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A Concise Review on Recent Pharmacological and Economical Activities of *Calotropis procera* (Ushar)

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ABSTRACT

Calotropis procera (family- asclepiadaceae), commonly known as milkweed is a perennial invasive species of arid and semi-arid regions. The plant contains a milky sap, which oozes out of any wound or injury anywhere on its aerial parts.All plant parts root bark, stem bark, leaf, flower, and latex and their extracts, fraction, and isolated compound exhibit anticoagulant, anti-hyperglycemci, anti-hyperdyslipidemic, anti-inflammatory, antioxidant, cough-suppressing, , and wound healing activity, anti-cancerous, anti tumour, anti fertility,anti-plasmodial, anti filarial activities.It is a multipurpose plant, which can be utilized for medicine, fodder, and fuel purposes, timber and fiber production, phytoremediation, and synthesis of nanoparticles,the present review is to put the valuable medicinal properties, socio-economic importance and knowledge gaps in ongoing research.

INTRODUCTION:

Ever since ancient times, in search for rescue for their disease, the people looked for drugs in nature, the decreasing efficacy of synthetic drugs and the increasing contraindications of their usage make the usage of natural drugs topical again.[1]Naturally, plants synthesize products beneficial for us namely as phytoconstituents that are used to perform biological functions, which also protect us against predators such as virus fungi and other microorganisms. The phytoconstituents obtained from the natural products are one of the most successful strategies for the discovery of new drugs.[2]

The Greek-Arabian traditional medicine knows the Calotropis plant under the name of Madar and Ushar, where from ancient times, extract, powders of different parts of Calotropis have been used. [3]. It is widely used in the Indian traditional medicinal system, C. procera is also used by various tribes of the world as a curative agent for ailments such as skin disease and elephantiasis.[2]C. procera is drought-resistant medicinal perennial shrub mostly found in arid to semi-arid areas. It is a major source of secondary metabolites including phenols, flavonoids, terpenoids, sugars, alkaloids, tannins cardenolides, glycoside, saponins and steroids It has medicinal properties as hepatoprotective, antioxidant, inflammatory, antimicrobial, and antimalarial[2]. It is vigorous used for the ailment of common diseases, i.e. fever, leprosy, eczema, diarrhea, dysentery and jaundice. [15]

Recent investigation has found that the alkaloids calotropin, calotaxein and uskerin are stimulant to heart (Ashwari, 2009).[9]

At present, it is being extensively explored for its potential pharmacological applications. Several reports also suggest its prospects in the food, textile, and paper industries. Besides, C. procera has also been acknowledged as an ornamental species. High pharmacological potential and socio-economic value have led to the pantropical introduction of the plant. Morpho-physiological adaptations and the ability to tolerate various abiotic stresses enabled its naturalization beyond the introduced areas. Now, it is recognized as an obnoxious environmental weed in several parts of the world.[5]Different parts of the plant have been reported to possess various phytochemicals containing cardiotonic agents such as calotropin, calotropagenin, calotoxin, calotropagenin and voruscharine, steroids, di and triterpenes such as stigmasterol, β-sitosterol, flavonoids, polyphenolic compounds, and various newer reported hydrocarbons and proteins.[2]

BOTANICAL DESCRIPTION:

***Calotropis procera* Synonym:**

Calotropis heterophylla Wall.,

Calotropis wallichii Wight,

Madorius procerus (Aiton) Kuntze,

Apocynum syriacum Garsault,

Asclepias patula Decne,

Asclepias procera Aiton

Calotropis busseana K. Schum [10,11]

C. hamiltoni wall[5]

Scientific Classification: [2,3,8]

Table No. 1: Scientific Classification

Kingdom	Plantae
Subkingdom	Tracheobionta
Super division	Spermatophyta
Division	Magnoliophyta
Class	Magnoliopsida
Subclass	Asteridae
Order:	Gentianales
Family	Apocynaceae
Subfamily	Asclepiadaceae
Genus	Calotropis
Species	*C. procera*

Regional names:

English: swallow wort, rubber tree, apple of sodom

Urdu: aak

Arabic: ashar

Hindi: madar, safed-ak

Sanskrit: alarka

Bengali: akanda

Punjab: shaker-al-lighal

Kannar: ekke

Telugu: mandaramu

Tamil: erukku

Gujarati: akanda

Malayalam: bukam

Bombay: mandara

Sind: ak

Afghanistan: spalwakka

French: pomme de sodome ,[2,12,13,30,]

Geographic Distribution:

C. procera is a perennial shrub belongs to the family Apocynaceae. It is native of Africa, Arabian peninsula, Western Asia, the Indian subcontinent and Indo-China[.5.] It grows in almost all parts of Punjab, Pakistan as wild shrub especially in plains, pasture and roads way (Azhar et al., 2014).[15]

Morphology:

C. procera is a woody erect perrenial shrub, 2.5-6 m in height. (Fig 1-4)

Aerial part/Stem-glabrous, internode with grey green pruinose bloom, bark is corky, furrowed, grey.

Latex-A copious amount of white sap generates on cut of plant part.

Leaves- elliptic 18cm long and 15cm wide, opposite-decussate with grey- green waxy appearance, venation obscure with secondary veins per side of midrib, tip acute, base cordate, petiole and peduncle 3cm long.

Flower- campanulate(bell shape), petals are arranged in pentamerous form, small and cream or greenish-white at the base and purple violet at the extremity of the lobes. Pedicle cream and glabrous, sepals ovate, corolla tube cream, lobes lanceolate-ovate, anther appendages truncate-obtuse.[18]

Seed- 8mm long, small flat obovate, with silky white pappusat (tuft of silky hairs)

Fruit-Pear-shaped, fleshy grey-green fruits 8 - 12 cm long.

Root-It has deep root system, simple and branched and corky bark root.[16,30]

Inflorescence: polychasial cymes.

Pollination happens through insects, mostly through bees or butterflies(entomophily).

Fig 1 shows single flower

Fig 2 shows complete plant

Fig 3 shows seeds with plant cotton,

Fig 4 shows latex-milky sap

Table No. 2: Part used as medicine

Plant part	Length	Shape	Colour
Stem	25cm	-	Grey green waxy
Leaves	18cm , (13cm broad)	elliptic	Grey green waxy
Flower	3.8 – 5.1	Bell(campanulate)	White at base, purple at tips
Fruit	8-12 cm	Pear	Grey green
Seeds	8mm	Obovate, coma	brown
Seed hairs	2-3 cm	-	White

Part used as medicine:

Stem, stem bark, leaf, flower, latex, seed, root, root bark.

Description of C. procera according to Unani literature:[1,17,19,20,21]

Mijaz (temperament): flower, leaf, stem, root-- Har(hot)3, Yabis (dry) 3

Latex (doodh)--- Har (hot)4, Yabis (dry) 4

Afal (actions):

Latex: lazai/muhij (derivative), muhaliq (hair remover), jazibsamhaiwanat (antidote),akal (corrosive), muqarah (ulcerative),mushily qawi (purgative), muqi (emetic), muatis (sneezing agent), qataibalgham (expectorant),

Fresh leaf: musakinalam (analgesic), muhalil sard auram (anti-inflammatory), qatai, akal (corrosive)

Dry leaf: jail (cleaning), akal (corrosive), mujafif (siccative), munafisbalgham (expectorant), muqi (emetic), muqatae

Leaf decoction: muhamir (rubrificant), akal (corrosive), qatai

Flower: muqawie meda (gastric tonic), qataebalgham (expectorant), muhalil (Anti-inflammatory), musakin (analgesic),

Bark root: muadil (moderator), lazai/muhij (derivative) medawa ama, muariq (diaphoretic), muqawi (tonic), qataiwamukhrijbalgham (expectorant), mughshi, qatilkirmshikam (vermicide)

Istemal (therapeutic use):

Latex: daad (eczema), ganj (alopecia), bawasirmassa (haemorrhoidal mass), wajaulmafasil (rheumatoid arthritis), zeq un nafs (bronchial asthma), damma (asthma), khansi (cough), wajaulmafadilbalghami-ghatiya or naqras (gout), musqitjineen (abortificant)

Fresh leaf: wajaulmafasil (rheumatoid arthritis), kan ki dard e gosh me (otalgia), behra pan (deafness)

Dry leaf: muzminzaqam (chronic infectious disease), regenerate new tissues, damma (asthma). Khansi (cough)

Flower: wajaulmasafil (rheumatoid arthritis), dardkamar (backache)

Bark root: naqras (gout), atishak (syphilis), juzam (leprosy), qataeghashi, haiza (cholera),

Decoction bark root- tap larza (fever&shivering)

Gond: mulaiyantabawamunafisbalgham

Cotton: habisuddam (haemostatic)

Miqdar e khurak(dose):

powder bark root-2-3 rati, dry leaf – 2 rati to 1masha (gm), flower-2-4 rati, decoction flower-4 masha, latex (doodh)- 4 drops to 1 masha, gond – 1 masha

Mashurmurakkab (compound formulations): hab gul aak, habushar, raughan gul aak

Muzir (adverse effect): muqarah (ulcerative), for liver and lungs

Musleh (corrective): ghee, milk, oil substance, sheraghokru, vomiting

Badal(substitute): Jamalgutta

Phytochemicals:

Phytochemical studies on Calotropis procera have afforded several types of compounds such as Cardenolide, triterpenoids, alkaloids, resins, anthocyanins and proteolytic enzymes in latex,

flavonoids, tannins, sterol, saponins, cardiac glycosides, Flowers contain terpenes, multiflorenol, and cyclisadol.

Leaves: The leaves contain mainly the a-amyrin, a-amyrin ac-etate, ß-sitosterol, urosolicacid, cardenolides, calotropin, calotropagenin.

Latex: The latex contains caoutchouc, calotropin, calotoxin 0.15%, calactin 0.15%, uscharin 0.45%, trypsin, voruscharin, uzarigenin, syriogenin and proceroside.

Flower: The flower contains the flavonoids, queretin- 3- ratinoside, sterol, calactin, calotoxin, calotropagenin, calotropin, polysaccharide D-arabinose, glucose, glucosamine and L-rhamnose. Flow-ers also contain enzymes 3-proteinase and calotropain (protease).

Other chemical constituents of C. procera flowers are lupeol, uscharin, proceroside, proceragenin (cardenolide), syriogenin, taraxast-20(30)-en-3-(4-methyl-3- pentenoate), 3-thiazolinecardenolide, gigantin, giganteol, isogiganteol, uscharidin, uzarigeninvoruscharin a-calotropeol, 3-epimoretenol, a- lactuceryl acetate anda-lactuceryl isovalerate.

Bark: Root bark of C.procera contains triterpenes, A newnorditerpenyl ester, named Calotropterpenyl ester, and two unknown pentacyclictri terpinoids, namely calotropursenyl acetate andcalotropfriedelenyl acetate, akundarol isovalerate, mundarolisovalerate and quercetin -3- rutinoside.[14, 19, 39]

Four new ursane-type triterpenes calotroprocerol A, calotroproceryl acetate A, calotroprocerone A, andcalotroproceryl acetate B from the root bark of C. procera were isolated and structure elucidated in addition to five known compounds. Two labdane-type di terpenicgalactosides have been isolated for the first time from the roots of C. procera, and structures are established as Labdan18-ol-β-D-galactofuranoside and Labdan-3 β-ol-11, 15-olide18,20-dioic acid-3 β-D-galactofuranoside. The ethyl acetate fraction of the methanolic extract the root barks of C. procera (Asclepiadaceae) resulted inthe identification of a new cardenolide glycoside named procera side A. Three new cardenolides, along with eight known ones, were isolated from the latex of C. procera. Two new cardenolides, named ischarin and ischaridin, were isolated from C. procera Ait. (Asclepiadaceae). Then-BuOH fraction of the root bark of C. procera (Ait) R.Br. Seven new oxypregnaneoligoglycosides: Calotroposides H-N (1-7) were isolated and identified. [6]

Pharmacological activity:

According to the literature, pharmacological activity done recently are listed as Shown in table 3.

Anti-histaminic and bronchodilator activities:

The aqueous and methanol extracts of C. procera were investigated for anti-histaminic and bronchodilatory activities using histamine-induced contraction of isolated guinea pig tracheal chain (at 0.5 ml, 1 ml and 2 ml, and stock concentration of 0.5 mg/ml), contraction of isolated guinea pig ileum strip test (at 0.1, 0.2, 0.4, 0.8 and 1 ml, and stock concentration of 10 mg/ml), and haloperidol induced catalepsy test in rats (at 200 mg/kg and 300 mg/kg doses). Both extracts of C. procera significantly relaxed ($p<0.01$) contraction of isolated guinea pig trachea. The extracts also significantly inhibited ($p<0.001$) contraction of isolated guinea pig ileum. The aqueous extract did not significantly inhibit haloperidol-induced catalepsy. However, methanol extract significantly inhibited ($p<0.05$) haloperidol-induced catalepsy at 300 mg/kg. The aqueous and methanol root bark extract of C. procera was found to possess anti-histaminic and bronchodilatory activities in in vivo and in vitro antiasthmatic test on animal models, with the methanol extract having greater activity than the aqueous extract, thus support the folkloric use of the plant in inflammatory and allergic conditions including asthma.[23]

Anti hyperglycaemic activity and Anti Dyslipidemic activity:

Diabetes was induced by streptozotocin. *C. procera* flowers aqueous extract (CFEX) was given orally in doses of 10,20,30,40 and 50 mg/kg body weight. Serum levels of total cholesterol, triglycerides, HDL and LDL were measured at the beginning of experiment and at intervals of 1 day, 1 week, 2 weeks and 3 weeks and compared with those in positive controls treated with glibenclamide and untreated negative control animals. Results: Weight loss in CFEX-treated animals was not significantly different from positive control group. Decrease in serum glucose levels, comparable to positive controls, was observed in animals treated with CFEX 20,30,40 and 50 mg/kg body weight. The TC, TG and LDL significantly decreased while a significant increase in HDL was seen. C. procera flowers extract has shown antihyperglycemic and antidyslipidemic effects in experimental diabetic rats and may have the potential of a potent antidiabetic agent. [24]

Anti-fertility activity/Anti-Implantation activity

The effect of ethanolic extract of the roots of C.procera has been studied in albino rats to explore its antifertility and hormonal activities. A strong antiimplantation (inhibition 100%) and uterotropic activity was observed at the dose level of 250 mg/kg (1/4 of LD(50). No antiestrogenic activity could be detected.[25]

Anti-Arthritic activity:

This study was designed in Wistar rats for the investigation of antiarthritic activity and acute toxicity of Swallow wort. Arthritis was induced in Wistar rats by injecting 0.1 mL of Freund's complete adjuvant (FCA) on the 1st and 7th days subcutaneously into the subplantar region of the left hind paw. Evaluation of our experimental findings suggested that antiarthritic activity of methanol fraction of Swallow wort (MFCP) was greater than ethyl acetate fraction of Swallow wort (EAFCP), equal to standard ibuprofen, and slightly lower than standard indomethacin. MFCP significantly reduced paw edema on the 17th, 21st, 24th, and 28th days. It also showed significant effect ($p < 0.01$) on arthritic score, paw withdrawal latency, and body weight. The inhibition of serum lysosomal enzymes and proinflammatory cytokines along with the improvement of radiographic features of hind legs was also recorded with MFCP. Finally, it was concluded that MFCP can be a feasible therapeutic candidate for the treatment of inflammatory arthritis.[26]

Anti convulsant activity:

C.procera has been widely used traditionally for its analgesic and anti-inflammatory effects. It is also reportedly used in ethnomedicine for mental health disorders including epilepsy even in the absence of supporting scientific data. Thus, the potential of the plant to affect neurological functions was evaluated. Methods. Irwin's test was performed to determine the effect of the oral administration of the extract (30–3000 mg kg−1) on gross behavior and physiological function. The activity meter, rotarod, pentylenetetrazol- (PTZ-) induced convulsion, pentobarbitone-induced sleep test, and the tail immersion tests were used to evaluate the spontaneous activity, neuromuscular function, convulsive threshold, sedation, and analgesic effects of the C.procera extract (30–1000 mg/kg), respectively, in mice. C procera extract (CPE) exhibited significant anticonvulsant and analgesic effects. There was a significant increase in withdrawal latency of the CPE-treated animals in the tail immersion test for analgesia, while latency and duration of PTZ-induced convulsions were positively modulated.

C. procera extract showed significant central nervous system depressant effects in pentobarbitone-induced hypnosis at 100–1000 mg/kg and spontaneous activity test (30–1000 mg/kg). The extract also depicted impaired motor coordination at 100–1000 mg/kg dose levels. LD50 was estimated to be above 1000 mg kg−1. C. procera extract has significant central nervous system depressant and analgesic effects in mice. [27]

Anti-plasmodial / Antimalarial activity:

The plant's anti-plasmodial agent was extracted using 0.2 M-phosphate buffer (pH 7.0), followed by precipitation using acetone. 90 mice were divided into three main groups of 30 mice each, used for the curative, suppressive and prophylactic tests, respectively. The 30 mice in each of the main groups five groups of 6 mice were divided. The mice in the group 1, 2 and 3 (test groups) were made to receive graded doses of 25 mg/kg, 50 mg/kg and 75 mg/kg of the extract of C. procera latex intraperitoneally. The phytochemical constituents of the plant and its intraperitoneal median lethal dose (LD50) were also undertaken. The freeze-dried acetone extract exhibited acute toxicity with median lethal dose (LD50) of 745 mg/kg b.w in mice. The highest percentage of parasite suppression (61.85%), parasite cure (50.26%), and parasite prophylaxis (65.47%), were obtained for the groups treated with 75 mg/kg b.w/day of the extract. The least percentage of parasite suppression (44.74%), parasite cure (35.21%), and parasite prophylaxis (45.21%), were obtained for the groups treated with 25 mg/kg b.w of the extract. Also, a dose-dependent percentage of parasite suppression (53.03%), parasite cure (39.70%), and parasite prophylaxis (49.82%) were obtained for the groups treated with 50 mg/kg b.w. This is comparable to the groups treated with standard chloroquine. The extract also produced a significant elevation in body weight of the animals for suppressive and curative tests. However, there were observable significant decreases in body weight of the animals in the case of prophylactic test.

This study showed that the phosphate buffer extract of C. procera latex possesses anti-plasmodial activity. The results of this study can be used as a basis for further phytochemical investigations in the search for new and locally affordable antimalarial agents.[28]

Anti filarial activity:

In the present study, the antifilarial activity of ethanolic extract (A001) and its hexane fraction (F001) of C. procera flowers was investigated using the human filarial parasite Brugiamalayi.

Methods: A001 and F001 were tested for antifilarial activity using motility and 3-(4,5-dimethylthiazol-2- yl)-2,5 diphenyltetrazolium bromide (MTT) assays (in vitro) and in the rodent models B. malayi- Merionesung uiculatus and B. malayi-Mastomys coucha. In the rodent models, A001 and F001 were administered orally for 5 consecutive days, and the adult worm burden and course of microfilaraemia were determined.

Results: Both A001 and F001 showed microfilaricidal and macrofilaricidal activity in vitro. In animal models, A001 killed ~49-54% adult worms. In M. coucha model, F001 killed 12-60% adult worms in a dose (125-500 mg/kg) dependent manner; A001 and F001 suppressed microfilaraemia till days 91 and 35 post initiation of treatment, respectively. HPTLC revealed 0.61% lupeol, 0.50% β-sitosterol and 1.50% triacontanol in F001.Whether this activity is due to lupeol, β-sitosterol and triacontanol found in the hexane fraction remains to be investigated. This is the first report on the antifilarial efficacy of flowers of the plant C. procera.[29]

Wound healing activity:

A methanolic extract of the leaves of C.procera was subjected to chromatography over silica gel column to isolate as six phytoconstituents, and their structures were characterized as n-nonanyl octadec-9-enoate (n-nonanyl oleate, 1), lup-12, 20 (29)-dien-3β-olylhexadecanoate (lupenyl palmitate, 2), 1-methyl-4-(2′-n-decanyl)-cyclohex-1-en-5-one (3), (Z)-eicos-9-enoic acid (gadoleic acid, 4), n-decanoyl-α-L-arabinopyranoside (n-capryl arabinoside, 5) and stigmast-5- en- 3β- ol- 3-O-β-D-glucopyranosyl-(1→2)-β-D-glucopyranoside-2″-hexadecanoate (β-sitosterol-diglucosyl palmitate, 6). The structures of all these natural products have been established based on spectral data analyses for the screening of the wound healing activity of all 6 compounds, and we found Compound-1, 2, 4, and compound 6 having excellent results during wound healing in rats. This results authenticate the beneficial effects of Compound-1, 2, 4, and 6 for an accelerated wound healing activity.[30]

Anthelmintic activity:

The crude latex of C.procera was evaluated for anthelmintic activity using adult earthworms. Both fresh as well as aqueous extracts of dried latex exhibited a dose-dependent inhibition of spontaneous motility (paralysis) and evoked responses to pin-prick. With higher doses (100mg/ml of aqueous extract of dry latex and 100% fresh latex) the effects were comparable with that of 3% piperazine. However, there was no final recovery in the case of worms treated with latex in contrast to piperazine with which the paralysis was reversible and the worms

recovered completely within 6 hours. The results show that latex possesses wormicidal activity and thus, may be useful as an anthelmintic.[31]

Anti-Tumor studies:

The objective of the present study was to investigate the antitumor potential of ethanolic root extract of C. procera against canine mammary tumor cell line (CF41-Mg). MTT, western blot, and flow cytometry assays were carried out to evaluate the possible cytotoxicity and apoptosis induction of the extract. MTT results showed that the extract had a potent cytotoxic activity in a dose-dependent manner with an IC50 of 9.00 μg mL-1. Based on the results of flow cytometry and western blotting, IC50 concentration of the extract induced significant apoptosis in the studied cell line, possibly through down-regulation of Bcl-2 expression. The results of the present study clearly indicated that the root extract of C. procera had promising anti-cancer activity and could be considered as a candidate for the treatment of mammary tumors.[32]

Anti-inflammatory and Antioxidative activity:

The present study was carried out to evaluate the protective effect of its methanol extract (MeDL) against inflammation and oxidative stress in monoarthritis induced by Freund's complete adjuvant (FCA) in rats. Intra-articular injection of FCA produced inflammation of the joint with a peak effect occurring on day 4 where a maximum increase in the levels of myeloperoxidase and inflammatory mediators like PGE2, TNF-α, and nitric oxide was observed. This was associated with oxidative stress with a marked reduction in the levels of glutathione, catalase, superoxide dismutase and glutathione peroxidase and an increase in the lipid peroxidation as indicated by the higher levels of thiobarbituric acid reactive substances (TBARSs). Subsequently on day 28 the histological analysis of the joint also revealed arthritic changes. Daily treatment of rats with MeDL (50 and 500 mg/kg) and standard anti-inflammatory drug rofecoxib (20 and 100 mg/kg), produced a significant attenuation in the inflammatory response and ameliorated the arthritic changes in the joint. The protection afforded by MeDL and rofecoxib was more pronounced than that of phenylbutazone and was associated with the normalizing of the levels of inflammatory mediators and biochemical parameters of oxidative stress. However, the overall protection afforded by rofecoxib was better than that of MeDL.[33]

Anti-cancerous activity:

To evaluate the anticancer property of the dried latex (DL) of C. procera, a tropical medicinal plant, in the X15-myc transgenic mouse model of hepatocellular carcinoma and to elucidate its mechanism of action in cell culture.

The young transgenic mice were orally fed with the aqueous suspension of DL (400 mg/kg for 5 d/wk) for 15 wk and their liver was examined for histopathological changes at 20 wk. Serum levels of vascular endothelial growth factor (VEGF) were also measured in these animals. To characterize the active fraction, DL was extracted with petroleum ether followed by methanol. The methanolic extract was sub-fractionated on a silica gel G column using a combination of non-polar and polar solvents and eleven fractions were obtained. Each fraction was analyzed for cytotoxic effect on hepatoma (Huh7) and non-hepatoma (COS-1) cell lines and non-transformed hepatocytes (AML12) using tetrazolium (MTT) assay. Finally, the mechanism of cell death was investigated by measuring the levels of Bcl2, caspase 3 and DNA fragmentation. DL treatment of mice showed complete protection against hepatocarcinogenesis. No adverse effect was observed in these animals. The serum VEGF level was significantly lowered in the treated mice as compared to control animals. Cell culture studies revealed that the methanolic extract of DL as well as its fraction 8 induced extensive cell death in both Huh-7 and COS-1 cells while AML12 cells were spared. This was accompanied by extensive fragmentation of DNA in Huh-7 and COS-1 cells. No change in the levels of canonical markers of apoptosis such as Bcl2 and caspase 3 was observed. DL of C. procera has the potential for anti-cancer therapy due to its differentiable targets and non-interference with the pathway of apoptosis.[34]

Table No. 3: Pharmacological activity

Plant part	Pharmacological activity
Leaf	Anti hyperglycemic effect Anti malarial Anti plasmodial Anti hyperbilirubinemic Anti microbial activity Wound healing activity Anthelmintic effect

Latex	Anti diarrhoeal activity Anti convulsant Neuroprotective Anti oxidant activity Anti cancer Anti inflammatory Anti tumour Wound healing antinociceptive
Flower	Hepatoprotective activity Anti malarial Antibacterial Anthelmintic Antiparasitic Antifertility Anti microbial Antipyretic Antitumour
Stem bark	Anti inflammatory Anti ulcer activity
Seed	Anti microbial Antibacterial
Root	Anti fertility Anti tumour studies Anti-implantation activity Anti oxidant Anti cancerous Oestrogenic functionality Anti inflammatory Anti ulcerative

Root bark	Anti tumour Oestrogenic functionality Wound healing activity Anti-histaminic and bronchodilatory activities

Toxicity study:

C. procera leaves and root-bark aqueous extracts were evaluated for their toxic and behavioral effects using adult mice. Toxicity studies were carried out using Organisation for Economic Cooperation and Development guidelines 423 and 407 for acute and subacute evaluation. Behavioral studies were performed using a traction test, fireplace test, hole-board test and forced-swimming test to evaluate the sedative, anxiety and depressive-like activities of the extracts. Very low acute toxicity was observed in mice that received both leaves and root-bark extracts. The subacute test showed some morphological, biochemical and hematological changes in the treated groups. The behavioral assessment demonstrated anxiety effects on mice for C. procera leaf extract (400 mg/kg of b.w).The acute use of C. procera (leaves and root-barks) aqueous extracts could be considered as low toxic. However, their repeated uses could have harmful effect on some organs. Likewise, a single dose up to 400 mg/kg b.w of these extracts produce no sedative or depressive-like effect, but they possess possible dose-dependent anxiety effect. Yet, more studies are necessary to relate these results to the chemical profile of the plant extracts. [11]

The latex is toxic and can cause rash, blisters and serious inflammations in sensitive persons and it may lead to blindness. Ingesting larger doses of latex produce toxic symptoms like burning in the throat, irritation of the stomach, nausea, vomiting, diarrhoea, tremors, vertigo and convulsions. [20,21]

Recent advancement- socio-economic use:

Non-medical socio-economic uses of *Calotropis procera* listed- shown in table 4.

- Phytoremediation: *C. procera* is a phytoaccumulator of several heavy metals such as manganese, lead, chromium, iron, copper, nickel, cobalt, strontium, and cadmium (D'Souza

et al., 2010; Almehdi et al., 2019; Ullah and Muhammad, 2020). As determined from biophysical measurements, roots and leaves of C. procera are also tolerant against aluminum toxicity (Hussain et al., 2018). *C. procera* can also be used as a photo-monitoring tool to assess metals in the environment (Gajbhiye et al., 2019). It has also been observed that old leaves of the plant have a greater ability to accumulate heavy metals compared to any other plant parts (Almehdi et al., 2019). This suggests that C. procera uses the metabolically less active leaves as sinks for heavy metals (Almehdi et al., 2019).[5]

- Recently, seed hair from Calotropis has beenpresented as a potential silk replacer.
- Seed hair has beentested as a thermal insulating material and has been found comparable to Rockwool mineral fibers in its insulating properties.
- Insulating material from a composite of C. procera fibres and phenol-formaldehyde resins has been shown to have high water repellency. C. procera flax has been forwarded as abinding material for the improvement of acoustic plaster. C.procera fibers were tested as reinforcement material in an epoxymatrix, too.[35,36]
- The heat values of whole plant fractions extracted with benzene, with petroleum ether and with ethyl acetate have been given as 9.6 kcal/g, 13.7kcal/g, and 7.4 kcal/g, respectively. [37]
- C. procera-silver nanoparticles were prepared by mixing 3% extract of latex and 3% silver nitrate solution, characterization of silver nanoparticles done by using Xray diffraction, UV-visible spectrophotometer, transmission electron microscopy and fourier transform infrared spectroscopy. The silver nanoparticles were evaluated against bacteria *(Pseudomonas, 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 Ag0). [38]
- The plant yields valuable hydrocarbons and holds the potential to produce bioenergy and biofuel, which could be used as diesel substitutes in the future (Kumar, 2018). Studies also recommend the use of its enzyme extract to tenderize muscle foods such as pork, beef, and chicken (Rawdkuen et al., 2013), dehair crude leather (Lopéz et al., 2017), and coagulate

milk for the production of fresh cheese (Abebe and Emire, 2020). C. procera leaves are also a potential source of natural colorants for textile fabrics (Hussaan et al., 2017).[5, 39,40]

Table No. 4: Non-medicinal uses of *Calotropis procera*

Plant part	Non medicinal use
Wood	Building material(light weight wood) Bioenergy Biofuel
Stem	Roof making
Stem fibre	Paper Nags Nets Rope making
Seed	Biodesel Stuffing for pillows and mattresses
Seed hair	Silk replacer
Latex	Natural rubber Synthesis of nanoparticles
Dried leaf powder	Adsorbent for dyes Biogas Fodder during dry periods Petrocrops
Dried flower	Sugar substitute
Root and leaf	Phyto remediation of heavy metals

CONCLUSION

C.procera is a plant with medicinal and socio-economical important species and also an invasive species. The latex may be hydrocracked to obtain hydrocarbons. There is need of more research work on *Calotropis procera* to obtain petroleum products. In conclusion, as per the available literature its pharmacological use has proven by few of recent pharmacological activities done on the potential herbs which exhibits same action of drug. The present review

article may be useful to provide concise recent activities and additional information about the invasive potential herb.

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