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Review Article

A Comprehensive Review of the Pharmacological Potential of Green Synthesized Nanoparticles from *Calotropis procera*

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ABSTRACT

Calotropis procera is a versatile plant widely recognized for its applications in traditional medicine, fodder, fuel, timber, fibre production, and phytoremediation. In recent years, it has also gained attention in nanotechnology research as a green source for nanoparticle synthesis. Green-synthesized nanoparticles have emerged as a major focus due to their environmentally friendly, sustainable, and biocompatible nature. Among various biological sources, plants like *C. procera* are commonly employed for nanoparticle synthesis owing to their inherent safety, rich phytochemical profile, and ecological benefits. This review summarizes in-depth analysis of global research on *Calotropis procera*-based nanoparticles by examining literature from major scientific databases, including PubMed, Scopus, Web of Science, and Google Scholar, covering studies published up to 2025. This review provides a comprehensive overview of the botanical characteristics, key phytochemical constituents, and traditional uses of *Calotropis procera*. It also explores the different types of nanoparticles synthesized from *C. procera* and their major pharmacological activities, including antimicrobial, antidiabetic, anti-inflammatory, anti-cancerous, larvicidal, immunomodulatory, anti-hypertensive, anti-oxidant and hepatoprotective activity, as well as the toxicity profile of *C. procera*-derived green nanoparticles. In conclusion, nanoparticles synthesized from *Calotropis procera* hold significant promise as therapeutic agents due to their diverse pharmacological properties. Through this review, a strong platform is established for future research on *C. procera*-based nanoparticles for clinical and other applications.

Keywords: *Calotropis procera*, Green synthesized Nanoparticles, Pharmacological Properties, Phytochemical Composition, Toxicity.

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INTRODUCTION

Medicinal plants are an essential part of daily life and are widely utilized for treating a variety of diseases and health conditions.[1] Plant-mediated Nanoparticles (NPs) are increasingly favored over chemically synthesized alternatives due to their environmentally friendly nature and reduced ecological impact.[2]

Calotropis procera (*C. procera*), a member of the Asclepiadaceae family, is known by various names worldwide, such as swallowwort, Sodom apple, dead sea apple, and milkweed. In India, it is commonly identified as orka in Oriya, madar in Hindi, alarka in Sanskrit, and akanda in Bengali. In Ayurvedic medicine, particularly in the formulation Arkelavana, it is referred to as Aak. Renowned for its potent medicinal properties, *C. procera* is highly valued in traditional medicine for its therapeutic potential.[3] The genus name *Calotropis* originates from Greek, signifying "beautiful," a reference to the plant's visually attractive flowers. The species name *procera*, on the other hand, is derived from Latin and is associated with the plant's distinctive waxy coating found on its leaves and stems.[4] It thrives and sustains growth under harsh environmental conditions such as drought, high salinity, extreme temperatures, low humidity, and intense sunlight.[5]

Over the past few decades, nanotechnology has experienced tremendous growth, not only in the diversity of its applications-including biomedical, healthcare, drug delivery, environmental protection, electronics, magnetics, space science, sensors, and energy storage and conversion-but also in the rising number of industrial R&D companies actively and effectively incorporating nanotechnology into their respective fields.[6] Nanoparticles (NPs), owing to their nanoscale dimensions (1-100 nm), exhibit unique physicochemical and biological characteristics. Depending on their shape, size, and dispersion, NPs exhibit superior characteristics and enhanced functionality compared to their bulk material counterparts.[7,8] Moreover, the increased surface area-to-volume ratio of nanoparticles is crucial and significantly enhances their efficiency in various

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biological applications. The use of individual phytochemicals leads to the production of highly stable Nanoparticles (NPs). The quality of nanoparticles is affected by the hydroxyl functional groups present in these phytochemicals.[9] To boost antioxidant performance, nanotechnology enhances the stability of bioactive molecules, improves their bioavailability, and ensures accurate delivery to specific biological targets.[10]

Despite the increasing interest in plant-mediated green synthesis of nanoparticles, there is a lack of comprehensive reviews focusing specifically on *Calotropis procera*. Although several primary studies have reported the synthesis and pharmacological evaluation of nanoparticles derived from different parts of this plant, no single review article has consolidated these findings. Most existing literature either focuses on general green synthesis methods or on other medicinal plants, leaving a significant gap in understanding the full therapeutic potential and mechanistic insights of *C. procera*-based nanoparticles. Moreover, the integration of its ethnobotanical relevance, phytochemical richness, and toxicity profile in the context of nanoparticle synthesis remains underexplored.

This review is the first to comprehensively compile and critically evaluate the green synthesis of a wide range of nanoparticles-such as silver, gold, copper, and various metal oxides-using different parts of *Calotropis procera*. It highlights the unique correlation between the plant's diverse phytochemical profile and the pharmacological activities exhibited by these biosynthesized nanoparticles, including antidiabetic, larvicidal, antimicrobial, anticancer, antioxidant, hepatoprotective, immunomodulatory, antihypertensive, and anti-inflammatory effects. The review further strengthens its scientific value by incorporating a detailed toxicity profile, offering insights into both safety and efficacy. To enhance clarity and accessibility, all pharmacological activities have been concisely summarized in a tabular format. By integrating aspects of ethnopharmacology, nanobiotechnology, and therapeutic potential, this work provides a novel and holistic perspective on the biomedical relevance of *C. procera*-based nanoparticles.

BOTANICAL PROFILE

C. procera is a perennial, evergreen shrub or soft-wooded tree that can grow up to 2.5 m in height, with a maximum height of 6 m. The stem is typically unbranched and simple, with a woody base covered in fissured, corky bark. When any part of plant cut or broken, the plant releases white latex. Its root system consists of a taproot extending approximately 3 to 4 m deep and woody at base.[11] The leaves are arranged in an opposite-decussate pattern, simple, subsessile and exstipulate. They have a slightly leathery texture and are covered with a fine layer of soft hairs, which may occasionally cause a stinging sensation.[12]

TRADITIONAL USES

India is a prominent tropical country abundant in natural resources and traditional knowledge related to their use. *C. procera* is one such significant medicinal plant, highly valued for its rich ethnobotanical applications and substantial economic importance.[13] Traditionally, some parts of the plant are known for their medicinal benefits to treat various ailments. The whole plant has been utilized for managing rheumatism, fever, indigestion, colds, eczema, diarrhea, boils and jaundice. The root has been employed in the treatment of eczema, leprosy, elephantiasis, asthma, cough, rheumatism and diarrhea, while the stem has been used for conditions such as leprosy, intestinal worms and leukoderma.[14,15] The latex used in medications for treating *Tinea capitis* in children due to its antifungal properties, also has a historical record of more drastic applications inducing abortion in women.[16] The flowers were thought to enhance digestion, alleviate mucus buildup, and boost appetite. The blooming tops were utilized for managing asthma. Moreover, the root bark was applied in the therapy of elephantiasis.[12,17]

PHYTOCHEMICAL COMPOSITION

Phytochemical analysis of *C. procera* has identified the presence of numerous bioactive constituents in substantial quantities, including alkaloids, flavonoids, tannins, saponins, anthraquinones, sesquiterpenes, steroids, terpenes, and cardiac glycosides.[18,19] The major cardioactive glycosides identified in *C. procera* include calactin, calotoxin, usharin, usharidine, and vouscharin. Among the plant parts, the latex exhibits the highest concentration of cardenolides, with uscharin and calotropagenin being the dominant compounds. In the leaves, calotropin and calotropagenin are primarily found, while the stem contains key cardenolides such as uscharidin, calotropin, proceroside, and calactin. The root bark primarily contains calotoxin and calactin, while the fruit pericarp is abundant in coroglaucigenin and uzarigenin. The seeds possess about 0.23-0.47% cardenolides, with coroglaucigenin or frugoside being the major constituents.[12,20,21] Rutin (quercetin-3-rutinoside) is the major flavonoid found in *C. procera*, with its concentration differing among various parts of the plant. In addition to flavonoids, the plant is rich in a range of bioactive compounds including fatty acids, resins, proteolytic enzymes, amino acids, hydrocarbons, and essential minerals.[22]

The flowers of *C. procera* are abundant in a wide range of bioactive compounds. These include flavonoids such as quercetin-3-rutinoside and sterols like β-sitosterol, β-sitost-4-en-3-one, stigmasterol, as well as α- and β-amyrins. In addition, they contain polysaccharides composed of sugars like D-arabinose, glucose, glucosamine, and L-rhamnose, along with significant cardenolides such as calactin, calotoxin, calotropagenin, and calotropin.[23,24]

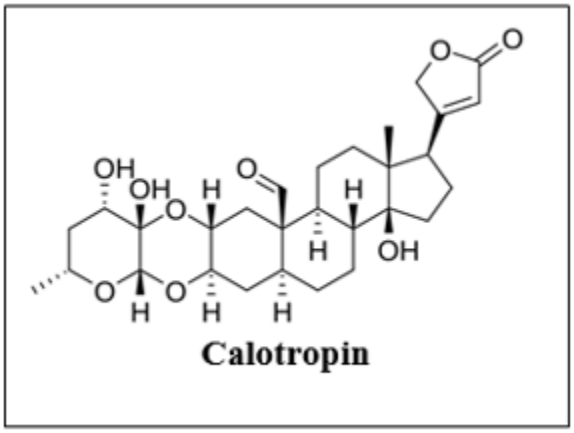
The roots of *C. procera* contain key phytochemicals such as cardenolides (calotoxin, *procera* genin), terpenes (calotropenol, calotropenyl acetate), and steroidal compounds like stigmasterol, β-sitosterol, and procesterol.[25,26]

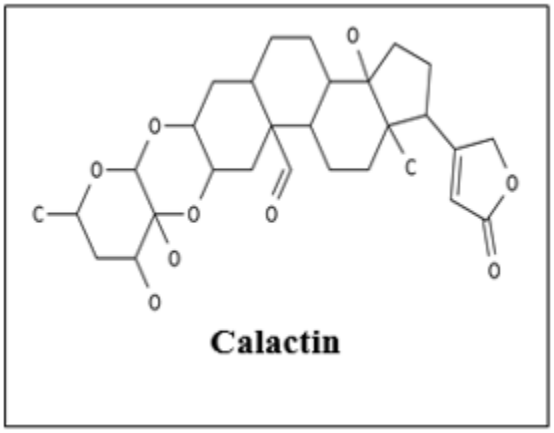
The leaves of *C. procera* are rich in important phytochemicals, including cardenolides such as calactin, calotoxin, calotropagenin, and calotropin. They also contain key flavonoids like kaempferol, isorhamnetin-3-O-rutinoside, and rutin, which contribute to antioxidant activity. Additionally, the leaves possess β-sitosterol and stigmasterol (steroidal compounds), ascorbic acid, and notable volatile constituents like R-limonene and tridecane.[27-29]

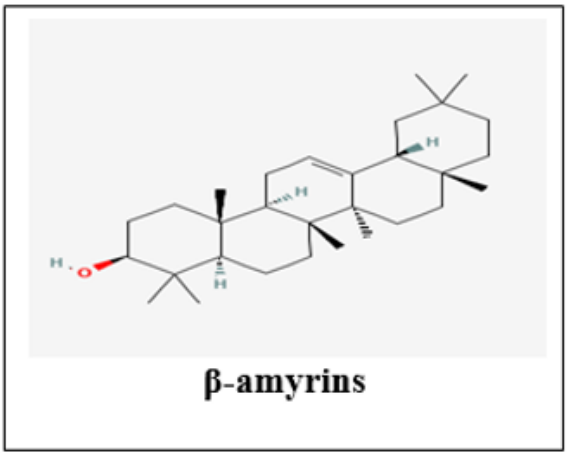
The latex of *C. procera* contains several important bioactive compounds, notably cardenolides such as calactin, calotoxin, uscharin, and procegenins A and B. Key steroids include β-sitosterol and ursolic acid derivatives. It is also rich in proteins and enzymes like cysteine peptidases (CpCP-1, CpCP-2, CpCP-3) and procerain B. Among lignans, notable compounds include (+) Pinoresinol 4-O-[6 -Oprotocatechuoyl]-β-D glucopyranoside and its glycosylated derivatives.[30,31]

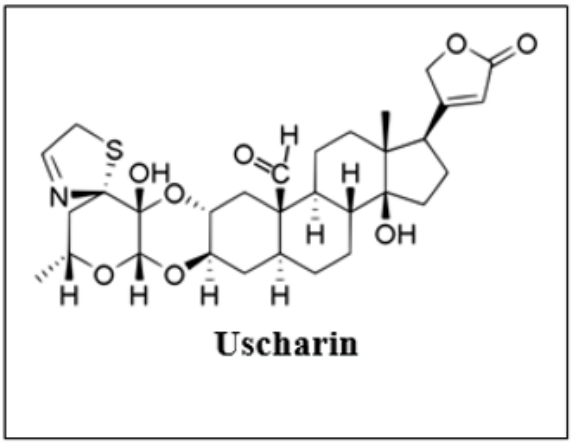
Structure of various phytochemicals have been illustrated in Figure 1.

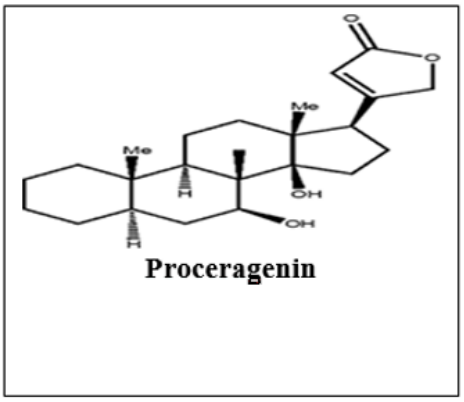
Major Phytochemical Structures of *Calotropis procera*



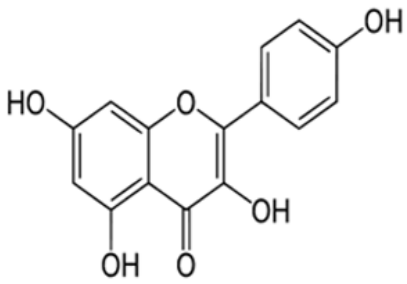




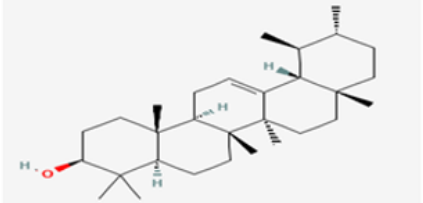




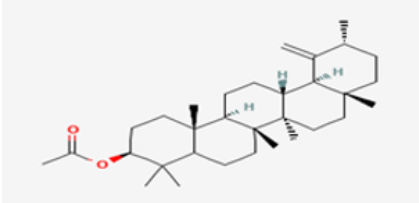
Proceragenin



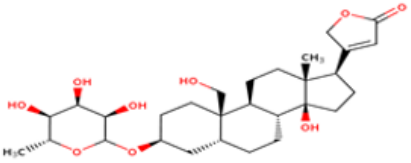
kaempferol



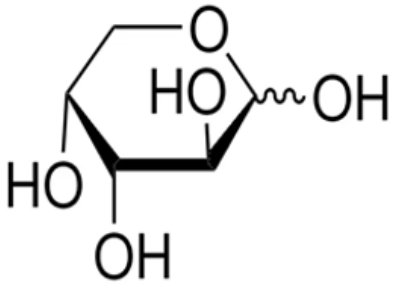
α- amyrin



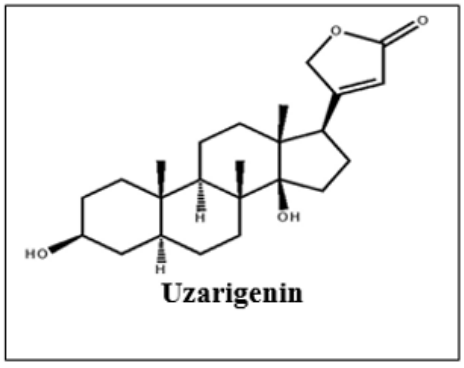
Calotropenyl acetate



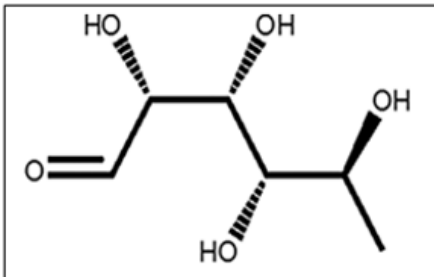
Frugoside



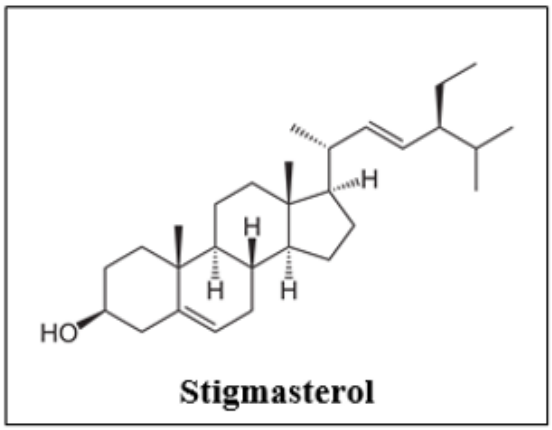
D-arabinose



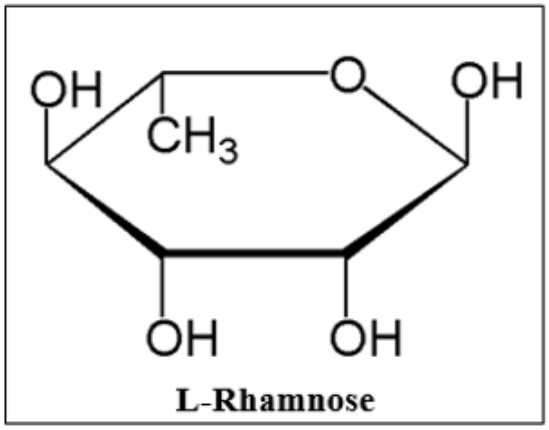
Uzarigenin



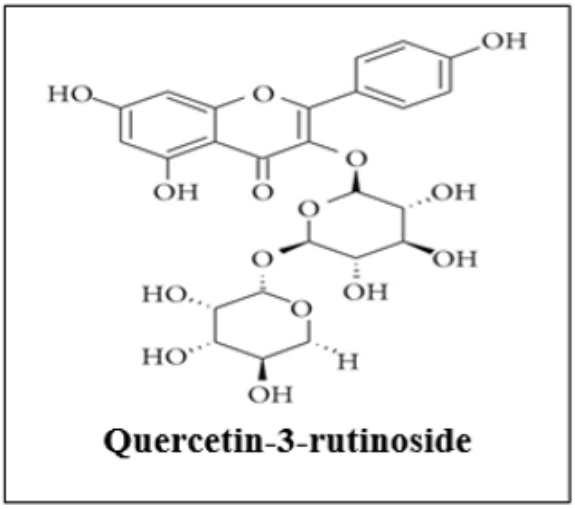
L-rhamnose



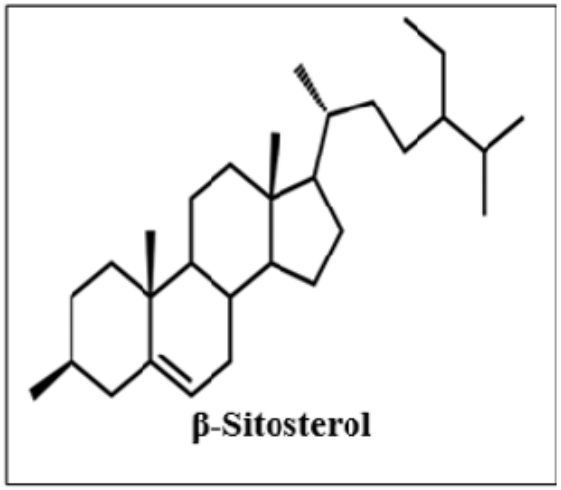
Stigmasterol



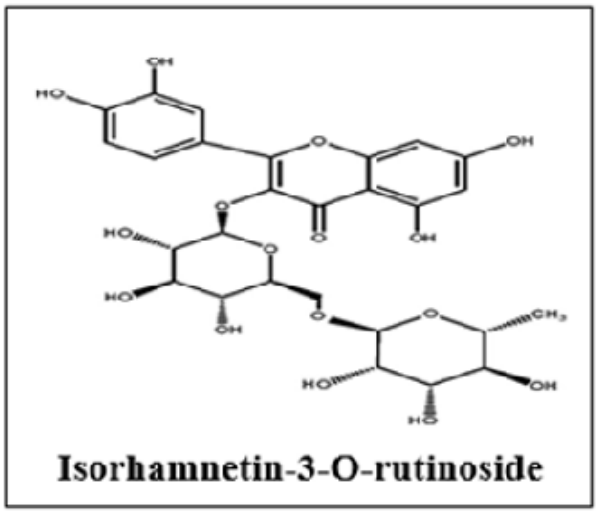
L-Rhamnose



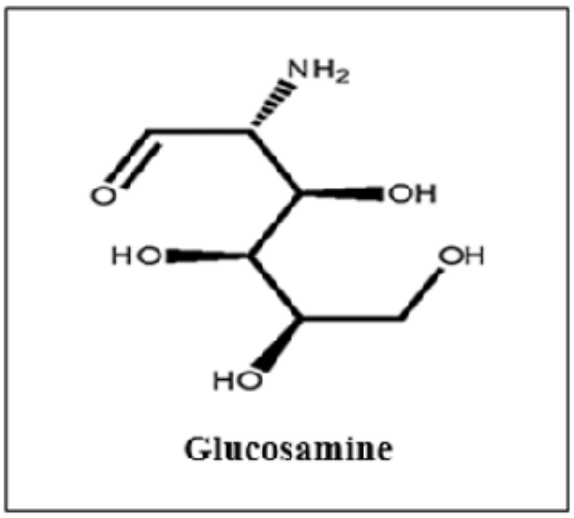
Quercetin-3-rutinoside



β-Sitosterol



Isorhamnetin-3-O-rutinoside



Glucosamine

Figure 1: Structure of various phytochemical of *C. procera*

Varieties of Nanoparticles Synthesized using *C. procera*

Various nanoparticles such as silver, gold, copper, copper oxide, zinc oxide, iron oxide, magnetite, cerium oxide, and titanium dioxide have been synthesized using different parts of *Calotropis procera*, including leaves, latex, flowers, and roots. The different types of nanoparticles derived from the plant are illustrated in the accompanying (Figure 2).

Silver Nanoparticle (AgNPs)

Silver Nanoparticles (AgNPs) are among the most widely studied nanomaterials due to their unique and desirable characteristics. These include excellent conductivity, chemical stability, catalytic efficiency, enhanced Raman effects, and antimicrobial activity, attracting significant research interest across disciplines.[32] Various parts of the *C. procera* plant have been utilized for the synthesis of Silver Nanoparticles (AgNPs), each demonstrating distinct pharmacological activities. Maisam *et al*., (2025) reported the green synthesis of Silver Nanoparticles (AgNPs) ranging in size from 30 to 130 nm using aqueous extracts from the flowers and latex of *C. procera*. The antibacterial potential of these biosynthesized AgNPs was evaluated through an *in vitro* study against *Escherichia coli, Bacillus subtilis, Staphylococcus aureus*, and *Pseudomonas aeruginosa*, using varying concentrations of 100, 125, 150, 200, 250, and 500 µL. The results demonstrated a clear dose-dependent response, with higher concentrations leading to increased inhibition zones. These findings highlight the effectiveness of *C. procera*-mediated AgNPs as antibacterial agents, with a strong correlation between nanoparticle concentration and antimicrobial activity.[33] Other studies also highlighted the green synthesis of Silver Nanoparticles (AgNPs) using *C. procera*, demonstrating their potential for a wide range of therapeutic applications. The biosynthesized AgNPs exhibited notable activities, including anti-diabetic, antioxidant, anti-inflammatory,[34] hepatoprotective,[35] anticancer,[36] immunomodulatory,[37] and larvicidal effects. This eco-friendly approach not only supports sustainable nanoparticle production but also underscores the multifunctional biomedical potential of *C. procera*-mediated AgNPs.[38]

Gold Nanoparticles (AuNPs)

Gold nanoparticles have gained significant interest among various metallic nanoparticles due to their exceptional properties and broad applicability, particularly in the fields of medicine and biology.[39] Their high biocompatibility,[40] adjustable surface plasmon resonance,[41] minimal toxicity,[42] and strong optical scattering and absorption capabilities make them ideal candidates for biomedical applications.[43]

In a study conducted by Shittu and Stephen (2016), gold nanoparticles (AuNPs) with an average size of 45 nm were synthesized using an aqueous leaf extract of *C. procera* and evaluated for their cytotoxic activity against the MCF-7 breast cancer cell line through an *in vitro* MTT assay. The results demonstrated a clear dose-dependent cytotoxic effect, where increasing concentrations of AuNPs led to a progressive decline in cell viability. Notably, the IC_{50} value was determined to be 0.312 mg/mL, indicating significant antiproliferative potential of the plant-mediated AuNPs against cancer cells. This study highlights the promising application of *C. procera*-derived gold nanoparticles in cancer nanomedicine.[44]

The study also reported that the biosynthesized AuNPs using *C. procera* exhibited notable antimicrobial, antioxidant, and antihypertensive activities, suggesting their multifunctional therapeutic potential. These findings underline the versatility of *C. procera*-mediated gold nanoparticles as promising agents for biomedical applications.[45]

Zinc Oxide Nanoparticles (ZnONPs)

Zinc oxide Nanoparticles (ZnONPs) have attracted significant research interest for their roles in catalysis, gas sensing, and biomedical applications.[46,47] Furthermore, ZnO nanoparticles are considered cost-effective and safe; the U.S. FDA has classified zinc oxide as a GRAS (Generally Recognized As Safe) metal oxide.[48] In a recent *in vivo* study by Sharma *et al*., (2025), zinc oxide nanoparticles (ZnO NPs) with an average size of 18.20 nm were synthesized using an aqueous leaf extract of *C. procera* and evaluated for their efficacy against root-knot nematodes (*Meloidogyne incognita*) in bitter gourd plants. The nanoparticles were applied at varying concentrations, and the results revealed a significant improvement in plant growth parameters along with a reduction in nematode infestation. These findings highlight the potential of *C. procera*-mediated ZnO nanoparticles as a sustainable and effective nanobiocontrol agent in agricultural pest management.[49] In addition to their nematicidal effect, other studies have also reported that *C. procera*-derived nanoparticles exhibit strong antimicrobial, antioxidant, and anticancer activities, underscoring their multifunctional potential in both agricultural and biomedical applications.[50,51]

Copper oxide nanoparticles (CuONPs)

K. Rayapa Reddy reported the green synthesis of CuO nanoparticles using *C. procera*, a plant belonging to the Asclepiadaceae family. These nanoparticles, characterized by their narrow band gap, have found widespread application in various fields, particularly in catalysis and photocatalytic processes.[52,53] CuO nanoparticles (CuONPs) synthesized using *C. procera* leaf extract demonstrated strong adsorption capacity for Cr(VI), indicating their potential as an effective and eco-friendly alternative for removing hexavalent chromium from aqueous environments.[54] Sethupandian *et al*., (2023) demonstrated the green synthesis of Copper Oxide (CuO) nanoparticles using an aqueous seed extract of *C. procera*. The biosynthesized CuO nanoparticles were evaluated for their antibacterial activity through *in vitro*

assays against both Gram-positive (*Staphylococcus aureus*) and Gram-negative bacteria, including *Escherichia coli, Pseudomonas aeruginosa, Vibrio cholerae*, and *Aeromonas hydrophila*. The results revealed significant antibacterial efficacy, with the nanoparticles exhibiting inhibitory effects against all tested bacterial strains, indicating the broad-spectrum antimicrobial potential of *C. procera*-mediated CuO nanoparticles. These findings suggest their promising application in controlling bacterial pathogens through environmentally friendly nanomaterials.[55]

Copper nanoparticles (CuNPs)

Copper nanoparticles have made remarkable advancements in the fields of nanotechnology and nanomedicine over the past decade, owing to their outstanding catalytic, optical, electrical, antifungal and antibacterial properties.[56] Copper nanoparticles (Cu NPs) were synthesized through a green approach by Harne *et al*., (2012) using an aqueous latex extract of *C. procera* and investigated their biocompatibility through *in vitro* studies on three different cell lines. The results revealed that Cu NPs exhibited excellent cell viability across all tested concentrations. This suggests that the copper nanoparticles synthesized using *C. procera* latex possess high biocompatibility, making them promising candidates for biomedical applications. While the study did not show direct anticancer activity, the demonstrated safety profile of these nanoparticles supports their potential use as nanocarriers or in combination therapies for cancer treatment.[57]

Cerium oxide (CeO_2) nanoparticles

Cerium oxide (CeO_2) is a semiconductor metal oxide characterized by a band gap energy of approximately 3.19 eV and is widely used in bioimaging, catalysis, antibacterial applications, and sunscreens formulations, with various synthesis methods underscoring its industrial and biomedical relevance.[58] Muthuvel *et al*., (2020) reported the green synthesis of cerium oxide nanoparticles (CeO_2-NPs) using an aqueous flower extract of *C. procera*, resulting in nanoparticles with an average size of 21 nm. The antibacterial activity of the synthesized CeO_2-NPs was evaluated *in vitro* against both Gram-positive (*Bacillus subtilis, Staphylococcus saprophyticus*) and Gram-negative (*Escherichia coli, Pseudomonas aeruginosa*) bacterial strains at concentrations ranging from 5 to 100 µg/mL. At the highest tested concentration, the nanoparticles exhibited strong antibacterial efficacy against all microorganisms. These findings highlight the potent broad-spectrum antibacterial potential of *C. procera*-mediated CeO_2 nanoparticles, making them promising candidates for antimicrobial applications.[59]

Iron oxide nanoparticles (FeONPs)

Ali *et al*., (2020) synthesized iron oxide nanoparticles (~32 nm in size) using an aqueous leaf extract of *C. procera* and evaluated their antifungal activity through an *in vitro* study against *Alternaria alternata*. The nanoparticles were tested at various concentrations (0.1 to 1.0 mg/mL). The highest concentration showed the most effective fungal inhibition, with a growth suppression rate of 81.9%, which was nearly equivalent to that of a standard chemical fungicide (82.2%). These results suggest that *C. procera*-mediated iron oxide nanoparticles are not only effective but could serve as an eco-friendly alternative to conventional fungicides in managing plant fungal pathogens.[60]

Titanium oxide nanoparticles (TiO_2 NPs)

Titanium dioxide (TiO_2) nanoparticles have attracted widespread interest due to their remarkable antibacterial and antifungal properties, effective ultraviolet (UV) light filtering capabilities, and exceptional catalytic and photochemical performance. These multifunctional characteristics make them highly valuable for various industrial, environmental, and biomedical applications.[61-63] In a recent study, Fatima *et al*., (2025) synthesized titanium dioxide nanoparticles (TiO_2 NPs) using an aqueous latex serum extract of *C. procera* and evaluated their insecticidal activity against different developmental stages (2nd and 4th instar nymphs and adults) of the dusky cotton bug (*Oxycarenus* spp.). The study demonstrated a strong dose-dependent insecticidal effect, with the highest mortality rates observed in second instar nymphs (90-95%) and the lowest in adults (around 70%). Overall, the TiO_2 nanoparticles achieved up to 95% control of the insect population, indicating that *C. procera*-mediated TiO_2 NPs are highly effective as a botanical nanoinsecticide, particularly against early-stage pests.[64]

Magnetite nanoparticles (Fe_3O_4 NPs)

Magnetite nanoparticles (Fe_3O_4) have attracted considerable scientific attention owing to their excellent biocompatibility, low cytotoxicity, simple synthesis methods, and eco-friendly biodegradability.[65] Kalu *et al*., (2022) reported the green synthesis of magnetite nanoparticles, with sizes ranging from 62.83 to 134 nm, using an aqueous leaf extract of *C. procera*. The antimicrobial potential of these nanoparticles was assessed *in vitro* at a concentration of 100 mg/mL against some microorganisms, including two Gram-positive bacteria (*Staphylococcus aureus* and *Bacillus subtilis*), two Gram-negative bacteria (*Escherichia coli* and *Klebsiella pneumoniae*), and two fungal strains (*Aspergillus niger* and *Fusarium oxysporum*). The nanoparticles exhibited notable inhibition against Gram-positive bacterial and fungal strains, while showing limited activity against Gram-negative bacteria. These findings suggest the potential of *C. procera*-mediated magnetite nanoparticles as effective agents against specific bacterial and fungal pathogens. Moreover, the eco-friendly and cost-effective green synthesis approach offers a promising alternative for developing magnetite-based nanomaterials, encouraging further studies focused on their optimization, mechanism of action, and application in biomedical and agricultural fields.[66]

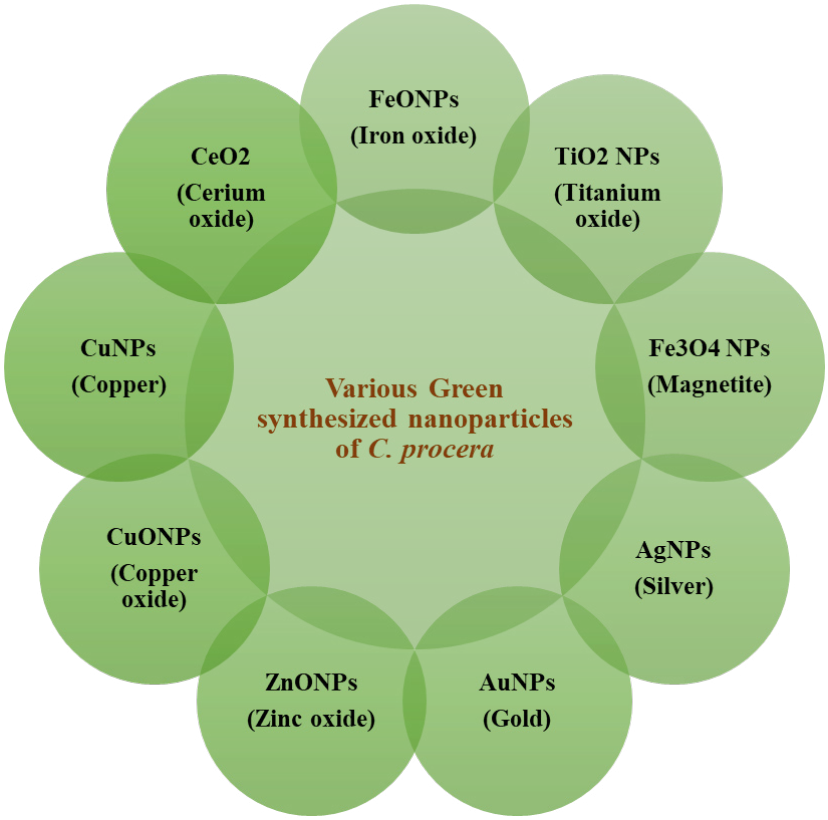


Figure 2: Different types of Nanoparticles of *C. procera*.

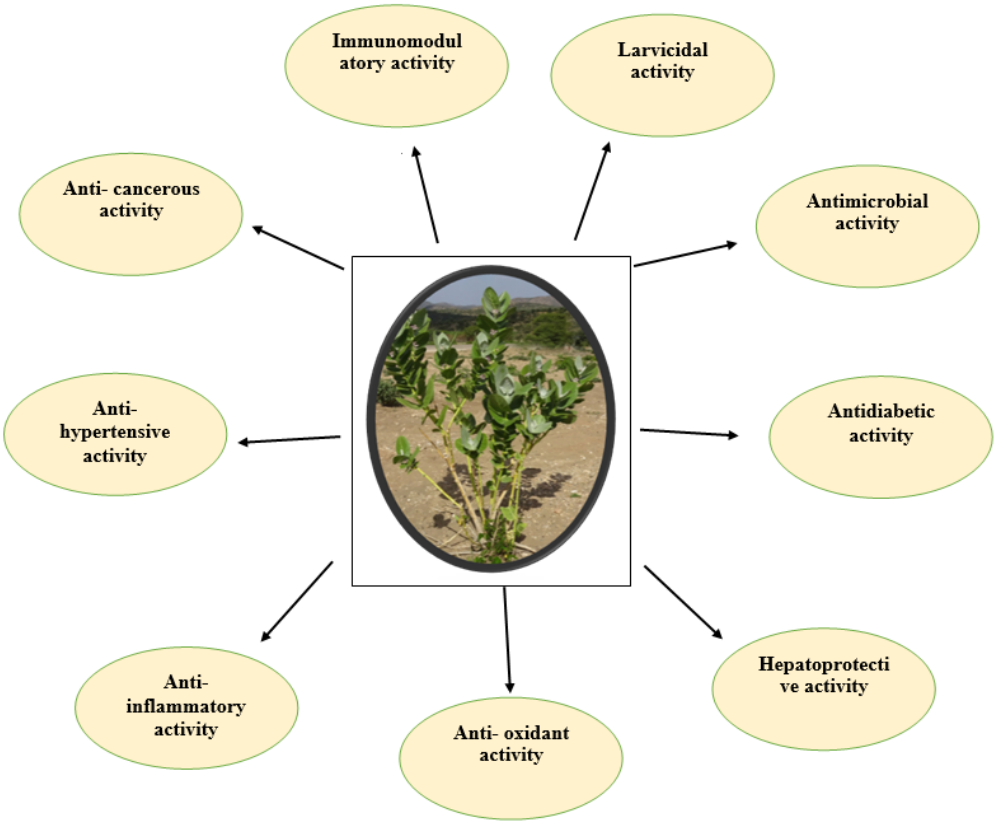


Figure 3: Different pharmacological activities of *C. procera*.

Pharmacological activity of nanoparticles synthesized using *C. procera*

Calotropis procera-mediated nanoparticles have been extensively studied for their broad spectrum of pharmacological properties, attributed to the plant's abundance of bioactive compounds. Various nanoparticles synthesized from different parts of the plant-such as leaves, roots, latex, and flowers-have demonstrated significant therapeutic potential. These include anti-inflammatory, antimicrobial, antioxidant, anticancer, antidiabetic, antihypertensive, immunomodulatory, and larvicidal activities. The key pharmacological activities are summarized in Table 1, which presents details including the year of publication, type and size of nanoparticles, plant part and extract used, dosage, mode of administration, duration of treatment, experimental model, and observed effects.

Various pharmacological activities have been illustrated in Figure 3.

POSSIBLE MECHANISMS OF VARIOUS PHARMACOLOGICAL ACTIVITIES

Figure 4 presents a comprehensive summary of the underlying mechanisms responsible for the various pharmacological activities described in Table 1, offering a visual representation to enhance understanding of their mode of action.

Table 1: Various pharmacological activities of Green synthesized nanoparticles using *C. procera*.

	Name of Nanoparticles/size	Part Used	Type of plant extract	Animal model	Dose duration and route	Observation and results	References
Antimicrobial activity	AgNPs/ 30 to 130 nm	Flowers and Latex	Aqueous extract	*In vitro study* against *E. coli, B. subtilis, S. aureus,* and *P. aeruginosa.*	100, 125, 150, 200, 250 and 500 µL	The antibacterial activity of the nanoparticles was dose-dependent, with higher concentrations resulting in greater inhibition across all tested bacterial strains.For *P. aeruginosa*, the lowest inhibition zone of 10.5 mm was observed at 100 µL, while the highest inhibition zone of 21.5 mm was recorded at 500 µL.For *B. subtilis*, the inhibition zone was observed minimum of 17 mm at 100 µL and maximum of 28 mm at 500 µLFor *S. aureus*, the smallest inhibition zone was 19.5 mm at 100 µL, increasing to 25 mm at 500 µL.For *E. coli*, the inhibition zone was found 12.5 mm at 100 µL and maximum of 25 mm at 500 µL.	[33]
	AgNPs/ 29-46 nm	Leaves	Aqueous extract	*In vitro* study against Gram-positive *(B. subtilis, B. megaterium)* and Gram-negative *(S. flexneri)* bacteria and against the fungi *(T. viride, P. crysogenum,* and *A. niger)*	100 µL	The zone of inhibition results demonstrated by AgNPs revealed antibacterial activity against *B. megabacterium* (18±1.89 mm), *B. subtilis* (20±1.95 mm), and *S. flexneri* (21±1.99 mm).Antifungal activity was also observed, with inhibition zones against *A. niger* (22±2.14 mm), *P. chrysogenum* (20±1.98 mm), and *T. viride* (18±2.16 mm).	[34]

	AuNPs	Leaves	Aqueous extract	*In vitro* study against fungal strain *A. niger, A. flavus, F. poae, F. solani* and *P. avenatum*	150 µL/ mL	The AuNPs exhibited notable antifungal activity at a concentration of 150 µL/mL, showing mycelial inhibition rates of 70.0%, 60.0%, 60.4%, 72.2%, and 82.0% against *F. solani, F. poae, A. niger, A.flavus*, and *P. avenatum*, respectively, when compared to the mycelial growth observed in the control group.	[45]
	AgNPs/ 15.30 - 17.66 nm	Leaves	Aqueous extract	*In vitro* study against *P. aeruginosa*, *E. sichuanensis*, *E. coli*, *S. aureus*, *S. agalactiae*	10 and 20 µL	The synthesized AgNPs exhibited potent antibacterial activity, as evidenced by the zones of inhibition observed against various bacterial strains: *E. coli* (18.1±0.2 mm), *E. sichuanensis* (16.8±0.5 mm), *P. aeruginosa* (14.4±0.3 mm), *S. aureus* (22.2±0.5 mm), and *S. agalactiae* (21.5±0.1 mm).	[67]
	AuNPs /41.88 nm	Leaves, root, stem, and flower	Methanolic extract	*In vitro* study against *S. larcymans* (fungal strain)	5, 10, 15, 20, 30, 40 and 50 µL	AuNPs of plant extract exhibited antifungal activity by producing a zone of inhibition measuring 3.2 mm at a concentration of 50 µL, 3.0 mm at 40 µL, and 2.1 mm at 30 µL.	[68]
	ZnO NPs/ 100-200 nm	Leaves	Aqueous extract	*In vitro* study against human *pathogenic* bacteria *E. coli, P. aeruginosa, K. pneumoniae, S. aureus* and plant isolated bacteria *X. axonopodis.* Fungal strain- *Aspergillus* sps. and *Penicillium* sps.	10, 20 and 30 µL for bacteria100, 200 and 300 µL for fungal strain	The green-synthesized ZnO nanoparticles demonstrated potent antibacterial activity against both human and plant pathogens at all tested concentrations. The highest zone of inhibition was observed at the 30 µL concentration. Interestingly, as the concentration of ZnO nanoparticles increased beyond 30 µL, a reduction in the inhibition zone was noted. Thus, the maximum antibacterial effect was achieved at 30 µL. According to the MIC data, complete inhibition of all tested microorganisms was achieved at concentrations ranging from 50 to 12.5 µg/mL of nano-ZnO. The antifungal assay results indicated that all concentrations of ZnO nanoparticles significantly inhibited spore germination.	[51]

	AgNPs	Latex from young twigs	-	*In vitro* study against *S. aureus, E. coli, E. coccus, E. faecalis, P. aeruginosa* and *K. pneumonia* bacterial strain.	10-100µg/mL	L-AgNPs displayed potent and concentration-dependent antibacterial activity against a variety of pathogenic microorganisms. The degree of microbial inhibition varied significantly among the different tested bacterial strains. The antibacterial effect was significantly more prominent against Gram-negative organisms compared to Gram-positive ones.	[38]
	CuONPs1/20-50 nm	Seed	Aqueous extract	*In vitro* study against gram positive bacteria *(E. coli, S. aureus)* and *gram* negative bacteria *(P. aeruginosa, Vibrio cholera* and *A. hydrophila)*	-	The green synthesized CuONPs exhibited strong toxicity against various pathogenic bacterial species and showed antibacterial activity against all tested bacterial strains.The zones of growth inhibition were observed in the following decreasing order: *V. cholerae, E. coli, P. aeruginosa, S. aureus*, and *A. hydrophila.*	[55]
	AgNPs/ 20-30 nm	Leaves and Flowers	Aqueous extract	*In vitro* study against *Streptococcus* spp, *Salmonella* spp, *E. coli,* and *S. aureus*	0.1, 0.25 and 0.5 mg/mL	The antimicrobial potential of C.p-AgNPs was investigated and found to exhibit dose-dependent inhibition. At 0.25 and 0.5 mg/mL, AgNPs effectively inhibited bacterial growth, yielding inhibition zones of 12 mm and 16 mm for *E. coli*, 7 mm and 12 mm for *S. aureus*, 10 mm and 13 mm for *Streptococcus*, and 9 mm and 14 mm for *Salmonella* spp., respectively.	[69]
	AgNPs/average sizes 14-25 nm	Stem	Aqueous extract	*In vitro* study against bacterial isolates such as *E. coli, P. aeruginosa, B. cereus and S. aureus* and against some pathogenic fungi*; F. oxysporum, Rhizopus* sp. *A. niger* and *A. flavus*	-	The inhibition zones were observed for *E. coli* (12 mm), *P. aeruginosa* (19 mm), and *B. cereus* (29 mm), while *S. aureus* showed no susceptibility. In antifungal activity, *A. niger* exhibited a 14 mm zone of inhibition, whereas *F. oxysporum, Rhizopus* sp., and *A. flavus* showed no observable inhibition.	[70]

	Fe_3O_4 NPs/62.83- 134 nm	Leaves	Aqueous extract	*In vitro* study against two Gram-positive bacteria *(S. aureus* and *B. subtilis),* two Gram-negative bacteria *(E. coli* and *K. pneumoniae),* and two fungal strains *(A. niger* and *F. oxysporum).*	100 mg/mL	The antimicrobial efficacy was demonstrated by inhibition zones ranging from 7.1 mm to 22.5 mm against *K. pneumoniae, S. aureus, B. subtilis, A. niger, and F. oxysporum*, whereas no inhibitory effect was detected against *E. coli.* The results of this study also revealed that the antimicrobial activity against Gram-positive bacteria was significantly higher compared to the other tested microorganisms, while the activity against fungal isolates was significantly greater than that observed against Gram-negative bacteria	[66]
	ZnO NPs/ 25.7 nm	Leaves	Aqueous extract	*In vitro* study against bacteria *E. coli, E. fecalicus, Klebsiella* sp., *Salmonella* sp., *streptococcus pyogens, S. aureus, Proteus* sp., *Pseudomonas* sp., and fungal strain *C. albicans.*	40, 80, and 120 µL	The study revealed that varying concentrations of green-synthesized ZnO nanoparticles exhibited notable antimicrobial sensitivity, with the maximum zone of inhibition observed at the concentration of 120 µg/mL. In the antifungal study, the ZnO nanoparticles exhibited the greatest inhibition at the highest concentration tested.	[71]
	Zno NPs/ 12.08 nm	Leaves	Aqueous extract	*In vitro* study against *E. coli*	-	The green-synthesized nanoparticles significantly enhanced the antimicrobial effect, increasing the inhibition zone to 49%	[72]
	CP-AgNPs/ 28.72 nm	-	Latex	*In vitro* study against *P. aeruginosa, K. pneumoniae, S. aureus* and *B. subtilis*	64, 32, 16, 8, 4, 2 and 1 µg/mL	The MIC of CP-AgNPs was found to be 4 µg/mL against *P. aeruginosa and B. subtilis*, and 8 µg/mL against *K. pneumoniae and S. aureus*. The MBC for all tested bacterial strains was determined to be 32 µg/mL. CP-AgNPs inhibited biofilm formation by all four bacterial strains by approximately 80%.	[73]

	AgNPs/10nm	-	-	*In vitro* study against *S. aureus,* MRSA, *S. typhimurium* and *E. coli*	1.6 to 4 mg	The bacterial inhibition was concentration-dependent. AgNPs exhibited antibacterial activity, with inhibition zone values ranging from 8 to 10 mm against *S. aureus* and MRSA, and from 7 to 9 mm against *S. typhimurium* and *E. coli*.	[74]
	AgNPs/ 70- 80 nm	Flowers	Aqueous extract	*In vitro* study against *S. aureus* and *P. acnes*.	10, 15, 20, 25 and 30 µg/g	*S. aureus* exhibited the highest zone of inhibition (13.5±1 mm), while *P. acnes* showed (8±1 mm). The bacterial strains displayed no resistance to the flower extract control and showed only a minimal inhibitory response to the silver nitrate control.	[36]
	AgNPs and honey/ 60-85 nm	Leaves	Aqueous extract	*In vitro* study against Gram positive *(S. aureus* and *B. subtilis)* and Gram negative *(P. mirabilis* and *E. coli)* bacteria.	20% AgNPs and 20% honey	AgNPs demonstrated effective antimicrobial activity by inhibiting the growth of both bacterial and fungal pathogens. The maximum zone of inhibition was observed against *Bacillus subtilis* (29±0.040 mm), while the minimum inhibition was recorded against *Micrococcus luteus* and *K. pneumoniae* (19±0.037 mm).	[37]
	AgNPs/ 38-44 nm	Roots	Aqueous extract	*In vitro* study against *S. typhi, S. flexneri, B. subtilis, E. coli, S. aureus, Enterococcus* sp., *K. pneumoniae, P. aeruginosa, S. epidermidis, and E. faecalis*.	10, 25, 50 and 100 µg	Among all the tested pathogenic bacterial strains, *S. flexneri, E. coli, P. aeruginosa*, and *E. faecalis* exhibited the highest sensitivity towards AgNPs, as evidenced by their lowest observed MIC value of 3.12 µg/mL. *S. typhi* and *B. subtilis* also showed considerable susceptibility to AgNPs, with an MIC value of 6.25 µg/mL, suggesting moderate antibacterial activity. On the other hand, a relatively higher degree of resistance was recorded for *S. aureus, Enterococcus* species, *K. pneumoniae*, and *S. epidermidis*, which demonstrated reduced sensitivity by exhibiting a MIC value of 12.5 µg/mL.	[75]

	FeO NPs/32 nm	Leaves	Aqueous extract	*In vitro* study against fungi *A. alternata*.	1.0, 0.75, 0.5, 0.25 and 0.1 mg/mL	A concentration of 1.0 mg/mL showed the highest and most comparable level of effectiveness. At this concentration, iron oxide nanoparticles and chemical fungicides exhibited growth inhibition rates of 81.9% and 82.2%, respectively. Interestingly, at lower concentrations, the nanoparticles demonstrated even greater inhibitory effects than the chemical fungicide.	[60]
	CeO_2-NPs/ average size 21 nm	Flower	Aqueous extract	*In vitro* study against Gram positive (*B. subtilis, S. saprophyticus*) and Gram negative (*E. coli, P. aeruginosa*).	5, 10, 20, 40, 80 and 100 µg/mL	The biosynthesized CeO_2 nanoparticles exhibited strong antibacterial activity against all tested microorganisms at a concentration of 100 µg/mL. The observed zones of inhibition were 23±0.48 mm for *E. coli*, 21±0.84 mm for *P. aeruginosa*, 21±0.78 mm for *S. saprophyticus*, and 20±0.41 mm for *B. subtilis*	[59]
	Latex silver nanoparticles (LAg-NPs)/ 2.26-30 nm.	Leaves	Latex	*In vitro* study against Gram-negative bacteria *(E. coli and P. aeruginosa*), Gram-positive bacteria (*S. aureus and B. subtilis)* and fungal strains of (*C. albicans and A. niger*).	25, 50, 75, 100 and 125 µg / mL	The silver nanoparticles exhibited varying degrees of growth inhibition across all tested strains. The largest inhibition zone was observed at the concentration of 125 µg/mL for all microorganism, indicating a concentration-dependent antimicrobial effect.	[4]

	ZnO NPs/ 100-200 nm	Leaves	Aqueous extract	*In vitro* study against- Human pathogen (*E. coli, P. aeruginosa, K. pneumoniae, S. aureus)* -plant pathogenic organism *(X. axonopodis)* and -Fungal strain *(Pencillium* sps., *Aspergillus* sps.*)*	For bacteria-10, 20 and 30 µL For fungal-100 µL, 200 µL, and 300 µL	For human pathogen- All tested microorganisms were completely inhibited at nano-ZnO concentrations ranging from 50 to 12.5 µg/mL.The MIC of ZnO NPs showed the most effective inhibition against all tested bacteria at a concentration of 50 µg/mL.For plant *pathogen*-ZnO nanoparticles exhibited the highest zones of inhibition, measuring 16 mm and 18 mm respectively, at a concentration of 30 µg/mL against *X. axonopodis*. Interestingly, the zone of inhibition for plant pathogenic strains decreased with increasing concentrations of ZnO nanoparticle.For fungi- Various concentrations of ZnO nanoparticles resulted in significant inhibition.The greatest inhibition was observed at the highest concentration of nanoparticles.	[76]
	LAgNPs/ average size 12.33 nm	-	Latex serum	*In vitro* study against *bacteria (E. coli, P. aeruginosa, Serratia* sp.)- and fungi *(T. rubrum, C. albicans, A. terreus)*	-For bacteria105, 10, 20 µL- for fungi 10, 25, 50 µL	The MIC of LAg-NPs was 5 µL for *E. coli*, and 10 µL for *Serratia* sp. and *P. aeruginosa*. Among the fungal strains, the MIC was 10 µL for *C. albicans*, while *T. rubrum* and *A. terreus* found 25 µL.	[77]
Antidiabetic activity	AgNPs/ 29-46 nm	Leaves	Aqueous extract	*In vitro* study	250 µL	The results showed that AgNPs demonstrated α-amylase inhibitory activity of 83.29±0.26%, significantly higher than the inhibition observed with metformin, which was 2.40±0.18% at the same tested concentration.	[34]

Hepatoprotective activity	CPLE AgNPs/ 9- 48 nm	Leaves	Methanolic extract	*Plasmodium berghei*-Infected Liver in Mice	10, 25 and 50 mg/kg, orally CPLE AgNPs for 7 days	Administration of CPLE-AgNPs to infected mice led to a marked reduction in parasitemia, (treated with 50 mg/kg CPLE AgNPs showed < 3% parasitemia). CPLE-AgNPs decrease the expression of hepatic cytokines, including IL-1β and IL-10. The treatment of mice with CPLE-AgNPs led to a reduction in the activities of ALP, AST, and ALT enzymes. Histopathological analysis revealed significant improvement in liver tissue architecture, hepatic lesions were notably reduced, liver damage score decreased and reduced infiltration of inflammatory cells.	[35]
Anti- oxidant activity	CPL-AgNPs/29-46 nm	Leaves	Aqueous extract	*In vitro* study	50 µL	The hydrogen peroxide scavenging assay revealed inhibition values of 29.31±0.21% for CPL-AgNPs and 0.13±0.19% for ascorbic acid, indicating that CPL-AgNPs possess significantly stronger scavenging activity. Furthermore, the reducing power assay confirmed that AgNPs exhibited a 4.38% reducing power activity, compared to 2.08% for the standard antioxidant BHT, even at very low concentrations.	[34]
	AgNPs	Leaves	Aqueous extract	*In vitro* study	1, 2, 3, 4 and 5 mg/mL	The antioxidant activity of the AgNPs increased progressively with rising concentrations. The DPPH assay results demonstrated that both the synthesized AgNPs and the standard antioxidant effectively inhibited DPPH radicals. The synthesized AgNPs displayed a dose-dependent ABTS radical scavenging activity, though their effectiveness was comparatively lower than that of the standard antioxidants. The FRAP assay revealed their ability to donate electrons. This reducing capacity increased with rising concentrations; however, it was still lower compared to that of the standard antioxidants.	[78]

	AuNPs	Leaves	Aqueous extract	*In vitro* study	50, 100, 150 and 200 µL/ mL	The DPPH radical scavenging activity of the AuNPs was recorded as 89.66%, 84.23%, 81.09%, and 80.64% at concentrations of 50, 100, 150, and 200 µL/mL, respectively.	[45]
	ZnO NPs and Fe NPs/ 32.67-202 nm	Aerial parts (stem, leaf, fruit, flower)	Aqueous and hydroalcoholic extracts	*In vitro* study (A-431 cell lines)	10, 20, 40, 60, 80 and 100 µL/ mL	Results from both ABTS and DPPH assays revealed that ZnO NPs showed the most effective scavenging activity against DPPH radicals (IC_{50}=148.46 µg/mL), whereas FeNPs demonstrated comparatively lower activity. Conversely, FeNPs exhibited the highest ABTS radical scavenging potential (IC_{50}=52.81 µg/mL), with ZnO NPs displaying slightly reduced efficacy in comparison.	[50]
	AgNPs/ 70- 80 nm	Flowers	Aqueous extract	*In vitro* study (A-431 cell lines)	10, 15, 20, 25 and 30 µg/ mL	The nanogel exhibited strong DPPH radical scavenging activity, with its antioxidant potential ranging from 38% to 87.49% across concentrations of 10 to 30 µg/g. The DPPH assay further confirmed that the nanogel formulation possessed superior antioxidant efficacy, showing an IC_{50} value of 14.94±0.59 µg/mL, which was more potent than that of ascorbic acid (IC_{50}=32.24±0.62 µg/mL).	[36]
Anti- inflammatory activity	AgNPs/29-46 nm	Leaves	Aqueous extract	*In vitro* study	-	AgNPs showed anti-inflammatory activity with inhibition of albumin denaturation (%) of 2.08±0.08 (%) which was compared with standard aspirin at 2.54±0.11 (%).	[34]
	AgNPs	Latex from young twigs	-	*In vitro* study	20, 40, 60, 80 and 100µg/ mL	The green-synthesized nanoparticles demonstrated significant inhibition of red blood cell (RBC) lysis. *In vitro* anti-inflammatory evaluations showed that the membrane-stabilizing potential of L-Ag NPs (82.73%) was comparable to that of the reference drug Aceclofenac (75.16%). Furthermore, the proteinase inhibition exhibited by L-Ag NPs (84.06%) and Aceclofenac (81.90%).	[38]

Anti-hypertensive activity	AuNPs	Leaves	Aqueous extract	*In vitro* study	50, 100, 150 and 200 µg/ mL	The results demonstrate that the nanoparticles were more effective at a lower concentration (80.71±13.91% inhibition) and less effective at high concentration (37.84±0.09064%) in inhibiting Angiotensin I-converting enzyme activity. This study proposes that a lower concentration of the nanoparticles could be an effective option for managing hypertension	[45]
Anti- cancerous activity	ZnO NPs and Fe NPs/ 32.67-202 nm	Aerial parts (stem, leaves, fruits, flowers)	Aqueous and hydroalcoholic extracts	*In vitro* study (A-431 cell lines)	up to 1000 µg/mL	The results highlight the effectiveness of CP aqueous extract-mediated nanoparticles, with CZnQ emerging as the most potent candidate against the tested cell lines. After 72 hr of exposure, CZnQ significantly reduced cancer cell viability to 0.61% at a concentration of 1000 µg/mL, with an IC_{50} value of 188.97 µg/mL.	[50]
	AgNPs	Fresh leaves and flowers	Hot water extract, Acetone extract and Chloroform Extract	*In vitro* study Dalton's Lymphoma Ascites cells (DLA)	12.5, 25, 50, 100 and 200 µL/ mL	These results indicate a dose-dependent correlation between AgNP concentration and cytotoxicity. An increase in AgNP concentration leads to a higher percentage of cell death, demonstrating that the nanoparticles become more toxic to cells at elevated doses.	[79]
	AgNPs/ 70- 80 nm	Flowers	Aqueous extract	*In vitro* study (A-431 cell lines)	10, 15, 20, 25 and 30 µg/g	A progressive decline in cell viability was detected with increasing concentrations of nanogel, ranging from 10 to 30 µg/g, suggesting a dose-dependent cytotoxic effect. The IC_{50} values for the standard compound (Doxorubicin) and the nanogel were determined to be 27.74 µg/mL and 23.88 µg/mL, respectively.	[36]
	AgNPs/ 38-44 nm	Roots	Aqueous extract	*In vitro* study HEPK (Keratinocytes) cells	0.78, 1.56, 3.125, 6.25, 12.5, 25, 50 and 100g/ mL	The MTT assay results revealed that the AgNPs were non-toxic to mammalian cells compared to the positive control TNF-β, although cell viability decreased progressively with increasing concentrations.	[75]

	AuNPs/ average 45 nm	Leaves	Aqueous extract	*In vitro* study (MCF-7cell line)	0.156, 0.312, 0.625, 1.25, 2.5 and 5 mg/mL	The cytotoxicity results from the MTT assay demonstrated that cell viability declined progressively with increasing concentrations of gold nanoparticles, ranging from 0.156 mg/mL to 5 mg/mL. This dose-dependent reduction in cell viability resulted in a calculated IC_{50} value of 0.312 mg/mL.	[44]
	CuNPs	Latex	Aqueous extract	*In vitro* study (HeLa, A549 and BHK21 cell lines)	0, 20, 40, 60, 80, 100, 120, 140 and 160 µM	Copper nanoparticles tested all three cell lines exhibited excellent cell viability even at concentrations up to 120 µM. The absence of cytotoxic effects in all three cell lines indicates that the copper nanoparticles synthesized using latex possess outstanding biocompatibility.	[57]
	AgNPs and honey/ 60-85 nm	Leaves	Aqueous extract	*In vitro* study (HeLA and HepG2cells)	20% AgNPs and 20% honey	The combination of honey and AgNPs resulted in a reduced growth suppressive effect compared to honey alone.	[37]
Larvicidal activity	TiO_2NPs	Latex	Aqueous serum extract	Against 2nd, 4th instar nymphs and adult of dusky cotton bug (*Oxycarenus* spp.)	600, 900, 1200, and 1500 ppm	The nanoparticles achieved up to 95% control of the insect population, with the highest effectiveness observed in second instar nymphs (between 90 and 95% mortality) and the lowest in adult stages (70% mortality). The total mortality percentage showed directly proportional to the concentration of the synthesized nanoparticles used.	[64]
	ZnO NPs/ average size18.20 nm	Leaves	Aqueous extract	Against Root-Knot Nematodes (*Meloidogyne incognita* affected bitter gourd plants)	50, 100, 200, and 500 ppm	*In vivo* bioassay result showed that the treatment of bitter gourd plants affected by *M. incognita* with ZnO nanoparticles led to significant improvements in growth indices and a marked reduction in root gall formation. Plants treated with 500 ppm ZnO nanoparticles showed the most enhanced growth performance, including the highest shoot length (197.13 cm), root length (17.22 cm), fresh shoot weight (387.76 g), earliest flowering (29 days), and the lowest number of root galls (8.23), compared to control and other concentration groups.	[49]

	AgNPs/ 42 nm	young twigs	Latex	Against 4th instar larvae of *Aedes aegypti*	20, 40, 60, 80 and 100 µg/ mL	The larval mortality rate of mosquitoes increased proportionally with the concentration of AgNPs. The lethal concentration (LC_{50}) of L-AgNPs was determined to be 63.09 µg/mL.Morphological analysis showed that no external abnormalities were observed in the untreated larvae. However, larvae exposed to lower concentrations of AgNPs exhibited increased pigmentation and gut blackening. At higher concentrations, more severe effects were observed, including body shrinkage, disrupted and disorganized gut structure, and ruptured cuticle.	[38]
	ZnONPs	Leaves	Aqueous extract	Against second, third, fourth, fifth and sixth instar larvae of *Spodoptera frugiperda*	100, 200, 300, 400 and 500 ppm	The first instar larvae exhibited the highest mortality rate of 85%, followed by 80%, 76%, 71%, 66%, and 55% for the second, third, fourth, fifth, and sixth instar larvae, respectively, at a concentration of 500 ppm. A decline in mortality frequency was observed with decreasing concentrations.ZnO nanoparticle treatment induced significant physical developmental abnormalities across all life stages-larvae, juveniles, and adults-in both males and females, disrupting normal body development and thereby contributing to the suppression of *S. frugiperda* populations.	[80]
	ZnONPs	Leaves	Aqueous extract	Against *larvae of Spodoptera litura*	100, 200, 300 and 400 ppm	ZnO nanoparticles induced increasing levels of mortality across different concentrations-100, 200, 300, and 400 ppm-with the highest mortality observed at 400 ppm compared to the lower concentrations. No mortality was recorded in the control group. The LC_{50} was calculated to be 232.55 ppm, while the LC_{90} value was determined to be 530.81 ppm. Also, the weight of the pest showed a progressive decrease with increasing concentrations of the treatment.	[81]

	AgNPs	Leaves	Aqueous extract	Against *Tribolium castaneum* pest	0.714, 1.0, 1.28, 1.57 and 1.85 mg/ cm2	The study showed that AgNPs exhibited significant toxicity against *T. castaneum*, with the highest mortality observed at a concentration of 1.85 mg/ cm^2, and there was no mortality observed in control group. These findings confirm that increase the concentration of AgNPs leads to a corresponding rise in *T. castaneum* mortality.	[82]
Immunomodulatory activity	AgNPs/ 60-85 nm	Leaves	Aqueous extract	*In vitro* study *(*Rat splenocytes*)*	100 µg/mL	The MTT assay results indicated that AgNPs inhibited the proliferation of rat splenocytes.	[37]

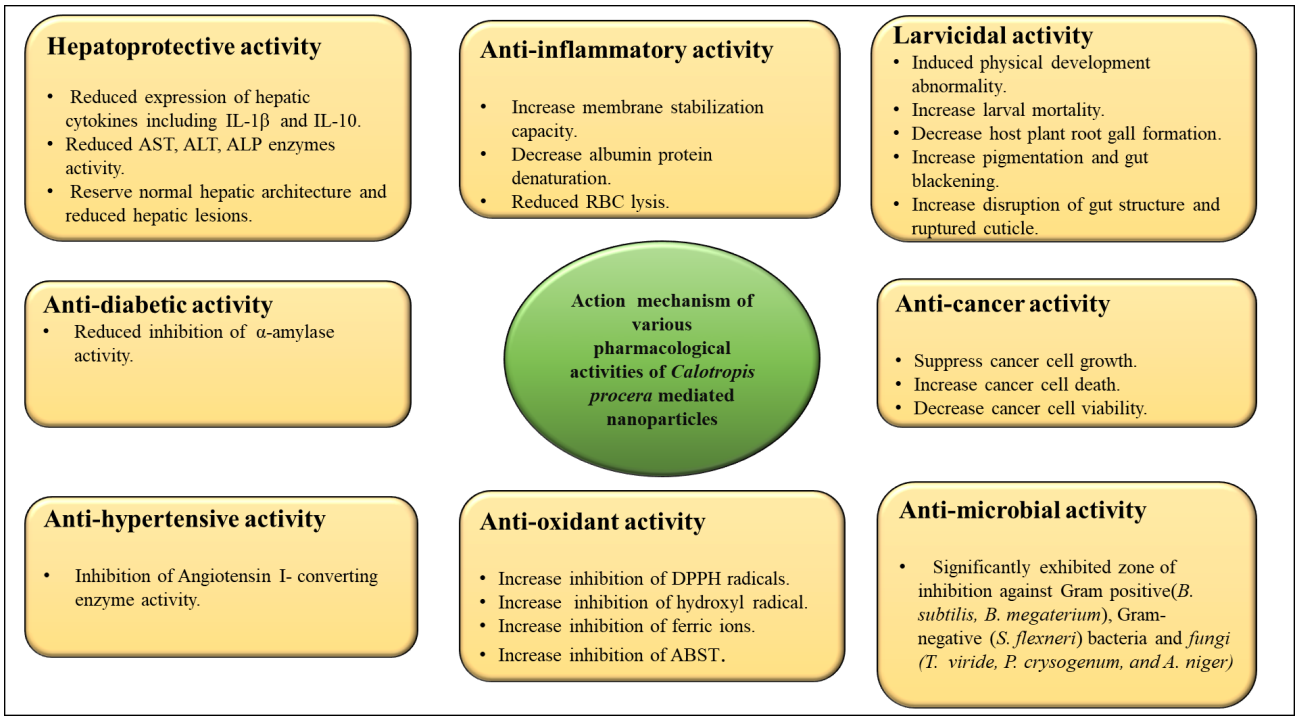


Figure 4: Mechanisms of Major pharmacological activities.

TOXICITY PROFILE

Assessing the toxicity profile is a vital step when exploring the medicinal potential of any plant, as it ensures safe and effective therapeutic use. Toxicological evaluations help identify possible adverse effects, determine lethal dose limits, and assess the overall risks linked to plant-derived compounds. *C. procera*, a widely recognized medicinal plant, contains a range of bioactive constituents that may offer therapeutic benefits but can also produce toxic effects, depending on the dosage and mode of administration. The latex of *C. procera* is recognized for its high toxicity. One study reported toxic effects in 29 individuals who accidentally came into contact with the latex through ocular exposure. These patients experienced sudden, painless vision loss accompanied by photophobia. Clinical observations revealed conjunctival congestion and varying levels of corneal edema, along with the presence of Descemet's membrane folds in all cases.[83-86] An acute toxicity study conducted on male rabbits using the up-and-down method estimated the LD_{50} of *C. procera* leaf extract to be approximately 2435.25 mg/kg of body weight.[27,87]

The study suggests that green-synthesized nanoparticles derived from *C. procera* could exhibit potential toxic effects, particularly at higher concentrations or with prolonged exposure. For example, *in vivo* study, ZnO and TiO_2 nanoparticles synthesized using *C. procera* were orally administered to albino mice at doses ranging from 100 to 300 mg/kg BW over a period of 7 to 21 days. The results revealed histopathological alterations in kidney tissues, indicating possible nephrotoxic effects. These findings suggest that while *C. procera*-mediated nanoparticles may possess desirable biological activities, their safety profiles require

careful evaluation.[88] Further research is needed to assess organ effects, dosage impact, and long-term safety before using these nanoparticles in medical or environmental applications.

CONCLUSION

Calotropis procera is a widely recognized medicinal plant, long valued in traditional medicine for its diverse therapeutic applications. Nanoparticles synthesized using various parts of *C. procera*-including its leaves, roots, flowers, and latex-have shown significant pharmacological potential as promising agents for the development of novel, plant-based therapeutics. These green-synthesized nanoparticles, such as silver, zinc oxide, iron oxide, and gold nanoparticles, exhibit a broad spectrum of pharmacological activities, including antimicrobial, anti-inflammatory, antioxidant, anticancer, and larvicidal effects. However, the use of *C. procera* in nanoparticle synthesis raises toxicity concerns, primarily due to the presence of cardenolides and other toxic phytoconstituents. This review highlights the botanical profile, major phytochemical constituents, and traditional medicinal uses of *C. procera*, along with the various types of nanoparticles synthesized using this plant. It further explores the therapeutic applications and safety profile of *C. procera*-based nanoparticles, emphasizing their potential in the treatment of a wide range of health conditions. By compiling and critically analyzing the existing literature, this review provides valuable insights into the pharmacological activities and biological mechanisms of *C. procera*-derived nanoparticles. It underscores the need for detailed toxicological evaluations and clinical investigations to ensure their safe application. Ultimately, this review aims to support and guide future research toward the development of effective, biocompatible, and clinically relevant *C. procera*-based nanotherapeutics.

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ABBREVIATIONS

LD_{50}: Lethal dose; **IC_{50}:** Inhibitory concentration; **TNF:** Tumor necrosis factor; **LC_{50}:** The lethal concentration; **IL:** Interleukin; **BW:** Body weight; **AST:** Aspartate Aminotransferase; **DPPH:** 2,2-Diphenyl-1-Picrylhydrazyl; **ALT:** Alanine Aminotransferase; **ALP:** Alkaline Phosphatase; ABTS: 2,2'-Azinobis(3-E thylbenzothiazoline-6-Sulfonic Acid); **FRAP:** Ferric Reducing Antioxidant Power; **MIC:** Minimum Inhibitory Concentration; **MBC:** Minimum Bactericidal Concentration; **IZ:** Inhibition Zone; **RBC:** Red Blood Cells; ***E. coli*:** *Escherichia coli*; ***P. aeruginosa*:** *Pseudomonas aeruginosa*; ***E. faecalis*:** *Enterococcus faecalis*; ***S. typhimurium*:** *Salmonella typhimurium*; ***S. saprophyticus*:** *Staphylococcus saprophyticus*: ***S. aureus*:** *Staphylococcus aureus*; ***C. albicans*:** *Candida albicans*; ***B. subtilis*:** *Bacillus subtilis*; ***B. megaterium*:** *Bacillus megaterium*; ***S. flexneri*:** *Shigella flexneri*; ***T. viride*:** *Trichoderma viride*; ***P. crysogenum*:** *Penicillium crysogenum*; ***P. mirabilis*:** *Proteus mirabilis*; ***K. pneumoniae*:** *Klebsiella pneumoniae*; ***F. poae*:** *Fusarium poae*; ***F. solani*:** *Fusarium solani*; ***P. avenatum*;** *Penicillium avenatum*; ***E. sichuanensis*:** *Enterobacter sichuanensis*; ***S. pyogenes*:** *Streptococcus pyogenes*; ***A. flavus*:** *Aspergillus flavus*; ***A. niger*:** *Aspergillus niger*; ***S. agalactiae*:** *Streptococcus agalactiae*; ***S. larcymans*:** *Serpula larcymans*; ***S. typhi*:** *Salmonella typhi*; ***S. epidermidis*:** *Staphylococcus epidermidis*; ***X. axonopodis*:** *Xanthomonas axonopodis*; ***P. acnes*:** *Propionibacterium acnes*; ***A. alternata*:** *Alternaria alternata*; ***E. coccus*:** *Entero coccus*; **MRSA:** Methicillin-Resistant *Staphylococcus aureus*; ***S. larcymans*:** *Serpula larcymans*.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

AUTHOR CONTRIBUTIONS

GSB: Conceptualization, writing original draft, Review and editing, Visualization. **AJ:** Review and editing. **TJ:** editing. **RNJ:** Writing original draft, Review and editing.

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