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Pharmacology of Natural Products: An recent approach on *Calotropis gigantea* and *Calotropis procera*

Farmacología de productos naturales: un enfoque reciente en *Calotropis gigantea* y *Calotropis procera*

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ABSTRACT

Introduction: Since ancient times, people have used medicinal plants to treat varied diseases. Medicinal plants are the important source of drugs, and many of them that are currently available in the pharmaceutical market are obtained from plant sources. *Calotropis gigantea* and *Calotropis procera* are small shrub, which are used conventionally to treat many diseases such as cancer, diabetes and intestinal disease in African and Asian countries. There have been always an increased focus on primary health care: basic health care which is effective and affordable by developing countries.

Objective: This paper aims to review the pharmacological and pharmacognostical features of *Calotropis gigantea* and *Calotropis procera*

Method: Brief review on recent literature carried out using Scopus, Google scholar.

Result and Discussion: Several studies provide evidence of their antioxidant, analgesic, anti-inflammatory, anti-diarrheal, anticonvulsant, anti-malarial, hepatoprotective, antitumor, antimicrobial and anti-nociceptive properties.

Conclusion: Species of *Calotropis* not widely recognized showed different pharmacological actions, due to the presence of effective secondary metabolites.

Key words: *Calotropis gigantea*; *Calotropis procera*; Pharmacognosy; Pharmacology.

RESUMEN

Introducción: Desde la antigüedad, las personas han utilizado plantas medicinales para tratar diversas enfermedades. Las plantas medicinales son la fuente importante de los fármacos, y muchas de ellas, que están actualmente disponibles en el mercado farmacéutico, se obtienen de fuentes vegetales. *Calotropis gigantea y Calotropis procera* son arbustos pequeños que se utilizan convencionalmente para tratar muchas enfermedades como el cáncer, la diabetes y las enfermedades intestinales en países africanos y asiáticos. Siempre se ha prestado una mayor atención a la Atención Primaria de salud: la atención básica de la salud es eficaz y asequible para los países en desarrollo.

Objetivos:

Este trabajo tiene como objetivo revisar las características farmacológicas y farmacognosóticas de *Calotropis gigantea* y *Calotropis procera*.

Método: Breve revisión de la literatura reciente realizada utilizando Scopus, Google scholar.

Resultado y discusión: Varios estudios proporcionan evidencia de sus propiedades antioxidantes, analgésicas, antiinflamatorias, antidiarreicas, anticonvulsivas, antipalúdicas, hepatoprotectoras, antitumorales, antimicrobianas y anti-nociceptivas.

Conclusión: Especies de *Calotropis* no ampliamente reconocido mostraron diferentes acciones farmacológicas, debido a la presencia de metabolitos secundarios efectivos.

Palabras clave: *Calotropis gigantea; Calotropis procera;* Farmacognosia; Farmacología.

INTRODUCTION

From ancient time plants were used for the treatment of several diseases. Ayurveda reveals the importance of Arka species (*Calotropis gigantea* and *Calotropis procera*), figure 1. both the species were used as an alternative to one another and possess similar effects. The plants were widely used in the Ayurveda, Unani and Afghan medicines to treat several diseases, namely tumors, leucoderma, ulcer, piles, leprosy, dysentery, asthma, spleen and liver.[1,2] *Calotropis* species are evergreen perennial shrub reaching 2.4-3 m high; bark yellowish white, furrowed, rough, corky; branches stout, terete, less or more covered with fine appraised cottony pubescence. Leaves are opposite-decussate, sessile, elliptic-oblong or obviate-oblong, acute, thick and pale in green, clothed beneath and less or more above with fine cottony tomentum, about 10-20 by 3.8-10 cm, base narrow, chordate. Flowers are regular, bisexual, purple or light greenish yellow with faint odor, 3.8-5 cm dia. In umbellate lateral cymes; periodicals are much longer than the flowers, the pedicels are overspread with cottony wool, buds ovoid, calyx divided to the base, consist 5 white sepals 4mm, ovate, acute, cottony, corolla 2 cm long, lobes of the corona 1.3 cm long, broadly in 5mm at the middle, smaller than the column, slightly thickened margin, the apex rounded with two obtuse auricles just below it. Follicles are 9-10 cm in length, wide, abundant, plump ventricose, green. Green color spongy fruits consist of light brown seeds 6 x 5 mm. Ovate, flattened, arrow margined, minutely tomentose, brown; coma 2.5-3.2 cm long and the hairs at the one end. The roots are deep plump taproot with less lateral roots near surface. 3 Figure 1. a. *Calotropis gigantea*, b. *Calotropis procera*.

Figure 1. a. ***Calotropis gigantea***

b. ***Calotropis procera***

The latex is used in different conditions as leucoderma, tumors, expectorant, analgesic, anticonvulsant, anti-inflammatory, piles, leprosy, asthma, enlargement of spleen and liver, joint swelling.[4, 5] The use of different parts of Calotropis species recorded for a number of activities like jaundice, lice treatment, headache, sore gums and mouth, ulcer, aborficient, anthelmintic, cough and dysentery.[6] Its taxonomy[7, 8] is presented in table 1.

Geographic Distribution:

Calotropis species are drought-resistant, relatively salt and drought-tolerant. Air pollination generally takes place and also with the animals. Such species easily take place as a weed to the roadside, lagoon edge and in overgrazed native pastures. It also grows easily in sandy soil in areas of low rainfall. *Calotropis* species are inhabited to India, Nepal, Pakistan, Iran, Iraq, Oman, Yemen, Vietnam, Afghanistan and Zimbabwe.[9,10]

Traditional Uses:

Calotropis species is used for the treatment of bronchitis, pain, asthma, leprosy, ulcers, piles, spleen, tumors, liver, abdomen and dyspepsia; it is also used frequently for cold, fever, diarrhea, rheumatism, indigestion, eczema and jaundice. Different parts of the plant were used for the treatment of several diseases such as stem for skin disease, intestinal worms, leprosy, leucoderma; the roots are used for the treatment of leprosy, asthma, cough, elephantiasis, rheumatism and diarrhea; latex and leaves are used for swelling and joint pain; oil massage can be used for paralyzed part; juice of *Calotropis* was used for purgation.[11]

PHARMACOLOGICAL ASPECTS

Antibacterial and Antifungal Potentials:

Calotropis gigantea ethyl acetate extract was used for the isolation of 1Di-(2-ethylhexyl) phthalate (compound 1) and anhydrosophoradiol-3-acetate (compound 2). For anti-bacterial activity study isolated compound, *Kanamycin* and *Nystatin* disc used as a positive control for the study. Antibacterial activity of sample were tested by using 30, 60 and 90 µg/disc and for antifungal 100, 200 and 400 µg/disc used. The 1Di-(2-ethylhexyl) phthalate (Compound 1) showed better activity when compared against gram positive (*Bacillus subtilis, Staphylococcus aureus* and *Sarcina lutea*) and gram negative (*Shigella sonnei, Escherchia coli, Shigella shiga* and *Shigella dysenteriae*). Compound 1 was inactive against *B.megaterium*, compound 2 showed medium activity against *S. aureus, S.lutea* and *E.Coli*. Compound 1 showed lowest MIC at 32 µg/ml against *B. subtilis* and *S. lutea*, where as compound 2 showed lowest MIC at 64 µg/ml against *S. aureus*. The test extract for antifungal activity produce a zone of inhibition between 7 mm to 15 mm against *A. flavus* and *A. fumigates*, whereas compound 1 exhibits activity against *A. flavus*. Compound 2 does not show any activity. [12]

Whereas the ethanolic extract of *C.gigantea* were tested against of *E. coli, Salmonella typhi, Pseudomonas aeruginosa, Vibrio cholerae* and *Staphylococcus aureus* showed high antibacterial activity at 8-11 mm range.[13]

Calotropis procera-silver nanoparticles were prepared by mixing 3% extract of latex and 3% silver nitrate solution, characterization of silver nanoparticles done by using X-ray diffraction, UV-visible spectrophotometer, transmission electron microscopy and fourier transform infrared spectroscopy. The silver nanoparticles were evaluated against bacteria (*Pseudomnas aeruginosa, Escherichia coli* and *Serratia sp*.) and pathogenic fungi (*Aspergillus terreus, Candida albicans* and *Trichophyton rubrum*). The silver nanoparticles exhibit strong antibacterial and antifungal activity. The silver nanoparticle shows the strong antibacterial potential by reducing the silver ions (Ag^+ to Ag^0). [14]

Anti-Diarrheal Effect:

Dried latex similar to phenylbutazone and atropine produced a marked decrease in defecation frequency and severity of diarrhea in 80% castor oil treated rats. For detail evaluation anti-diarrheal activity of C. *procera* latex different parameters were used like intestinal transit time, castor oil-induced fluid accumulation (enteropooling) and electrolyte concentration in intestinal fluid. The dried latex showed 27-37 % reduction in intestinal transit when compared to castor oil treated and normal animals. Unlike atropine dried latex of *C. Procera* inhibits castor oil induced enteropooling significantly. However the dry latex did not alter the electrolyte balance in the intestinal fluid when compared to castor oil-treated rats.[15]

Whereas the ethanolic root extract of *C. gigantea* used to study the anti-diarrheal potential. 100 mg/kg, 200 mg/kg and 400 mg/kg doses of extract were used. The 200 and 400 mg/kg dose showed appreciable anti-diarrheal activity.[16]

The 70% hydroethanolic extract of *C. procera* (*CP*) and *C. gigantea* (*CG*) leaves were used for castor oil induced diarrhea model for the study. The extract reduced the number of fecal boluses and improved the severity of the diarrhea condition. Dose dependant increase in latent period also observed. The CP showed a more prominent effect than the CG extract with reference to loperamide. [17]

Hepatoprotective Activity:

From 50% ethanolic stems extract of *C. gigantea* were used for the study. Wistar rats with 250 and 500 mg/kg dose of extract, 2 mg/kg dose of carbon tetrachloride were used. Changes in biochemical parameters like Aspartate transaminase (AST), Alanine aminotransferase (ALT), Glutathione (GSH), Lipid peroxidation (LPO), Superoxide dismutase (SOD), Catalase (CAT) and Glutathione peroxidase GPx were evaluated. ALT and AST levels significantly decrease in extract treated rats. GSH, SOD, CAT, GPx and catalase level significantly increased in extract and silymarin treated rats, Thiobarbituric acid reactive substances (TBARS) level significantly reduced by extract and silymarin. The histological study showed fatty changes, tissue necrosis and infiltration of lymphocytes and kupffer cells near to central vein and cellular damage in CCl4 treated rats. Whereas animals pretreated with extract and subsequently given CCl4 showed the normal architecture of the liver. [18]

A 70 % aqueous ethanolic extract of *C. procera* flowers used to study hepato-protection against paracetamol-induced hepatitis model. Biochemical changes in markers of hepatic damage, like Serum glutamic oxaloacetic transaminase (SGOT), Serum glutamic pyruvic transaminase (SGPT), bilirubin, Alkaline phosphatase (ALP), cholesterol, High density lipoprotein (HDL), and tissue glutathione (GSH), were evaluated in both treated and untreated groups. Paracetamol (2 gm/kg) reported to enhance the biochemical markers like SGOT, SGPT, bilirubin, ALP and cholesterol levels, HDL serum levels reduce and the extract treated group showed the tissue level of GSH and also dose-dependently restored the altered levels of biochemical markers to almost normal levels. [19]

Calotropis procera latex used for evaluation of anti-oxidant and anti-apoptotic on catfish. The chemical pollutant 4-nonylphenol exposed to catfish. The apoptotic cell raised the level of different enzymes like catalase, acetylcholinesterase, super oxide dismutase, glutathione S-transferase and cortisol significantly and latex treated cells showed significantly reduced the levels of these enzymes. Latex treated group showed total phenol content, reducing power and total anti-oxidant capacity increased significantly when compared 4-nonylphenol treated. It showed that the *Calotropis procera* latex possesses anti-oxidant and anti-apoptotic activity against the 4-nonylphenol toxicant. [20]

Antitumor studies:

Ehrlich's ascites carcinoma (EAC) model used to study anti-tumor activity of isolated compound anhydrosophoradiol-3-acetate (A3A) from flowers of *C. gigantea* was in Swiss albino mice.

The isolated and purified compound characterized by mass and NMR spectral data. The effects of A3A at 10 and 20 mg/kg dose on survival time, viable cell count and body weight changes studied, the treated mice showed increased in life span, and decreased the viable tumor cell count significantly.[21]

Ehrlich's ascites carcinoma (EAC) model used to study anti-tumor activity of methanolic root extract of *C. gigantea* in Swiss albino mice. The methanolic extract, petroleum ether fraction, chloroform fraction was used. Methanolic extract at 10 and 20 mg/kg, petroleum ether extract at 80 mg/kg and chloroform extract at 20, 40 mg/kg showed decreased the viable cells significantly. The highest life span increased by chloroform extract (40 mg/kg) it was 57.70% when compared with the control group, whereas in standard bleomycin it was 96.97%. The significant decrease in ALP and SGOT level observed in extract treated mice when compared with the standard. Methanolic extract increased SGPT when compared with tumor bearing mice.[22]

The HepG2 cancer cells used for anti-cancer study against different extract like methanolic extract (CM), hexane extract (CH), aqueous extract (CW) and ethylacetate extract (CE) of root of *C. Procera*. Tetrazolium bromide (MTT) calorimetry study used for the cellular proliferation activities. Different doses of extract 1.0, 5.0, 10.0 ad 25.0 µg/ml showed CM, CH and CE possessed cytotoxicity, whereas CW did not show any cytotoxic activity. The extract treated cells exhibits typical changes in morphological characters of apoptosis. The plant extract arrests the HepG2 cell at S phase and prevent them entering to G2/M phase and initiated apoptosis.[23]

Anthelmintic Activity:

The *Calotropis procera* flower extract was compared with levamisole for its in-vitro and in-vivo anthelmintic activity. The in-vitro study showed that the crude aqueous extract (CAE) and crude methanolic extract (CME) of flowers showed a significant effect ($P<0.05$) on live Hemonchus. The crude powder (CA) and extract were administered to sheep which was naturally infected with gastrointestinal nematodes for in-vivo study. The CAE and CP treated sheep showed 88.4 and 77.8 % reduction in percentage of egg count at 3000 mg/kg, was recorded on 7 and 10 post-treatment respectively. Whereas CME treated sheep showed the reduction percentage in egg count only about 20.9 %. From the above findings, it was concluded that the plant extract showed significant activity against nematode, where as in levamisole it was 97.8-100 %. [24]

The methanolic extract of *Calotropis gigantea* leaves showed prominent anthelmintic activity when compared against

Indian earthworms. The 10.0, 15.0 and 20.0 mg/ml extract was used for the evaluation of anthelmintic activity. The 20.0 mg/ml dose showed highest activity when compared with Albendazole. [25]

Anti-Hyperglycemic Effect:

Hypoglycemic activity of *C. Gigantea* leaves extract was studied, diabetes induced by standard drug streptozotocin. The extract administered for 21 days it lowered the Total Cholesterol (TC), Triglycerides (TG), Very Low Density Lipoprotein (VLDL), Low Density Lipoprotein (LDL) and enhance cardio protective High Density Lipoprotein (HDL) level in treated animals. STZ treated animal showed increases in kidney weight due to proliferation of glomerular cell while extract treated animal showed decreases in kidney weight near to normal value. Urea and creatinine level significantly reduced in extract and STZ treated animal. Extract treated animal prevent elevation of tissue lipid in diabetic animal. Histopathological study showed prominent effects of extract treated animal when compared to control groups. [26]

The hydro alcoholic extract of *Calotropis procera* leaves was used for the study. Extract at a dose of 300 and 600 mg/kg/day, insulin (6U, s.c) or metformin (500 mg/kg/day) were administered to streptozotocin induced diabetes rats for four weeks. Result showed significant decreased in food intake in the group receiving extract (300mg/kg/day). Whereas group treated with 600 mg/kg/day showed decreases in food intake only in the first week of the study when compared with diabetic control. The animals treated with extract at 300 and 600 mg/kg showed significantly reduced in uric acid, ALT and AST level when compared with the diabetic control group, and increases in creatinine, total cholesterol and triglycerides. The extract showed significantly increased in adipose tissue and Soleus muscle relative mass, but decrease relative mass of the kidney when compared with the diabetic control group.[27]

Anti-Ulcer Activity:

The hydro alcoholic and chloroform extract of *Calotropis procera* stem bark was used for evaluation of anti-ulcer and anti-inflammatory activity. The carragennan-induced paw oedema model used for anti-inflammatory activity and ulcer induced by aspirin and ethanol at for evaluation of anti-ulcer activity in albino rats. The extract treated animals showed significant activity when compared to standard drugs. The anti-ulcer activity of extract was proved by histopathological examination.[28]

The chloroform and ethanol extract of *Calotropis gigantea* flowers used for the evaluation of anti-ulcer and anti-inflammatory activity. The carrageenan-induced paw oedema and cotton pellet induced granuloma model used for the study of anti-inflammatory activity. The aspirin and ranitidine used for the study of anti-ulcer activity. The extract significantly reduced rat paw oedema, dry weight granuloma and both the extract treated group significantly protect from pyloric ligation and aspirin induced gastric ulcers.[29]

Anti-Convulsant and Sedative Activity:

To study anti-convulsant and sedative activity in mouse the latex proteins of *Calotropis procera* were used. The convulsions were induced by pentylenetetrazol, Pilocarpine and strychnine for the anti-convulsion activity and the pentobarbital induced sleep model used for the sedative potential determination. The plant extract does not show significant effects on Pilocarpine and strychnine induced convulsion when compared with standards. The plant extract showed significant effect in pentylenetetrazol induced seizures model the extract showed at high dose (50 or 100 mg/kg), the extract proteins showed central depressant property.[30]

For the evaluation of anticonvulsant, sedative and muscle relaxant activity the ethanol extract of *Calotropis gigantea* was orally administered to the experimental animal. Strychnine and maximal electroshock induced convulsion models were used for the study. Actophotometer and Rota rod apparatus were used for the evaluation of sedative actions. The extract treated animals showed significant anticonvulsant activity against maximal electroshock induced convulsion, but no marked effect were observed against strychnine model. The extract showed significantly muscle relaxant activity and decrease in motor coordination in mice reported. [31]

Anti-malarial activity:

The ethanolic extracts of *Calotropis procera* leaves were fractioned with petroleum ether, chloroform and ethyl acetate respectively. The extract was evaluated averse to brine shrimp larvae and also subjected to anti-malarial parasites bioassay. The extract showed anti-malarial activity.[32]

The mosquito repellant activity of *Calotropis gigantea* flower extract was studied. The different extract of the plant was used for the study against the three day blood starved female *Culex quinquefasciatus mosquito*. The ethanolic extract showed high mosquito repellant activity against the female *Culex quinquefasciatus mosquito* as compared to the petroleum ether and chloroform extract. The dose dependant mosquito repellant activity of the extract was found[33] .

Wound healing activity:

C. gigantea root bark extract was used for the evaluation of wound healing activity. The different models like a dead space wound, incision and excision were used for the study. The extract was formulated in ointment base and topically applied on albino rat in excision model. Ethanol extract of *C. gigantea* was administered orally at different doses in incision model and dead space wound models. Excision model showed an increased percentage of wound contraction, decreased fibrosis. Breaking strength was increased in incision and dead space wound model[34].

The *C. procera* latex was used for the wound healing study. Excision was made on the back of guinea pig. Sterile preparation of latex was made and applied daily two times for 7 days. The latex treated animal showed increasing collagen fibers, DNA and increased protein synthesis resulting in the healing of the wound area [35].

CONCLUSION

It is estimated by the World Health Organization that about 80 % of the population in developing countries rely on herbal medicines for primary health care needs. Recently botanical and traditional uses of organic compounds, especially which are obtained from plant origin, had received greater affection because of their efficacy and safety for human consumption.

A detailed review of published data on *Calotropis procera* and *Calotropis gigantea* depicts their popularity as a remedy in different cultural groups, also Ayurveda and traditional practitioners for treating a range of disease. Many of researcher are mainly focusing on the therapeutic potential of *Calotropis* species as it is considered to have many more therapeutic potential than which is currently known.

REFERENCES

1. Kiritikar K, Basu B. Indian Medicinal Plants. *Int B Distrib*. 1987;III(2 Edn):1432–6.
2. Bairagi SM, Aher AA, Nema N, Pathan IB. Evaluation of anti-diarrhoeal activity of the leaves extract of *Ficus Microcarpa L. (Moraceae*). *Marmara Pharmaceutical Journal*. 2014;3(18):135-135. Doi:10.12991/mpj.2014187240
3. Rahimi M. Pharmacognostical Aspects and Pharmacological activities of *Calotropis procera*. *Bulletin of Environment, Pharmacology and Life Sciences*. 2015;4(2):156-162.
4. Nalwaya N, Pokharna G, Deb L, Jain NK. Wound healing activity of latex of *Calotropis gigantea*. *International Journal of Pharmacy and Pharmaceutical Sciences*. 2009;(1):176–81.
5. Arya S, Kumar VL. Antiinflammatory efficacy of extracts of latex of *Calotropis procera* against different mediators of inflammation. *Mediators of Inflammation*. 2005;2005(4):228–32. Doi:10.1155/MI.2005.228
6. Verma VN. The chemical study of *Calotropis*. International Letters of Chemistry, Physics and Astronomy. 2014;1:74-90. 10.18052/www.scipress.com/ILCPA.20.74
7. Oloumi H. Phytochemistry and Ethno-Pharmaceutics of *Calotropis procera*. *Ethno-Pharmaceutical Products*. 2014;1(2):1–8.
8. Joseph B, George J, Jeevitha M V, Charles S. Pharmacological and biological overview on *Calotropis gigantea*: a comprehensive review. *International Research Journal Pharmaceutical and Applied Sciences* [Internet]. 2013;3(5):219-223, 5 . Available from: http://www.irjpas.com/zip.php?file=File_Folder/IRJPAS 3(5)219-223.pdf&id=308&quat=3
9. Sharma AK, Kharb R, Kaur R. Pharmacognostical aspects of *Calotropis procera* (Ait.) R. Br. *International Journal of Pharma and Bio Sciences*. 2011;2(3):480–8.
10. Parihar G, Sharma A, Ghule S, Sharma P, Deshmukh P, Srivastava DN. Anti inflammatory effect of *Calotropis procera* root bark extract . *Asian Journal of Pharmacy and Life Science*. 2011;1(1):29–44.
11. Evans WC. Trease and Evans' Pharmacognosy.2005:41-47.
12. Habib MR, Karim MR. Antimicrobial and Cytotoxic Activity of Di-(2-ethylhexyl) Phthalate and Anhydrosophoradiol-3-acetate Isolated from *Calotropis gigantea* (*Linn*.) Flower. *Korean Society of Mycology*. 2009;37(1):31–6.
13. Radhakrishnan K, Thangamani P, Balakrishnan V. Antibacterial and phytochemical analysis of stem and root extracts of *Calotropis gigantea* against selected pathogens. *Malaya Journal of Biosciences*. 2014;1(1):49–55. Available from: http://www.malayabiosciences.com/download.php?id=10
14. Mohamed NH, Ismail MA, Abdel-Mageed WM, Mohamed Shoreit AA. Antimicrobial activity of latex silver nanoparticles using *Calotropis procera*. *Asian Pacific Journal of Tropical Biomedicine* . 2014;4(11):876–83. Doi:10.12980/APJTB.4.201414B216, Available from: http://linkinghub.elsevier.com/retrieve/pii/S2221169115300344
15. Kumar VL, Basu N. Anti-inflammatory activity of the latex of *Calotropis procera*. *Journal of Ethnopharmacology*. 1994;44(2):123–5.
16. Rahman R, Rahman F, Shashank B, Rajasshekar S, Gangadhar B, Chandrashekhar S, Evaluation of *Calotropis Gigantea* root in experimental diarrhoea. *International Journal of Pharmacy & Industrial Research*. 2012; 2(1):10-15.
17. Murti Y, Singh SP, Devender P. Comparison of anti-diarrheal activity of hydroethanolic extract of *Calotropis Procera* and *Calotropis Gigantea* leaves. *Journal ofPharmaceutical and Scientific Innovation*. 2012 ;1(4):32-33.

18. Lodhi G, Singh HK, Pant KK, Hussain Z. Hepatoprotective effects of *Calotropis gigantea* extract against carbon tetrachloride induced liver injury in rats. *Acta Pharmaceutica*. 2009;59(1):89–96. Doi: 10.2478/v10007-009-0002-2.

19. Ramachandra Setty S, Quereshi AA, Viswanath Swamy AHM, Patil T, Prakash T, Prabhu K, *et al*.. Hepatoprotective activity of *Calotropis procera* flowers against paracetamol-induced hepatic injury in rats. *Fitoterapia*. 2007;78(7–8):451–4. Doi:10.1016/j.fitote.2006.11.022

20. Sayed AELD, Mohamed NH, Ismail MA, Abdel-Mageed WM, Shoreit AAM. Antioxidant and antiapoptotic activities of *Calotropis procera* latex on Catfish (*Clarias gariepinus*) exposed to toxic 4-nonylphenol. *Ecotoxicology and Environmental Safety*. 2016;128:189–94. Doi: 10.1016/j.ecoenv.2016.02.023

21. Habib MR, Karim MR. Effect of anhydrosophoradiol-3-acetate of *Calotropis gigantea* (*Linn*.) flower as antitumoric agent against Ehrlich's ascites carcinoma in mice, *Pharmacological Reports*. 2013; 65: 761-767.

22. Habib MR, Karim MR. Evaluation of antitumour activity of *Calotropis gigantea L*. root bark against Ehrlich ascites carcinoma in Swiss albino mice. *Asian Pacific Journal of Tropical Medicine*. 2011;4(10):786–90. Doi:10.1016/S1995-7645(11)60194-6.

23. Mathur R, Gupta SK, Mathur SR, Velpandian T. Anti-tumor studies with extracts of *Calotropis procera (Ait.)* R.Br. root employing Hep2 cells and their possible mechanism of action. *Indian Journal of Experimental Biology*. 2009;47(5):343–8.

24. Iqbal Z, Lateef M, Jabbar A, Muhammad G, Khan MN. Anthelmintic activity of *Calotropis procera (Ait*.) Ait. F. flowers in sheep. *Journal of Ethnopharmacology*. 2005;102(2):256–61. Doi: 10.1016/j.jep.2005.06.022

25. Dongare SD, Mali SS, Dhanawade PP, Patrekar PV. In-vitro anthelmintic activity of *Calotropis Gigantea* against Indian earth worm Pheretima Posthuma. *International Journal of Institutional Pharmacy and Life Sciences*.2015;5(1):117-123.

26. Singh K, Rao V, Hussain Z, Pahuja. Evaluation of anti-diabetic and antioxidant activity of extract of *Calotropis Gigantea* linn in streptozotocin induced diabetic rats. *The Pharma Innovation*. 2014; 2(11):1-12.

27. Mário C.L. Neto, Carlos F. B. de Vasconcelos, Valerium N. Thijan, Germana F. R. Caldas, Alice V. Araujo, Joao H. Costa-Silva. Evaluation of antihyperglycaemic activity of *Calotropis Procera* leaves extract on streptozotocin-induced diabetes in wistar rats. *Revista Brasileira Farmacognosia*. 2013;23:913-919. Doi: 10.1590/S0102-695X2013000600008.

28. Tour NS, Talele GS. Gastric antiulcer and anti-inflammatory activities of *Calotropis Procera* stem bark. *Revista Brasileira Farmacognosia Brazilian Journal Pharmacognosy*. 2011;21(6): 1118-1126. Doi:10.1590/S0102- 695X2011005000175.

29. Kshirsagar A. Patil PA, Purnima A, Hulkoti B. Anti-inflammatory and anti-ulcer effects of *Calotropis Gigantea* R. Br. Flowers on rodent. *Journal of Natural Remedies*. 2008; 8(2):183-190. Doi:10.18311/jnr/2008/332

30. Raquel Cristina de Sousa Lima , Márcia Calheiros Chaves Silva , Carlos Clayton Torres Aguiar, Edna Maria Camelo Chaves, Katia Cilene Ferreira Dias, Danielle Silveira Macedo. Anticonvulsant action of *Calotropis procera* latex proteins. *Epilepsy & Behavior*. 2012; 23: 123–126. Doi:10.1016/j.yebeh.2011.11.008

31. Ghule SD, Vidyasagar G, Bhandari A, Sharma P, Gunjal AP. CNS activity of leaves extract of *Calotropis gigantea. Asian Pacific Journal of Tropical Disease*. 2014;4(S2):S902–5. Doi:10.1016/S2222-1808(14)60755-6

32. Mudi SY, Bukar A. Anti-plasmodia activity of leaf extract of *Calotropis Procera linn*. *Biokemostri*, Nigeria. 2011;23(1):29-34.

33. Dhivya R, Manimegalai K, Mosquito repellent activity of *Calotropis gigantea (Apocynaceae*) flower extracts against the filarial vector *Culex Quinquefasciatus*. *Hygeia:Journal For Drugs And Medicine*. 2013; 5 (2): 56-62.

34. Deshmukh PT, Fernandes J, Atul A, Toppo E. Wound healing activity of *Calotropis gigantea* root bark in rats. *Journal of Ethnopharmacology*. 2009;125(1):178–81. Doi: 10.1016/j.jep.2009.06.007

35. Rasik AM, Raghubir R, Gupta A, Shukla A, Dubey MP, Srivastava S, *et al*.. Healing potential of *Calotropis procera* on dermal wounds in Guinea pigs. *J Ethnopharmacology*. 1999;68(1–3):261–6.

Table 1-Taxonomy of *Calotropis procera* **and** *Calotropis gigantea*

Kingdom	**Plantae**	**Plantae**
Subkingdom	Tracheobionta-Vascular plants	Tracheobionta-Vascular plants
Superdivision	Spermatophyta -Seed plant	Spermatophyta -Seed plant
Division	Magnoliopsida -Dicotyledons	Magnoliopsida -Dicotyledons
Subclass	Asteridae	Magnoliopsida
Other	Gentianales	Gentianales
Family	Asclepiadaceae -Milkweed	Apocynaceae- Milkweed
Genus	Calotropis R. Br.	Calotropis R. Br.
Species	*Calotropis Procera* (Aiton)	*Calotropis gigantea*