



Unveiling Biological and Therapeutic Properties of Calotropis Procera: A Promising Traditional Medicine

¹Dr. Deepankar Misra, ²Dr. Tarun Vyas, ³Dr. Akansha Misra, ⁴Dr. Ranjeeta Mehta, ⁵Dr. Vashishtha Singh, ⁶Dr. Harshika Jain

¹Professor and Head, Department of Oral Medicine and Radiology, Institute of Dental Studies and Technologies, Kadrabad, Modinagar, Ghaziabad (U.P.) India.

²Reader, Department of Oral Medicine and Radiology, College of Dental Science and Hospital, Amargadh, Bhavnagar, Gujarat, India.

³Professor, Department of Oral and Maxillofacial Pathology, Institute of Dental Studies and Technologies, Kadrabad, Modinagar, Ghaziabad (U.P.) India.

⁴Associate professor, Department of Oral Medicine and Radiology, Seema Dental College & Hospital, Pashulok, Veerbhadra Road, Rishikesh (Uttarakhand) India.

⁵Senior Lecturer, Department of Oral Medicine and Radiology, Institute of Dental Studies and Technologies, Modinagar, Ghaziabad, (U.P.) India.

⁶Post Graduate Student, Department of Oral Medicine and Radiology, Institute of Dental Studies and Technologies, Kadrabad, Modinagar, (U.P.) India.

Corresponding author:

Dr. Deepankar Misra

Professor and Head, Department of Oral Medicine and Radiology, Institute of Dental Studies and Technologies, Kadrabad, Modinagar, Ghaziabad (U.P.) India.

(Received: 07 January 2024

Revised: 12 February 2024

Accepted: 06 March 2024)

KEYWORDS

Calotropis procera;
Phytochemistry;
Traditional
medicine;
Pharmacognosy;
Anti-cancer; Anti-
inflammatory;
Antioxidant, Oral
Health, Dental
Disorders,
Dentistry

ABSTRACT:

Since the dawn of civilization, people have utilized plants as a secure and efficient form of treatment for a variety of illnesses. A number of traditional medicines are formed from certain plants with medicinal and therapeutic properties. It has long been known that Calotropis procera offers potential as a therapy for many different conditions. This xerophytic, erect shrub is native to the tropics of Asia and Africa, where it reaches a height of roughly 6 meters. Numerous illnesses, such as rheumatism, fever, diarrhea, diabetes, malaria, asthma, and many more, have been treated using its constituents.

The latex has demonstrated strong benefits against inflammation, cancer, wound healing, hepatoprotection, inflammation prevention, nerve regeneration, antiulcer, insecticidal, and antimalarial bacteria. The study also discovered that consuming too much has detrimental impacts on health. The study found a wealth of documentation supporting the biological assessment of C. procera in both in vitro and in vivo animal models. However, human safety and efficacy remain to be fully investigated, and more carefully planned clinical trials are needed to validate preclinical results. Establishing a standard dose and ensuring its safety are crucial.

This review provides the biological information that is currently available about the potential therapeutic and biological uses of C. procera for the management of various illnesses with an insight on its potential applications in oral health and dentistry.

1. INTRODUCTION

Herbal remedies have been employed over thousands of years to cure ailments in individuals as well as

animals.^[1] Plants have historically been trusted as a reliable source of both preventive medicine and therapy in many cultures. In many parts of the developing



world, herbal remedies continue to be the main source of healthcare.^[2] Traditional medicines are used to address prevalent healthcare concerns by 80% of the global population, primarily in developing countries. In nearly all cultural backgrounds, they are used as nutrition and as a medicine.^[3,4] Even more astounding is the fact that plants serve as the foundation for around 25% of modern medications.^[4] Their use greatly enhances the provision of basic medical care and they are seen as indispensable sources of medicinal items, including herbal remedies. The healthcare and biopharmaceutical sectors have made bioactive plant products an essential component of their scientific and technological advancement.^[5] A species of plant in the Asclepadiaceae family called *Calotropis procera* (*C. procera*), commonly known as "Madar," has been utilized for centuries in ancient therapy. This shrub is continuously subjected to harsh conditions, but it nevertheless yields latex and grows well in natural environments.^[5,6] The plant discharges a creamy latex substance, which is particularly prevalent in its aerial segments, when it is wounded. In addition to being rich in beneficial additional chemicals and enzymes, it shields the plant against damage and has been revered in traditional medicine for its diverse therapeutic properties.^[5,6] Indigenous communities have utilized various parts of the plant for centuries, recognizing its potential in treating a range of ailments. The latex extracted from *Calotropis procera* has demonstrated notable anti-inflammatory properties, making it valuable in managing conditions like arthritis and skin disorders. Additionally, the plant exhibits antimicrobial effects, contributing to its application in wound healing and skin infections.^[7,8]

The roots of *C. procera* have been traditionally employed for their analgesic qualities, offering relief from pain associated with conditions such as rheumatism and muscular injuries. Its efficacy in addressing respiratory issues has also been acknowledged, attributing the plant's use in overall well-being.^[8] Furthermore, it has shown potential as an anti-cancer agent, with certain compounds exhibiting cytotoxic effects on cancer cells that has sparked interest in its potential role in modern medicine.^[9] This review aimed to conduct a thorough literature assessment on the biological and therapeutic importance

of its constituent parts. This article also discusses its potential benefits for dental health and how its ingredients are used in dentistry.

2. METHODS

An electronic search through PubMed, Scopus and Google Scholar for "Calotropis procera", "antioxidant", "traditional medicine", "anti diabetic", "anti bacterial", "anti viral", "anti microbial", "ethnopharmacology", "toxicity", investigating a number of studies. Then, we consecutively screened abstracts and, full-text articles published in English. A total of 138 articles were found in PubMed and 9 duplicate papers were excluded. Additionally, 85 articles were excluded as they were case reports, case series, editorials, letter to editor, commentaries and conference proceedings. Finally, 45 papers published in last 20 years were analyzed in this article. In Figure 1, were analyzed in this review.

3. REVIEW

Anti inflammatory property

In pharmacologic models of formaldehyde-induced arthritis, cotton pellet granuloma, and carrageenin-induced foot oedema in rats, significant dose-related activity was demonstrated for a chloroform-soluble fraction ($p < 0.001$). When it came to preventing the development of foot oedema, the extract at a specific and substantial doze was effective.^[10] Macroscopic and microscopic analyses has revealed that colonic mucosal damage in colitic rats is much decreased after receiving Methanol extract of dried latex (MeDL) therapy, and oxidative stress level in tissues and proinflammatory mediators were recovered.^[11] Also the plant extract exhibits the strongest anti-inflalmmatory effects with IC50 values of 7.6 μM against 5-LOX and 2.7 μM against 15-LOX.,^[12] The extract administered at 100 and 200 mg/kg, significantly reduced inflammation. At these dozes, the extract shows 21.6 and 71.6% inhibition, respectively. This extract at doses 50 and 500 mg/kg has also proven to decrease inflammation in rats with arthritis.^[13] In vivo testing at dosages of 200 and 400 mg/kg, respectively has also shown considerable anti-inflammatory effectiveness employing hydroalcoholic and chloroform extracts of this plant.^[14]



Anti microbial property

Studies have demonstrated both antibacterial and antifungal properties of *C. Procera* in its different forms. These properties have been found in cardenolide (proceragenin) against *S. aureus*, *S. pyogenes* and *S. saprophyticus* and in the ethanol extract of the leaves and latex against *E. coli* and *P. aeruginosa* of this plant. Water-soluble extract (250 µg/mL) has been found effective against *C. perfringens* and *S. faecalis*. The maximum efficiency against the examined bacterial strains has been demonstrated by the crude flavonoid fraction and the leaf and bark extracts prepared with 50% methanol are effective against *B. subtilis* and *K. pneumoniae*.^[16]

Many antifungal properties have also been found in its extract, however, ethanol and chloroform extracts showed remarkable performance over water extract and were effective against *C. albicans*.^[16] Crude flavonoids were the most effective portion of flavonoids, which had 30 mm-diameter inhibitory zones against *C. albicans*, *T. rubrum* and *A. terreus* after being treated with Latex silver nanoparticles. The IC₅₀ values of all the peptidases (procerain and procerain B) evaluated in previous studies were approximately 50 µg/mL thereby inhibiting the fungi *in vitro*.^[17]

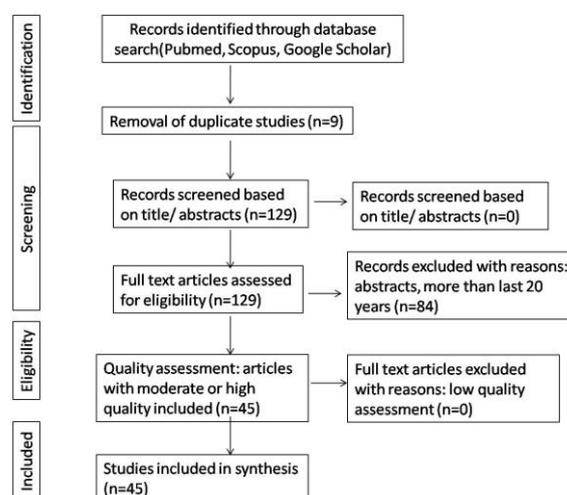
Antioxidant and anti-cancer property

Studies have demonstrated that the plant extracts accounts for 42–90% free radical scavenging activity with 2,2-Diphenylpicrylhydrazyl (DPPH) radical scavenging assay. Also in the assays using hydrogen peroxide and hydroxyl radicals, the methanol extract exhibited maximum scavenging activity (83.63%) at 500 µg/mL over ferric thiocyanide, while the DPPH assay revealed least activity (50.82%).^[18] The use of dry latex of this plant for 31 days, decreases Thiobarbituric acid-reactive substances (TBARS) levels. Root extracts and ethanol floral extract have lowest level of antioxidants (IC₅₀ = 0.27 mg/mL, IC₅₀ = 142 µg/mL), while lyophilized latex extracts and aqueous flower extract have greatest values (IC₅₀ = 0.060 mg/mL, IC₅₀ = 85 µg/mL) as a radical scavenger.^[19] For DPPH, the ethyl acetate extract has the most radical scavenging activity (95%), followed by ethanolic floral extract (88.1%) and aqueous extract of methanol (85.5%).^[20] Antioxidant property by the phenolics is exhibited by

the location of the functional groups surrounding their nucleus and the quantity and configuration of their H-donating hydroxyl groups present within calotropogenin, calotropin, latex and calotoxin parts of the plant.^[21]

Wound healing Activity

In a study topical application of sterile latex solution has improved wound healing due to its ability to stimulate collagen, DNA, and protein production resulting in re-epithelization of the wound.^[22] Similar studies on rats demonstrated faster wound healing time and wound contraction after application of the extract.^[23]



4. DISCUSSION

4.1 Provenance of the plant and phytochemistry

C. procera, erect, velvety woody shape achieves a height of 2.5–6 m. It is found everywhere in the world because it prefers temperatures that are warm, dry, sandy, and alkaline soils. It grows well in a range of various habitats, such as sand dunes, highway channels, swamps, waste dumps, and derelict areas.^[24] It harbors a rich tapestry of phytochemical constituents, contributing to its diverse therapeutic properties. The phytochemical profile of this plant encompasses a variety of compounds, each playing a distinct role in its pharmacological activities.^[25]

Alkaloids and Terpenoids:

Calotropin and Uscharin are notable alkaloids found in *C. procera*, contributing to its anti-inflammatory



properties. These compounds have been associated with inhibiting inflammatory mediators. Terpenoids like β -sitosterol contribute to the overall pharmacological profile of *C. procera* and is a phytosterol with potential anti-inflammatory and analgesic effects. Tannins, including gallic acid, contribute to the astringent properties of *C. procera*. These compounds may play a role in wound healing and tissue repair.^[26]

Flavonoids and Glycosides:

C. procera contains flavonoids with antioxidant properties such as Quercetin and Kaempferol Derivatives. These compounds play a role in scavenging free radicals and contribute to the plant's overall therapeutic potential. An active glycoside found in the latex of *C. procera*, known for its antimicrobial properties is Calotropin, which contributes to the plant's efficacy in addressing various microbial infections. Certain parts of *C. procera* contain cardiac glycosides, such as calotoxin. However, caution is advised in their use due to potential toxic effects, emphasizing the importance of proper dosage and preparation.^[27,28]

4.2 Biological and Therapeutic activities pertaining to oral health

C. procera emerges as a versatile traditional medicine, offering a spectrum of therapeutic benefits. From addressing inflammatory and microbial challenges to providing relief in pain management of various dental disorders, the plant also holds promise across various healthcare domains.

4.2.1 Anti-Inflammatory and Analgesic Activity:

The presence of compounds like calotropin and uscharin present in the latex of this plant attribute to this activity. These compounds inhibit the synthesis of prostaglandins, suppress pro-inflammatory cytokines and inhibit NF- κ B activation ultimately leading to overall anti-inflammatory effect. Root extracts of *C. procera* showcase analgesic properties, offering relief from pain associated with rheumatism and muscular injuries thereby attributing in pain management.^[29]

4.2.2 Antimicrobial Potency:

The robust antimicrobial activity against bacteria and fungi is due to presence of proceroside, proteolytic enzymes, syriogenine, cardenolides, carbohydrates, cardiac-active glycosides, calactin, calotropain, calotoxin, alkaloids, tannins, flavonoids, and procerain present in the plant. It disrupts the integrity of cell

membrane, inhibits the ergosterol synthesis and alters the fungal cell wall components collectively contributing to the antifungal effect.^[30,31]

4.2.3 Antioxidant and Anti-Cancer Potential:

Flavanol glycosides, cardenolides and lignans present in this plant exhibit promising cytotoxic effects on cancer cells, suggesting a potential role in cancer treatment. The exploration of its anti-cancer pharmacology opens avenues for further research in oncological applications.^[29]

4.2.4 Wound Healing activity

The extract from this plant contains triterpenoids such as amyirin, flavonoids, cardiac glycosides, cardenolide anthocyanins, mudarine, lupeol, sitosterol, flavanols, resin, a nontoxic proteolytic enzyme called calotropin, and a strong bacteriolytic enzyme called calactin. These products stimulate the proliferation of fibroblasts and collagen deposition, facilitating tissue repair and regeneration. Additionally, these extracts exhibit analgesic effects, which alleviate pain associated with wounds. The plant's ability to enhance angiogenesis, the formation of new blood vessels, further supports tissue repair by ensuring an adequate blood supply to the wounded area.^[32]

4.3 Biological and Therapeutic activities pertaining to general and overall health

4.3.1 Respiratory Health Benefits:

The plant's products are effective in managing respiratory conditions such as asthma and bronchitis. Active compounds contribute to bronchodilation and anti-inflammatory effects, supporting its traditional use in respiratory ailments.^[33]

4.3.2 Antifertility Activity:

This is attributed to its ability to disrupt various stages of reproductive function. It may inhibit spermatogenesis in males and interfere with ovarian function in females, leading to contraceptive effects.^[34]

4.3.3 Antiglaucoma Activity:

Studies have shown that extracts of *C. procera* possess is believed to reduce intraocular pressure, which is a key factor in the pathogenesis of glaucoma, thereby helping to manage the condition.^[35]

4.3.4 Antimalarial Activity:

Its bioactive compounds have been found to inhibit the growth and replication of the malaria parasite, making it



a promising candidate for malaria treatment and prevention.^[36]

4.3.5 Antidiarrheal Activity:

The products of this plant have the ability to reduce intestinal motility and secretion, alleviating diarrhea by exerting an inhibitory effect on various pathways involved in diarrheal mechanisms.^[37]

4.3.6 Anticonvulsant Activity:

Calotropis procera demonstrates anticonvulsant effects, making it potentially useful in the management of epilepsy and other seizure disorders. Its bioactive constituents modulate neurotransmitter activity and neuronal excitability, thereby reducing the frequency and severity of seizures.^[38]

4.3.7 Antidiabetic Activity:

Studies have indicated that *Calotropis procera* exhibits antidiabetic properties by lowering blood glucose levels and improving insulin sensitivity. Its mechanisms of action include enhancing pancreatic function, promoting glucose uptake by cells, and inhibiting carbohydrate digestion and absorption.^[39]

4.3.8 Hepatoprotective Activity:

Calotropis procera demonstrates hepatoprotective effects, which can help safeguard the liver against various insults and toxins. It aids in the regeneration of liver cells, reduces oxidative stress, and inhibits inflammation, thereby promoting liver health and function.^[40]

4.4 Toxicology:

Despite its therapeutic promise, it's essential to approach the use of *C. procera* with caution, as improper dosage or preparation can lead to adverse effects. Integrating traditional knowledge with contemporary research will enhance our understanding of this plant's medicinal potential and pave the way for its responsible incorporation into modern healthcare practices. Caution is warranted in the utilization of *C. procera*, as certain parts of the plant contain toxic compounds, including cardiac glycosides. Improper dosage or preparation may lead to adverse effects. Rigorous studies on toxicology are imperative to establish safe usage guidelines and mitigate potential risks associated with its traditional medicinal applications.^[41]

5. CONCLUSION:

Nature contains vast array of compounds that may be used to create remedies for a variety of chronic diseases. Numerous therapeutic plants and their components have been shown to –provide great therapeutic benefits and one such plant is *C. procera*. *Calotropis procera*'s journey from phytochemistry to pharmacology unfolds a narrative of diverse therapeutic potential. As research progresses, understanding its toxicological aspects becomes paramount for safe integration into healthcare practices. This comprehensive review sheds light on the intricate interplay of phytochemical constituents, pharmacological actions, therapeutic applications, and the imperative need for cautious exploration in the realm of *C. procera*.

REFERENCES:

1. Kundu S. A mini review on *Calotropis procera* and tapping its phytochemical and pharmacological potential. *The Journal of Phytopharmacology*. 2021;10(4):277-80.
2. Batool H, Hussain M, Hameed M, Ahmad R. A review on *Calotropis procera* its phytochemistry and traditional uses. *Big Data Agric*. 2020;2(11):29-31.
3. Quazi S, Mathur K, Arora S, Wing P. *Calotropis procera*: An overview of its phytochemistry and pharmacology. *Indian Journal of Drugs*. 2013;1(2):63-9.
4. Paul A, Kumar A. Review on pharmacological properties of Aaka (*Calotropis procera*). *International Journal of Economic Plants*. 2018;5(3):157-62.
5. Dhalendra G, Rathore P, Satapathy T, Roy A. Pharmacognostical, phytochemical and pharmacological study of *Calotropis procera*: A review. *Research Journal of Pharmacy and Technology*. 2014;7(3):346-51.
6. Mali RP, Rao PS, Jadhav RS. A review on pharmacological activities of *Calotropis procera*. *Journal of Drug Delivery and Therapeutics*. 2019 Jun 15;9(3-s):947-51.
7. Balekar N. *Calotropis procera*: A phytochemical and pharmacological review. *Thai Journal of Pharmaceutical Sciences (TJPS)*. 2016 Sep 30;40(3).



8. Murti Y, Yogi B, Pathak D. Pharmacognostic standardization of leaves of *Calotropis procera* (Ait.) R. Br. (Asclepiadaceae). *Int J Ayurveda Res.* 2010 Jan;1(1):14-7.
9. Meena AK, Yadav A, Rao MM. Ayurvedic uses and pharmacological activities of *Calotropis procera* Linn. *Asian journal of traditional medicines.* 2011 Apr 20;6(2):45-53.
10. Basu A, Chaudhuri AK. Preliminary studies on the antiinflammatory and analgesic activities of *Calotropis procera* root extract. *J Ethnopharmacol.* 1991 Mar;31(3):319-24.
11. Kumar VL, Pandey A, Verma S, Das P. Protection afforded by methanol extract of *Calotropis procera* latex in experimental model of colitis is mediated through inhibition of oxidative stress and pro-inflammatory signaling. *Biomed Pharmacother.* 2019 Jan;109:1602-1609.
12. Abdel-Mageed WM, Mohamed NH, Liu M, El-Gamal AA, Basudan OA, Ismail MA, Quinn RJ, Liu X, Zhang L, Shoreit AA. Lipoxygenase inhibitors from the latex of *Calotropis Procera*. *Arch Pharm Res.* 2016 Mar 9.
13. Kumar VL, Roy S. *Calotropis procera* latex extract affords protection against inflammation and oxidative stress in Freund's complete adjuvant-induced monoarthritis in rats. *Mediators Inflamm.* 2007;2007:47523.
14. Tour N, Talele G. Anti-inflammatory and gastromucosal protective effects of *Calotropis procera* (Asclepiadaceae) stem bark. *J Nat Med.* 2011 Jul;65(3-4):598-605.
15. Pattnaik PK, Kar D, Chhatoi H, Shahbazi S, Ghosh G, Kuanar A. Chemometric profile & antimicrobial activities of leaf extract of *Calotropis procera* and *Calotropis gigantea*. *Nat Prod Res.* 2017 Aug;31(16):1954-1957.
16. Nenaah G. Antimicrobial activity of *Calotropis procera* Ait. (Asclepiadaceae) and isolation of four flavonoid glycosides as the active constituents. *World J Microbiol Biotechnol.* 2013 Jul;29(7):1255-62.
17. Freitas CDT, Silva RO, Ramos MV, Porfirio CTMN, Farias DF, Sousa JS, Oliveira JPB, Souza PFN, Dias LP, Grangeiro TB. Identification, characterization, and antifungal activity of cysteine peptidases from *Calotropis procera* latex. *Phytochemistry.* 2020 Jan;169:112163.
18. Kumar S, Gupta A, Pandey AK. *Calotropis procera* Root Extract Has the Capability to Combat Free Radical Mediated Damage. *ISRN Pharmacol.* 2013 Oct 9;2013:691372.
19. Roy S, Sehgal R, Padhy BM, Kumar VL. Antioxidant and protective effect of latex of *Calotropis procera* against alloxan-induced diabetes in rats. *J Ethnopharmacol.* 2005 Dec 1;102(3):470-3.
20. Mohamed MA, Hamed MM, Ahmed WS, Abdou AM. Antioxidant and cytotoxic flavonols from *Calotropis procera*. *Z Naturforsch C J Biosci.* 2011 Nov-Dec;66(11-12):547-54.
21. Soobrattee MA, Neergheen VS, Luximon-Ramma A, Aruoma OI, Bahorun T. Phenolics as potential antioxidant therapeutic agents: mechanism and actions. *Mutat Res.* 2005 Nov 11;579(1-2):200-13.
22. Rasik AM, Raghubir R, Gupta A, Shukla A, Dubey MP, Srivastava S, Jain HK, Kulshrestha DK. Healing potential of *Calotropis procera* on dermal wounds in Guinea pigs. *J Ethnopharmacol.* 1999 Dec 15;68(1-3):261-6.
23. Tsala DE, Nga N, Thiery BN, Bienvenue MT, Theophile D. Evaluation of the antioxidant activity and the healing action of the ethanol extract of *Calotropis procera* bark against surgical wounds. *J Intercult Ethnopharmacol.* 2015 Jan-Mar;4(1):64-9.
24. Bairagi SM, Ghule P, Gilhotra R. Pharmacology of Natural Products: An recent approach on *Calotropis gigantea* and *Calotropis procera*.
25. Yogi B, Gupta SK, Mishra A. *Calotropis procera* (Madar): A medicinal plant of various therapeutic uses—A review. *Bull. Env. Pharmacol. Life Sci.* 2016 Jun 7;5(7):74-81.
26. Wadhvani BD, Mali D, Vyas P, Nair R, Khandelwal P. A review on phytochemical constituents and pharmacological potential of



- Calotropis procera. RSC Adv. 2021 Nov 4;11(57):35854-35878.
27. Dogara, A.M. A systematic review on the biological evaluation of Calotropis procera (Aiton) Dryand. *Futur J Pharm Sci* 2023;9:16.
28. Kaur A, Batish DR, Kaur S, Chauhan BS. An Overview of the Characteristics and Potential of Calotropis procera From Botanical, Ecological, and Economic Perspectives. *Front Plant Sci*. 2021 Jun 17;12:690806.
29. Sivapalan S, Dharmalingam S, Venkatesan V, Angappan M, Ashokkumar V. Phytochemical analysis, anti-inflammatory, antioxidant activity of Calotropis gigantea and its therapeutic applications. *J Ethnopharmacol*. 2023 Mar 1;303:115963.
30. Al-Rowaily SL, Abd-ElGawad AM, Assaeed AM, Elgamal AM, Gendy AE, Mohamed TA, Dar BA, Mohamed TK, Elshamy AI. Essential Oil of Calotropis procera: Comparative Chemical Profiles, Antimicrobial Activity, and Allelopathic Potential on Weeds. *Molecules*. 2020 Nov 9;25(21):5203.
31. Saher U, Ovais Omer M, Javeed A, Ahmad Anjum A, Rehman K, Awan T. Soluble laticifer proteins from Calotropis procera as an effective candidates for antimicrobial therapeutics. *Saudi J Biol Sci*. 2023 Jun;30(6):103659.
32. Rabelo ACS, Noratto G, Borghesi J, Souza Fonseca A, Cantanhede Filho AJ, Costa Carneiro FJ, Abreu-Silva AL, Miglino MA. Calotropis procera (Aiton) Dryand (Apocynaceae): State of the art of its uses and Applications. *Curr Top Med Chem*. 2023;23(23):2197-2213.
33. Timalsina D, Pokhrel KP, Bhusal D. Pharmacologic Activities of Plant-Derived Natural Products on Respiratory Diseases and Inflammations. *Biomed Res Int*. 2021 Oct 4;2021:1636816.
34. Kamath JV, Rana AC. Preliminary study on antifertility activity of Calotropis procera roots in female rats. *Fitoterapia*. 2002 Apr;73(2):111-5.
35. Basak SK, Bhaumik A, Mohanta A, Singhal P. Ocular toxicity by latex of Calotropis procera (Sodom apple). *Indian J Ophthalmol*. 2009 May-Jun;57(3):232-4.
36. Hoopes GM, Hamilton JP, Kim J, Zhao D, Wiegert-Rininger K, Crisovan E, Buell CR. Genome Assembly and Annotation of the Medicinal Plant Calotropis gigantea, a Producer of Anticancer and Antimalarial Cardenolides. *G3 (Bethesda)*. 2018 Feb 2;8(2):385-391.
37. Kumar S, Dewan S, Sangraula H, Kumar VL. Anti-diarrhoeal activity of the latex of Calotropis procera. *J Ethnopharmacol*. 2001 Jun;76(1):115-8. doi: 10.1016/s0378-8741(01)00219-7. PMID: 11378292.
38. Obese E, Biney RP, Henneh IT, Adakudugu EA, Anokwah D, Agyemang LS, Woode E, Ameyaw EO. The Anticonvulsant Effect of Hydroethanolic Leaf Extract of Calotropis procera (Ait) R. Br. (Apocynaceae). *Neural Plast*. 2021 Jun 26;2021:5566890.
39. Kazeem MI, Mayaki AM, Ogungbe BF, Ojekale AB. In-vitro Studies on Calotropis procera Leaf Extracts as Inhibitors of Key Enzymes Linked to Diabetes Mellitus. *Iran J Pharm Res*. 2016 Winter;15(Suppl):37-44.
40. Ramachandra Setty S, Quereshi AA, Viswanath Swamy AH, Patil T, Prakash T, Prabhu K, Veeran Gouda A. Hepatoprotective activity of Calotropis procera flowers against paracetamol-induced hepatic injury in rats. *Fitoterapia*. 2007 Dec;78(7-8):451-4.
41. Bezerra CF, Mota ÉF, Silva ACM, Tomé AR, Silva MZR, de Brito D, Porfírio CTMN, Oliveira AC, Lima-Filho JV, Ramos MV. Latex proteins from Calotropis procera: Toxicity and immunological tolerance revisited. *Chem Biol Interact*. 2017 Aug 25;274:138-149.