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Comprehensive Exploration of the Pharmacological Importance of *Calotropis* (AKK) Species: A Review

Qura Tulain[1], Maria[1], Dr. Tahir Yasin[2] & Muhammad Asif Raheem[3*]

[1]*Department of Chemistry & Biochemistry, University of Agriculture Faisalabad, Faisalabad, Pakistan.* [2]*University of Health Sciences, Lahore, Pakistan.* [3]*Applied Biotechnology, University of Westminster, 115 New Cavendish St., London W1W 6UW, UK. Corresponding Author (Muhammad Asif Raheem) Email: asifraheem74641@gmail.com*[*]

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ABSTRACT

Plant have been used for medical purpose from the past and today their use become more. The ethno-pharmacology is as old as man himself. Herbal medicines show a significant therapeutic diversity. *Calotropis* species includes *Calotropis acia* bunch, *Calotropis gigantea* and *Calotropis procera* are used in several traditional medicines to treat different diseases. The bark and leaves of *Calotropis* plant have shown anti-diarrheal activity, antimicrobial activity, antifungal activity, anti-inflammatory activity, antioxidant activity, anti-tumor activity, anti-malarial activity, analgesic activity, antifertility activity, pregnancy interceptive activity, anthelmintic activity, hepatoprotective activity, antinociceptive activities, anti-hyperglycemic activity, anti-convulsant, sedative activity and antinociceptive activities. In this review we are going to discuss about Calotropis, its species with different activities which are useful for humans to treat different disease.

Keywords: *Calotropis*; Ethno-pharmacology; Herbal medicines; *Calotropis acia* bunch; *Calotropis gigantea*; *Calotropis procera*; Anti-diarrheal activity; Antimicrobial activity; Anti-inflammatory activity; Antioxidant activity; Anti-tumor activity; Antifertility activity.

1. Introduction

All over the world, numbers of drugs are prepared form different plants that are used for medical purpose. About more than 50,000 species of plants are used for the benefits of plant. In different countries about 80% people depend on plants for medicines. The use of plants for medical purposes is increasing daily throughout the world. Medical plants are much source of different beneficial components that are helpful for treatment of different diseases (Egamberdieva *et al.*, 2021). The composition of every plant is different. Color, taste, and other properties present in all plants differentiate them from each other (Derkach and Tarasenko, 2021).

Since past, humans have effectively used plant extracts for treating sickness, wounds and during therapy for effective treatment. As a genus *Calotropis* was first described in 1810 that belong to flowering plants genus in family *Apocynaceae*. Its natural habitats include southern Asia and northern Africa. Because of the latex that they generate, they are usually referred to as milkweeds. *Calotropis* species are classified weeds in several regions of the globe, including the United States (Bairagi *et al.*, 2018).

There are mainly three species of *Calotropis* includes *Calotropis procera*, *Calotropis acia* buch and *Calotropis gigantea*. The blossoms give fragrance that is mostly utilized in the production of floral tassels in several civilizations of mainland Southeast Asia. It is recognized by a variety of colloquial names, in English it is called as Swallowwort, in Hindi it is known as Madar, and in Sanskrit it is famous by Alarka, it has also common names as Ark, Swallow wart, and milkweed. It is a common wasteland weed in Indonesia, Malaysia, China, and India, and it may be present in many regions of globe having hot temperature and in those that have sandy and much dry soils in which alkaline concentration is moreover high. It is likewise found in the United States and Canada (Rahmatullah *et al.*, 2010).

Pharmaceutical corporations have focused their attention on plants as potential sources of new pharmaceuticals, and they are now performing considerable work on plant extracts for bringing new drugs in profession of medicines, which is a priority for them. With current review, we want to bring attention towards *Calotropis procera and Calotropis gigantea* pharmacological results in general (Kundu, 2021).

1.1. Study objectives

- Explore historical and contemporary uses of *Calotropis* species in traditional medicine.
- Evaluate pharmacological activities including anti-diarrheal, antimicrobial, anti-inflammatory, antioxidant, anti-tumor, and anti-malarial properties.
- Assess therapeutic potential compared to conventional treatments.
- Identify research gaps and limitations for further investigation.
- Propose future research directions for understanding mechanisms of action and optimizing dosage forms.
- Advocate for integrating indigenous knowledge into healthcare for enhanced disease management.

2. Morphology of plant

It is a tall shrub having wax like leaves and stems that secrete milk like liquid when crushed. Because of the size of its leaves (which are 4 to 10 cm broad and 5 to 20 cm long), it is best suited for growing in groups. Each of its five petals is white with purple-colored ends, and the center is a purplish crown-like shape. Its blooms are 20-30 mm in diameter. Its fruit is a big bladdery 'pod' that is greyish green in color and is 8-12 cm in length. When the fruit reaches maturity, it splits apart to release many seeds, each of which is crowned by a tufted silk-like white coloured, long hairs (Punia, 2013).

Figure 1. *Calotropis procera* is a big shrub having waxy-like leaves and stems that produce milk-like liquid when crushed (Tahri *et al*., 2021)

A layer of light white colored hairs covers the surface of the new stems, which have green showing grayish color and are smooth textured (they are hoary). The bark of mature stems is severely fissured and cork-like in appearance, and it has a light brown color (Akhtar *et al*., 2019).

Figure 2. *Calotropis* Flowers: Large, purplish, sometime white, not scented, bracteates, complete, actinomorphic, hypogynous and cyclic (Pavani *et al*., 2020)

Aside from being huge and quite thick (5-30 cm long and 4-15 cm wide), the leaves are grayish green color having and complete edge. Leaves are spherical or egg like (ovate) in shapes, with pointy ends that are short and sharp (acute apices). In contrast, their lower sides can be thickly surrounded by small white colored hairs or have a cluster of hairs like structures at the bottom of the middle vein on their top surfaces (glabrous, midrib) (Nguyen *et al*., 2017).

Figure 3. *Calotropis* is leaves are large, bushy shrub with decussate, leaves with acute, inflorescence with purple corolla and erect lobes (Nguyen *et al.*, 2017)

Peduncles, or the major stem of these clustered flowers are 20 to 55 mm in length and every bloom of flower has a stalked structure also called a pedicel that is 15 to 25 mm in length. Flowers having five surrounding petals (7 to 10 mm in length and 6 to 10 mm wide) having whitish or pinky in color with considerably deeper purple colored or purplish-brown like ends and a central corona that is like crown similarly purple in color, are produced by this species. Aside from that, they contain five sepals (each approximately 3 mm wide and 5 mm in length) that have either oval shape or egg like forms, as well as five stamens and mostly flowering happens during the winter months (Narayanasamy *et al.*, 2020).

Figure 4. *Calotropis* fruits are ellipsoid or ovoid, containing 350–500 seeds with tufts of white, silky hair or pappus (Narayanasamy *et al.*, 2020).

The skins of the fruits are thick and spongy and they split open as they reach maturity. Several brown colored and flattened shaped seeds (about 6 mm length and 4 mm broad) present in each fruit, each of which is crowned with an elongated tuft of large, whitish, silky like hairs (35 to 50 mm in length) (Oun & Rhim, 2016).

Figure 5. *Calotropis* seeds contain white, silky floss that is a potential silk replacer (Oun & Rhim, 2016)

2.1. Species

Calotropis acia bunch

Caloropis procera

Calotropis gigantea

2.2. Common name

In English: *Calotropis*, calotrope, giant milkweed, Dead Sea fruit, swallow-wort, desert wick, Sodom apple, mudar fiber, rubber tree, rubber bush, rubber tree.

In French: algodón de seda, pomme de Sodome, arbre a soie du Senegal, arbre á soie, cotonsoie.

In Italian: calotropo.

In Arabi: kisher, usher, Dead Sea plant, oshar, debaj.

In Hindi: akada, madar, aak, akdo.

In Punjabi: akk.

3. Pharmacological Activities of *Calotropis*

People utilize the bark of different parts of tree to cure different diseases. Although major security issues present but *Calotropis* has been using to treat different diseases such as digestive diseases like constipation, diarrhea and ulcers of stomach; pain giving ailments as cramps, toothache, and pain of joint; and infections that occurred due to parasites such as worm infestation.

3.1. Antioxidant activities of *Calotropis procera* and *Calotropis gigantea*

Anti-hyperglycemic and antioxidant characteristics of *Calotropis procera* dry latex (DL), which has high anti-inflammatory action, were investigated in rats having alloxan produced diabetes (Yesmin *et al.,* 2008).

DL caused a rise in liver level of endogenous antioxidants such as catalase, superoxide dismutase (SOD) and glutathione in alloxan producing diabetic rats. DL showed as effective as a commonly prescribed diabetes medication (Ramkumar *et al.,* 2014).

The hydro-alcoholic solvent (70:30) was used to extract the powdered crude medicines, which were extracted using a twofold maceration method. The antioxidant activity of hydroalcohlic extract of *Calotropis gigantea* leaves (HECGL) was explored utilizing in-vitro models Ascorbic acid was used in the ascorbic acid reducing power test, while curcumin equivalents were used in the nitric oxide scavenging activity experiment. At the same time, the phenolic content of the extracts was evaluated using the Folin-Ciocalteau reagent and the total tannins and total flavonoids were checked using rutinein order to assess their contribution to total antioxidant activity, respectively (M. Shahid *et al*., 2015).

HECGL exhibited the highest DPPH radical scavenging activity and the highest nitric oxide scavenging activity when compared to a specific concentration. The reducing power of HACGL was shown to rise when the concentration of the extract was increased. It has a phenolic content which is represented as gallic acid equivalents (M. Shahid *et al*., 2016).

3.2. Antimicrobial activity of *Calotropis procera* and *Calotropis gigantea*

Extracts of *Calotropis procera*, both ethanolic and aqueous, were shown to have an inhibiting impact on the development of the isolates under investigation. Compared to extract of aqueous roots and leaves, ethanolic extract of leaves and roots had a much larger impact on the test subjects' blood glucose levels (Amini *et al.,* 2021). In antimicrobial assay, media is used known as nutrient agar. By measuring zone of inhibition results were measured (Bilal *et.al.,* 2020).

The extract petroleum ether of *Calotropis procera* showed the most potent antibacterial property opposite to *Klebsiella pneumonia* and *Pseudomonas aeruginosa*, while the chloroform extract showed the most potent antibacterial activity against *Pseudomonas aeruginosa* ATCC and *Klebsiella pneumonia* (Kareem *et al.* 2008).

Potential antibacterial property of methanol and aqueous extracts of *Calotropis procera* leaves was determined against Gram negative bacteria (*Shigella dysenteriae, Plesiomonasshigelloide),* Gram positive bacteria (*Staphylococcus epidermidis, Staphylococcus aureus, Streptococcus pyogenes* and *Staphylococcus saprophyticus*). Even at low quantities, it was clear that both extracts were effective against the microorganisms when tested (Mako *et al*, 2012).

The biofertilizer potential of leftover biomass produced from two components of the Akk plant, such as the flowers and leaves, was analyzed in terms of its use as a substrate for plant bacterial growth and subsequent inorganic phosphate solubility. After isolating antioxidants from the leaves and flowers of Akk with various solvent systems, residual biomass was observed. In comparison with the control, the treatment with residual biomass of Akk considerably (p0.05) increased the growth of Enterobacter sp. Fs-11 and Rhizobium Sp. E-11 (without residual biomass). Aqueous ethanol obtained residual biomass had the maximum phosphate solubility, whereas aqueous acetone extracted residual biomass had the lowest compared to the control (M. Shahid *et al*., 2016).

Partly purified extract of *C. gigantea* latex showed the antifungal activity against a variety of pathogenic fungi of humans. In vitro tests were performed on the latex's ethanolic extract to see how well it worked against fungus strains. The disc flow technique was used to find out the inhibitory effect. Using the serial dilution approach, it was possible to find out the minimum fungicidal concentration (MFC) and the minimum inhibitory concentration (MIC) (Saratha & Subramanian, 2010). Ethanolic extract contain several physiologically active chemicals including flavonoids, triterpenoids, alkaloids, phenols, saponins and glycosides indicates that the extraction is rich in biologically active molecules. The latex extract exhibits a large zone of inhibition that increases in size with increasing dosage. The minimum inhibitory concentration and maximum inhibitory concentration of extract of latex in contrast to strains of fungus range from (1mg-8mg) and the findings are equivalent to those obtained with Amphotericin B (Usha *et al.,* 2009).

3.3. Anti-diarrheal activity of *Calotropis procera*

The anti-diarrheal action of the dried-out latex of *Calotropis procera*, is a powerful agent against inflammation. Phenyl butazone and atropine, single eaten dose caused a substantial reduction in rate of constipation and diarrhea using oil called castor oil treated in rats. The protection against diarrhea disease in 80% of rats is cured with the help of oil (castor) (Kumar *et al.,* 2001).

Its influence on intestinal transit, castor oil produced fluid of intestine which concentration increase (enter pooling) and concentration of electrolyte in the fluid of intestine to better identify with its anti-diarrheal effect's mechanism. As dry latex was used for animals, the intestinal transit decreased by 27 to 37% and when comparison done to control and castor oil was used for treatment of animals, DL in contrast to atropine, had a considerable inhibitory effect on castor oil-induced enter pooling. When compared to rats treated by oil of castor, it had no effect on the content of electrolyte in the fluid of intestine, which was unexpected (Chitme *et al.,*2004).

3.4. Anti-inflammatory activity of *Calotropis procera*

An investigation into the anti-inflammation characteristics of *Calotropis procera* latex was conducted using a rat foot oedema model generated because of carrageenan and formalin. Only one dosage of aqueous solution of dry

latex was shown efficient for the severe inflammatory reaction at a statistically significant level (Obese *at al*., 2018).

3.5. Anti-tumor activity of *Calotropis procera*

Large number of different kinds of components found in medicinal plants, which are valuable to produce active pharmaceutical compounds, which are synthesized from these plants. *Calotropis procera* is a shrub that required medium water with flexible, large, many shrubs with less flowering kindling's or minute trees that belong to the *Asclepiadaceae* family that is found all over the hot and subtropical places of Africa and Asia. It is widely recognized in traditional medicine for its cleaning and anti-ageing characteristics, ascytotoxic, anti-coagulant, and anticancer capabilities (Mathur *et al.*, 2009).

This plant which includes a variety of chemical elements including cardiac glycoside, triterpenes, flavonoids, steroids, and various phenolic extracts in different portions of plant, is famous for its wide biological and pharmacological properties, including *Calotropis procera* extracts and portions of plants have shown substantial cytotoxic, anti-proliferative and anti-tumor action in a variety of and tumor cells and lines of cell and in vivo and in vitro, indicating that the herb has tremendous promise as an anticancer adjuvant (Meena *et al.*, 2011).

3.6. Anti-malarial activity of *Calotropis procera*

In vitro tests having Plasmodium falciparum MRC20-CQ-sensitive parasites, the extracts of ethanol from various portions of *Calotropis procera* revealed IC50 values for the different sections of *Calotropis procera.* Buds and flowers extracts were the most helpful against MRC76 CQ-resistant bacteria. Even though they are 220 to 440 times slow effecting than CQ. Extracts obtained additional investigation to identify the active ingredients. The findings of this study provide acceptence to the ethno-botanical usage of this plant (Bairagi, *et al.*, 2018).

3.7. Analgesic Activity of *Calotropis gigantea* and *Calotropis procera*

The analgesic activity of alcoholic compound of *Calotropis gigantea* flowers was investigated using chemical and thermal models to determine if the extract has analgesic properties. In a test known as an acetic acid-produced writhing test, a reduction in the digit of writhes was found (Pathak & Argal, 2007). Blossoms were picked in April and identified. Sprain, stiff joints and discomfort are all treated with *Calotropis gigantea*. It is also used to relieve earache and toothache (Singh *et al.*, 2014).

Flavonoids, long-chain fatty acids having volatile nature and triterpenoids discovered and separated in large quantities. Ethanol was used to macerate the dry powder of flower of *C. gigantea* for 72 hours. Using a concentrated extract, the extract was suspended in a solution (Adak & Gupta 2006). The acetic acid-produced writhing and warm plate technique were used to investigate the analgesic effectiveness of the drugs (Argal & Pathak, 2006).

The extract obtained from ethanolic compounds of flower of the *C. gigantea* resulted in significant reduction in the amount of writhing and time spent licking the paws. In activity a substantial increase was noticed after time about thirty minutes of and the maximal analgesic result was obtained after time about ninety minutes of dosing with the

hot plate approach. The effects are equivalent to those of a typical medication dose. Findings seem to support the plant's historic usage as a possible painkiller (Dewan *et al.*, 2000).

Calotropis procera extract of leaf was studied for its analgesic and anti-inflammatory properties, the results revealed that it has both. The extract was evaluated using different tests like the paw lick induced by formalin and paw oedema induced by carragenaan tests, as well as in mice using the tail flick and writhing induced by acetic acid tests (Mossa *et al.,* 1991Substantial analgesic activity was shown by the use of acetic acid producing writhing in mice (Basu & Chaudhuri, 1991).

The injection of the extract was repeated in the presence of naloxone and opioid antagonist, writhing acetic acid-induced and for the paw lick formalin-induced models, as well when an opioid antagonist absents. Ethanolic extract displayed a significant anti-inflammatory or analgesic impact on the subjects (Mascolo *et al.*, 1988). A substantial difference was found between the extract and Indomethacin when it came to inhibiting paw oedema production. Itching was greatly decreased treated with the extract, and the results were equivalent to those obtained with Indomethacin (Soares *et al.*, 2005). At the body weight, suppressed the writhing movement in a manner equal to aspirin. The same trend was discovered in mice using the tail flick technique as well. The findings of the research revealed that the analgesic or anti-inflammatory activity of the leaf extract is mediated by both peripheral and central mechanisms of action respectively (Das *et al.,* 2011).

Analgesic and the anti-inflammatory activity of the extracted compounds were not inhibited by the opioid competitor naloxone; it cannot be assumed that opioid receptors are involved in the extract's core mechanism of action. As a result, it was determined that these actions are induced by contact with extra nociceptive ways (Meena *et al.*, 2011).

3.8. Antifertility activity of *Calotropis procera*

It has been claimed that the dry latex and extract from chloroform of roots have anti-inflammatory properties (Upadhyay, 2014). The flowers' aqueous extract has been shown to have analgesic, anti-inflammatory and antipyretic properties, according to research. It has been discovered that the alcoholic extract from various portions of the plant exhibits antibacterial and spermicidal properties (Kumari & Chaudhary, 2021). The impact of extract from ethanolic compounds of the roots of *Calotropis procera* was identified to determine if it had antifertility and hormonal actions. Anti-implantation and action known as uterotropic drug was detected, which was quite high (Mali *et al.*, 2019).

3.9. Pregnancy interceptive activity of *Calotropis gigantea*

The milk like juice of the *Calotropis gigantea* shrub has been claimed to be a strong gastrointestinal irritant and purgative, and it also has been used to induce abortion purpose in certain cases, according to reports (Srivastava *et al.,* 2007). The latex of plant demonstrated 100% efficacy when an abortifacient after being spread on the uterine horn of rats (Lodhi *et al.,* 2009). For many tribal societies, inducing abortion by inserting branches of this plant into the vagina or the uterus has been a regular technique for many years (Singh *et al.,* 2014). It has been said that taking a paste of its seeds with countryside liquor on an empty stomach after menstruation will prevent conception in women for more than one year (Kumar *et al.,* 2010).

Calotropis gigantea is also said to have abortifacient, emmenagogue, ecbolic and uterotonic properties, according to certain reports. The leaves of this plant are used to make a tincture that is used to cure intermittent fevers, while the powdered blossoms of this plant are used to treat colds, coughs, asthma, and indigestion, among other ailments (Mishra *et al.,* 2017). The roots of this plant were shown to have pregnancy-interrupting effect in mature Sprague–Dawley colony-bred rats when supplied during peri-implantation or the pre-implantation stages, according to the findings of our research (Kumar *et al.,* 2013).

3.10. Anthelmintic activity of Latex of *Calotropis procera* and *Calotropis gigantea*

Adult earthworms were used in the anthelmintic activity. Both aqueous and fresh extracts of dry latex revealed a dosage dependent reduction of paralysis as well as other responses to pinpricking when applied topically (Iqbal *et al.,* 2005). The paralysis was reversible in the case of worms treated with piperazine and the worms recovered entirely (Al-Qarawi *et al.,* 2001). Because of the findings, it seems that latex has wormicidal action and may thus be beneficial as an anthelmintic. Earthworms were used to test the anthelmintic activity of the compound (Cavalcante *et al.,* 2016).

Paralytic effect was checked in worms by dividing an experiment into different stages (Bairagi *et al.,* 2018). The worms were immediately put in fresh water and examined to see whether they were able to recover from their inhibition of reaction to external stimuli. It was determined how long it would take for a person to fully heal or die. The mean paralytic score was plotted versus time, and the results were compared to a reference standard of piperazine (Tejaswini *et al.,* 2021).

Calotropis gigantea roots were used to test the effects of aqueous and alcoholic extracts of peeled roots on the earthworm Pheritimaposthuma (earthworm) at different doses for paralysis and death time (Argal *et al.,*2007). Each individual earthworm was timed, and the mean time was calculated for each earthworm. In this experiment, it was discovered that the CGR could cause dose-related paralysis and death in earth worms. The time it took for animals to become paralyzed and die at different concentrations was very similar to the time it took for mice to become paralyzed and die at the standard dose albendazole (De *et al.,* 2019). At the close concentrations albendazole had almost the same impact as albendazole. The aqueous extract outperformed the alcoholic extract in terms of effectiveness (Mushir *et al.,* 2016).

3.11. Hepatoprotective activity of *Calotropis procera* and *Calotropis gigantea*

Xenobiotics, viral infections, chronic alcoholism, and drugs are just a few of the exogenous and endogenous challenges that the liver must deal with. The liver is an essential organ of vital importance as it is concerned in the maintaining metabolic works and help detoxification from these challenges (Setty *et al.,* 2007). Ultimately, if the natural defensive systems of the liver are overcome throughout all these exposures to the stresses, hepatic damage will emerge consequently. It is usually the case that liver injury is coupled with necrosis at cellular level, a rise in per oxidation of tissue liquid, and a decrease level of GSH in the liver (Alqasoumi *et al.,*2012). Additionally, blood levels of various biochemically prepared indicators, such as cholesterol, triglycerides, phosphatase, bilirubin, and alkaline phosphatase are higher in this population (Chavda *et al.,* 2010).

Although contemporary medicine has seen tremendous progress, artificial medications are not accessible to treat hepatic problems despite this development. There are, however, numerous plants and herbal formulations that have been reported to have therapeutic effect in the treatment of hepatic diseases (Qureshi *et al.,* 2007). During one of our countryside surveillances, we discovered a widely propagated herb, *C. procera*, which purported to have protective properties but was really a weed. Plant was discovered to contain flavonoids, tannins, alkaloids, sterols, triterpenes, and cardiac glycosides among other things (Sharma *et al.*, 2011).

Reports indicate that plant flowers exhibit anti-inflammatory, analgesic, antipyretic, larvicidal and antibacterial characteristics, in addition to their larvicidal action. The latex of this plant was shown to have wound-healing and analgesic properties, according to certain reports. Several studies have shown that the roots have anti-ulcer properties and anti-fertility. The use of this plant as a hepatoprotective agent, on the other hand, is not supported by scientific evidence or accounts in the current literature. As a result, the current investigation was carried out in order to investigate the hepatic protective efficacy of extract obtained from the hydro-ethanolic extract obtained from flowers of *C. procera* in rats that had been subjected to paracetamol-induced liver damage. Using *Calotropis procera* flowers, a hydro-ethanolic extract (70 percent) was produced and evaluated for its hepatic protective efficacy for paracetamol inducing hepatitis disease in rats. It was determined if there was a difference in the amount of indicators present biochemically for liver damage such as tissue GSH, ALP, SGPT, bilirubin, SGOT, HDL or cholesterol, in the treated and untreated groups (Agbaje & Ogunleye, 2016). It was discovered that paracetamol increased blood levels of SGPT and SGOT enzymes, as well as bilirubin and cholesterol, while simultaneously decreasing HDL the serum concentration and GSH the tissue level. The hydro-ethanolic extraction of C. procera flowers has been shown to restore abnormal amount of biochemically prepared markers to near-normal amount in a dosage-dependent way (Alrheam, 2015).

Hepatoprotective activity of suspensions of alcoholic extraction of bark and root of the herb *Calotropis gigantea* in amount 0.6 percent CMC (Deshmukh *et al.*,2008). An alcoholic extraction of the bark or root of *Calotropis gigantea* demonstrated a statistically significant defense result by normalizing the amount of alanine amino transferase, alkaline phosphatase, aspartate amino transferase, lactate de and total bilirubin (TB) for the sake of comparison, silymarin, a well-known hepatically protective medication (Ingawale *et al.*, 2013).

3.12. Antinociceptive activities of *Calotropis procera*

A dose-dependent anti-nociceptive effect was shown in all trials using the protein part latex delivered to male rats. It was discovered that acetic acid-induced abdominal constriction was inhibited at various dosages when comparison was done to the control group (Obese *et al.,* 2021). Nociception induced by formalin in the first and second phases was reduced by lateral protein. and this result was not inverted before treatment with compound naloxone in the first and second phases, respectively, when latex protein was administered (Ramos *et al.,* 2007). When compared with controls, an increase in response time was found, with naloxone having no influence on the result. Conclusion: The part of fraction obtained from the complete *Calotropis procera* latex displays anti-nociceptive effect that is self-determining of the opioid method, as shown by the results of this study (Mahmoud *et al.,* 2009).

3.13. Anti-hyperglycemic activity of *Calotropis procera*

The anti-hyperglycemic effects of *Calotropis procera* extracts were examined in Male Wister Albino rats its impact (Roy *et al.,* 2005). The pet ether, aqueous and methanol extracts of the leaves of *C. procera* were provided as a one dosage each day. Result was conducted on rats suffering from diabetes to determine the impact of *C. procera* on blood glucose levels (VH & Ajay, 2009). The rats having diabetes' serum lipid profile (total triglycerides, very low density, phospholipids, cholesterol low density and high-density lipoprotein) was checked using a lipid profiling method (Mali *et al.,* 2019). It was also determined if the activities were comparable to the impact provided by glibenclamide 500 mg/kg, a typical anti-diabetic medication.

According to the findings of this inquiry, there is pharmacological proof to carry the tradition state that it is drug having anti-diabetic. Inhibition of hyperlipidaemic activity the blood was tested for total cholesterol, LDL-C, HDL-C, triglycerides, and VLDL-C, among other things. In this study, the total cholesterol was determined using the Liebermann Burchard Reaction Method. Friedwald's approach was used to assess LDL cholesterol in an indirect manner. The Hantzsch condensation technique was used to quantify the number of triglycerides (TG) (Kumar & Padhy, 2011).

3.14. Anti-Convulsing and Sedative Activity of *Calotropis procera*

The latex proteins of *Calotropis procera* were employed to investigate anti-convulsing and sedative activity in mice. When testing for anti-convulsing activity, the convulsions were caused using pentylenetetrazol, Pilocarpine, and strychnine. The sedative potential was determined using the pentobarbital-induced sleep model, which was employed in conjunction with the anti-convulsing activity. When compared to industry standards, the plant extract had no significant impact on Pilocarpine and strychnine-induced convulsions. A substantial impact of the plant extract was seen in the pentylenetetrazol-induced seizures paradigm. At high doses, the extract proteins exhibited central depressive properties, as shown by the extract proteins (Obese *et al.,* 2021).

The ethanol extract of *Calotropis gigantea* was provided orally for checking its anticonvulsant, sedative, and muscle relaxant effects. The assessment of sedative effects was carried out with the use of an actophotometer and a Rota rod equipment (Asif, 2014). The anticonvulsant activity of the extract treated mice was substantial against maximum electroshock generated convulsion, but no meaningful impact was detected against the strychnine model. In mice, the extract demonstrated considerable muscle relaxant action as well as a loss in motor coordination, according to the findings (Auditeau *et al.,* 2019).

3.15. Antinociceptive activities of *Calotropis procera*

It was determined in this study that proteins from the lateral parts of *Calotropis procera* had an anti-nociceptive impact (Obese *et al.,* 2021). It was discovered that acetic acid-induced abdominal constriction was inhibited as compared to the control group (Padhy & Kumar, 2005). Nociception induced by formalin in the first and second phases was reduced by latex protein, and this effect was not reversed by pretreatment with naloxone in the first and second phases, respectively, when latex protein was administered (Meena *et al.,* 2010). After 60 minutes of latex treatment, compared to controls, an increase in response time was found, with naloxone having no influence on the result (Oloumi, 2014).

4. Conclusion and Future Recommendations

The WHO has estimated that 80% of the population of the world depends on parts or products of plants. From last few years' plants have more attention for medical field as they are easy to handle, much safe for human and other organisms. Scientists try to obtain more and more compound to make pharmaceutical product for the welfare of humans. From all other plants *Calotropis* has also attention because it shows anti-diarrheal activity, antimicrobial activity, antifungal activity, anti-inflammatory activity, antioxidant activity, anti-tumor activity, anti-malarial activity, analgesic activity, antifertility activity, pregnancy interceptive activity, anthelmintic activity, hepatoprotective activity, anti-nociceptive activities, anti-hyperglycemic activity, anti-convulsing and sedative activity and anti-nociceptive activities. Future research should prioritize investigating the mechanisms of action underlying *Calotropis* species' pharmacological activities and optimizing their dosage forms for enhanced efficacy. Controlled clinical trials are imperative to validate the safety and efficacy of *Calotropis*-based treatments, while collaboration between traditional healers and scientific researchers can integrate indigenous knowledge into mainstream healthcare for more holistic patient care. Such efforts will maximize the therapeutic potential of *Calotropis* species and contribute to the development of effective treatments for a range of health conditions.

Declarations

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Competing Interests Statement

The authors declare no competing financial, professional, or personal interests.

Consent for publication

The authors declare that they consented to the publication of this study.

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