Review Article

Calotropis gigantea Linn. - An Indian Traditional Medicine Treasure

Ghegade R. Y.*[1], Aher A. N[2].
[1]Research Scholar, Dept. of Pharmacognosy, MVPs College of Pharmacy, Nasik, Maharashtra, India.
[2]Associate Professor, Dept. of Pharmacognosy, MVPs College of Pharmacy, Nasik, India.
Affiliated to Savitribai Phule Pune University, Pune Maharashtra, India.
***Corresponding author's E-mail:** raoghegade1@gmail.com

Received: 24-02-2021; **Revised:** 18-04-2021; **Accepted:** 28-04-2021; **Published on:** 15-05-2021.

ABSTRACT

Calotropis belongs to two species, the majority of which are native to India, Indonesia, Malaysia, Thailand, and Sri Lanka. *Calotropis gigantea*, also known as giant milk weed plant that grows in large quantities, is a member of the Apocynaceae (Asclepidiaceae) family of latex-producing plants. Traditionally *C. gigantea* is used to treat a variety of diseases and ethno-medicinal claims. In the last few decades, sophisticated analytical methods have been used to study *C. gigantea* for its medicinal properties and a number of bioactive compounds have been isolated and analyzed from various parts of the plant**.** Analgesic, antimicrobial, antioxidant, anti-pyretic, insecticidal, cytotoxic, hepatoprotective, pregnancy-interrupting, purgative, procoagulant, and wound-healing properties have been identified and found to be effective which make it a valuable source of therapeutic compounds. This review attempts to cover ethnobotany, pharmacology, phytochemistry, and phytopharmacological activities of *C. gigantea.*

Keywords: *Calotropis gigantea*, phytochemistry, pharmacological activity, ethnobotany.

QUICK RESPONSE CODE →

DOI: 10.47583/ijpsrr.2021.v68i01.024

DOI link: http://dx.doi.org/10.47583/ijpsrr.2021.v68i01.024

INTRODUCTION

Arka (*Calotropis gigantea*), an effective Ayurvedic medicine, has been used in this country since ancient times. It is mentioned by the earliest Hindu authors, and the ancient name of the plant that appears in Vediyesc literature is Arka, which refers to the shape of leaves that was used in sacrifical rites. *Calotropis gigantea* (Linn.) R.Br. and *Calotropis procera* (Ait.) R.Br. are two common species of Calotropis described by Sanskrit authors. *C. gigantea* or giant milk weed, is a common wasteland weed found in Bangladesh, Burma, China, India, Indonesia, Malaysia, Pakistan, Philippines, Thailand, and Sri Lanka. *C. gigantea* is commonly found in India and is used for a variety of medicinal purposes in the conventional medical system.[1-2] *C. gigantea* has recently been scientifically documented for a variety of medicinal properties, including analgesic, antimicrobial, and cytotoxic activity in the flowers [3]. Anti-diarrhoeal activity[4-6], hypoglycemic activity [7], antibacterial activity [8-10], and antioxidant activity [11, 12] have been identified for the plant's leaves and areal sections whereas roots have been confirmed for anti-pyretic effect [13]. *Calotropis gigantea* has been the subject of many reviews to date wherein various pharmacological studies on *Calotropis gigantea* conducted in the last few years were included in this study in addition it is attempted to summarize recent works and current developments in the field of modern phytomedicine regarding *Calotropis gigantea's* phytochemistry and pharmacology from various parts of the world.

Botanical Description of Calotropis giganteaa

A tall shrub with a back that is yellowish white and furrowed and branches are stout, terete, and covered in fine appressed cottony pubescence (especially the younger ones). Leaves are sessile, elliptic-oblong or obovate-oblong, acute, thick, glaucous-green, clothed beneath and more or less above with fine cottony tomentum; base narrow, cordate. Flowers are odorless and purplish or white in color. Sepals 6 by 4 mm, ovate, acute, cottony; calyx divided to the base. Corolla flower that grows in the 2 cm or more in length; lobes 1.3-1.6 cm long, deltoid-ovate, subacute, revolute, and bent with age; corona's 1 lobe 3cm long by 5 mm wide, pubescent on the slightly thickened margin, with a rounded apex and two obtuse auricles below. 9-10 cm green follicle is long, broad, thick, fleshy, and ventricose. Brown coma, multiple seeds, 6 by 5 mm, widely ovate, flattened closely margined, minutely tomentose long up to 2.5-3.2 cm.[14-16]

Description of the Plant (*Taxonomical classification*) [17]

Kingdom: Planatae

Subkingdom: Tracheobionta

Superdivision: Spermatophyta

Division: Magnoliophyta

Class: Dicotyledones

Sub class: Asteridae

Series: Bicarpellatae

Order: Gentianales

Family: Apocynaceae

Subfamily: Asclepidiaceae

Genus: Calotropis

Species: Calotropis gigantea

Vernacular Names [18]

Hindi : Akand, Ark, Madar

Sanskrit : Arka, Aditya, Mandara

Marathi : Akand, Rui

Part used : Leaves, root, root bark, latex, stem bark, flowers.

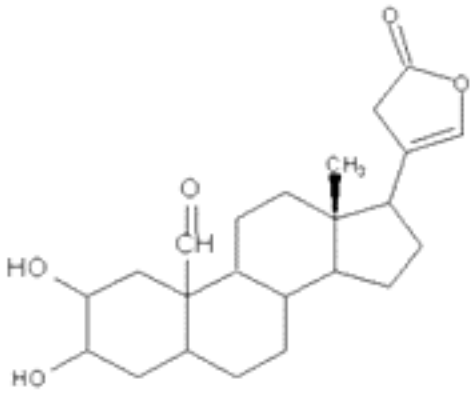
Morphological/ Botanical Description [19-20]

Sr. No	Part of Plant	Particular Characteristics
		Morphology- *Calotropis gigantea*
1.	**Root**	Simple, branched, woody at the base and covered with a fissured; corky bark; branches somewhat succulent and densely white tomentose; early glabrescent. All parts of the plant exude white latex when cut or broken
2.	**Leaves**	Opposite-decussate, simple, subsessile, exstipulate; blade oblong, obovate to broadly obovate, 5-30 X 2.5-15.5 cm, apex abruptly and shortly acuminate to apiculate, base cordate, margins entire, succulent, white tomentose when young, later glabrescent and glacouse.
3.	**Flowers**	Bracteate, complete, bisexual, action-morphic, pentamerous, hypogynous, pedicellate, pedicel 1-3 cm long
4.	**Calyx**	Sepal 5, Polysepalous, 5 lobed, shortly united at the base, glabrescent, quincuncial aestivation
5.	**Androecium**	Stamens five, gynandrous, anther dithecous, coherent
6.	**Bark & Branches**	The bark is thick, rough and corky and a yellow-brown colour; twigs are green and fleshy and may have a covering of tomentum (white fur like hairs)
7.	**Fruit**	A simple, fleshy, inflated, subglobose to obliquely ovoid follicle up to 10 cm or more in diameter.
8.	**Seeds**	Many, small, flat, obovate, 6 × 5 mm, compressed with silky white pappus, 3 cm or more long.

Chemical Description:[21-32]

Cardenolide, triterpenoids, alkaloids, resins, anthocyanins, proteolytic enzymes in latex, flavonoids, tannins, sterols, saponins and cardiac glycoside a few of the compounds discovered through phytochemical research on Calotropis. Terpenes, multiflorenol, and cyclisadol are found in flowers.

Sr. no	Part of Plant	Chemical Constituents
1.	**Stem Bark**	Giganteol, α and β calotropeol, β-amyrin
2.	**Root**	Calotropnaphthalene [naphthalene derivative], Calotropis sesquiterpenol, Calotropis esterterpenol [terpene derivatives], calotropbenzofuranone [aromatic product] and sucrose
3.	**Seed**	Oil extracted from seeds contains palmitic, oleic, linoleic and linolenic acid. The unsaponifiable fraction contains phytosterol, stigmasterol , melissyl alcohol and laurane
4.	**Flower**	Ester of α-and β-calotropeols
5.	**Leaves**	Sapogenins, holarrhetine; cyanidin-3-rhamnoglucoside; taraxasterol isovalerate. mudarine and three glycosides calotropin uscharin, calotoxin along with phenol
6.	**Latex**	Water and water soluble substance (86-95.5%) and caoutchouc (0.6-1.9%). The coagulam consist of caoutchouc (5.1-18.6), resin (73.6-87.8) and insoluble matter (4.5-13.8%). α- and β-calotropeols ; latex-protease, calotropains FI & FII, flower β-amyrin, stigmasterol. Calotoxin, uscharin, and calactin. Two new triterpine ester-3'-methyl butanoates of α-amyrin and taraxasterol isolated from latex
7.	**Root Bark**	Root bark contains β-amyrin, two isomeric crystalline alcohols, giganteol and isogiganteol



Calotropoginin

Phytopharmacological Evaluation of *Calotropis gigantea Linn*

Anticancer activity

Calotropis gigantea produces specialized secondary metabolites known as cardenolides, which have anticancer and antimalarial properties. GM Hoopes, in his research, produced a high-quality de novo assembly for *C. gigantea*, representing 157, 284, 427 BP with a N50 scaffold size of 805, 959 BP, with quality assessments suggesting a near-complete representation of the genic space. To help in the annotation and construction of a gene expression atlas, transcriptome data in the form of RNA-sequencing libraries from a developmental tissue series was created. 18, 197 high-confidence genes were annotated using an ab initio and evidence-driven gene annotation pipeline. [33]

Treatment with anhydrosophoradiol-3-acetate (A3A) isolated from the flower of Calotropis gigantea decreased the viable tumor cells and body weight gain, altered hematological (Hb, RBC and WBC) and biochemical parameters more or less to normal level thereby increasing the life span of Ehrlich's ascites carcinoma (EAC) bearing mice. Results of this study conclude that in vivo, the A3A was effective in inhibiting the growth of EAC with improving in cancer induced complications. [34]

CNS Activity

C. gigantea ethanolic extract was supplied orally to laboratory animals in doses of 100, 200, and 500 mg/kg body weight. On a maximal electroshock test and a strychnine-induced convulsions model, the anticonvulsant properties were investigated. The actophotometer was used to test the sedative property, and the rota rod was used to test the skeletal muscle relaxant property. Only strychnine-induced seizures were protected by this extract, which had no or a mild effect on electroshock-induced seizures. In mice, locomotor activity was found to be reduced, as was motor coordination. The extract was found to be healthy up to a dose of 2000 mg/kg in the acute toxicity sample. [35]

The CNS activity of an alcoholic extract of peeled roots of *Calotropis gigantea* R.Br. (Asclepiadaceae) was evaluated in albino rats at doses of 250 and 500 mg/kg bodyweight. Eddy's hot plate approach and acetic acid-induced writhings also demonstrated strong analgesic efficacy. The pawlicking time was extended, and the number of writings was reduced substantially. The onset of pentylenetetrazole-induced convulsions was delayed, and the severity of the convulsions was reduced, indicating significant anticonvulsant activity. The rats given the extract spent more time in the open arm of EPM, indicating that it has anti-anxiety properties. There was a decline in locomotory operation. The time it took to fall off (motor coordination) was also reduced. The sedative effect of the extract triggered a potentiation in the pentobarbitone-induced sleep. Up to a dose of 1 g/kg, no mortality was observed. These findings demonstrate the extract's analgesic, anticonvulsant, anxiolytic, and sedative properties. [36]

Wound Healing activity

Wistar albino rats of either sex weighing 180–200 g were topically treated with extract formulated in ointment using simple ointment BP as a base. In an excision wound model, a 5% (w/w) ointment was used once a day. Incision and dead space wound healing models were treated with ethanolic extract of *Calotropis gigantea* at doses of 100, 200, and 400 mg/kg. A 5 percent Povidone iodine ointment was applied topically to rats in the regular classes. On full epithelization, the percentage wound closure; epithelization duration, hydroxyproline content, and scar area were assessed. The percentage of wound contraction was increased when *Calotropis gigantea* was added topically to an excision wound model. Scar area and epithelization time were decreased. In incision wound and dead space wound breaking strength of wounds and hydroxyproline was increased. The size of the scar and the time it took for it to heal were both reduced. The breaking strength of wounds and hydroxyproline were increased in incision wounds and dead space wounds.[37] Using excision and incision wound models, *Calotropis gigantea* latex demonstrated wound healing activity in albino rats. When compared to controls, latex-treated animals had an 83.42 percent reduction in wound area. The norm was 1% w/w framycetin sulphate cream. When opposed to controls, wounds treated with the extract epithelized faster. The breaking power of granulomas increased significantly ($p<0.001$). [38]

Hepatoprotective activity

In male Wistar rats with liver damage caused using carbon tetrachloride, 2 mL kg-1 twice a week; ethanolic extract (50%) of stems of *Calotropis gigantea* R. Br. (Asclepiadaceae) at doses of 250 and 500 mg kg-1 was studied for hepatoprotective function. *C. gigantea* extract was compared to the regular drug silymarin for its protective effect. The aspartate amino transferase (AST), alanine amino transferase (ALT), glutathione (GSH), lipid peroxide (LPO), super oxidedismutase (SOD), glutathione peroxidase (GPx), and catalase (CAT) enzymes were all checked. [39] The hepatoprotective efficacy of leaf extracts of *Calotropis gigantea* in various solvents, including petroleum ether, acetone, chloroform, and methanol, was evaluated

using acetaminophen-induced hepatotoxicity models. The SGPT level was significantly reduced by chloroform and methanolic extract, while the SGOT level was significantly reduced by methanolic extract and Silymarin. Hepatoprotective activity was found in both the methanolic and chloroform extracts of the leaves. Acetone and petroleum ether extracts, on the other hand, showed no or just a small reduction in various liver enzymes. [40]

Antivenom activity

Calotropis gigantea methanolic extract was tested for its ability to neutralise venom (*Vipera russelli*) effects such as lethality, necrotizing activity, edoema, and haemorrhagic activity. The lethal effects of 2LD50 and 3LD50 venom in mice were effectively neutralised by oral administration of extract at 200 and 400 mg/kg (in-vivo neutralization). The plant extracts neutralised 2LD50 and 3LD50 of venom in in-vitro tests at 100, 200, and 400 mg/kg. Induction of haemorrhage and necrosis was also effectively inhibited. The antinecrotic effect of plant extract was important at doses of 200 and 400 mg/kg. At 60, 120, 180, and 240 minutes, the effect of methanolic extract on edoema caused by viper venom was investigated. At 240 minutes, plant extract at doses of 200 mg/kg and 400 mg/kg demonstrated substantial anti-inflammatory activity, with an effect comparable to that of standard antivenom. [41]

Anti viral activity

(+)-pinoresinol 4-O-[60-Ovanilloyl] is a new lignan glycoside isolated from the latex of *Calotropis gigantea*. -b-D-glucopyranoside (1), as well as two known phenolic compounds, 69-O-vanilloyltachioside (2) and 69-O-vanilloylisotachioside (3), and one authentic compound, (+) pinoresinol 4-O-b-Dglucopyranoside, were screened for A/PR/8/34 (H1N1) inhibitory activity in MDCK cells using the cytopathic effect. (Compound 1 had an inhibitory effect on A/PR/8/34 H1N1) The CPE inhibition assay was used to test its in vitro inhibitory activity against a panel of human and avian influenza viruses. It had an inhibitory effect on both subtypes A and B of human influenza viruses, but had no effect on avian influenza viruses. Furthermore, a plaque reduction assay demonstrated its activity against human influenza viruses subtype A. Compound 1 exerts its antiviral activity at the early stages of viral replication, according to the time course suggested by the assay. Compound 1 effectively inhibited influenza virus-induced activation of the NF-kB pathway in a dose-dependent manner, but had no effect on virus-induced activation of the Raf/MEK/ERK pathway, according to a mechanistic analysis. Further research revealed that 1 effectively prevented nuclear translocation of the transcription factor NF-kB caused by the influenza virus, as well as nuclear export of viral ribonucleoproteins. [42]

CONCLUSION

Calotropis gigantea Linn, in its different parts the root, root bark, leaves, flower, and latex of plants are used ethnomedicinally to treat a number of human illnesses. The current analysis aims to compile the plant's morphological characteristics, therapeutic uses, ethno-pharmacological records, and all pharmacological studies performed on it along with its phytochemistry review. These results support the use of plants in conventional medicine while also laying the groundwork for further research into the plant's pharmacological and therapeutic potential.

ACKNOWLEDGEMENT:

Author is thankful to Principal and Management of NDMVPs, College of Pharmacy, Nashik. Special thanks to Prof. H. U. Chikhale to accomplish this review.

CONFLICT OF INTEREST:

We declare that we have no conflict of interest.

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Source of Support: None declared.

Conflict of Interest: None declared.