 100 µg/mL concentration, and an

increase in reduction power with increasing extract concentration.

Additionally, when the leaf and flower extracts of Calotropis gigantea were tested for antioxidant potency, it was discovered that the methanolic extract had a noteworthy 64% free radical scavenging activity, whereas the acetone and chloroform extracts had only 30% and 37%, respectively [57].

12. Larvicidal Activity

Calotropis procera showed high larvicidal effect when tested against Anopheles labranchiae mosquito larvae, with an LC50 (24 hours) ranging from 28 to 325 ppm. The detrimental effects of crude extracts of Calotropis procera (from both leaves and flowers) on the termite species Heterotermes indicola and Coptotermes mesheimi have been studied [58]. The ethanolic extract of Calotropis gigantea has been shown in earlier studies to have larvicidal effects on Ae. aegypti larvae, with an LD50 value of 351.43 ppm.

Calotropis gigantea and Calotropis procera had the same effect on Ae. aegypti larvae, according to the LC50 value of all sections for the larvicidal action [59]. Calcotoxin and calcotropin are the main compounds that may be responsible for the larvicidal characteristics of the Calotropis species.

13. Comparative Study

Numerous plant parts are used as medicines to treat common ailments, such as the leaves, stem, flowers, and root bark of Calotropis gigantea and Calotropis procera. Their comparative analyses, however, have received less attention. R. A. Sharma et al. published a comparative study of the phytochemistry and pharmacology of Calotropis gigantea and Calotropis procera [60]. These plants'



phytochemical composition contained a variety of active compounds. Every element of Calotropis

The Ayurvedic medical system recommends using the root, stem, leaf, and flower of *gigantea* and *procera* to cure a variety of illnesses. Phytochemical examination of plant parts has been the subject of certain comparative (qualitative or quantitative) research [61]. Pratibha and associates conducted a phytochemical analysis of root extracts using four distinct solvents: ethanol, water, ethyl acetate, and chloroform [61]. According to their findings, both species' root extracts contained flavonoids, alkaloids, and phenolic compounds. However, the *Calotropis gigantea* root extract in ethanol had significantly higher levels of phenolic and flavonoid components.

Srivastava and colleagues examined the physicochemical and phytochemical properties of both *Calotropis* species [62]. The results of the physicochemical studies showed that *Calotropis procera* has more extractive properties than *Calotropis gigantea*. The phytochemical composition and, specifically, the quantity of β -sitosterol were examined using HPTLC. Both species were found to contain β -sitosterol; however, the roots of *Calotropis gigantea* (2.79%) and *Calotropis procera* (1.07%) differed slightly. The antioxidant potential of extracts from the leaves, roots, and latex of *Calotropis gigantea* and *Calotropis procera* was compared by the H. V. Patel group.

The methanolic leaf extract of *Calotropis procera* was shown to have higher larvicidal and antioxidant qualities than *Calotropis gigantea* after the larvicidal and antioxidant qualities were assessed using radical (DPPH) scavenging against *Ae. Aegypti* larvae.

14. Antidiabetic activity:

According to several research, *Calotropis gigantea* exhibits antidiabetic efficacy by lowering increased blood glucose levels (Rathod et al. 2011). *Calotropis gigantea* plant extracts have a hypoglycemic impact. When diabetes mellitus is present, *Calotropis gigantea* prevents weight loss. In the pancreatic islet, *Calotropis gigantea* increases the number of granulated cells and normal beta cells. According to reports, the plant extract effectively lowers increased serum glucose levels in experimental animals (Jatin et al. 2014, Manivannan and Shopna. 2017). [63]

15. CNS Activity:

Calotropis gigantea extract aided in the early stages of neuronal growth. Collateral branching is improved, and axonal and dendritic lengths, numbers, and branching orders are increased in *Calotropis gigantea*. Because it contains the flavonoids chrysin and apigenin, *Calotropis gigantea* exhibits neuropharmacological activity such as antidepressant, sedative and hypnotic, antianxiety, anticonvulsant, analgesic, and neurogenesis (Argal and Pathak. 2006, Kaur et al. 2014, Khan et al. 2014, Lima et al. 2012, Ghule et al. 2014). [63]

16. Anti-malarial:

Malaria is a deadly parasite illness that causes death. *Calotropis gigantea* shown antimalarial activity against *Plasmodium berghei* and *Plasmodium falciparum*. When it comes to chloroquine-sensitive *Plasmodium falciparum*, *Calotropis gigantea* exhibits outstanding antiplasmodial action (Satish et al. 2017, Kaushik et al. 2015, Kovendan et al. 2012). [63]

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