World Journal of Pharmaceutical and Life Sciences
WJPLS
www.wjpls.org
SJIF Impact Factor: 7.409

PHARMACOLOGICAL AND BOTANICAL PROFILE OF CALOTROPIS PROCERA-A MULTI-POTENTIAL PLANT TO HUMANKIND

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Article Received on 23/08/2024 **Article Revised on 13/09/2024** **Article Accepted on 03/10/2024**

ABSTRACT
Medicinal plants are a rich source of pharmaceuticals; in fact, the majority of drugs on the market are derived from various types of plants or herb species. Many crude products not only provided the basis for many medicines, but they also had significant therapeutic effects. *Calotropis procera* Linn is an ayurvedic plant that has long been used to make traditional medicines to treat a wide range of diseases. It is regarded a medicinal plant belonging to the Asclepiadaceae family, which is distributed throughout India and other tropical areas. The collected product from roots, barks, leaves, flowers, and other parts has a variety of therapeutic properties that are extremely beneficial. *C.procera* possess a wide range of pharmacological activities such as anticancer, antidiabetic, analgesic, anti-inflammatory, anthelmintic, antimicrobial, antidiarroheal, anticonvulsant, hepatoprotective, antioestrogenic, antiulcer, antimalarial, anti-fertility etc. The phytochemical constituents of this plant revealed that it includes cardiac glycosides, triterpenoids, flavonoids, cardenolide, tannis, saponins, resins. Latex of *C.procera* contain a powerful bacteriolytic enzyme called calactin, which is a cardiotoxin and a robust nontoxic proteolytic enzyme called calotropin. *Calotropis procera's* macroscopic and microscopic features, as well as its general phytochemical constituents and pharmacological action, are the subject of the current review.

KEYWORDS: Medicinal plants, Therapeutic activity, Calotropin, Macroscopic character, Traditional medicine.

INTRODUCTION
Humans have relied heavily on plants for shelter, medicines, scents, meals, tastes, clothes, and fertilizers etc.[1] The World Health Organization (WHO) classifies medicinal plants as those that contain chemicals for therapeutic purposes or serve as substrates for the production of valuable pharmaceuticals.[2] This plant-based traditional medicine system continues to play an important role in health care, with around 80% of the world's population relying on traditional medicines for primary care.[3] Various studies have shown that plants are an important source of medication discovery and development.[4] Historically, folks have pursued natural therapies to mitigate diverse ailments. The reliance on plants as a medicinal resource is widespread in developing nations, with traditional medicine serving as a fundamental component of healthcare for approximately 80% of the population.[5] In China, traditional tribal medicines account for around 40% of the entire medicinal intake. India, Pakistan, Japan, Thailand, and Sri Lanka are nations where the practice of traditional medicine is prevalent.[6] *Calotropis procera* Linn is a significant plant in herbal medicine. It is popularly known as French cotton, which is used as medication fairly throughout the greater part of India and is referred to as a topical plant growing at around 1050 meters.[7] *Calotropis procera* is a perennial shrub belonging to the Apocynaceae family. It is widely accessible throughout Africa, America, and Asia. The shrub is indigenous to Punjab, Pakistan, and is well-suited to many habitats, such as plains, pastures, and roadside regions.[8] *Calotropis procera* likely arrived in Australia as garden plants in the early 1900s. It expanded over Katherine and Roper River in the 1950s. This species is widespread in northern Australia.[9]

C. procera is a plant whose maximum height ranges from 2.5 to 6 meters. The plant is named because of its fleshy, grayish-green leaves that bear a resemblance to wax. Its breadth ranges from 2.5 to 10 cm, while its length ranges from 15 to 30 cm. The plant produces fleshy fruits and has a compact root structure.[10] Carpenter bees primarily pollinate *C. procera.*[11] The plant in question is a blossoming species commonly

referred to as Arka, or Sodom apple. It is commonly grown in tropical and subtropical parts of Asia and Africa. This plant is renowned for its abundant production of latex.[12] The plant possesses a diverse array of secondary metabolite categories, including flavonoids, cardenolides, alkaloids, tannins, triterpenes, and proteolytic enzymes. These chemicals have demonstrated a variety of biological actions, such as hepatoprotective, antifertility, antimalarial, anticancer, anti-inflammatory, and analgesic etc properties.[13]

Common name[14,15]

Arabic: Dead Sea plant, debaj, usher, oshar, kisher; **Turkish:** ipekag **French:** pomme de Sodome, algodón de seda, arbre á soie, coton soie, arbre a soie du Senegal; **Bengali:** Akada, Akauwa, Rui, **English:** Calotrope, Calotropis, Dead Sea fruit, Desert wick, Giant milkweed, Swallow-wort, Mudar fibre, Rubber bush, Rubber tree, Sodom apple; **Hindi:** madar, akada, akdo, aak; **Swahili:** mpamba mwitu; **Spanish:** Bomba, Algodón extranjero, cazuela **Somali:** Boah, Bo'ah; **Marathi:** Mandara, Alaka, Ravi, Rui; **Oriya:** Arakh **Punjabi:** aK; **Tamil:** Vellerukku, Erukku; **Telugu:** Jilledu; **Urdu:** Madar, aak; **Iran (Persian):** Kharak **German:** wahre mudarpflanzer, gomeiner; **Nigeria (Hausa and Yoruba)**: Tumfafiya, Bomubomu and Kayou **Pakistan:** Spalmai or Spalmey, **Morocco (Darija):** Tourja **Thailand:** NR **Bangladesh:** Akondo gach **Ethiopia:** Bunagadhee, Ttobia **Brazil (Portuguese):** Flor de seda, ciu´ me, ciumeira **Plant taxonomy.[16]**

Table 1: *Calotropis procera* Plant Taxonomical Data.

Rank Description	
Kingdom	Plantae
Subkingdom	Tracheobionta
Superdivision	Spermatophyta
Division	Magnoliophyta
Class	Magnoliopsida
Subclass	Asteridae
Order	Gentianales
Family	Asclepiadaceae
Genus	Calotropis

Geographic distribution

C. procera is native to North and Tropical Africa, Western and South Asia and Indochina up to the Arabian Peninsula, and it is widely distributed in Australia, American countries and West indies.[17] The plant is also found in Afghanistan, Algeria, Australia, Bangladesh, Bolivia, Brazil, Cameroon, Chad, Ecuador, China, Colombia, Cuba, Ecuador, Egypt, Eritrea, Ethiopia, Ghana, Guatemala, Guinea-Bissau, Haiti, Israel, Jordan, Lebanon, Mauritania, Mexico, Mozambique, Nepal, Puerto Rico, Peru, Nicaragua, Pakistan, Paraguay, Saudi Arabia, Senegal, Sudan, Tanzania, Uganda, United Arab Emirates, Uruguay, Venezuela, Yemen, and Zimbabwe are among the countries where it grows.[18] This plant *Calotropis procera* is also widespread in tropical Asia. It grows in almost all parts of Punjab Pakistan as wild shrub especially in plains, pasture and roads way.[19]

Macroscopic description

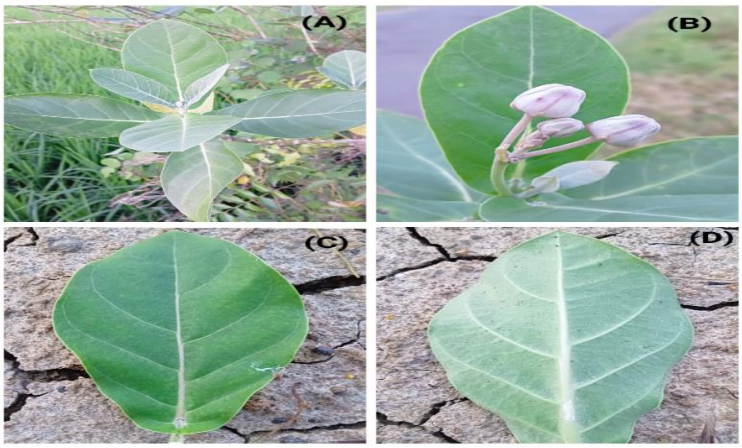


Figure 1: A) *Calotropis Procera* plant, B) Bellshaped summetrical flower of *Calotropis Procera,* C) Oblong-obviate leave with hairy covering, D) Lower leaf surface with venation.

Root

The root is characterized by its simplicity, branching, and woody nature at the base. It is coated with a fissured, corky bark. The branches have a deep and sturdy root system with only a few branches.[20]

Bark

The bark is corky, furrowed, and light gray.[21]

Leaves

In addition to being opposite-decussate, simple, subsessile, and exstipulate, the leaves also have a fine layer of soft hairs that can sting and are somewhat leathery.[22] The plant has opposing, sessile, oblong-obviate leaves that range in length from 7 to 18 cm and in width from 5 to 13 cm. The leaves have a pointy to blunt tip. A fine, hairy covering like leather covers the leaves.[23]

Flowers

Flowers are bellshaped, resembling a campanula, with bracts, having all the necessary parts, capable of both male and female reproduction, symmetrical in shape, with five petals, positioned below the ovary, attached to a stalk, arranged in many clusters, forming anumbrellalike structure, and supported by a stem.[24]

The flowers are composed of 5 small triangular sepals thatare dirty white in color. Petalsare measuring 1cm x 1cm, which have a white base and purple points. Surrounding a white 5lobed stigma are 5 stamens with purple tips. The calyx is separated all the way to the base, smooth, and has five sepals that are elliptical and pointed, measuring 2.5 mm.[25]

The androecium consists of five stamens that are gynandrous, with anthers that are dithecous and coherent. The gynoecium consists of two carpels that are separate from each other, andthe styles are fused at their tip. The stigma is peltate and has five lateral stigmatic surfaces. The anthers are fused to the stigma, creating a structure called a gynostegium.[26]

Fruits

Fruits are a straightforward, green, fleshy, inflated, and somewhat spherical to diagonally egg-shaped follicle. Fruits are characterized by their grey-green colour and typically measure approximately 8-12 cm in size.[27]

Seeds

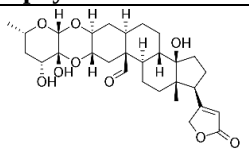
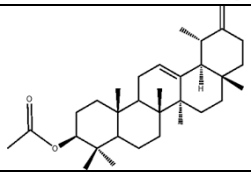
The dimensions of the seed are 6 by 4 millimeters, with a broadly oval shape. It has a sharp tip and a flattened appearance, with narrow margins. The surface is covered in a fine layer of tomentose hairs and is light brown in color.[28]

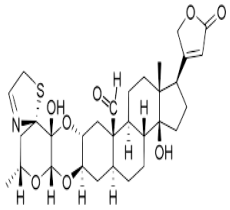
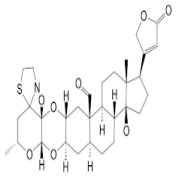
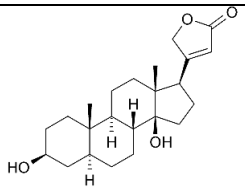
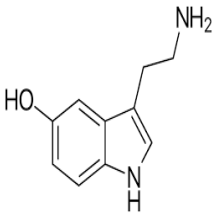
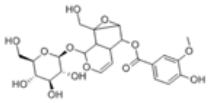
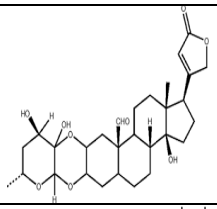
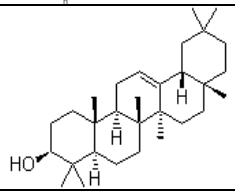
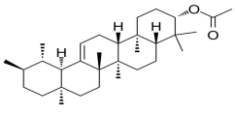
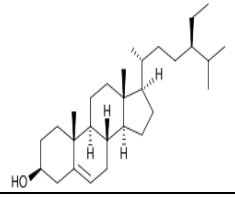
Microscopic description

Microscopic analysis of a transverse root cut shows that the outermost cork tissue has 4–8 rows of tangentially elongated, radially organized cells, followed by 3-6 rows of irregular, thick-walled secondary cortex cells without calcium oxalate crystals or starch grains. The cortex has large polyhedral parenchymatous cells and spherical starch granules. Some cortical cells have calcium oxalate rosette crystals and brown laticifer cells. Sive components and thick-walled sieve tubes make up phloem parenchyma. Phloem cells, which are more visible in the inner area and that the unit crosses to tetraseriate medullary rays, contain calcium oxalate crystals, starch grains, and laticifers like the cortex: Only the phloem contains the cambium, 2–5 rows of thin-walled cells with tangential elongations. Xylem is the root's central vascular network. The tracheid, fibers, and xylem parenchyma contain vessels organized radially in groups of 2-7. solitary vessels, cylindrical with bordered pits on their walls, xylem fibres long, lignified with large lumen, tapering on ends, simple pits on walls. Radially elongated cells packed with starch like cortical cells make up medullary rays 1-4. Medullary rays are striate and trimerite outside and uni or biseriate inside.Under a microscope, a vertical leaf slice is dorsiventral, with an elevated midrib on the bottom and uniformly extended wings. Upper and lower epidermis are thick and cuticulated with small cubical cells. The top epidermis has striations and rubiaceous stomata. Only the midrib has collenchymatous hypodermal area. Mesophyll is divided into upper palisade and lower spongy. Three to four layers of compactly packed chloroplast cells form the palisade. They are modest and abundant in the wings, but one large arch-shaped vascular bundle is in the midrib. Leaf laticifers canals carry milky-white fluids, another unique feature. Epidermal peeling also shows a few uniseriate trichomes. Lime oxalate crystals are single and clustered. Dense, striated cuticle covers upper and lower epidermis. Below upper epidermis, three layers of tightly structured palisade parenchyma. Intercellular gaps and irregular central cells characterize spongey parenchyma tissues. Laticifers and vascular bundles are scattered here.The petiole has a single, massive, bicollateral, arc-shaped vascular bundle, whereas the epidermis and ground tissues are parenchymatous.[29]

Phytochemistry

C. procera is rich in a diverse array of phytochemicals such as cardiac glycosides, flavonoids, terpenoids, steroids/ phytosterols, phenolics, tannins, proteins, amino acids, resins, enzymes, and fatty acids.[30]

Sl No	Name of compound	Molecular Formula	Molecular Weight	Nature of compound	Structure of phytoconstituents	Pharmacological activity	References
1	Calotropin	$C_{29}H_{40}O_9$	532.6 g/ml	Cardenolide glycoside.		Cytotoxic and antitumor effect, Anthelmintic activity,. Antioxidant effect	[31]
2	Calotoxin	$C_{29}H_{40}O_{10}$	548.6 g/ml	Cardiac glycosides		Asthma, epilepsy, cancer, sexual disorders, skin diseases	[32]

3	Uscharin	$C_{31}H_{41}NO_8S$	587.7 g/ml	Cardiac glycosides		Insecticidal Activity, Vasodilatation Effect, CNS Activity.	[33]
4	Voruscharin	$C_{31}H_{43}NO_8S$	589.7 g/ml	Steroid glycosides		Wound healing potential, Antiplasmodial activity, Hepatoprotective activity	[34]
5	Uzarigenin	$C_{23}H_{34}0_4$	374.5 g/ml	Cardenolide glycoside.		lesser vomiting action,	[35]
6	Syriogenin	$C_{23}H_{34}0_5$	390.5 g/ml	Steroid glycoside		Potentiation of serotonergic neurotransmission, Therapeutic activity in depression, anxiety, obsessional and impulse control disorders.	[36]
7	Proceroside	$C_{29}H_{40}O_{10}$	548.6g/ml	Glycoside		various diseases like snake bite, body pain, asthma, epilepsy, cancer, sexual disorders.	[37]
8	Calotropagenin	$C_{23}H_{32}O_6$	404.5 g/ml	Cardiac glycoside		Digestive disorders, toothache, cramps, joint pain, and many others.	[38]
9	β-amyrin	$C_{30}H_{50}O$	426.7 g/ml	Pentacyclic triterpenoid		Exhibits long-lasting ant nociceptive and anti-inflammatory	[39]
10	α-Amyrin acetate	$C_{32}H_{52}O_2$	468.8 g/ml	Triterpenoid		Possesses anti-inflammatory, antispasmodic, and relaxing properties.	[40]
11	B-sitosterol	$C_{29}H_{50}O$	414.71 g/ml	Natural Triterpenoid		By reducing the amount of cholesterol that can enter the body, beta-sitosterol may help lower cholesterol levels	[41]

Bark Root

The root bark of *C. procera* contains triterpenes, including a novel norditerpenyl ester called calotropterpenyl ester, as well as two unidentified pentacyclic triterpenoids known as calotropursenyl acetate and calotropfriedelenyl acetate. Additionally, it contains akundarol isovalerate, mundarol isovalerate, and quercetin-3-rutinoside. The compounds benzoyllineolone, benzoylisolineolone, calotropterpenyl ester, calotropursenyl acetate, and calotropfriedelenyl acetate were also discovered to be present in the root bark.[42] The stem bark was analyzed for phytochemicals and found to contain a range of secondary metabolites including polyphenols, triterpene glycosides, flavonoids, and coumarins.[43] A new cardenolide compound, 2-oxovoruscharin, was extracted from the root bark and subsequently transformed into its semisynthetic derivative, known as UNBS1450.[44]

Leaves

The phytochemical screening revealed the presence of tannin, saponin, alkaloids, flavonoids, steroids, phenolics, reducing sugar, and terpenoids. However, terpenoids were not found in both the ethyl acetate and n-hexane extracts, and cardiac glycoside was also absent.[45]

Flower

The flower contains polysaccharides that consist of D-arabinose, glucose, glucosamine, and L-rhamnose. Additionally, it contains flavonoids such as queretin-3-ratinoside, calactin, calotoxin, calotropagenin, and calotropin. Flowers contain various enzymes and compounds such as 3-proteinase, calotropin (protease), lupeol, uscharin, proceroside, proceragenin (cardenolide), syriogenin, taraxast-20(30)-en-3-(4-methyl-3-pentenoate), 3-thiazoline cardenolide, gigantin, giganteol, isogiganteol, uscharidin, vuzarigeninvoruscharin, a-calotropeol, 3-epimoretenol, alactuceryl acetate, and a-lactucerylisovalerate.[46]

Latex

The latex of this substance contains various compounds, including caoutchouc, calotoxin (0.15%), proceroside 18, syriogenin, trypsin, uzarigenin, uscharin (0.45%), and voruscharin. It also contains a potent bacteriolytic enzyme and a highly toxic glycoside called calactin (0.15%). Additionally, it contains calotropin D I, calotropin D II, calotropin-F I, calotropin F II, and a non-toxic proteolytic enzyme called calotropin (2%-3%). Calotropin exhibits a higher degree of proteolytic activity compared to papain. Additionally, bromelain has the ability to coagulate milk and digest meat, gelatine, and casein.[47]

Pharmacological Activity

Analgesic activity

An analgesic effect against acetic acid-induced writhings was observed after administering a single oral dosage of dry latex, with doses ranging from 165 to 830 mg/kg. The analgesic effect was shown to be dose-dependent. The impact of dry latex at a dosage of 415 mg/kg was more prominent in comparison to an oral dosage of 100 mg/kg. Aspirin dosage.[48]

In their study, Saba et al. (2011) employed an ethanolic extract derived from the plant's leaf to conduct several tests on mice and rats. These tests included acetic acid-induced writhing and tail-flick tests in mice, formalin-induced paw lick test, and carrageenan-induced paw oedema test in Wistar rats. This study revealed that the plant exhibited analgesic effects in both the central and peripheral regions. It was also noteworthy that naloxone and opioid antagonists had no impact on the analgesic properties of this extract, it can be inferred that the extract likely interacts with other nociceptive pathways.[49] Basu et al. (1991) determined that the ethanolic extract derived from the flowers of the plant exhibited a mild analgesic effect. The root extract's chloroform fraction exhibited promising analgesic effects on Acetic acid administration in rats.[50]

Anticancer activity

According to Choedon et al. (2006), the dried latex of this plant caused significant cell death in both hepatoma (Huh-7) and non-hepatoma (COS-1) cell lines. The dry latex (DL) of *Calotropis procera* inhibits the growth of roots and the mitotic activity of the tip meristem of *Allium cepa.* This model evaluates the cytotoxic and anti-mitotic effects of *C. procera* latex, which has cytotoxic properties comparable to established anticancer drugs such as podophyllotoxin and cyclophosphamide.[51] Mathur et al. (2009) investigated the cytotoxic effects of methanol (CM), hexane (CH), water (CW), and ethyl acetate (CE) extracts of *C. procera* on Hep2 cells using the MTT assay to measure cell viability. According to their analysis, the ethyl acetate (CE) sample had the highest potency level as a growth inhibitor.[52] Oliveira et al. (2007) studied the cytotoxic activity of laticifer proteins (LP) recovered from the latex of *C. procera* and found significant cytotoxicity with IC50 values ranging from 0.42 to 1.36 µg/mL against SF295 and MDA-cell lines.[53] Bou Malhab LJ et al conducted a study and observed that the ethanolic extract of *C. porcera* is capable of cell inhibition in a dose-dependent manner. The IC50 values for MCF-7 and HCT-116 cells for that study at 24 hours were calculated to be 50 µg/mL and 55 µg/mL, respectively. The breast cell line experienced cell cycle arrest in the sub-G1 phase, while the human colon cells experienced cell cycle arrest in the G2-M phase.[54] In 2010, Hemerson I.F. et al. conducted a study that showed the substantial potential of ethyl acetate and acetone extracts of *C.procera* for causing cytotoxicity in both in-vitro and in-vivo settings. The IC50 values for these extracts ranged from 0.8 to 4.4 g/mL, indicating their potency. Additionally, the study found that these extracts exhibited reversible toxic effects on the liver and kidneys.[55] In a study conducted by Aparna L. Joshi et al. (2015), demonstrated that the methanolic extract of *C. porcera* has the ability to hinder the proliferation of

human skin melanoma cells (SK-MEL-2) at the G2/M phase, primarily due to its cardenolide concentration.[56] In a study conducted by Ayobami Matthew Olajuyin et al. (2021), it was discovered that the growth of H1299 lung cancer cells can be suppressed by using a methanolic extract derived from the leaves of *Calotropis procera*.[57] Ana Carolina Silveira Rabelo (2021) in their most recent study found that phenolic extracts from *C. porcera* effectively inhibited cell viability (specifically breast cell (4T1)) by selectively blocking Akt/mTOR Signalling. Additionally, these extracts induced apoptosis and reduced cell migration.[58] S.R.M. Ibrahim et al. discussed the cytotoxic effects of the *C. procera* aqueous solution on hepatocellular carcinoma, non-small cell lung cancer, glioblastoma, and prostate cancer cell lines in vitro.[59]

Antifertility studies

In a study conducted by Sharma and Jacob (2001), the researchers examined the impact of the water-based and methanol-based extracts of the plant's flower on male albino rats. The extracts were administered at doses of 10.0 or 5.0 mg per mouse every other day to assess their antifertility effects. This study provided evidence that the flower of *C. procera* had a notable inhibitory effect on sperm production in albino mice. However, it did not have any noticeable influence on sexual desire or behaviour, despite the specific dosages and experimental schedule employed.[60] Kamath & Rana (2002) found that the ethanolic extract of this plant's root had a strong anti-implantation (100%) and uterotropic effect at low doses. There was a lack of evidence indicating any antiestrogenic activity.[61]

Antihelmintic study

Qarawi et al. (2001) conducted a study where they tested *C. porcera* latex on sheep to evaluate its effectiveness against *Haemochus contortus* larvae. After 20 minutes of treatment, the latex showed a larvicidal effect in vitro that depended on the dose.[62] In another subsequent study on the anthelmintic effects of the plant's latex, Shivkar and Kumar (2003) employed mature earthworms. Both fresh and aqueous latex extracts demonstrated a dose-dependent inhibition of spontaneous mortality. The latex of the plant exhibited vermifugal characteristics.[63]

Iqbal et al. (2005) conducted research both inside and out side of a living organism to examinecomparative effects of levamisole with *C. porcera* flower extract.*Calotropis procera* flowers demonstrated potent anthelmintic activit y against worms, it was inferior to levamisole.[64] Sing et al. (2015) showed via their research that several leaf extracts of the plant had in vitro antihelmintic efficacy against Indian earthworms *Pheritima posthuma*, utilizing piperazine citrate as the reference standard. Nevertheless, the hydroethanolic extract of *Calotropis procera* leaves, at a concentration of 70%, exhibited superior efficacy compared to the n-butanol and chloroform extracts.[65] Aggarwal et al. (2016) conducted a study to compare the efficiency of ethanolic and aqueous extracts of *C. Procera's* flower with albendazole. They used in vitro system to study the worm mortality suppression on live *Gastrothylax indicus* worms. The mortality index (MI) was 0.90 for *C. procera* and 1.0 for albendazole. The extracts exhibited a %WMI (percent mean worm motility inhibition) range of 70% to 100%.[66]

Antihyperglycemic activity

Bhaskar and Sumant (2009) showed in their studies anti-diabetic solid characteristics of the *C. procera* root extracts. Antidiabetic research using petroleum ether, methanol, and an aqueous plant extract at 250 mg/kg daily for 15 days produced results. Conventional medicine Glibenclamide (500 g/kg) was investigated to be compared.[67] Strong antihyperglycemic action of hydroalcoholic extracts of the plant leaves was claimed by Mário C.L. Neto et al. (2013). These dried extracts at a dose (300 and 600 mg/kg) not only greatly lower blood glucose levels but also greatly improve metabolic health, therefore enhancing the oral tolerance for glucose.[68] In 2016, Kazeem et al. looked at the α-amylase and α-glucosidase inhibitory potential of *Calotropis procera* leaf. The ethanolic and aqueous extracts clearly inhibit the carbohydrate hydrolyzing enzymes α-amylase and α-glycosidase, hence producing their anti-diabetic action.[69]

Hepatoprotective activity

According to Setty et al.(2007), hydroalcoholic extracts of *C.porcera* flower exhibit hepatoprotective effect in rats against paracetamol-induced hepatitis.These extracts (200mg/kg, 400mg/kg) reduced SGPT, SGOT, ALP, bilirubin, and cholesterol levels to near-normal levels in a dose-dependent manner.[70] In the same year, Qureshi et al. (2007) discovered that 70% ethanolic extracts of this plant's bloom exert hepatoprotective action. They also discovered that the plant has hepatoprotective properties due to its antioxidant activity.[71] In a study, Prakash et al (2011) discovered that a methanolic extract of the plant's root bark has hepatoprotective efficacy against CCl4-induced liver damage. This extract has the capacity to lower the body's biochemical hepatotoxic substances.[72] In their study, Dahiru et al. (2013) examined the effectiveness of ethanolic extracts from the root bark of a plant in protecting the liver against damage caused by CCl_4 in female rats. The analysis revealed that the extracts did not exhibit any hepatoprotective properties in this study.[73] Alrheam (2015) discovered that aqueous, chloroform, and ethanol extracts and latex of this plant had a propensity to lower acid phosphatase, alkaline phosphatase, aspartate aminotransferase, alanine aminotransferase, and total protein, albumin, and bilirubin levels in CCl_4-induced rats.[74] Agarwal and Murti (2016) discovered that aqueous leaf extracts of *C.porcera* have hepatoprotective efficacy at dosages of 150, 400, and 800mg/kg in their study.[75]

Inflammatory activity

Kumar & Basu (1994), suggested that *Calotropis procera* latex exhibits anti-inflammatory properties in rat paw oedema models, with a single dose significantly reducing inflammation.[76] In their research, Mansouri & Hemmati (2015) found that in a carrageenan-induced rat paw oedema model, the dry latex of plants with acetone and aqueous extracts demonstrated the best oedema inhibition.[77] According to Kumar et al. (2001), *C. porcera's* dry latex can be used to reduce inflammation in a variety of acute and chronic inflammation models, including those that cause vascular permeability, UV-induced erythema, cotton pellet granuloma, Freund's adjuvant-induced oedema, carrageenan-induced oedema, and Freund's adjuvant-induced oedema.[78] In their investigations, Arya and Kumar et al. (2005) showed that the latex of *C. porcera* has a strong anti-inflammatory effect against formalin and carrageenan. In this study, they employed a rat paw oedema model to test the effectiveness of the plant against inflammation brought on by histamine, serotonin, compound 48/80, bradykinin (BK), and prostaglandin E2 (PGE2). Additionally, they proposed a method for how blocking histamine, BK, and partially PGE2 might reduce inflammation in latex.[79] Tour and Talele (2010) demonstrated in their research that extracts of the plant's stem bark have anti-inflammatory and antiulcer efficacy against carrageenan-induced paw oedema in albino rats.[80] In their investigation, Saba et al. (2011) found that ethanolic extract of *C. porcera* leaf (100 mg/kg, 200 mg/kg, 400 mg/kg) had anti-inflammatory effects against the formalin-induced licking of the paws, the carrageenan-induced swelling of the paws in Wistar rats, and the acetic acid-induced writhing and tail flicking tests in mice. The research revealed that both centrally and peripherally, this extract mediated.[81] Singh et al, (2021) in the study evaluated the antiarthritic activity of swallow wort leaf fractions in Wistar rats, comparing them to standard ibuprofen and indomethacin. Results showed that methanol fraction of swallow wort (MFCP) had greater antiarthritic activity than ethanol fraction of swallow wort (EAFCP), reducing paw edema and affecting arthritic score, paw withdrawal latency, and body weight. MFCP also inhibited serum lysosomal enzymes and proinflammatory cytokines, improving hind leg radiographic features.[82]

Anti-diarrhoeal activity

In their experiment, Kumar et al. (2001) found that rats fed with castor oil also demonstrated anti-diarrheal action from dry latex (500 mg/kg) of *C. porcera*. The dry latex showed a substantial decrease in feces frequency, and diarrhoea severity, and provided protection from diarrhoea. DL dramatically reduced enteropooling caused by castor oil without affecting the electrolyte content, in contrast to atropine.[83] According to Awouters et al.(1975) in comparative trials using the conventional medication Loperamide and *C.porcera* leaf extracts assessed for anti-diarrheal efficacy of 40–50gm albino rats against Castor oil–induced Diarrhea.[84] In their comparison study, Murti et al. (2012) found that the leaves of *Calotropis procera* and *C. gigantea* showed considerable anti-diarrheal activity in rats, with *C. Porcera* displaying greater results than *C. gigantea* and loperamide.[85] In the research they carried out, Abhinayani et al. (2013) demonstrated that Calotropis procera leaves' aqueous and alcoholic extracts effectively decreased castor oil-induced diarrohea in rats, with aqueous and alcoholic dosages greatly lowering fecal output and dropping frequency.[86]

Anti convulsant activity

Jalalpure et al. (2008) conducted a study to examine the anticonvulsant effects of *Calotropis procera* root extracts against seizures induced by MES, PTZ, lithium-pilocarpine, and electrical kindling. Although the water extract successfully inhibited convulsions, the chloroform extract exhibited noticeable effects. The results suggest potential benefits for both absence and tonic-clonic seizures.[87] In line with research conducted by Babu and Karki (2011), the anticonvulsant and sedative properties of *C. procera* latex proteins were tested in mouse models of convulsions caused by pentylenetetrazol (PTZ), pilocarpine, and strychnine. The higher latencies to convulsions and death were indicative of the central nervous system depressing impact of diazepam and *C. procera* latex proteins.[88] The study conducted by Obese et al. (2021) investigates the efficacy of hydroethanolic leaf extract from *Calotropis procera* in reducing seizures in mouse models. The results indicate that CPE (100-300 mg/kg) significantly reduces the occurrence and length of strychnine-induced clonic seizures, delays the onset of picrotoxin and tonic convulsions, and completely avoids the occurrence of these seizures.[89] Additionally, it has a potent anticonvulsant action and lower mortality in convulsions brought on by pilocarpine.

Anti-microbial activity

Kareem et al. (2008) investigated the antibacterial properties of *Calotropis procera* leaf and latex extracts against six bacterial strains, including *Escherichia coli*, *Staphylococcus aureus*, *Staphylococcus albus*, *Streptococcus pyogenes*, *Streptococcus pneumoniae*, as well as three fungal species. The results indicate that ethanol was the most efficacious extractive solvent for the leaf and latex of *C. procera*. The water extract proved ineffective against the test fungus, while the ethanolic extracts exhibited the most extensive zone of inhibition against *E. coli*. The ethanol extract of *C. procera* latex exhibited the most potent antifungal activity against *Candida albicans*, with a minimum inhibitory concentration (MIC) for fungi between 5.0 and 20.0 mg/ml.[90] **Nenaah and Ahmed (2011)** employed the disc diffusion bioassay and Minimal Inhibitory Concentrations (MICs) to illustrate the antibacterial properties of *Calotropis procera* leaves, flowers, and latex. The results indicated that methanolic extracts from leaves and latex exhibited the highest antibacterial activity against *Escherichia coli*, *Staphylococcus*

epidermidis, and *Bacillus spp*. The optimal outcomes were derived from the latex methanolic extract.[91] **Nenaah (2013)** claimed in his experiment that the crude flavonoid fraction was the most potent among four bioactive components derived from the bioassay-guided fractionation of the MeOH extract. The extracts of *C.procera* exhibited antibacterial effectiveness against bacterial strains and the fungus *Candida albicans*, with minimum inhibitory concentrations ranging from 0.04 to 0.32 mg/ml.[92] **Mohamed et al. (2014)** synthesized silver nanoparticles by combining 3% latex serum extract with the same volume of silver nitrate (2 mmol/L) solution in a round flask and heating in a water bath at 80 °C. By using agar-well diffusion techniques, the antibacterial activity of the green-produced AgNPs was assessed against bacteria, dermatophytes, and phytopathogenic fungi and compared to the crude untreated latex. The antibacterial effectiveness of the green-produced AgNPs was found to be greater than that of raw latex.[93] A recent research by **Saddiq et al. (2022)** revealed that a plant extract from *C. procera* had substantial antibacterial activity against Staphylococcus aureus, Klebsiella pneumonia, and Escherichia coli, with MIC zones of 18.66 mm, 21.26 mm, and 21.93 mm. Bacillus subtilis and actinobacteria, including possible Streptomyces strains, were moderately inhibited by it.[94]

Oestrogenic activity

In their study, **Circosta et al. (2001)** demonstrated that *Calotropis procera* roots' ethanolic and aqueous extracts had an effect on rats' oestrogenic functioning and the estrous cycle. In 60% and 80% of the treated rats, respectively, both extracts disrupt the regular cycle, prolonging the dioestrous stage and momentarily inhibiting ovulation. In contrast, the extracts show no oestrogenic action in young female rats that have had bilateral ovariectomies.[95] Ethanolic extract of *Calotropis procera* roots exhibited substantial antiimplantation and uterotropic effect in albino rats at a level of 250 mg/kg, with no antiestrogenic activity found, according to study by **Kamath and Rana (2002)**.[96] Another study by **Ahirwar et al. (2006)** found that alcoholic extract of *C.procera* increased glycogen and protein content and activity of acid and alkaline phosphatase in uterus and cervix with increasing weights in ovariectomized rats, ovariectomy lowered the animals' levels of both proteins and glycogen. When coupled with ethinylestradiol, *Calotropis procera* roots' estrogenic effects were confirmed in adult rats having ovariectomies.[97] In a research, **Ahmad et al (2009)** examined the estrogenic effects of ethanolic and aqueous extracts of *Calotropis procera* of shade-dried roots, branches, and leaves on immature female rats. For ethanolic extracts, body weight and weights of the ovaries and uterus did not differ between treated and control groups. Serum estradiol concentrations did not differ between rats of all groups. Same results observed for aqueous extracts. Control showed higher estrogen level.[98]

Antimalarial activity

Sharma and Sharma (2000) discovered that ethanol extracts from the leaves, stems, roots, flowers, and buds of *Calotropis procera* demonstrated in vitro antimalarial efficacy against both chloroquine (CQ)-sensitive and CQ-resistant strains of *Plasmodium falciparum*.[99] **Mudi and Bukar's (2011)** investigation involved the soaking, pulverization, and drying of *Calotropis procera* leaves in ethanol. Bioassays for anti-parasitic efficacy indicate that CP1-04 has the highest activity. Compound CP1-04-61 has been found to be effective against malaria.[100] **George et al. (2016)** identified the erythrocyte membrane stabilizing properties of the aqueous and methanolic extracts of *C. porcera* leaf. The in vitro antiplasmodial activity of these extracts was examined against chloroquine-sensitive (MRC2) and chloroquine-resistant (RKL9) strains of Plasmodium falciparum.[101] **Adejoh et al. (2021)** report that the phosphate buffer extract of *C. procera* latex exhibits anti-plasmodial activity.[102]

Antiulcer activity

According to **Basu et al. (1998)**, *C. procera* root extract has analgesic, antipyretic, anti-inflammatory, and significant antiulcer properties. Research indicates that it inhibits gastric ulcerations, protects the gastric mucosa, and safeguards rats and guinea pigs against histamine-induced ulcers.[103] **Tour and Talele (2011)** assert that research on the stem bark of *Calotropis procera* (Apocynaceae), conducted via cold maceration, demonstrated antiulcer efficacy in both chloroform extract (CH) and hydroalcoholic extract (HE). The histological examination of the removed rat stomach substantiated the findings about antiulcer action.[104] **Taweel et al. (2017)** demonstrated in their study that the ethanolic extract of the plant's leaves exhibits antiulcer activity.[105] The study by **Thobaiti and Konozy (2022)** elucidates the hemagglutinating properties of *Calotropis procera* leaves, their capacity to protect the stomach from ethanol-induced lesions, and endorses ProLec as an effective treatment for gastric ulcers.[106] **Sing et al.'s (2023)** study investigated the anti-ulcer and antioxidant effects of *C. procera* leaf extract in rats with ulcers produced by pylorus ligation. The extract was administered orally for a consecutive duration of 15 days. *C. procera* (Aiton) ethanol leaf extract exhibits considerable antiulcer and antioxidant properties.[107]

CONCLUSION

The WORLD HEALTH ORGANOZATION has roughly calculated more than 83 % of the world's population in developing counties be conditional on primarily on herbal medicine for their basic health requirements. In the last few years ethno-botanical & pharmacological also traditional use of herbal crude product, have gained much more recognition when we compared to marketed product of the drugs. Not only they are good in therapeutic efficacy range but also there is a concept to believe by human that herbal product is meant to be sae for the entire human usage. A detailed review of this

review paper on Calotropis procera make manifest that it is a well-received medication source in a range of variety of ethnic groups. The scientist is inspecting another therapeutic property of Calotropis procera as it is likely to have many more function than are currently well known for us.

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