SJIF Impact Factor (2024): 8.675| ISI I.F. Value: 1.241| Journal DOI: 10.36713/epra2016 ISSN: 2455-7838(Online)
EPRA International Journal of Research and Development (IJRD)
Volume: 9 | Issue: 11 | November 2024 - Peer Reviewed Journal

AN OVERVIEW OF CALOTROPIS PROCERA'S PHYTOCHEMICAL COMPONENTS AND PHARMACOLOGICAL POTENTIAL

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ABSTRACT

Calotropis procera is a member of the Apocynaceae family and subfamily Asclepiadoideae. It is commonly known as Aak or Madar in Hindi and milk weed in English. Despite being a wasteland plant, its blossoms are dedicated to Lord Shiva, a Hindu god, making it a sacred plant. The herb is used by tribes worldwide to treat a wide range of illnesses, including skin conditions, sexual dysfunction, cancer, asthma, epilepsy, bodily discomfort, and snake bites. Numerous phytoconstituents, including cardenolides, oxypregnanes, terpenoids, flavonoids, and steroids, are present in this plant. Despite the abundance of articles regarding the chemical makeup, pharmacological activity, and ethnomedicinal uses of Calotropis procera that come up in literature searches, there aren't any recent papers that give a summary of the toxicity and therapeutic potential of the plant. In light of this, the review's goal is to present a comprehensive overview of the phytochemistry, pharmacology, toxicity, and therapeutic potential of Calotropis procera while also highlighting information gaps to serve as a source of inspiration for further investigation. Other names for Calotropis procera include Aak and Madar. The phytochemistry, toxicity, pharmacology, and therapeutic potential of Calotropis procera are all systematically summarized in this paper.

KEYWORD : *Calotropis procera calotropin , Aak , Milkweed , Calotropis gigantea*

INTRODUCTION

Calotropis is a member of the Apocynaceae family, also referred to as Aak or milkweed.
This genus of plants is called milkweed because various plant sections exude a white, sticky latex.
Calotropis procera (Rakta arka) and Calotropis gigantea (Sweata arka), two common species in the genus Calotropis, are said to have important pharmacological qualities for Ayurvedic toxicology and treatments. C. acia and C. sussuela are other species. Calotropis procera (Aiton) W. T. Aiton is an erect, deciduous evergreen perennial shrub commonly known as 'Sodomaomena' or 'Madar bush'. It is known as "Akanda" in Bengali and "Aak" in Hindi. It is widely used in the traditional medical systems of India, Arabia and Sudan to treat global ailments.Dangas tribe in Gujarat, 1 Singhum tribe in Bihar, 2 Ghatigaon forest tribe in Gwalior, 3 Andhra Pradesh tribe4 used this plant to treat various diseases like earache, cough, fever, stomachache. Dysentery and elephantiasis.Calotropis procera is more poisonous than Calotropis gigantea and is thought to be even more poisonous than cobra venom. Interestingly, the cobra and other poisonous snakes cannot even stand its smell; Therefore, snake charmers of Bengal use this plant to control or tame cobras.5Previous reviews 6-16 have discussed the phytochemistry, ethnobotany and pharmacological potential of Calotropis procera. A review of Calotropis species 17-20 comparing procera and gigantea discusses their therapeutic importance. This review summarizes the phytochemistry, pharmacology, commercial aspects, traditional medicinal uses, toxicology and recent research on Calotropis procera. The future scope of Calotropis procera was also confirmed, explaining its multiple biological functions and mode of action.

Scientific Classification

Kingdom	Plantae
Clade	Tracheophytes
Clade	Angiosperms
Clade	Eudicots
Clade	Asterids
Order	Gentianales
Family	Apocynaceae
Subfamily	Asclepiadoideae
Tribe	Asclepiadeae
Genus	Calotropis R.Br.[1]

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Toxicity

C. procera is distributed in many regions of the world. What makes its phytochemistry interesting is the secretion of a milky and poisonous latex from all parts of the plant. Latex is called plant mercury because it has mercury effects on the human body.21Every part of this plant is poisonous, but the stem (latex) and roots are more poisonous than the leaves. The leaves of this plant contain three toxic glycosides, calotropin, calotoxin and uscarin, while its latex contains calotropin, calotoxin, and calactin, which are corrosive and poisonous in nature. In addition, the concentration of calactin, a poisonous glycoside, increases as a defense mechanism against locust or insect attack and is the reason why cattle or other livestock do not eat the plant.In addition, osmotin, a laticin protein purified from latex, protects plants against phytopathogens.23 Its milk is irritating, neurotoxic and anticholinergic, causing toxicity and fatal complications. The sap and latex of madar have a bitter taste and a burning pain that causes salivation, stomatitis, vomiting, diarrhea, dilated pupils, titanic strangulation, collapse and death. The time to death varies from half an hour to eight hours.24 When latex enters the eye, it causes keratitis, corneal swelling and blurred vision without pain.25–27 In some cases, permanent damage of endothelial cells was observed, which was obvious. . . after three weeks.5.28C. Procera was found to be toxic to chicken embryos at a dose of 100 mg kg-1. Its toxicity has caused hepatocellular degeneration in the liver, brain congestion, dilation of central veins, sinuses, underdeveloped lungs and kidneys.29 Therefore, considering the toxic effects of certain extracts and glycosides, further research should focus on clarifying toxicity and safe use. C. longa.

2.The ability to survive in extreme climatic conditions.

Another interesting feature of this plant is its ability to withstand adverse environmental conditions such as lack of water, dry environment or any harsh climate. To understand this, Akhkha30 studied the effects of water deficit stress and found that although the photosynthetic machinery remained unchanged, the rate of photosynthesis actually increased under mild water conditions (50%), which could be considered a compensatory mechanism. In addition, Ramadana et al.31 investigated the effect of light and irrigation on β-sitosterol accumulation in C. proceras. They hypothesized that the β-sitosterol biosynthetic pathway supported the plant's tolerance to drought and light intensity.

1. **Commercial prospective**

Use As Biofuel :- C. procera is rich in hydrocarbons and contains biologically degradable materials similar to that found in other agricultural crops. Traore32 conducted fermentation experiments and found that it is a good substrate for biogas synthesis. Barbosa et al.33 found that oil composition of its seeds varies from 19.7 to 24.0% which proves its future potential as biodiesel, specially in those areas where people rely mainly on wood as source of energy production.

Use as Biopesticide :- To evaluate the biological role of latex, the insecticidal activity of Calotropis procera latticifer proteins (LP) against various crop pests was determined. Diets containing 4% latex reduced weight gain (ED50 = 3.07%) and affected survival (LD50 = 4.61%) in third stage Ceratitis capitata.34 Crude fraction of flavonoids (Cf), latex protein fraction (LP) and methanol extract of leaves showed. Significant insecticidal activity .35 These studies suggest that it can be developed as a natural biopesticide.

In Future of Industry :- For Cheese Production

In West Africa, the crude aqueous extract of C. procera is used as a milk coagulation enzyme in the traditional cheese making method.36 It showed optimal activity at 75 °C, which is required for cheese. 37 The plant enzyme calotropin is more effective than papain, physin and bromelain, and can also cause curdling of milk, disintegration of meat, casein and gelatin.38,39 These studies supported its traditional use as a cheese-making agent.

As Surfactant

C. procera milk latex was used as a surfactant for the facile synthesis of Eu3+-activated La(OH)3 and La2O3 nanophosphors via a green-mediated hydrothermal route. The latex reflected a good splitting ability in controlling the morphology and phase of the nanophosphorus.40 Thus, its latex can be a good source of natural surfactant..

As Corrosion Inhibitor

It shows anti-corrosion effect of C. procera extract was investigated by weight loss, electrochemical, SEM and UV methods, a significant anti-corrosion effect was shown on mild steel in sulfuric acid environment.41 So it can be used as a green corrosion. An inhibitor.

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As Dehairing Agent Of Leather

C. procera latex peptidases showed a complete senescence process when analyzed against typical skin substrates, although no changes in skin structure were observed. Thus, it can be a suitable environmentally friendly depilatory agent compared to the toxic sodium sulfite used in tanneries.42.

Ethnomedicinal Use

Misra et al. compiled an overview of the Ayurvedic, Unani and folk use of various parts of C. procera and C. gigantea for the treatment of various diseases.43 The ethnomedicinal use of C. procera plant parts in the treatment of various diseases was summarized..



Fig.(1) **Calotropis procera plant**

An Important Milestone in Calotropis Phytochemistry.

The phytochemistry of Calotropis procera has always attracted the attention of researchers because, despite its toxicity, it still has wide applications in the traditional system of medicine. Starting in 1936, calotropin 55 was identified as the first compound from this plant by Hesse et al. In addition, Hesse and his collaborators56,57 isolated cardiotoxins or cardiac glycosides, namely calotropin, calotoxin, calactin, uscarin, voruscarin and uscaridine.58 The root powder of this plant was used tribally to induce abortion in women and as a remedy. . uterotonic medicine since ancient times. It was later discovered that this was caused by the compound calotropin. Gupta et al59 administered calotropin to gerbils and rabbits and found a 65% and 94% decrease in sperm count.In 1955, Rajagopalan et al.60 identified the chemical constituents of the seeds viz. coroglautsigenin, corotoxigenin and frugoside (cardenolides). Later, Bruschweiler et al.61 identified three more cardenolides, viz. uzarigenin, siriogenin and proseroside. Quaquebeke et al.62 isolated a new cardenolide, 2'-oxovoruscarin, from the root bark and converted it into a semi-synthetic derivative, i.e., UNBS1450. Akhtar and Malik63 isolated a new cardenolide named proceragenin from the hexane-insoluble fraction of C. procera.An interesting property of the plant is its ability to slow Alzheimer's disease and #039 (AD), the main cause of neurodegenerative dementia. Its dried latex showed the weakening of β-amyloid accumulation in the mouse brain and the protective function of the brain.64 Therefore, it is necessary to evaluate the mechanism of the metabolites, so that it can lead to a promising direction to search for new ones. Scaffolds for AD. Therapy In 2015, Mohamed et al. isolated three non-glycosidic cardenolides from the latex, namely calactoprosin, prokegenin A and prokegenin B. 65The patent claimed that a polar extract of C. procera exhibited dose-dependent antiulcerative colitis activity in mammals and was found to be more. Effective than the standard drug Prednisolone.66.

Pharmacology

Over the last many years, researchers have carried out numerable pharmacological activities, which are summarized in Table 2

Brief summary of the pharmacological properties

S. no.	Pharmacological activities	Parts/extracts/possible chemical constituents	References
1	Wound healing potential	Latex: aqueous extract	67
		Latex	68
		Bark: ethanolic extract	69
		Leaves: aqueous extract	70
		Bark: aqueous extract	71
2	Anticoccidial activity	Dried leaves powder	72
3	Toxicity activity	Leaves: aqueous extract	73 and 74
		Leaves and stem bark extracts	75

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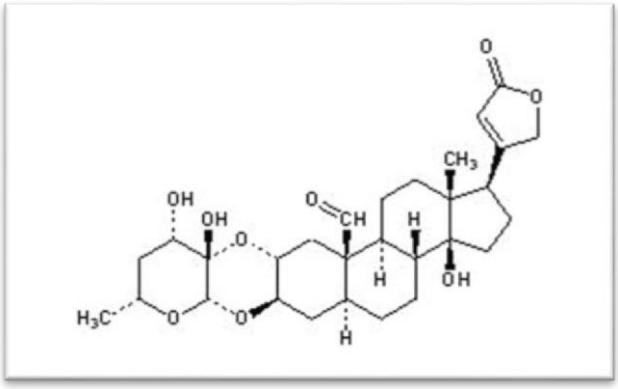
		Leaves and stem: ethanolic extract	29
		Leaves: ethanolic extract	79
4	Biopesticidal/insecticidal activity	Leaves: extract	80 and 81
		Leaves: methanolic extract, latex protein fraction, flavonoids (quercetin-3-*O*-rutinoside)	35
5	Antimycoplasmal activity	Leaves: acetone extract	82
6	Hepatoprotective activity	Root bark: methanolic extract	83
		Flowers: hydroethanolic extract	84
		Roots: chloroform extract	85
7	Antimicrobial/antibacterial activity	Leaves: methanolic extract, flavonoids (quercetin-3-*O*-rutinoside)	86
		Leaves and latex: ethanol, aqueous, and chloroform extract	87
		Leaves and stem: aqueous, ethanolic, methanolic extract	88 and 89
		Endophytic fungi of *C. procera*	90
		Seeds: chloroform extract	91
		Root: pet. ether, methanolic extract	92
		Flowers: ethanolic extract	93
		Latex	94
		Leaves: methanolic extract	95
		Leaves, flower, root bark: ethanolic extract	96
		Leaves and latex: aqueous, ethanolic extract	97 and 98
		Leaves: aqueous, methanolic extract	99
		Latex: aqueous extract	78
8	Central nervous system activity	Latex proteins	100
9	Antioxidant activity	Leaves, flower, fruit, latex	101
		Leaves: aqueous, methanolic extract, quercetin and its derivatives	76
		Leaves: aqueous and methanolic extract	102
		Leaves, flowers and fruits: methanolic extract	103
		Bark: ethanolic extract	69
10	Antinociceptive activity	Latex protein	104
11	Antihelmintic activity	Flowers: crude powder, aqueous and methanolic extract	105
		Latex: fresh, dried aqueous extract	106 and 107
12	Antiinflammatory activity	Dry latex	108 and 109
		Stem bark: chloroform and hydro-alcoholic extract	110
		Latex: hexane, dichloromethane, ethyl acetate, *n*-butanol and aqueous extract	77
		Latex: pet. ether, acetone, methanol extract	111
		Leaves: aqueous extract	112
		Flowers: ethanolic extract	93
13	Antidiarroheal activity	Bark: Arkamula Tvarka (Ayurvedic preparation)	45
		Latex	113
14	Antifungal activity	Aqueous bark extract	114
		Leaves: aqueous, methanol, acetone and ethanol extract	115
		Root bark	116
	Antimycotic activity against dermatophytes	Latex	117
	Antimycofloral activity (fungi in wheat)	Fresh latex	118
15	Larvicidal activity	Crude latex and ethanolic extract of leaf	119
		Leaves: ethanolic extract	120
		Leaves: aqueous extract	121
		Flower, young bud, mature leaves and stems: ethanolic extract	122

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		Flowers: aqueous extract	123
16	Tobacco mosaic virus (TMV) inhibitor activity	Latex	124
17	Antifertility activity	Ethanolic extract of roots	125
		Leaves: ethanolic extract	79
		Roots (calotropin)	59
	Abortifacient activity	Latex	126
	Antisperm activity	Root: chloroform extract	127
	Oestrogenic/antiovulatory activity	Roots: ethanolic and aqueous extract	128
18	Plasma clotting activity	Protein fraction isolated from fresh latex	129
19	Antiplasmodial activity	Different plant parts: ethyl acetate, ethanolic and acetone extract	130
		Leaves extract	131
20	Antipyretic activity	Dry latex: aqueous extract	132
		Flowers: ethanolic extract	93
21	Antiasthmatic activity	Flowers	133
22	Anticonvulsant activity	Root extracts	134
23	Cytotoxic activity	Root (2″-oxovoruscharin)	62
		Laticifer proteins (LP) recovered from latex	135
		Root: methanolic, aqueous, ethyl acetate, hexane extracts	136
		Plant: methanolic extract	137
		Stems: uzarigenin	138
		Root bark: calotroprocerol A	139
		Root: alcoholic, hydro-aqueous and aqueous	140
		Leaf: ethanolic extract	149
24	Analgesic activity	Flowers: Ethanolic extract	93
25.	Antihyperglycemic activity	Leaves: pet ether, methanol and aqueous extracts	141
26	Antiarthritis activity	Latex	142
		Protein sub fraction of latex	143
27	Antimolluscicidal activity	Latex: 95% aqueous ethanol (uscharin)	144
28	Antitermites activity	Latex	145
29	Antimigraine activity	Dried terminal leaves	146
30	Anti-ulcer activity	Root: chloroform extract	147
		Plant: 50% ethanolic extract	148
		Leaf: ethanolic extract	149
		Stem bark: chloroform and hydroalcoholic extract	110
31	Spasmolytic activity	Plant: aqueous extract	150
32	Allelopathic activity	Leaves: aqueous extract	151
33	Anti-keloidal activity	Latex	68
34	Anti-hyperbilirubinemic activity	Leaves: aqueous extract	70
35	Antiapoptotic activity	Latex	152

Phytochemistry:- C. procera contains cardenolides, flavonoids, sterols, oxypregnanes, triterpenoids, glycosides and other compounds described in Table 11.7. Flavonoid and its glycosides are the most important compounds isolated from C. procera leaves. Steroids and cardenolides (are the main secondary metabolites found in latex. Cardenolides have also been reported from other plant families of Apocynaceae or Asclepiadaceae, such as Strophanthus, Cerbera, Apocynum, Nerium and Thevetia.159 They are traditionally used to treat congestive heart failure.160 Cardenolides are C23 steroids with an asteroid glycoside. Part at C-3 and the lactone part at C-17.6 Cardiac glycosides may be new antitumor agents because cancer cells are more sensitive to these compounds.159 Terpenoids (ursane, oleanane-type and pentacyclic triterpenes, etc.) isolated from flowers, rhizomes and latex. Oxypregnane glycosides 5) were recently reported from the root bark of this plant.153,154 They have a steroid backbone containing a 2deoxysugar moiety. These oxypregnanes have a benzoyl group at C-12 and a straight sugar chain of 5-7 units linked to the aglycone at C-3.6 Some glycosides , wood glycosides terpene glycosides and caffeic acid derivatives 9) was also isolated from this plant..

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Structure of Calotropin

CONCLUSION, DISCUSSION

This review summarizes the research progress on the phytochemistry and pharmacology of C. procera. There were acquisitions in the study; However, we found some shortcomings in our research, which are as follows 1) C. procera has been used by people and tribes since ancient times; further research can be done on when the traditional use of C. procera begins.(2) The secondary metabolites of a plant vary according to several factors such as region, environment, soil quality, age of the plant, etc. In addition, latex and rhizome seem to be the most studied plant constituents, flowers, pods and pods have not been studied much. Fyoconstituentsis seeds were implemented. Further investigation of these components may lead to the discovery of new phytoconstituents of interest.(3) The device can be used commercially because scientific studies have shown its use as a cheese-making agent, skin depilatory agent, natural surfactant, biopesticide and corrosion inhibitor.(4) Many efforts have been made to confirm its cytotoxic and anti-inflammatory potential. Some were made for its migraine, plasmodial and anticonvulsant effects. Further research in these areas can provide medicine with effective and promising new drugs.(5) Most of the cytotoxic actions performed are in vitro, except that performed with UNBS1450; semi-synthesized cardenolide. Further studies should be conducted to investigate its in-vivo potential.(6) The right method of administration and the right dose can turn a terrible poisonous substance into an excellent medicine, while a medicine can become a deadly poison if the doses and method of administration are not done. Human practitioners used C. procera as an antifertility and uterine tonic. Further studies using positive controls, toxicity and side effect studies may lead to the discovery of effective and natural contraceptives.(7) The active ingredients underlying many activities are unknown, apart from the known cytotoxic, antibacterial, antifertility, mollusc and insecticidal activities. More research can be done to know the active ingredients to make effective medicines.(8) Renewable and environmentally friendly energy sources are the need of the hour, Calotropis procera is a rich source of various hydrocarbons, so it can be a promising biofuel.In general, this document covers pharmacology, toxicology, traditional uses, use of secondary metabolites, clinical trials and quality control. However, there seems to be a good correspondence between pharmacological functions and traditional uses. Further research in this area is needed to determine the active principles and underlying mechanisms..

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