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Pharmacological, biological activities and phytochemical constituents of *Calotropis gigantea*

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ABSTRACT

Calotropis gigantean is a class of *calotropis* belonging to the family Apocynaceae. C. Gigantea is resident in Cambodia, Indonesia, Malaysia, the Philippines, Thailand, Sri Lanka, India, China, Pakistan, Nepal, BoocBooc in Somalia and tropical Africa. This herb produced large amount of latex thus includes in latex bearing plants generally known as giant milk weed. *C. Gigantean* is known for a multiplicity of pharmacological properties in ancient medicinal system and utilizes to cure a various disease. From few decades, it is broadly studied for its pharmacological as well as medicinal properties by highly developed scientific techniques and various medicinally active compounds obtained from the different parts of the plant and this are analysed pharmacologically. The plant is reported for its various activities like: analgesic, antimicrobial, antioxidant, anti-pyretic, insecticidal, cytotoxicity, hepatoprotective, pregnancy interceptive properties, pro-coagulant activity and wound healing, Antivenom activity, CNS activity. The therapeutic properties of calotropis gigantean plant signify it as aimportant source of therapeutic compound. This study is combined information about the ethnobotany, pharmacology, phytochemistry and natural medicinal activities of the C. *gigantea*.

Keywords: *Calotropis gigantea*, Antimicrobial activity, Cytotoxicity, Ethnobotany, Phytochemistry.

INTRODUCTION

History:

Calotropis gigantea is anative plant of India, China and Malaysia and distributed in the following countries: Afghanistan, Algeria, Antigua and Barbuda, Argentina, Australia Burkina Faso, Antilles, Arab Jamahiriya Bahamas, Barbados, Bolivia, Brazil, Cameroon, Chad, Cote d'Ivoire, Colombia, Cuba, Democratic Republic of Congo, Dominica, Dominican Republic, Egypt, Eritrea, Ethiopia, Ecuador, French Guinea, Grenada, Guadeloupe, Guatemala, Guyana Paraguay Haiti, Gambia, Ghana, Honduras, India, Iran, Iraq, Israel, Jamaica, Kenya, Kuwait, Lebanon, Libyan, Martinique, Mexico, Montserrat, Mauritania, Morocco, Mozambique, Myanmar, Mali, Nepal, Niger, Nigeria, Netherlands Nicaragua, Oman, Pakistan, Panama, Peru, Puerto Rico, Saudi Arabia, Senegal, Somalia, Sudan, Syrian Arab Republic, StLucia, St Vincent, Surinam, Thailand, Tanzania, Trinidad Uganda, Uruguay, United Arab emirates, Vietnam, Venezuela, Yemen. [1]

Scientific classification: -

Kingdom	:	Planatae
Subkingdom	:	*Tracheobionta*

Superdivision	:	*Spermatophyta*
Division	:	*Magnoliophyta*
Class	:	Dicotyledones
Sub class	:	*Asteridae*
Series	:	Bicarpellatae
Order	:	Gentian ales
Family	:	Apocynaceae
Subfamily	:	Asclepidiaceae
Genus	:	*Calotropis*
Species	:	*Calotropis gigantean*

Vernacular Names: -

Common names: Crown Flower, Swallow Wort, Giant Milkweed,

Hindi: Aak, Alarkh, Akanda, Bara Akand, Safedaak, Sveta Arka, Madar,

Gujarati: Aakando

English: Bowstring hemp, crown plant, Crown flower, giant Indian milkweed, madar.

Malaysia: kemengu Remiga, rembega,

Indonesia: Bidhuri, sidaguri, Rubik.

Philippines: Kapal-kapal.

Laos: dokkap, dokhak, Kok may,

Thailand: paanthuean (northern), Po thuean, rak (central).

French: Faux arbre de soie, mercure vegetal

Morphology and Distribution

Calotropis gigantea is a minor tree or a shrub, 4–10m tall. Its stem is straight, about 20 cm in diameter. The leavesare broadly elliptical in shape, with the size of 9–20 cm × 6–12.5 cm but subsessile. The inflorescence stalk is 5–12 cm elongated; the stalk of flower is 2.5–4 cm extended. Sepal lobes are broadlyegg-shaped with a size of 4–6 mm × 2-3 mm. The diameter of Petal is 2.5–4cm. The plant hasbunches of waxy flowers that are either buff white or lavender in colour. Each flower contains of fivepointed petals and a tiny, stylish "crown" rising from thecentre. The plant has elliptical, lightgreen leaves and milky stem. The petal parts are generally triangular 5–8 mm ×10–15 mm; they are creamand pale lavender coloured near the tips. Calotropis is drought resistant shrub, it is naturally grows up to 900 meters all over the country [2]. It is a plant which is not consumed byanimals [3]. It grow well on poor soils particularly where overgrazing has removed competition from native grasses [4].

Herbs and plants have been in use as a source of therapeutically active compounds in old medicinal system since prehistoric time [5]. There is a continuous needed of the growth of new effective antimicrobial drugs because of the coming out of new infectious diseases and drug resistance [6] The plant opposed tovariouscommunicable diseases and to the intenseunkindsituation are partly recognized to the presence of hydrolytic enzymes of the latex especially proteases [7, 8]

Table 1: Therapeutic activities of phytoconstituentsisolated from Calotropisgigantean [9].

Species/plant parts	Compounds isolated	Therapeutic activity
Root bark	Milky sap extract, β-sitosterol , Sterols Giganticine Stigmasterol,	Anti syphilis, Purgative, anti-worm, insecticidal, antipyretic, contraceptive, anti-oxidant Anticoccidial, anti-diarrhea, analgesic, anti-tumor Anti metastatic, anticancer,
Latex of Flower	20-Epoxy-cardenolides Di-(2-ethylhexyl) phthalate Glyceryl mono-oleolyl-2-phosphate Proceranol 2. Glyceryl-1,2-dicapriate-3-phosphate Procerursenyl acetate 1.Methyl myrisate, 19-Nor-and18,	Pro-coagulant Fibriogenolytic, Cytotoxic and antimicrobial, wound healing, ant-proliferative Cytotoxic, anti-oxidant Toxic, pesticidal.
Leaves	19-Nor- and 18,20-Epoxy-cardenolides, 16alpha-hydroxycal actinic acid methyl ester, 15beta-hydroxycardenolides	anti-inflammatory myocardium, stimulatory effect on smooth muscle motility, Analgesic, antiplasmodial, ant proliferative,
Flower	Di-(2-ethylhexyl) Phthalate Anhydrosophoradiol-3-acetate	sedative, antipyretic Analgesic, anti-convulsant, ant arthritis,
Dried Latex	Calotropins DI, Calotropins DII. Calotropain-F1 andCalotropain-FII 3′-methylbutanoates of α-amyrin, ψ-taraxasterol,	allergic, larvicidal, anti-helmintic, ascaricidal, Protective to oxidative stress and renal damage, insecticidal, schizonticidal, anti-fungal, insecticidal, anti-oxidant anticancer, insecticidal, proteolytic activity, anti-mycoplasmal, anti-bacterial,
Roots	Calotropisesterterpenol, Calotropbenzofuranone, Calotropone,	Anthelmintic, antimicrobial, Wound healing activity*)*
Arial parts	Calotropisesjuiterpenol, Frugoside Coroglaucigenin, Isorhamnetin-3-O-rutinoside, Isorhamnetin-3-O-Glucopyranoside Taraxasteryl acetate [18]	Asthma, CNS activity, A Novel Insect Antifeedant Non protein Amino Acid, antitumor, cytotoxic. Coagulant, hepatoprotective, ant venom

Pharmacological Activity	Part of plant used	Extract	Model	Interpretation	Reference
1) Anti diarrheal activity	Aerial parts	anti-diarrheal activity	Castor oil model of diarrhoea in rats	C. gigantean extract helpful in a broad range of diarrheal states, functional diarrhoeas, radiation diarrhea or the diarrhea due to abnormal secretary mechanisms like in cholera or E.coli enterotoxin induced diarrhea.	[10, 11]
2) Antimicrobial a) Anthelmintic	Roots	Aqueous and Alcoholic extract	Anthelmintic activity animal model paralysis and death of individual earthworm	The aqueous extract has a better anthelmintic activity as compared to the alcoholic extract at all the doses	[12, 13]
b) Antibacterial	Leaves	Aqueous, extracts	Mueller Hinton agar plates (Gram positive bacteria like B.subtilis)	Dichloromethane and Ethyl acetate extracts showed better and broader spectrum of activity compared to other extracts.	[14]
c) Anti-Candida activity(Anti-fungal)	Leaves	aqueous extract	Modified agar well diffusion technique.	The C. gigantean leaves aqueous extract of show the antibacterial Extract exhibited maximum antibacterial activity next toE. coli and lowly activity besideK. pneumonia	[15]
d) **Antifungal activities**	Leaves	Aqueous, petroleum ether methanol, ethanol extract	Agar well diffusion method in potato dextrose agar	The results prove Calotropis gigantea a potent source of natural anti-Candida compounds.	[16]
e) Antimicrobial Activity (Pathogenic Bacteria.)	Flower	ethyl acetate extract	disc diffusion method	Di-(2-ethylhexyl) phthalate and ethyl acetate extract exhibited a enhanced broad spectrum of antibacterial activity beside equally Gram positive and gram negative bacteria.	[17]
f) Antimicrobial Activity	root bark	petroleum ether, methanol extract, ethyl acetate and chloroform fractions	disc diffusion assay method	potent antibacterial photochemical present in root bark methanolic extract	**[18]**
	Latex	crude water extract of latex	agar well diffusion method on Mueller Sabouraud Dextrose agar and Hinton agar for fungi and bacteria in that order	C. gigantea latex aqueous extract having the considerable amount of antimicrobial activity next to a wide range of microorganisms	**[19]**
3)Procoagulant activity	crude latex	Crude latex extract	human blood samples	crude latex is abundant with cysteine protease(s) and are medicinallyimportant in controlling bleeding and wound healing.	[20]
a) Wound healing activity	root bark	Defatted by petroleum ether and soaked in ethanol and kept aside for 4 days. After that ethanolic layer be decanted off.	rats.(Wistar albino rats)	Calotropis gigantean a show wound healing activity in rats and thus helps to its conventional use.	[21]
b) Wound healing activity	latex	Latex extract	albino rats by excision and incision wound models	The latexextract of calotropis gigantean treated wounds are establish to epithelise quicker as compared to controls.	[22]
4)Anti diabetic Activity	Flowers	Liquid nitrogen and dissolved in PBS (pH 5) buffer to form aqueous fine flowers powder.	diabetic human blood sample	Acidic proteases from Calotropis gigantea showed anti-diabetic activity.	[23]
a)) Antidiabetic Activity	flower	Ethyl acetate and chloroform extracts	alloxan-induced and normal diabetic Wistar albino rats	The obtained results support whole *in vivo* antidiabetic activity of the extracts that may confirmedto be of therapeutically important to improve the organization of diabetes.	[24]
5) Asthama	root	methanolic extract	Male Wistar rats	*Calotropis gigantea* might be potential therapeutically active drug for treating asthma.	**[25]**
6) CNS activity analgesic and sedative	Peeled root	Alcoholic extract	Eddy's hot plate method using albino rats at different dose level of CNS activity.	alcoholic extract of thepeeled roots retains anxiolytic, Anticonvulsant, analgesic and sedative activity.	**[26]**
a) **Sedative and anxiolytic effects**	Leaves	ethanolic extract	Animal behaviour model in mice	C. gigantean was originate to have promising anxiolytic and sedative activity in mice	[27]

b) anticonvulsant	leaves	various extracts	MES induced seizures is abolishing HLTE (hind limb tonic extension) which is taken as the end point of the test rats	anticonvulsant activity shown by extract	[28]
7) Hepatoprotective effects	stems	Ethanolic extract (50 %)	Male Wistar albino rats	extract has a significant effect on liver damagesand on oxidative stress, causing in reduced lipid per oxidation and enhanced serum biochemical parameters like ASTand ALT.	[29]
8) Analgesic activity	flowers	alcoholic extract	thermal models in mice.	Flower extractgives a Significant decrease in the amount of jerk and stay in paw licking time.	[30]
9) Pregnancy interceptive properties	roots	Extract by using Different organic solvents	On the rats it show pregnancy interceptive effect	The extract also show100% efficiency at the amount of 12.5 mg/kgdose when administered in the Days 1-5 and 1-7 post costume schedules.	[31]
10) Antioxidant activity	Leaves	hydroalcohlic extract	in-vitro models like DPPH (1,1-Diphenyl-2-Picryl-Hydrazyl)	As the concentration of extract increases The antioxidant activity of the extract was also enhance	[30]
11) Antitumor activity	root bark	Methanolic extract and it's chloroform soluble fraction	Swiss albino mice	root bark Methanol extract of C. gigantea and its chloroform soluble fraction retainsimportant antitumor activity.	[32]
12) Anti-pyretic activity	roots	water: ethanol (50:50) extract	Typhoid vaccine and yeast induced pyrexia in Albino Swiss rats and rabbits	The root extract of *calotropis gigantea* significantly reduced the fever and body temperature was Regulated at the dose of 200 and 400 mg/kg body weight	[10]
13)Cytotoxic activity	Flower	Crude ethyl acetate extract	Ehrlich's as cite carcinoma in mice.	The flower extract also repairs the haematological and biochemical parameters (ALP, SGPT and SGOT, glucose, cholesterol, triglyceride, blood urea,) that wasalteredthroughout tumour progression, at 200 mg/kg body weight dose extract displaythe greatestAction.	[17]
a) Cytotoxic activity	Roots	ethanolic extract	Allium cepa root meristem (ACRM) models	This might be utilized for the growth of new anticancer drug leads	[33]
14)Anti venom activity	extract	methanolic extract	Wistar albino rats, and Swiss albino mice	From the Existing study confirms the strong anti snake venom effect of methanolic extract of C. gigantea.	[34]
15)Free radical scavenging activity	leaf and latex	ethanolic extracts	DPPH radical 1,1 DipthenylPicrylhydrazyl radicals	The latex extracts C. gigantean exhibited enhancedability to scavenge DPPH radicals whereas leaf extract exhibitedfair free radical scavenging activity.	[30]
16) Antitussive activity	flower	flower extract	Albino Wistar rats, guinea pigs and mice	Aqueous flower extract have the significant antitussive effect	[35]
17) A Novel Insect Antifeedant Non protein Amino Acid	Root	Root extract	spectroscopic methods	The result exhibitaimportantantifeedant effect beside nymphs of the return locust Schistocercagregaria	[30]

1) Anti Diarrheal Activity: [10, 11]

The anti-diarrheal effect of aerial part of hydroalcoholic (50:50) extract of *Calotropisgigantea*abeside castor oil-induced-diarrhoea model in rats by Chitme H.R. concluded that The aerial part extract having the antidiarrheal activity but for the best results additional studies are necessary to completely know the mechanism of anti-diarrheal action of C.gigantea extract.

2) **Antimicrobial Activity** [12-19]

The Antibacterial effect of Calotropis gigantea leaf extract by using Well plate method against certain Gram positive (B. subtilis, M. luteus, S. aureus) and Gram negative (K. pneumoniae, P. vulgar and E. coli) bacteria was studied by Argal A result shown that dichloromethane and Ethyl acetate extracts exhibited better and broader spectrum of activity when compared to other extracts.

3) Wound Healing Activity [20-30]

The therapeutic activity of *Calotropis gigantea* root bark was studied for wound healing effect in rats was examined with the help of excision, incision and dead space wound healing models by Deshamukh P. T. and from the study he concluded that *Calotropis gigantean* enhanced the wound healing effect in rats.

4) Antidiabetic Activity [23, 24]

Fresh flowers of *Calotropis gigantean* plant were harvested and gathered early in the morning and macerated with liquid nitrogen and dissolved in PBS (pH 5) buffer to form aqueous fine flowers powder. He studied the activity on human blood sample and concluded that acidic proteases from *Calotropis gigantean* showed anti-diabetic activity.

5) Asthama [25]

Study has shown that methanolic extract of root tested on MaleWistarratsCGiganteaproved potential therapeutic drug for treating asthma owing toits anti-inflammatory, anti-lipoxygenase and antioxidant activity.

6) **CNS activity** [26-28]

The alcoholic extract of *Calotropis gigantean* peeled roots possesses sedative, anxiolytic, anticonvulsant and analgesic activity tested by Eddy's hot plate method on *albino rats* but constituents responsible for activity are still unknown.

7) Hepatoprotective effects [29]

The hepatoprotective effect of *calotropis gigantean* stem ethanolic extract of on Wistar albino rats.study showed that it the lower lipid peroxidation and enhanced serum biochemical parameters such as ALT andAST.

8) Analgesic activity [30]

The analgesic effect of flower alcoholic extract on*thermal models in mice.* He concluded that the flower produced significant decrease in the amount of jerk and stay in paw licking time.

9) Pregnancy interceptive properties [31]

Thepregnancy interceptive activity of calotropis gigantean root extract was studied on rat to by *Srivastava S. R.* And from the results he concluded that The root extract exhibited 100% effectiveness at the dose of 12.5 mg/kg when administer in the Days 1-5 and 1-7 postcoitum schedules.

10) Antioxidant activity [30]

The leaves hydrochloric extract studided on in-vitro models like DPPH (1,1-Diphenyl-2-Picryl-Hydrazyl) free radical scavenging effect. The study shows that the antioxidant activity of the calotropisgiganteaextract was found to enhance with increasing the concentration of extract.

11) Antitumor activity [32]

The antitumor activity of the methanolic extract of root bark tested on Swiss albino mice for and concluded that C. gigantea root barkMethanol extract and its chloroform soluble portion possesses significant antitumor activity.

12) Anti-pyretic activity [10]

The Water : ethanol extract of root was studied on yeast and typhoid vaccine induce pyrexia in albino Swiss rat and rabbits and the effect of this study At the dose of 200 and 400 mg/kg body weight*(*intraperitoneal injection) extract considerably lower the fever and body heat was normalized.

13) Cytotoxic activity [17, 33]

Cytotoxic activity of flower extract in ethyl acetate was studied carcinoma in mice.The extract restores the haematological and biochemical parameters (ALP,blood urea,cholesterol, glucose, triglyceride,SGOT andSGPT) that was changedthrough tumour sequence, at the dose 200 mg/kg body weight extract show themost excellent activity.

14)Anti venom activity [34]

Calotropis gigantean Methanolicextract was used to study the antivenom effect on Wistar albino rats, and Swiss albino miceand current study confirms the strong anti snake venom effect of methanolic extract of *C. gigantea.*

15) Free redical scavenging activity [30]

The free radical scavenging activity studied on Leaf ethanolic extract or latex 1,1DipthenylPicrylhydrazyl radicals The latex extracts C. gigeanteashows betterability to scavenge DPPH radicals whereas leaf extract showed reasonable free radical scavenging activity.

16) **Antitussive activity** [35]

Jaliwala Y.A. studied the flower extract of *Calotropis gigantean* for its antitussive effect of by using the method Albino Wistar rats, guinea pigs and mice and concluded that Aqueous extract of *Calotropis gigantean* has shown important antitussive effect.

17) **A Novel Insect Anti feedant Non protein Amino Acid** [30]

A nonprotein amino acid, has been isolated from aroot bark methanol extract of *Calotropis gigantean* and its structure recognized by spectroscopic methods. It show a important anti feedant activity next to nymphs of the desert locust Schistocercagregaria.

CONCLUSION

From the above study the obtained results in this work show the diversity of medicinal effects of C. gigantea. The wide-ranging pharmacological outline exposed by *Calotropis gigantea* plant should be operated by the pharmaceutical industry for the improvement of novel drugs, so the beneficial arsenal for many diseases could be extended benefit to humankind.

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