

Pharmacological activities of *Calotropis gigantea*: A Perspective

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Abstract: *Calotropis gigantea* is a common wasteland weed with medicinal properties. Studies conducted indicates that the plant possess antibacterial, antiasthmatic, free radical scavenging, wound healing, vasodilation, procoagulant, antifertility, anti inflammatory, anticancer, cytotoxic, analgesic, anti pyretic, anti convulsant and anti diarrheal activities. Calotropnaphthalene, calotropisesjuiterpenol, calotropisesterterpenol, calotropbenzofuranone were the major phytochemical compounds derived from the root extract of the plant. Latex was found to contain the cardiac glycosides, calotopin, uscharin, calotoxin, calactin and uscharidin gigantol and hence possess the pharmacological activities. The plant was also mentioned in ayurveda and unani for the treatment of asthma and for many other diseases.

Key Words: Milkweed, latex, expectorant, locomotor, procoagulation.

Introduction

Medicinal plants are used widely for the promotion of primary health care needs of the people living in the rural areas [1]. The traditional medicines was derived from the medicinal plants, minerals and other organic matters. But the herbal drugs are obtained from the medicinal plants alone [2]. The inheritance of the utilization of plant as the source of medicine plays an essential component of the health care system in India. The formulations of the medicinal products were prepared by the practitioners in their own methods in Indian countries but require further documentation and research works to be carried out. But in the Western countries the utilization of herbal medicines is steadily under growth [3].

Plants are exploited for their medicinal source from the ancient period itself. The traditional and folk medicinal system used the plant products to treat various disease causing infections. In recent times, plants are explored extensively for detecting their medicinal properties as they have become the major source for drug discovery and development [4-6]. Plants are reported to possess antimicrobial, anticancer, antiinflammatory, antidiabetic, hemolytic, antioxidant, larvicidal properties etc. Therapeutic compounds were now altered by the medicinal plants due to their potent

Therapeutic compounds were now altered by the medicinal plants due to their potent medicinal properties. *C. gigantea* is one of the plant explored with many medicinal properties and they are easily available [7].

Calotropis gigantea Linn., which belongs to the family of *Asclepiadaceae* is a glabrous or hoary small tree that is commonly known as The swallow-wort or Milkweed [8]. It is found as a common wasteland weed in India. Traditionally *Calotropis gigantea* plants were used to treat some of the common diseases such as fevers, rheumatism, indigestion, elephantiasis, asthma, diarrhea and was also used as an analgesic. The plant was also reported to possess free radical scavenging and anti-diarrheal activity [9]. In Asia and Africa *Calotropis gigantea* is distributed as the laticiferous shrub [10]. The aqueous extract of *C. gigantea* latex was found to contain many of the hydrolytic enzymes. Among all, the proteases were found to be in relatively abundant range and could be probably responsible for the pharmacological properties possessed by the latex [11].

Calotropis gigantea is proudly known as the milkweed in the Asian countries such as India, Indonesia, Malaysia, Philippines, Thailand, Sri Lanka and China. Tribal people were utilizing the plant parts to cure various illnesses such as toothache, ear ache, sprain,

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anxiety, pain, epilepsy, diarrhoea and mental disorders. *C. gigantea* is also proved for its anti-*Candida* activity, cytotoxic activity, antipyretic activity and wound healing activity [12-15].

Plant Description

The genus *Calotropis* (Asclepiadaceae) comprises of about six species of shrubs that are distributed throughout tropical and subtropical African and Asian countries. Among them, two were called as the sister species (*Calotropis gigantea* L. and *Calotropis procera* L.) that occurs in China. *C. gigantea* possess a high biomass with fast growing perennial shrub in the Hainan province of China. Plant latex is found to contain a complex mixture of several hydrolytic enzymes. They also possess a rich source of wax, resins and other lipid like substances. But the physiological role of the latex in the plants is not yet clearly understood. Proteases in the latex make the plant resistant against many of the infectious diseases and aid the protection against extreme conditions. The latex possesses several pharmacological properties and hence exploited in the folk medicine [16].

Taxonomical Classification

Kingdom: Plantae

Division : Magnoliophyta

Class : Magnoliopsida

Sub-class : Asteridie

Order : Gentinales

Family : Asclepiadaceae

Genus : *Calotropis*

Species : *gigantea*

Synonyms

The plant has various names in different languages such as:

Sanskrit: Arka, Alarka

English: Gigantic swallow wort, Mudar

Hindi: Madar

Kannada: Ekkemale

Telugu: Mandaramu, Ekke, Jilledu, Arka

Malayalam: Errikka

Traditional Uses

Calotropis gigantea is found to be an important medicinal plant that is mentioned in Ayurveda and Unani for the treatment of asthma. According to Ayurveda, the dried whole plant was found to be the good tonic, expectorant, depurative, and anthelmintic agent and the dried root bark was found to be the febrifuge, anthelmintic, depurative, expectorant, and laxative. The powdered root was used in the treatment of asthma, bronchitis, and dyspepsia. The leaves were also used for the treatment of paralysis, arthralgia, swelling and fever. Flowers were bitter, astringent, stomachic, anthelmintic and tonic [17].

The latex was also used as bitter, heating, oleaginous, purgative, cures, leucoderma, tumours, ascites agent. The latex was used as caustic, acrid, expectorant, depilatory and was found to be useful in leprosy scabies ring worm of the scalp, piles, eruptions on the body, asthma, enlargement of spleen and liver, dropsy applied to painful joint swellings. The latex *C. gigantea* showed the digitalis like action on the heart. The latex was also used for the induction of abortion and infanticide [16]. *C. gigantea* was used in the treatment of sprain, stiff joints [10] and also several tribal people used the latex for easy delivery [11].

Phytochemical Constituents

Four new chemical constituents such as the naphthalene derivative which was named as calotropis naphthalene and two terpene derivatives namely calotropis esjuiterpenol and calotropis esterterpenol and finally an aromatic product designated as calotropbenzofuranone along with a known compound, sucrose was isolated from the roots of the *Calotropis gigantea* [17]. The *C. gigantea* possess the chemical constituents such as cardenolides, flavonoids, terpenes, pregnanes and a nonprotein amino acid [16]. Latex was found to contain the cardiac glycosides, calotropin, uscharin, calotoxin, calactin and uscharidin gigantol. Latex possess the protease calotropin DI and DII and calotropin FI and FII. The latex was investigated to contain some of the poisonous constituent that causes the caustic effect on the mucous membrane and tender skin [8]. The other constituents isolated were the glycosides and proteases [15]. Flavonoids, triterpenoids, volatile long chain fatty acids were also isolated from the plant parts [8].

Pharmacological Activities

Antibacterial Activity

Bacterial infections were the causative agents of various diseases in the world. Plants possess the antimicrobial components that are much active towards the infectious pathogens. *Calotropis gigantea*'s aqueous extract possess significant anti bacterial activity against various bacterial pathogens such as *Staphylococcus aureus*, *Escherichia coli*, *Bacillus cereus*, *Pseudomonas aeruginosa*, *Micrococcus luteus* and *Klebsiella pneumoniae*. with the formation of the maximum zone of inhibition. Amoxycillin (10 µg/disc) was used as positive control for *B. cereus* and *K. pneumoniae*, Penicillin G disc (10 µg/disc) *S. aureus* and *M. luteus* and Polymyxin-B (10 µg/disc) for *E. coli* and *P. aeruginosa* and Sterilized distilled water was used as negative control in the above experiment [7].

Antiasthmatic Activity

Bronchial asthma is a chronic inflammatory disease which is characterized by both bronchoconstriction and airway inflammation that leads to bronchial hyperresponsiveness [19].

The ethanolic extract of the roots of *Calotropis gigantea* were tested for their antiasthmatic activity in various in vivo and in vitro animal models. In vitro studies were done on isolated guinea pig ileum Preparation and in vivo studies on Acetylcholine and Histamine induced bronchospasm in guinea pigs. The extract showed relaxant activity in the histamine induced bronchocontraction in the guinea pig model and reveals their usefulness in the treatment of asthma disease [17].

Vasodilatation Effect

The latex of *Calotropis gigantea* possess various components that are helpful in the controlling mechanism of the heart muscle. The proteins in the crude latex extract are found to be highly basic with strong dilatation activity. The crude extract of the latex was found to produce the higher cardiac output with dilation effect in the tested green frog namely *Rana hexadactyla* but at the fixed dosage only. The over dosage of the same extract would cause the contractility of the cardiac muscle itself [16].

Free Radical Scavenging Activity

Free radicals were the major compounds responsible for various oxidative damages occurring in the cells. The effect of chloroform extracts of *Calotropis gigantea* leaf and flower on the free radical scavenging activity and lipid profile was measured in the streptozotocin-induced diabetic rats. The lipid peroxidation, superoxide dismutase, and catalase were the parameters measured in liver homogenate and others include the serum glutamic pyruvic transaminase, serum glutamic oxaloacetic transaminase, alkaline phosphatase, lipid profile in the blood serum. The study showed that the administration chloroform extract to the streptozotocin induced rats produced a significant reduction in the lipid peroxidation, serum glutamic pyruvic transaminase, serum glutamic oxaloacetic transaminase, alkaline phosphatase, cholesterol and triglyceride levels and also the significant increase in the superoxide dismutase and catalase levels [20]. The latex of *C.gigantea* was found to exhibit a greater capacity to scavenge DPPH radicals and hence possess antioxidant activity [21].

Wound Healing Activity

Wound can be defined as the loss or breaking of the cellular and functional continuity of the living tissues. Wound healing is a biological process that begins by trauma and often ends by the scar formation. The Latex of *Calotropis gigantea* showed the wound healing activity in the tested excision and incision wound models of the albino rats by causing a reduction in the wound area [8]. Similarly, the ethanolic extract of the bark of the plant possessed the rapid increase in the wound contraction in the excision wound model rats

and the increase in the breaking strength of wound in the incision and dead space wound model [9].

CNS Activity

Alcoholic extract of the peeled roots of *Calotropis gigantea* showed the prominent CNS activity in the albino rats. They showed the analgesic activity by means of delaying the paw licking time and reduction in the numbers of writhings. The delay in the onset of pentylenetetrazole induced convulsions and the decrease in its severity showed the significant anticonvulsant activity. The extract treated rats was found to show the antianxiety activity also. Decrease in the locomotor activity and the fall off time was observed. Thus, the plant possesses analgesic, anticonvulsant, anxiolytic and sedative effect [18]. The alcoholic extract of the flowers was also found to possess the respective analgesic activity in the thermal and chemical models of mice [10].

Procoagulant Activity in association with Fibrin(ogen)olytic Activity

The latex of *Calotropis gigantea* possesses certain components that are involved in the control of bleeding. The crude latex extract contains highly basic proteins that possess the stronger proteolytic activity. The crude extract has the ability to hydrolyse casein, human fibrinogen and crude fibrin clot. Hence, the crude extract is found to be pharmacologically hemorrhagic in nature and was found to reduce the coagulation time of citrated plasma and promotes blood coagulation. Procoagulation and blood clot hydrolysis are the important factors in wound healing process [11]. Further, the proteolytic action on fibrinogen subunits occurs in the order of Alpha > Beta > Gamma [22].

Anti-Fertility Activity

The *C. gigantea* roots were found to show the antifertility activity in the tested rats. The ethanol extract and the chloroform soluble fraction of *C. gigantea* roots showed the 100% pregnancy interceptive activity and were found to cause 7-25% loss in body weight at the minimum effective contraceptive dose (MED) in the tested rats [23].

Anti-Inflammatory Activity

C. gigantea showed the anti-inflammatory activity against carrageenan and kaolin induced rat paw oedema for acute inflammatory condition, cotton-pellet granuloma and adjuvant- induced arthritis model for chronic inflammatory condition. The alkaloid fraction showed the higher initial anti-inflammatory activity. The residual anti-inflammatory activity of alkaloid fraction of *C. gigantea* was achieved due to the greater protein binding nature of the compound or due to the non available of possible bioactive metabolites in order to retain the activity profile relation [24].

Analgic and Anti-Pyretic Activity

The ethanol extract of the flowers of *C. gigantea* showed the analgesic activity in the acetic acid induced writhing test model and hot plate model in mice and was found to be dose dependant in its action [25]. The roots of *C. gigantea* showed its antipyretic activity against yeast-induced pyrexia in rats and TAB (Typhoid) vaccine-induced pyrexia in rabbits. They also showed significant dose dependent activity after the intraperitoneal administration of the root extract [26].

Anticancer and Cytotoxic Activity

Three cardenolide glycosides that were found to be toxic to cell lines of human origin were isolated as the cytotoxic principles from the roots of the plant and were named to be calotropin, frugoside, and 4'-O-beta-D-glucopyranosyl frugoside [27]. In addition, two more new cardenolides along with 12 known compounds were also obtained from the dichloromethane extract of the leaves of *Calotropis gigantea* and was found to show a significant cytotoxic activity against the tested cancer cell lines [28].

Anti Convulsant Activity

The alcoholic extract of the peeled roots of "akond mul" (*Calotropis gigantea* L.) was found to show a significant dose dependent anti-convulsant activity against the pentylenetetrazole (PTZ) induced convulsions in rats. Animals treated with the extract exhibited the anti anxiety activity and decreased locomotor and motor coordination activity [29].

Anti-Diarrheal Activity

The hydro alcoholic extract of aerial parts of *C. gigantea* was found to show a significant anti-diarrheal activity against the castor oil induced diarrhoea model in rats. The plant extract causes the significant reduction in fecal output and frequency of droppings [33]. Anti-diarrhoeal activity of the ethanolic extract of *C. gigantea* flowers were also investigated against the castor oil induced diarrhoea model in rats and was found to reduce the number, frequency and wetness of faeces and the propulsion of charcoal meal [22].

Other Uses

The leaf extracts of *Calotropis gigantea* was also investigated to possess significant inhibition against the mitochondrial malate dehydrogenase and malic enzyme of a filarial worm *Setaria digitata* [30]. The ethanol extract of *Calotropis gigantea* was found to possess the antibacterial activity against both gram positive and gram negative bacteria [31]. The plant *Calotropis gigantea* was also found to show the inhibiting activity against *Sitophilus zeamais* and hence used as a potential pest control [32].

Conclusion

The vast study of the literature revealed the fact that the *Calotropis gigantea* is found to be an important source of many pharmacological applications. In spite of the poisonous constituents of the latex, the plant possesses many properties that have application in the present pharmaceutical world. Knowledge on the pharmacology of the plant is not the new discovery which we have found out. The pharmacology of the plant was known from the ancient period through great saints and ayurvedic practitioners. But the formulation they practiced and the documentation of their practices were disappeared due to the absence of technology. So, the compilation of the research works done on the pharmacology of the plant would be helpful to the scientists in order to convert the property as the useful drug product that is used to treat many of the infections and diseases affecting the life of the people in the present world.

References

1. Kamboj VP(2000). Herbal medicine. *Curr Med.* 78: 35-39.
2. Sath SD ,Sharma B(2004). Medicinal Plants in India. *Indian J Med Res.* 120: 9-11
3. Bent S(2004). Commonly used herbal medicines in the United States. A review. *Am. J. Med.* 116: 478-85
4. Rates SMK(2001). Plants as source of drugs. *Toxicon.* 39: 603-613
5. De Pasquale A(1984). Pharmacognosy: the oldest modern science. *Journal of Ethnopharmacology.* 11: 1- 16
6. Gordon MC, David JN(2005). Biodiversity: A continuing source of novel drug leads. *Pure Appl Chem.* 77: 7-24
7. Gaurav Kumar, Loganathan Karthik, Kokati Venkata Bhaskara Rao (2010). Antibacterial activity of aqueous extract of *calotropis gigantea* leaves – an *in vitro* study. *International Journal of Pharmaceutical Sciences Review and Research* 4(2):141-144
8. Narendra Nalwaya, Gaurav Pokharna, Lokesh Deb, Naveen kumar Jain(2009). Wound healing activity of latex of *calotropis gigantea*. *International Journal of Pharmacy and Pharmaceutical Sciences.* 1(1):176-181
9. Pradeep T. Deshmukha, Jennifer Fernandesb, Akarte Atul , Emmanuel Toppoa(2009). Wound healing activity of *Calotropis gigantea* root bark in rats. *Journal of Ethnopharmacology.* 125 : 178–181
10. Pathak AK, Argal A(2007). Analgesic activity of *Calotropis gigantea* flower. *Fitoterapia.* 78 : 40–42
11. Rajesh R, Raghavendra Gowda CD, Nataraju A, Dhananjaya BL, Kemparaju K, Vishwanath BS(2005). Procoagulant activity of *Calotropis gigantea* latex associated with fibrin(ogen)olytic activity. *Toxicon.* 46: 84–92
12. Gaurav Kumar, Karthik L, Bhaskara Rao KV(2010). *In vitro* anti-*Candida* activity of *Calotropis gigantea* against clinical isolates of *Candida*. *Journal of Pharmacy Research.* 3:539-542.
13. Wang Z, Wang M, Mei W, Han Z, Dai H(2008). A New Cytotoxic Pregnanone from *Calotropis gigantea*. *Molecules.* 13: 3033- 3039
14. Chitme HR, Chandra R, Kaushik S(2005). Evaluation of antipyretic activity of *Calotropis gigantea* (Asclepiadaceae) in experimental animals. *Phytotherapy Research.* 19:454-456
15. Saratha V, Subramanian S, Sivakumar S(2009). Evaluation of wound healing potential of *Calotropis gigantea* latex studied on excision wounds in experimental animals, *Med Chem Res.* 19:936-947
16. Sheelaa B, Mohamed Hussain S, Sampath Kumar P, Kalaichelvam VK, Venkatachalam VK(2010). Vasodilatation

- Effect of Latex from *Calotropis gigantea* in Green Frog *Rana hexadactyla*. *Asian Journal of Medical Sciences* .2(1): 22-24
17. Rahul Mayee, Ambrish Thosar, Arun kondapure(2011).Evaluation of antiasthmatic activity of *Calotropis gigantea* roots. *Asian J Pharm Clin Res.*4(2):3335
 18. Ameeta Argal, Anupam Kumar Pathak(2006). CNS activity of *Calotropis gigantea* roots. *Journal of Ethnopharmacology* .106: 142–145
 19. Sheth UK, Dadkar NK, Kamath NG(1972). Selected topics in experimental pharmacology. Vol 5, Kothari Book Depot, Bombay, India, 1972, 63.
 20. Rathod NR, Raghuvver I, Chitme HR, Chandra R(2009). Free Radical Scavenging Activity of *Calotropis gigantea* on Streptozotocin-Induced Diabetic Rats. *Indian J Pharm Sci.* 71(6): 615–621
 21. Ahmed M, Rana AC ,Dixit VK(2003). Free radical scavenging activity of *Calotropis* species. *Indian Drugs.* 40(11): 654-55
 22. Argal A and Pathak AK(2005). Anti-diarrhoeal activity of *Calotropis gigantea* flowers. *Indian J. Nat. Prod.*21(3): 42-44
 23. Srivastava SR, Keshri G, Bhargavan B, Singh C, Singh MM(2007). Pregnancy interceptive activity of the roots of *Calotropis gigantea* Linn. in rats. *Contraception.* 75(4):318-22
 24. Adak M, Gupta JK(2006). Evaluation of anti-inflammatory activity of *Calotropis gigantea* (AKANDA) in various biological system. *Nepal Med Coll J.* 8(3):156-61
 25. Pathak AK, Argal A(2007). Analgesic activity of *Calotropis gigantea* flower. *Fitoterapia.*78(1): 40-2
 26. Chitme HR, Chandra R, Kaushik S(2005). Evaluation of antipyretic activity of *Calotropis gigantea* (Asclepiadaceae) in experimental animals. *Phytother Res.*19(5): 454-6
 27. Kiuchi F, Fukao Y, Maruyana T, Obata T, Tanak M, Sasaki T, Mitkage M, Haque ME, Tsuda Y(1998). Cytotoxic principles of a Bangladeshi crude drug, akondmul (roots of *Calotropis gigantea* L.) .*Chem. Pharm. Bull (Tokyo)* . 46(3): 528-30
 28. Lhinhatrakool T, Sutthivaiyakit S(2006). 19-Nor- and 18, 20-epoxy-cardenolides from the leaves of *Calotropis gigantea*. *J Nat Prod.* 69(8):1249-51
 29. Argal A, Pathak AK(2006). CNS activity of *Calotropis gigantean* roots. *J Ethnopharmacol.* 106(1):142-5
 30. Banu MJ, Nellaippan K, Dhandayuthapani S(1992). Mitochondrial malate dehydrogenase and malic enzyme of a filarial worm *Setaria digitata*: some properties and effects of drugs and herbal extracts. *Jpn J Med Sci Biol.* 45(3):137-50
 31. Ali NA, Jülich WD, Kusnick C, Lindequist U(2001).Screening of Yemeni medicinal plants for antibacterial and cytotoxic activities. *J Ethnopharmacol.*74(2):173-9
 32. Haque MA, Nakakita H, Ikenaga H, Sota N(2000). Development-inhibiting activity of some tropical plants against *Sitophilus zeamais* Motschulsky (Coleoptera: Curculionidae) J. *Stored Prod Res.* 36(3):281-287
 33. Chitme HR, Chandra R , Kaushik S(2004). Studies on anti-diarrhoeal activity of *Calotropis gigantea* R. Br. in experimental animals. *J. Pharm. Pharmaceut. Sci.* 7(1):70-75
