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Review Article

Ethnomedicinal and Cytotoxic Activities of *Calotropis Procera*-A Review

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A B S T R A C T

Plants are major sources of drugs that we use today. One such plant is *Calotropis procera*which can be consider as a home for many phytochemicals. Each part of this plant is enriched with various phytochemicals having its own significance for human life. The phytochemistry of this plant reveals presence of triterpenoids, anthocyanins, flavonoids, cardiac glycosides, cardenolides, *α*–amyrin, *β*-myrin, lupeol, *β*-sitosterol, flavanols, mudarin, resin, a powerful bacteriolytic enzyme calactin, a non-toxic proteolytic enzyme calotropin. The plant exhibits antimicrobial, anthelmintic, anti-inflammatory, analgesic, antipyretic, anticancer, antiangiogenic, immunological, antidiabetic, cardio vascular, hypolipidemic, gastro protective, hepatoprotective, renal protective, antidiarrheal, anti-oxidant, anti-convulsant and wound healing effect. This review is an attempt to stack the phytochemical and pharmacological activities of *Calotropis procera* shrubs.

Key word: Cytotoxicity, melanoma, Glioblastoma, Hela cell lines, Neuritis, Hydrocele

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INTRODUCTION

*Calotropis procera*is a soft-wooded, perennial shrub belonging to the family Apocyanaceae. It is an evergreen xerophytic plant found in arid and semiarid habitats. It is commonly seen in India, Malaysia and Indonesia. The plant is grown in dry, sandy and alkaline soil. The two species of Calotropis reported in literature are *C. procera* and *C. gigantea*.The Hindu literature of Dhanvantari Nighantu reported three varieties of Calotropis. Viz., suklarah, rajarkah and sveta mandarah. The most commonly used variety in Indian traditional medicinal system is sveta mandarah.[1]

The word 'Calotropis' is derived from a Greek word, meaning beautiful which refers to its flowers. Whereas procera a Latin word referring to the cuticular wax present on leaves and stem[2].

Plant profile:

Calotropis procera (Raktha Arka) is an erect, tall large, highly branched and perennial shrub that grows to the height of 4-5 m with milky latex throughout the plant.The flowers are 5-20cm long, 4-6 cm wide, regular, bisexual, purple or light greenish yellow with faint odour and basically borne in pairs. Its stem is yellowish white, furrowed, rough, cory and branches are stout. Leaves are 10-20 cm long and 3.8-10 cm wide, opposite, decussate, elliptic-oblong, sessile, obviate, acute, thick and pale green in colour. Spongy fruits consist of light brown seeds of size 6×5 mm[3]

Table 1: Taxonomic classification[4,5]

Kingdom	**Plantae**
Sub kingdom	*Tracheobionta*
Super division	*Spermatophyta*
Division	*Magnoliophyte*
Class	*Magnoliopsida*
Subclass	*Asteriidae*
Order	*Gentianales*
Family	*Asclepiadaceae*
Genus	*Calotropis*
Species	Calotropis procera

Special characteristic of C*alotropisprocera*

Toxicity

The plant exudes milky and toxic latex which is referred as vegetable mercury as it shows mercury like effacts on human body. Every part of this plant is toxic, but stem (latex)and roots are more poisonous than leaves [6](Gupta et al., 2012). If latex enters into the eye, it causes kerato- conjunctivitis, corneal edema and dimness of vision without any pain.[7,8] The latex of plant is capable of causing hepatocellulardegeneration in liver, brain congestion, dilatation of central veins, underdeveloped kidneys, sinusoids[9].

Self defence mechanism

The toxic glycosides calactin, uscharin present in latex and leaves respectively are poisonous in nature. The concentration of calactin increases as a defence mechanism on grasshopper and insect attack and this is rationale behind the plant not being consumed by cattle or grazing animals[10].

Ability to survive under arid condition

Another interesting aspect of this plant is its ability to tolerate adverse environmental conditions like scarcity of water, arid environment or any kind of harsh climate. from the research article.[11]

Vernacular names[6]

Kannada:Yekkadagida

Hindi:Mudar, Akada, Akdo, Aak

Marathi:Rui, Mandara

Sanskrit:Arka, alaka, Ravi

Tamil:Vellerukku

Urdu: Madar, aak

Table 2: Ethnomedicinal Uses of *Calotropis Procera*

Plantpart	**Disease**	**Preparation/administration**	**References**
Root	Amoebicdysentery	Pastewith/withoutopiumtakenorally	11
	Elephantiasis	Pastemixedwithfermentedricewaterappliedontheaffected area	12-13
	Jaundice	Takenwithriceingroundedform	14
	Snakebite	Powderorallytaken.Pasteappliedonwoundsandinternally taken with ghee	12, 15
Latex	Boils	Appliedexternally	16
	Leprosy	Appliedontheaffectedarea	12
	Migraine	Applied ontheaffectedsideveinofforehead	11
Leaf	Cold,cough,asthmaandbronchitis	Warmedalongwithgheeandbandagedonthechestofinfants	11
	Eczemaandskineruptions	Appliedexternallyalongwithturmericand sesameoil	15
	Gonorrhoea	Decoction used forwashing andtaken orally	14
Flowers	Healthtonic	Oraladministrationofpowder	12
	Cough	Burnttoproduceash,thentakenwithhoney	11
	Epilepsy	Oraladministrationofpastewithblackpepper	16
Fruit	Eyedisorder	Decantedashwaterappliedoneyelids	11
	Anaemia	Mixedwithsamequantityofredchilli,mineralsaltandtaken with milk	16
Whole plant	Rheumaticpainandhyperacidity	Paste directlytaken	11

Young twigs	Purgative	Juice taken	17

CYTOTOXIC ACTIVITY OF CALOTROPIS PROCERA

Antiproliferative activity of *Calotropis procera* stem extracts

Thecytotoxicpotentialofstemorganicextractsfrom*Calotropisprocera*wasfirstlyevaluatedagainstcancer cell lines by MTT assay, by Henderson et, al.,[18]. Subsequently, samples considered cytotoxic were tested for antimitotic activity onsea urchin egg development and for *in vivo* antiproliferative activity in mice bearing Sarcoma 180 tumour. Amongthe five extracts (hexane, dichloromethane, ethyl acetate, acetone and methanol), ethyl acetate and acetone extractsdisplayed higher cytotoxic potential against tumour cells, with IC_{50} ranging from 0.8 to 4.4 µg/mL, while methanolicextract was weakly cytotoxic. Ethylactate extracts exhibited cell division inhibition capacity by antimitotic assay,revealing IC50 values lower than 5 µg/mL.

Cytotoxic activity of root bark of *Calotropis procera*

A study reported that, the methanolic extracts of root bark of *Calotropis procera* contain a novel cardenolide (2-Oxovoruscharin) which exhibits In vitroanti-tumor activity on a panel of 57 human cancer cell lines similar to Taxol. The root bark of *Calotropis procera* has shown high in-vivo tolerance of tumor growth and prolonged survival in human xenograft models of nude mice[19].

Anti-tumor activity of root extract of Calotropis procera

Mathur et, al., [20] studied the anti-tumor potentials of root extract of Calotropis procera against Hep 2 cancer cells. Methanolic, hexane, ethyl acetate and aqueous extracts of roots were tested against Hep2 cancer cells and cellular proliferationactivities was assayed by tetrazolium bromide (MTT) colorimetry. They concluded that root extracts of Calotropis procera inhibit the proliferation of Hep 2 cells via apoptotic and cell cycle description-based mechanism.

Cytotoxic activity of *Calotropis procera* on Human skin melanoma cells (sk-MEL-2)

Aparna L Joshi, et al. reported that, the cardiac glycosides of *Calotropis procera* are cytotoxic to the Human skin melanoma cells (sk-MEL-2). The SK-MEL-2 cells treated with C. procera methanolic extract (CPME) were analyzed for growth inhibition and apoptosis. The cell cycle analysis shows that CPME treated cell halt at G_2 /M phase. Significant cytotoxic activity of CPME against SK-MEL-2 may be attributed to its high cardenolide content.[21]

Cytotoxic activity of methanolic extract of vegetative stem of C. Procera against the human cancer cell line HT 29 and hepg 2 and Mouse fibroblast cell line NIH-3T3.

The sensitivity of cell lines NIH-3T3, HePG2 and HT-29 to the isolated compounds such as 5-Hydroxy-3,7-dimethoxyflavone-4-0-βglucopyranoside, 2β,19-epoxy-3β,14β-dihydroxy-19-methoxy-5α-(ard-20(22)-enol ide and β-anhydroepidigitoxigenin-3β-o-glucopyranoside, uzarigenin and β-anhydroepidigitoxigenin was evaluated by monitoring metabolic activities using the cell-titter-blue cell viability assay (Promega, Mannheim, Germany) and it was concluded that ugarigeni showed moderate cytotoxicity among all other chemical constituents[22].

Cytotoxic activity of ursine type triterpene from the root bark of Calotropis procera.

The antineoplastic activity of calotroprocerol A, calotroproceryl acetate A, calotroprocenone A, B, pseudo-taraxasterol E-octade-7-enoic acid against 3 Human cancer cell lines including the A549 non-small cell lung cancer (NSCLC), the U373 glioblastoma (GBM) and the PC-3 prostate cancer cell lines was determined the 3-(4,5-dimethylthiazole-2-yl)-2,5-iphenyltetrazolium bromide (MTT) assay. It was observed that Calotroprocerol A exhibited invitro growth inhibitory activity in all 3 cancer cell lines with effects compatible to those of cisplatin and carboplatin[23].

Cytotoxic activity of Calotroposides h-n against lung cancer

The investigation on N-Bu OH fraction of root bark of *C.procera* (Ait). R. Br. revealed the presence of Seven new oxypregnaneoligo glycosides: calotroposides H–N [24]. The in vitro growth inhibitory activity of the n-Bu OH fraction was evaluated against A549 non-small cell lung cancer (NSCLC), U373 glioblastoma (GBM), and PC-3 prostate cancer cell lines. Compounds calotroposides-K and calotroposides-M showed sub nanomolar growth inhibition activity with IC50 ranging from 0.5 to 0.7 lM against U373 glioblastoma (GBM) and PC-3 prostate cancer cell lines[25].

Anti-proliferative activity of c. Procera towards prostate cancer.

Calotroposides S possesses the 12-O-benzoylisolineolon aglycone moiety with eight sugar residues attached to C-3 of the aglycone. It showed potent anti-proliferative activity towards PC-3 prostate cancer, A549 non-small cell lung cancer (NSCLC), and U373 glioblastoma (GBM) cell lines with IC50 0.18, 0.2 and 0.06 µM, respectively[26].

Cytotoxic activity cardenolides from the latex of *Calotropis procera*.

Three new cardenolides were isolated from the latex of *Calotropis procera*. The growth inhibitory activity of the latex was evaluated against human A549 and Hela cell lines. Among the four extracts (hexane, chloroform, ethyl acetate and aqueous), chloroform extract displayed the highest potential cytotoxic activity, with IC50s of (0.985 lM, A-549) and (1.471 lM, Hela)[27].

Cytotoxic activity of root extracts of C.P against oral and CNS human cancer cell lines.

Alcoholic, hydro-aqueous and aqueous extracts of 10 µg/ml, 30 µg/ml and 100 µg/ml respectively were prepared and evaluated for anti- neoplastic activity against human oral (KB) and central nervous system (SNB-78) cancer cell lines through Sulforhodamine - B (SRB) assay. On evaluation of the fractions prepared from alcoholic and hydro-aqueous

extracts, it was observed that chloroform fraction from alcoholic extract was antiproliferative for oral (KB) cancer cell line and n-butanol fraction from alcoholic extract was antiproliferative for CNS cancer cell line than remaining fractions at three different concentration of 10 µg/ml, 30 µg/ml, 100 µg/ml in a dose-dependent manner [28].

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