Journal of Biomedical and Allied Research

ISSN: 2582-4937 Patial B, et al., 2022-J Biomed Allied Res **Review Article**

A Review on Biological Activities of **Indian Traditional Medicinal Plant: Calotropis Gigantea**

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Abstract

India, which is aptly referred to as the world's botanical garden, is the country that produces the most medicinal herbs. The Apocynaceae/Asclepiadaceae family member, Calotropis gigantea sometimes known as the Crown Flower, has special therapeutic characteristics that can be used on its own or in combination with other drugs to treat common illnesses. There is a surprising therapeutic diversity in herbal medications. Entire dried plant is employed as rejuvenating, parasitic worm expellers and mucus explusors in ayurveda. While latex of it cures vertigo, baldness, hair loss, and rheumatoid arthritis, and to treat asthma root in dry form is used, leprosy. Calotropis is employed as a homoeopathic remedy in addition to its conventional purposes. Significant medicinal benefits can be obtained from the plant's extracts from its many components. It is necessary to objectively investigate these treatments in order to determine their active principles and comprehend their pharmacological properties, such as prophylactic

protective, NSAID, antibacterial, antimicrobial, anti-oxidant, antiulcer ,helps in treating Covid-19, antimalarial, antipyretic, wound healing activity, cytotoxic properties, anti-asthmatic, procoagulant, CNS and anticonvulsant activity, pregnancy interceptive, anticancer, analgesic, antidiabetic, antidiarrheal, insecticidal, and hepatoprotective. It provides data about the mythical importance, herbal relevance, origin, pharmacogenetic illustration, herbal constituents, biological activities, and ethnopharmacological noteworthiness of Calotropis gigantea is summarized in the current review.

Keywords: Calotropis gigantean; Prophylytic protectant; Anti-inflammatory; Anti-bacterial; Anti-microbial; Cytotoxic; Antimalarial; Antipyretic; Wound healing; CNS; Anticonvulsant activity; Pregnancy interceptive; Anticancer; Analgesic; Antidiabetic; Covid-19.

Patial B | Volume 4; Issue 2 (2022) | Mapsci-JBAR-4(2)-028 | Review Article

Citation: Patial B, Thakur S, Ul Islam S, Ayush and Kumar A. A Review on Biological Activities of Indian Traditional Medicinal Plant: Calotropis Gigantea. J Biomed Allied Res. 2022;4(2):1-13.

DOI: https://doi.org/10.37191/Mapsci-2582-4937-4(2)-028

Introduction

Calotropis gigantea is also referred to as giant milk weed, crown flower, white ack. Freely found in about 9 Asian countries like; (India, Bangladesh, Burma, Indonesia. China, Malaysia, Pakistan, Philippines, Thailand, Sri Lanka) and all of these countries are home to this plant naturally. The plant's thick, oblong leaves which are light green in colour, has milky stems, oval shape, odorless in nature and waxy flower clusters are either lavender or white in colour. In India Calotropis gigantea is currently clinically proven to have a number of therapeutic benefits have analgesic properties [1]. This plant is found in the wastelands of Asia and Africa. It is also named as "shallow wort" be the possession of family the Apocynaceae. These plant fibres are known as madar or mader. It is referred to as "aak" "akauwa" or "arka" in India (Table 1). The blooms have analgesic properties [2], cytotoxic and antimicrobial activity [3]. The areal portions of the leaves also have antidiarrheal properties [4], anti-Candida campaign [5] and bacterial resistance [6], oxidation prevention performance [7]. It has been claimed that roots have antipyretic properties [8] with cytotoxic behaviour [9]. The part of the plant also found to be possessed CNS [10], insecticidal [11], antimicrobial [12], and pregnancy prevention capabilities [13]. The latex is also considered to have catharactive qualities, procoagulant activity [14] and rehabilitation i.e wound healing activity [15].

Family	Apocynaceae		
Subfamily	Asclepiadoideae		
Genus	Calotropis		
Species	Gigantea		
Kingdom	Plantae		
Synonyms	onyms crown flower, giant milk weed, white ack		

Table 1: Systematic position of the selected plant [16].

The stomachic, bechic, anti-asthmatic, and pain-relieving properties of C. gigantea blossoms are dynamic in medicine [16]. Lupus, tuberculous sickness, and syphilitic ulceration sorts of illnesses can be generally treated with roots [17], while outer swellings and the runs are dealt owith utilizing the plant's leaves and elevated parts [18]. The smooth juice of this plant has been utilized to prompt fetus removals in customary medication and has been depicted as serious areas of strength for an and gastrointestinal irritant [19]. Also, emmenagogue, uterotonic, ecbolic, and abortifacient properties of this plant have been reported [20,21]. The powdered petals of this plant are useful in treating colds, hacks, asthma, and heartburn, and the color of the leaves is utilized to fix discontinuous fevers [22,23]. The cardiovascular glycosides calotopin, uscharin, calotoxin, calactin, uscharidin, and gigantin are completely tracked down in the plant's bloom. The proteases calotropin DI, DII, FI and FII additionally present in the flower [24].

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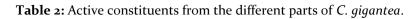
The alkaloids, tannins, flavonoids, and phenolic synthetic substances are the main artificially dynamic parts of plants (Table 2).

Various of these local restorative spices are used medically (Figure 1) [1,25].

Plant parts	Active constituent	Chemical nature	Structure
Flowers	Di-[2-ethylhexyl] Phthalate	Triterpenoids [3]	
Flowers	Anhydrosophoradiol-3-acetate	Triterpenoids [3]	HO cholesterol 1
Leaves	19-Nor-and 18,20-Epoxy-cardenolides	Cardenolides [26]	
Leaves	15beta-hydroxycardenolides	Cardenolides [27]	H
Leaves	16alpha-hydroxycalactinic acid methyl ester	Cardenolides [27]	Cardenolide 2
Arial parts	Isorhamnetin-3-O-rutinoside	Flavanol [28]	
Arial parts	Isorhamnetin-3-O-Glucopyranoside	Flavanol [28]	ОН
Arial parts	Taraxasteryl acetate	Flavanol [28]	llo flavonol 3
Latex	Calotropain-FI	Proteinases [29]	
Latex	Calotropain-FII	Proteinases [29]	NH NH
Latex	Calotropins DI	Proteinases [30]	
Latex	Calotropins DII	Proteinases [30]	Protease K 4
Roots	Calotropone	Cardiac glycoside [9]	HO HO HO HO HO HO HO HO HO HO HO HO HO H
Roots	Calotropises juiterpenol	Terpene [31]	
Roots	Calotropisesterterpenol	Terpene [31]	HO menthol 6

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Roots bark	Stigmasterol	Sterols [32]	HO registerol 7
Roots bark	Giganticine	Nonprotein amino acid [33]	он nicotinic acid 8



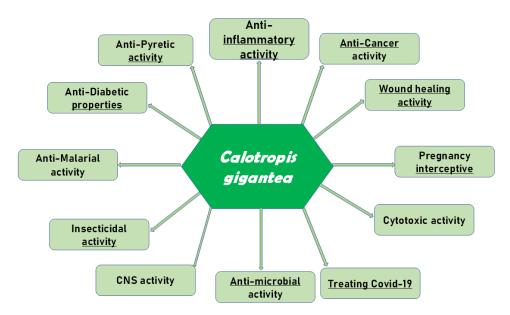


Figure 1: Therapeutic properties of *Calotropis gigantea*.

Antioxidant Activity

Antioxidants are crucial for defending against infections and degenerative disorders in humans. Namrata Singh.et.al in 2010 perform on DPPH [1,1-Diphenyl-2-Picryl-Hydrazyl] free radical forage activity and used it an invitro model to examine the antioxidant activity of hydroalcoholic extort of Calotropis gigantea leaves [HECGL]. Utilizing curcumin equivalents and the ascorbic acid reducing power assay, nitric oxide scavenging action is demonstrated. Along with the phenolic content of the extracts, total tannins and total flavonoids were evaluated using the Folin-Ciocalteau reagent to determine how much they contributed to the overall antioxidant activity. HECGL had maximal DPPH radical scavenging activity at 400g/ml [85.17%] and maximum nitric oxide scavenging activity at

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Wound healing activity

Nalwaya et al in 2009 used ablation and slit wound models, the wound healing capacity of Calotropis gigantean latex [200mg/kg/day] was examined in albino rats. Compared to controls, which had a wound area of 76.22%, latex-treated animals' wounds were 83.42% smaller wounds treated with the extract show a higher rate of epithelization than untreated wounds. Granuloma breaking strength [48534.64] increased significantly [p=0.001],

which is significant. A standard was established using the Framycetin Sulphate Cream (FSC), 1% w/w [15]. Ahmed Alafnan et al in 2021 concluded that the phytonutrient profile, oxidation protectant, effects on catalyst inhibition, and profile of specialized metabolites of Calotropis gigantea leaf extracts are investigated in this process. A substantial amount of phenolic and flavonoid content was discovered in the plant. According to the results of the UHPLC-MS analysis, the specialized metabolite outline showed presence of the various bioactive components that owned to important phytonutrient bands. Specialized metabolite and comprehensive bioactive makeup of the plant extract under research may be responsible for its significant antioxidant and enzyme inhibitory capabilities. So, it is important to consider this plant as an of essential source bioactive phytocompounds with oxidation prevention suppression and enzyme potential. Additionally, the most recent studies support the traditional medical system's usage of Calotropis gigantea leaves to speed up wound healing. However, it is strongly advised to conduct more research on the isolation of the harmful lead compounds [37].

Anti-inflammatory activity

Jagtap VA et al in 2010 observed the ethanolic extract of Calotropis gigantea, showing that this plant primarily suppresses the release of inflammatory mediators. To recognize and segregate the active ingredients liable to generate activity against inflammatory, however, as well as to clarify its antiinflammatory action mechanism or

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mechanisms, animal studies and other research are required [38].

Insecticidal activity

Alma et al in 2009 observed the toxicity of residual films, deodorant malignance, and impermeable effects in opposition to a variety of basal and grown-up forms of Tribolium castaneum were assessed for the methanolic distillate of the root bark of C. gigantea as well as its methyl trichloride and petroleum ether fractions. After petroleum ether fraction and chloroform fraction, methanol extract had the highest insecticidal activity against T. castaneum. A lack of fumigant toxicity was evident in any sample [11]. Elvian IN et al in 2021 performed on one of the high-value plants is the shallot (Allium ascalonicum). However, several unsettling microbes have reduced shallot output. One insect that affects shallot cultivation is Spodoptera exigua, which can reduce yields by up to 70%. To control the insect, farmers employ an excessive amount of synthetic pesticides. The usage of synthetic pesticides has a number of detrimental repercussions on both humans and the environment. Natural pesticides derived from plants can therefore be a different approach. One possible plant that could be used as a natural pesticide is the giant calotrope (*Calotropis gigante*). In order to provide repellent activity and cause damage to S. exigua second instar larvae, the research sought to determine the most effectual concentration and solvent abstract of Calotropis gigantea. By gradually macerating polar [ethanol] and non-polar [nhexane] solvents, the abstract [extract] was produced. The extracts' specialized metabolites were examined using chromatography [TLC]. Compared to nhexane extract, ethanol extract displays higher levels of toxicity and antifeedant action. The concentration that caused the most mortality, 91,674,41%, was 3%. In comparison to n-hexane extract, ethanolic distillate has an excessive group number of specialized metabolites [39].

Antimicrobial activity

Alma et al in 2008 reported that the petroleum ether, trichloromethane, and ethyl acetate fractions of a methanol extract from the root bark of Caltropis gigantea have antibacterial activity. It was shown that the methanol extract's chloroform fraction has antibacterial action in opposition to Sarcina lutea, B. megaterium, and P. aeruginosa. Petroleum ether fraction showed effectiveness against B. subtilis and Shigella sonnei while ethyl acetate fraction showed efficacy against P. aeruginosa and E. coli. [12]. Pati Kemala in 2022 performed green synthesis of AgNPs utilizing Calotropis gigantea leaf and flower extracts, which are found in the geothermal formation le Seu-Um, Aceh Besar, Indonesia. When AgNO₃ is used as a metal precursor, SPR peaks in the 410-460nm range have been observed at doses of 2,5 and 9mM. Identified ascetic groups in AgNPs-FCg and AgNPs-LCg were also displayed in the FTIR data. AgNPs-FCg and AgNPs-LCg also possess good stability, a domain-frame arrangement, and antibacterial efficacy in case of fungi, pathogens [Gram-positive bacteria, and Gram-negative bacteria]. It is well known that AgNPs-FCg has a bigger inhibition zone than

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AgNPs-LCg. It is encouraged to do more investigation within response activity escalation in order to lower the commonly agreed nano-particle size to evaluate less than those discovered in this research as a result of the data related nano-particle size [40].

Analgesic activity

Biswasroy et al in 2020, Singh et al in 2014 were exposed rats to the chemical and heat treatments responded favorably to an ethanol extract of Calotropis gigantea flower and bark [41,42]. Biswasroy et al in 2020 using the heated plate technique and an in-vivo ethanoic acid-induced convulsing test, the anxiolytic activity was evaluated for 90 minutes. 250 and 500mg/kg of CG flower administered orally produced analgesia in the amounts of 20.97% and 43%, respectively [41].

Cytotoxic activity

Kumar G et al in 2011 observed that the Cardenolide glycosides that are isolated from

the roots of Calotropis gigantea exhibit strong cytotoxicity toward a variety of human cell types. The main active components are frugoside, 4'-O-Dcalotropin, and glucopyransylfrugoside [9]. Perumal Gobinath et al in 2022 created a brand-new, environmentally friendly procedure for the high yield production of 1,4-dihydropyridine derivatives coupled to 3-amino thymoquinone. The cytotoxic effect of the 1,4dihyropyridine derivatives was evaluated making use of three cancer cell lines and normal cell lines. Human embryonic kidney cell [HEK₂₉₃], liver cell [LO₂], and lung cell assay using were subjected to MTT doxorubicin as the reference drug (MRC₅). When compared to other compounds, compound 9 [HepG₂, LC50-0.50 M, MCF₇, LC50-0.64M, HeLa, and LC50-0.52M] [structure given in Figure 2] was found to be extremely active. As outcome, compound 9 may serve as a highly significant compound for the continued development of an anticancer medication [43].

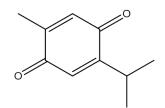


Figure 2: 2-Isopropyl-5-methyl-1,4-benzoquinone.

Chitme HR et al in 2004 observed that the Castor oil-induced diarrhea model in rats was used to test the anti-diarrheal actions of a hydroalcoholic [50:50] draw out of Calotropis gigantea's aerial component. The extract exhibited remarkable reduction in faecal production and dropping frequency [intraperitoneal dose] at a dose of 200 and 400mg/kg. The weight and volume of intestinal content were notably inhibited by the extract as well [4].

Anti-pyretic activity

In the system of traditional medicine in India, Calotropis gigantea root extracts have been

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Anti-diabetic activity

According to a study on CG leaf extract, [Haque et al in 2012] it drastically lowered blood glucose levels during a glucose tolerance test on mice that were already loaded with glucose. Significantly greater antihyperglycemic action is seen at oral dosages of 100, 200, and 400mg draw out per kg body weight. The study also discovered that, in compared to control animals, these doses resulted in a percent drop in blood glucose levels of 21.35, 25.39, and 28.54 [45]. Biswasroy et al, 2020, Jaiswal et al, 2013 observed the levels of LPO, SGPT, SGOT, alkaline phosphatase, cholesterol, and

triglycerides were remarkably reduced by the chloroform extract made from CG flower and leaf. This work was supported by the streptozotocin [STZ] induced model [41,46].

Anti-cancer activity

SP Avinash et al in 2012 observed the phytonutrient analysis and anticancer actions of Calotropis gigantea leaf draw out [extract] show that the alkaloids, glycosides, and tannins found in the target plant's leaves are what give the extract its biological activity. Additionally, the leaves could be more effectively pharmaceutical used in applications as antibacterial and anticancer agents [47]. Roihatul Mutiah et al in 2021 observed that the plant Calotropis gigantea contains the chemicals calotropin, calotroposide A, and oxypregnane oligoglikosida, which have been shown to have efficacy in preventing the proliferation of cancer cells by inducing apoptosis and suppressing ROS. The plant Calotropis gigantea should be onwards expanded into standardized herbal medications and phyto neutraceuticals, according to the results of this systematic review [48].

Pregnancy interceptive activity

Srivastava SR et al 2007 was performed on rats and rats show the pregnancy-interrupting action when Calotropis gigantea roots were dissolved in various organic solvents. The displayed extract 100% pregnancyinterceptive efficacy at a dose of 100mg/kg. Introduced in the Days 1-5 and 1-7 post coitum regimens, the extract likewise signified 100% effectiveness at a dose of 12.5mg/kg [13]. Singh N et al in 2014 studied that the pregnancy-

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interceptive effects of Calotropis gigantean root extracts in various organic solvents were assessed [in rats]. At a dose of 100mg/kg, the extract exhibited 100% contraceptive efficacy. Additionally, the extract demonstrated 100% effectiveness when given at doses of 12.50mg/kg on days 1 through 5 and 1 through 7 post coitum [49].

Hepatoprotective

Rats exposed to CCl₄-induced hepatotoxicity have good hepatoprotective effect from Calotropis gigantea leaf extract in a dosedependent manner [Tenpe CR in 2007] [50]. Biswasroy et al in 2020 discovered that when an animal was given an ethanol extract, the serum enzyme levels were dramatically reduced. In-vitro paracetamol-induced hepatotoxicity was used as the experimental method [41].

Treating Covid-19

In the field of drug discovery new era has developed by Mycal Dutta et al in 2021 with the growing usage of HTS and molecular docking modelling. Since the dawn of civilization, phytochemicals from medicinal plants have been employed for therapy. Recently, the subject of drug development has gained a new dimension thanks to advanced computer-aided programme and richer extraction techniques. By concentrating on one of the crucial enzymes needed for SARS-CoV-2 replication, this study offers critical information for the use of separated phytochemicals from C. gigantea for the procurement of COVID-19. Additional experimental research could be necessary to show the molecular activity of the

phytochemicals. In addition, there are a ton more of these bioactive elements from medicinal plants that exist in Bangladesh's rich biodiversity and require additional study. The study made plant-based treatment in opposition to COVID-19 possible, but more investigation and wet lab testing are necessary before it can be used on patients. [51].

CNS Activity and Anticonvulsant Activity

Argal A et al in 2006 observed that the oral administration of peeled roots alcoholic extract of Calotropis gigantea was studied for CNS exercise in albino rats at doses of 250 and 500mg/kg bodyweight. Notable analgesic effect was seen with both the Eddy's hot plate approach and acetic acid-induced writings. The quantity of writings was significantly decreased, and the paw licking period was postponed. Both the onset and severity of pentylenetetrazol-induced convulsions were displaying remarkable delayed, anticonvulsant efficacy. Rats imparted the extract consume more time in the open arm of the EPM, demonstrating the extract's antianxiety properties. The activity of the locomotor system decreased. Additionally, the motor coordination's fall-off period was shortened. Due to the sedative effects of the extract, the pentobarbitone-persuaded sleep was potentiated. Upto the dose of 1g/kg, no mortalities were detected. These detections reveal the extract's analgesic, anticonvulsant, and sedative effects [52]. Bairagi SM et al in 2018 studied that the Strychnine and electroshock generated convulsions were used to test the ethanolic extracts of Calotropis gigantea for their anticonvulsant

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and sedative effects. The extract-treated animals significantly reduced the amount of electroshock-induced convulsions they experienced, but had no discernible impact on the strychnine convulsion model. Additionally, the extracts demonstrated notable motor coordination impairment and muscle relaxant action [53].

Antimalarial activity

Shripad M.B et al in 2018 studied that the effectiveness of Calotropis gigantea flower extract as a mosquito repellant was investigated. The plant's unique extract was used in an experiment against a female Culex quinquefasciatus mosquito that had been blood-starved for several days. Comparing the alcoholic extract to the petroleumether and chloroform extracts, the alcoholic extract demonstrated a higher level of mosquito repellent effect opposite to the female Culex quinquefasciatus mosquito. The extract was discovered to have dose-dependent insect repellent properties [53].

Anthelmintic activity

It was shown that the time for an earthworm to become paralyzed and die in an aqueous extract was shorter than it was in an alcoholic extract. Both the paralysis and the time it takes to die are substantially longer in the animals treated with extracts than they are in the animals treated with albendazole. Compared to an albendazole concentration of 80mg/ml, a 100mg/ml dose of alcoholic and aqueous extract paralyzed the worms, but the time it took for them to die was excessive. Although the aqueous extract did not exhibit a clear zone of inhibition, both dosages of the alcoholic extract demonstrated a good zone of inhibition with no growth. Despite being lower than the standard drug, the zone of inhibition at a concentration of 50mg/ml was determined to be good [54]. (Ameeta Argal et.al, 2007).

Anti-asthmatic activity

Jaliwala YA et al in 2011 When compared to the control, the liquid flower draws out of Calotropis gigantean greatly reduced the whoop that hydrogen nitride and Sulphur dioxide caused in mice when administered at amount of 250mg and 500mg/Kg of body weight. The aqueous extracts significantly reduced the amount of cough that was caused by sour salt in cavies [250mg/kg and 500mg/kg body weight]. Additionally, the anti-asthmatic effects in guinea pigs were also noticeable in the liquid draw out at amounts of 250mg/kg and 500mg/kg when contrasted to the control [54].

Ansari Mushir et al in 2016 mentioned that the Calotropis gigantea has anti-asthmatic properties in ova albumin [OVA]-induced asthma. At amount of 100, 200, and 400mg/kg, the effects of Calotropis gigantea on dissimilar bodily corpuscles, catalysts, and histopathological changes were observed. Accordingly, plant concentrate may be useful in the treatment of asthma Inhibition of eosinophils, neutrophils, erythrocytes, and total leukocyte counts in mucous fluid by Calotropis gigantea at 200 and 400mg/kg was significant [p=0.05]. These findings imply that a plant's anti-inflammatory, antilipoxygenase, and antioxidant properties may make it a promising therapeutic medication for the treatment of asthma [55].

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Procoagulant activity

According to Singh N, Jain NK, et al in 2010 that it is well known that Calotropis gigantean's latex has strong procoagulant properties. The extremely basic proteins in the crude latex extract have a powerful proteolytic activity [7]. Mishra P et.al in 2017 performed that depends on dosage, human fibrinogen, cude fibrin, and latex hydrolyzed casein form a clot [56].

Joseph B et.al in 2013 performed due to their proteolytic character, proteins in the latex of Calotropis gigantea are what cause the procoagulant action. The fibrinogen subunits are digested by the extract; the alpha subunit is hydrolyzed first, followed by the beta and gamma subunits [57]. The more resistant gamma subunit is hydrolyzed either at extensive polypeptide concentrations or after a prolonged incubation period. Correlated to papain and trypsin, the plant extract withdraw hydrolyzes the crude fibrin clot considerably more forcefully. Additionally, it is discovered that the crude withdraw is extravasatic, producing skin hemorrhage at around >75 microns and promoting blood coagulation [7].

Conclusion

Significant medicinal benefits can be obtained from the various plant extracts. Identifying the active principles and comprehending the pharmacological actions, such as anti-fertility, anti-inflammatory, analgesic, anticancer. antidiabetic. antidiarrheal, insecticidal, anti-bacterial, anti-microbial, antioxidant, wound healing activity, treating Covid-19, anti-asthmatic, procoagulant, CNS and anticonvulsant, pregnancy interceptive, antidiabetic. antimicrobial, insecticidal, antiulcer, antipyretic, and hepatoprotective, are necessary for making these remedies acceptable to modern medicines. The information on the origin, pharmacognostic description, phytoconstituents, biological and ethnopharmacological activity, importance of Calotropis gigantea is summarized in the current review.

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