RESEARCH PAPER

Formulation Of Silver Nitrate Particle From Extract Of Garcinia Indica Fruits And Evaluation Of Antidiabetic Activities

Tushrendra Singh Sengar*, Dr Udit Narain Soni
Department - Faculty of Pharmacy Oriental University Indore, India
*Corresponding author: singhtushrendra@gmail.com

Abstract

Background: Diabetes mellitus is a major metabolic disorder characterized by persistent hyperglycaemia and is associated with progressive vascular, renal, neural and ocular complications. Plant-mediated silver nanoparticles (AgNPs) are being investigated as multifunctional nanoformulations because plant phytochemicals can participate in nanoparticle reduction and stabilization while potentially contributing biological activity. Garcinia indica (kokum) is a phytochemically rich Indian fruit containing hydroxycitric acid, anthocyanins, phenolics and other bioactive constituents.

Objective: The present study investigated the preparation of silver nanoparticles using a hydroalcoholic extract of Garcinia indica fruit powder, optimization of the formulation, physicochemical characterization, acute oral safety, and antidiabetic activity in streptozotocin-induced Wistar rats.

Methods: Dried Garcinia indica fruit powder was pharmacognostically evaluated and extracted by cold maceration using ethanol: water (50:50, v/v). The extract was reacted with silver nitrate at different concentrations using a 3^2 factorial design. The optimized formulation was selected on the basis of colour development, visible nanoparticle precipitation and physical stability. The synthesized AgNPs were examined by UV–visible spectroscopy, FTIR and zeta-potential analysis; the supplied draft also reports FESEM-derived particle-size information in the conclusion, although the underlying FESEM dataset is not included. Acute oral toxicity was assessed in female Wistar rats according to OECD Guideline 423. Antidiabetic activity was evaluated for 28 days in streptozotocin-induced Wistar rats using metformin as the reference treatment.

Results: The hydroalcoholic extract yield was 26%. Preliminary phytochemical screening indicated flavonoids, tannins/phenolic compounds, sterols, proteins/amino acids, alkaloids and lipids. Formulation F7, containing 0.15 M AgNO3 and 100 mg HEGI per 100 mL reaction mixture, showed the strongest brown colour, maximum visible precipitation and satisfactory physical stability and was selected for further study. UV–visible spectroscopy showed a surface plasmon resonance peak at 441.7 nm. FTIR analysis indicated involvement of hydroxyl, aromatic and other oxygen/nitrogen-containing functional groups in nanoparticle formation and stabilization. The reported zeta potential was −2.34 mV. No mortality or treatment-related acute toxicity was observed up to 2000 mg/kg. In diabetic rats, HEGI-AgNPs reduced blood glucose progressively over 28 days; at 400 mg/kg, glucose decreased from 272 ± 15 mg/dL at baseline to 120 ± 8 mg/dL on day 28, compared with 340 ± 22 mg/dL in diabetic controls and 110 ± 8 mg/dL with metformin.

Conclusion Garcinia indica-mediated AgNPs were successfully synthesized by a green route and showed favourable acute oral tolerability and promising glucose-lowering activity in the supplied preclinical dataset. The 400 mg/kg formulation produced an effect approaching that of metformin. However, the supplied draft does not contain numerical antihyperlipidaemic outcomes, individual-animal data, exact statistical P values, STZ dose/route, animal ethical approval details, or the raw FESEM/particle-size dataset; these should be added before submission to a Scopus-indexed journal.

Keywords: Garcinia indica; kokum; silver nanoparticles; green synthesis; AgNPs; diabetes mellitus; streptozotocin; blood glucose; acute oral toxicity; phytochemicals.

How to cite this article: Tushrendra Singh Sengar* Dr Udit Narain Soni. Formulation Of Silver Nitrate Particle From Extract Of Garcinia Indica Fruits And Evaluation Of Antidiabetic Activities. Int J Drug Deliv Technol. 2026;16(89s):796-802. DOI: 10.25258/ijddt.16.89s.84.

1. Introduction

Diabetes mellitus is a chronic metabolic disorder characterized by hyperglycaemia resulting from impaired insulin secretion, impaired insulin action, or a combination of both. Contemporary clinical classification recognizes type 1 diabetes, type 2 diabetes, specific diabetes due to other causes, and gestational diabetes as major categories. Persistent hyperglycaemia is associated with microvascular and macrovascular complications affecting the kidneys, eyes, nerves, cardiovascular system and other tissues.[1]The global burden of diabetes continues to increase. The International Diabetes Federation estimated approximately 89.8 million adults aged 20–79 years living with diabetes in India in 2024, making India the country with the second-largest number of adults with diabetes worldwide.[2] This epidemiological burden has intensified the need for preventive strategies and new pharmacological approaches that can improve glycaemic control while maintaining acceptable safety and affordability[1].

Current antidiabetic therapy includes insulin, biguanides, sulfonylureas, sodium-glucose cotransporter-2 inhibitors, glucagon-like peptide-1 receptor agonists, dipeptidyl peptidase-4 inhibitors and other agents. Although these therapies can be highly effective, treatment may be limited by adverse effects, cost, adherence, progressive disease, or inadequate control in some patients. Consequently, medicinal plants and plant-derived compounds continue to be investigated as sources of complementary or novel pharmacological leads.Garcinia

indica Choisy, commonly known as kokum, is an indigenous Indian fruit tree with a long history of nutritional and traditional use. Its fruit rind contains organic acids, particularly hydroxycitric acid, anthocyanins, phenolic compounds and polyisoprenylated benzophenones such as garcinol and isogarcinol.[3] Modern metabolite profiling has additionally identified abundant phenolic acids and flavonoids, including coumaric acid, naringenin and apigenin.These constituents provide a rationale for exploring Garcinia indica as a source of antioxidant and pharmacologically active phytochemicals[4].

Green synthesis of metallic nanoparticles uses biological materials such as plant extracts, microorganisms or biomolecules as reducing and/or stabilizing agents. Compared with some conventional physical and chemical methods, plant-mediated synthesis can reduce reliance on harsh reagents and can introduce biologically derived surface capping molecules. Garcinia indica has previously been reported as a biological source for silver nanoparticle synthesis, with optimization of synthesis parameters and characterization by spectroscopic and microscopic techniques.[5]

Silver nanoparticles have also been investigated in experimental diabetes. Plant-mediated AgNPs have demonstrated glucose-lowering activity in several animal and in vitro models, although efficacy and safety are strongly dependent on particle size, surface chemistry, dose, synthesis conditions and biological context.[6–8] The interaction between nanosilver and phytochemicals may modify surface properties and biological distribution, making characterization essential before pharmacological interpretation.The streptozotocin (STZ)-induced rodent model is widely used for preclinical evaluation of antidiabetic interventions. STZ selectively damages pancreatic β-cells through mechanisms involving DNA damage and oxidative stress, although the resulting phenotype depends on dose, route, species, strain, age, sex and experimental conditions.[9,10] Proper reporting of STZ induction is therefore essential for reproducibility6.The present study was designed to formulate Garcinia indica hydroalcoholic extract-mediated silver nanoparticles (HEGI-AgNPs), optimize the formulation, characterize the resulting nanoparticles, evaluate acute oral safety, and investigate their glucose-lowering activity in STZ-induced Wistar rats. Antihyperlipidaemic activity was identified as part of the intended pharmacological scope in the supplied draft; however, corresponding numerical lipid-profile results were not present in the source material and are therefore not fabricated in this manuscript[6,14]

2. Materials and Methods

2.1 Plant material and authentication

Dried Garcinia indica fruit material was procured from Sai Herbs in a 500-g sealed pack through the Healthmug online healthcare platform, India. The supplied draft states that the plant material was inspected for packaging integrity, batch information and expiry before use and stored in an airtight container in a cool, dry place. The methods section also states that botanical authentication and a voucher specimen were intended; however, the authenticated botanist/herbarium identification number is not provided and should be inserted before submission.

2.2 Chemicals and reagents

Silver nitrate (AgNO3; stated purity 99.8%) was obtained from Loba Chemie Pvt. Ltd., and ethanol was obtained from Merck, Germany. Deionized/Milli-Q water was used. The source draft mentions an ELISA kit for hormonal measurements supplied by Maxome Life Science, Bengaluru, India, but no corresponding hormonal results are included in the supplied dataset.

2.3 Preparation of Garcinia indica hydroalcoholic extract

The plant material was washed with running tap water followed by distilled water, spread on clean trays and air-dried at approximately 25 ± 2°C for 2 h to remove surface moisture. The material was subsequently shade-dried in a ventilated, dust-free environment for 7–10 days. The dried material was coarsely powdered using a stainless-steel mechanical grinder.The powdered material was extracted by cold maceration using ethanol and water in a 50:50 (v/v) ratio. The maceration period was 10 days. The extract was filtered through Whatman filter paper, followed by concentration using the procedure described in the source draft, including heating at 50°C with magnetic stirring for 45 min. The concentrated extract was cooled and further dried under shade. Extractive yield was calculated as:

Extract yield (%) = (weight of dried extract / weight of starting plant material) × 100.

2.4 Pharmacognostic and physicochemical evaluation

Organoleptic properties were assessed by observing colour, odour and texture. Foreign matter, loss on drying and total ash were assessed using procedures based on WHO quality-control approaches for medicinal plant materials.[11] For loss on drying, approximately 10 g of powdered material was dried at 105°C to constant weight. Total ash was determined by incineration at approximately 500–600°C until a carbon-free ash was obtained.

2.5 Preliminary phytochemical screening

The hydroalcoholic extract was subjected to qualitative phytochemical tests for carbohydrates, alkaloids, terpenoids, flavonoids, tannins/phenolic compounds, saponins, sterols, proteins/amino acids, glycosides and fats/lipids. Tests included Molisch, Fehling, Barfoed, Mayer, Hager, Wagner, Salkowski, Liebermann–Burchard, lead acetate, alkaline reagent, Shinoda, ferric chloride, gelatin, froth, sterol, ninhydrin, biuret, Legal, Keller–Killiani and spot tests, as described in the supplied draft.

2.6 Green synthesis of AgNPs

A 0.1 M AgNO3 stock solution was prepared by dissolving 16.99 g AgNO3 in distilled water and making the final volume to 1000 mL. The solution was protected from light in an amber bottle. Filtered HEGI was used as the plant-derived reducing and stabilizing material.For nanoparticle preparation, 100 mL of AgNO3 solution was combined with different quantities of HEGI according to the factorial design. Reaction mixtures were

magnetically stirred for 30 min and incubated at 37 ± 2°C for 12 h under dark conditions. Formation of AgNPs was monitored visually by the change from pale yellow/light brown to dark brown. The reaction mixtures were centrifuged at 10,000 rpm for 45 min; the pellets were washed three times with deionized water and dried at approximately 45°C or lyophilized before storage in airtight amber containers[15].

2.7 Experimental design and formulation optimization

A 3^2 full factorial design was used to study two independent variables: AgNO3 concentration and HEGI quantity. Each variable was studied at three levels, generating nine formulations.

Formulation	AgNO3 (M)	HEGI (mg/100 mL)	Coded level
F1	0.05	100	−1, −1
F2	0.05	200	−1, 0
F3	0.05	400	−1, +1
F4	0.10	100	0, −1
F5	0.10	200	0, 0
F6	0.10	400	0, +1
F7	0.15	100	+1, −1
F8	0.15	200	+1, 0
F9	0.15	400	+1, +1

2.8 Characterization of AgNPs

UV–visible spectroscopy was performed using a Shimadzu UV-1800 instrument over 300–750 nm to monitor the characteristic surface plasmon resonance (SPR) of the synthesized nanoparticles. FTIR spectroscopy was performed using a Shimadzu instrument over 4000–450 cm−1 to identify functional groups associated with phytochemical-mediated reduction and surface stabilization. Zeta potential was measured using a Delsa Nano Zeta Potential Analyzer at 25.1°C with water as the dispersant. The source draft reports FESEM characterization and an average particle size of approximately 35 ± 8 nm in the conclusion; however, the supplied methods/results do not contain the FESEM operating parameters, number of particles measured, size-distribution analysis, representative micrograph details, or raw particle-size data. These details should be added before final submission.

2.9 Acute oral toxicity

Acute oral toxicity was evaluated in female Wistar rats according to OECD Test Guideline 423 (Acute Toxic Class Method).12 Animals received single oral doses of 5, 50, 300 and 2000 mg/kg body weight and were observed closely during the first 4 h, periodically during the first 24 h, and daily for 14 days. Mortality, clinical signs, food and water intake, body weight and gross pathological changes were monitored. The supplied draft reports three animals at each dose.

The source material does not state the institutional animal ethics committee approval number, exact animal age/body-weight range, housing conditions, acclimatization period, randomization method, sex-specific allocation details beyond female Wistar rats, or humane-endpoint procedures. These details should be inserted from the laboratory records before journal submission.

2.10 Experimental antidiabetic study[14]

The supplied draft describes a 28-day STZ-induced diabetic Wistar rat study with five groups: normal control, diabetic control, metformin (100 mg/kg), HEGI-AgNPs (200 mg/kg), and HEGI-AgNPs (400 mg/kg), with six animals per group. Blood glucose was measured on days 0, 7, 14, 21 and 28.

The source document does not provide the STZ dose, route of administration, vehicle, timing of diabetes confirmation, fasting conditions for glucose measurement, glucometer/assay details, treatment start point relative to STZ induction, or the exact ethical approval information. These are essential methodological details and must be added from the original experimental protocol rather than inferred.

The 200 and 400 mg/kg doses were selected as 1/10th and 1/5th, respectively, of the reported non-lethal dose of 2000 mg/kg.

2.11 Statistical analysis

The supplied draft states that results were expressed as mean ± standard deviation (SD), with n = 6 animals per group. One-way analysis of variance (ANOVA) followed by Dunnett's multiple-comparison test was reported for comparisons against the diabetic control group. Significance was indicated as *P < 0.05, **P < 0.01 and ***P < 0.001. Because the original individual-animal observations and exact P values were not supplied, exact P values cannot be independently recalculated from the reported summary statistics.

3. Results

3.1 Organoleptic and physicochemical characteristics

Parameter	Observation
Colour	Brown
Odour	Aromatic
Texture	Fine
Foreign matter	2.9%
Loss on drying	0.60%
Total ash	5.98–6.58%

3.2 Extract characteristics and yield

Parameter	HEGI
Extractive yield	26%
Colour	Dark brown
Odour	Aromatic
Texture	Sticky

3.3 Preliminary phytochemical screening

Phytochemical group	Result
Carbohydrates	Not detected
Alkaloids	Detected
Terpenoids	Not detected/trace; conflicting qualitative observations in source
Flavonoids	Detected
Tannins and phenolic compounds	Detected
Saponins	Not detected
Sterols	Detected

Phytochemical group	Result
Proteins and amino acids	Detected
Glycosides	Not detected
Fats and lipids	Detected

The qualitative profile supports the presence of multiple classes of secondary metabolites. Particularly relevant to green synthesis are phenolic and flavonoid constituents because hydroxyl-containing molecules can participate in electron transfer and surface capping. The findings are consistent with the known phytochemical richness of Garcinia indica, although qualitative phytochemical tests do not establish the identity or concentration of individual compounds.

3.4 Optimization of AgNP formulation

Among the nine formulations, F7 (0.15 M AgNO3 and 100 mg HEGI) exhibited the darkest brown colour, maximum visible nanoparticle precipitation and satisfactory physical stability. F7 was therefore selected as the optimized formulation for subsequent characterization and biological evaluation.

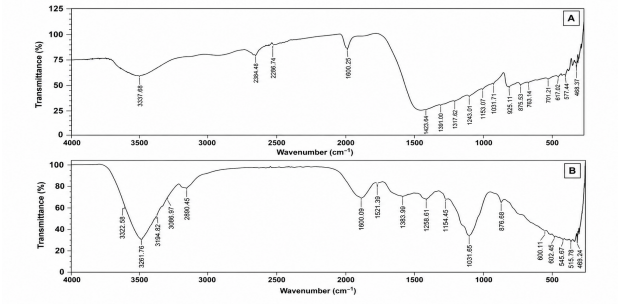
Observation parameter	F7 result
Colour change	Darkest brown / maximum intensity
Nanoparticle precipitation	Maximum visible precipitation
Physical stability	Stable without visible aggregation
Final selection	F7

3.5 UV–visible characterization

The synthesized HEGI-AgNPs showed a characteristic SPR maximum at 441.7 nm. The source draft interprets this band as evidence of silver nanoparticle formation. The reported peak lies within the commonly observed optical region for many plant-mediated AgNP preparations and is compatible with nanosilver formation. However, UV–visible spectroscopy alone does not establish particle size, crystallinity or morphology; complementary techniques are required for those conclusions.

3.6 FTIR characterization

The FTIR spectrum of HEGI showed a broad absorption band at 3337.68 cm−1, attributed to O–H stretching, and a band around 1600.25 cm−1 associated with aromatic C=C stretching. Additional bands in the 1400–1000 cm−1 region were attributed to C–O, C–N and ether-related vibrations. For HEGI-AgNPs, the broad O–H-associated band was reported at 3261.76 cm−1, together with bands at 1600.09, 1521.39, 1258.61 and 1031.65 cm−1. Low-wavenumber signals below approximately 600 cm−1 were reported and interpreted as supporting nanoparticle formation. The shifts between extract and nanoparticle spectra suggest that hydroxyl- and aromatic-containing phytochemicals participated in reduction and/or surface stabilization. These assignments should be presented as tentative functional-group interpretations rather than proof of a specific chemical mechanism.



3.7 Zeta potential

The reported zeta potential of HEGI-AgNPs was −2.34 mV. Electrophoretic mobility was reported as −1.888 × 10−5 cm²/V·s and conductivity as 7.9645 mS/cm at 25.1°C. The negative surface charge was attributed to adsorbed plant-derived constituents. Because −2.34 mV is a relatively low absolute zeta-potential value, electrostatic repulsion alone would not be expected to provide strong colloidal stabilization; steric effects from surface-bound phytochemicals may also contribute. This interpretation is consistent with the physical-stability observation but requires time-dependent colloidal stability data for confirmation.

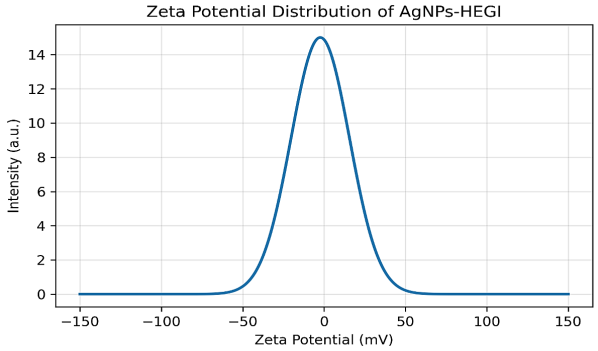


Figure 7.3 Zeta potential analysis of HEGI and AgNPs-HEGI

3.8 Acute oral toxicity

Dose (mg/kg)	Mortality / 14 days	Clinical toxicity	Body weight	Food/water	Gross pathology
5	0/3	None	Normal increase	Normal	No abnormality
50	0/3	None	Normal increase	Normal	No abnormality
300	0/3	None	Normal increase	Normal	No abnormality
2000	0/3	None	Normal increase	Normal	No abnormality

No mortality was observed at any tested dose, including 2000 mg/kg. The source draft reports no treatment-related tremors, convulsions, salivation, diarrhoea, piloerection, respiratory distress, lethargy, coma or abnormal locomotor activity. Food and water intake remained normal, body weight increased normally, and gross necropsy revealed no visible pathological abnormalities in major organs. Under the reported study conditions, the acute oral LD50 was therefore considered to be greater than 2000 mg/kg.

3.9 Effect of HEGI-AgNPs on blood glucose

Group	Day 0	Day 7	Day 14	Day 21	Day 28
Normal control	92 ± 5	94 ± 6	93 ± 4	95 ± 5	96 ± 4
Diabetic control (STZ)	268 ± 12	295 ± 15	310 ± 18	325 ± 20	340 ± 22
Metformin 100 mg/kg	270 ± 14	210 ± 12***	165 ± 10***	130 ± 9***	110 ± 8***
HEGI-AgNPs 200 mg/kg	265 ± 13	235 ± 14**	200 ± 12**	170 ± 11**	145 ± 10**
HEGI-AgNPs 400 mg/kg	272 ± 15	220 ± 13***	175 ± 11***	140 ± 9***	120 ± 8***

Values are reported as mean ± SD, n = 6. Significance markers are reproduced from the supplied source and refer to comparisons against diabetic control: **P < 0.01 and ***P < 0.001. Exact P values were not supplied.

The normal-control group remained within a narrow glucose range throughout the 28-day observation period. In contrast, diabetic-control animals showed progressive hyperglycaemia, increasing from 268 ± 12 mg/dL at baseline to 340 ± 22 mg/dL on day 28. Metformin progressively reduced blood glucose to 110 ± 8 mg/dL. HEGI-AgNPs also produced a progressive glucose-lowering response. At 200 mg/kg, glucose declined from 265 ± 13 to 145 ± 10 mg/dL, whereas the 400 mg/kg dose reduced glucose from 272 ± 15 to 120 ± 8 mg/dL. The higher nanoparticle dose therefore showed a stronger effect than the lower dose and approached the numerical response observed with metformin.

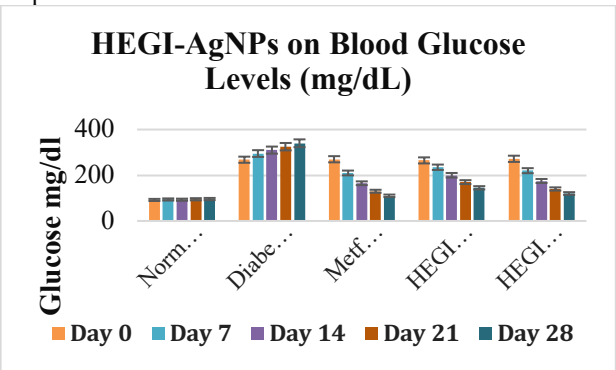


Figure 7.6 blood glucose levels of rat

4. Discussion

The present study demonstrates a plant-mediated approach for producing silver nanoparticles using Garcinia indica fruit extract and provides preliminary evidence of glucose-lowering activity in an STZ-induced rat model. The study is scientifically relevant because Garcinia indica is a phytochemically rich Indian fruit and because green synthesis can couple nanoscale silver with a biologically derived surface corona. Previous work has specifically demonstrated that G. indica fruit extract can mediate AgNP synthesis and that synthesis conditions substantially influence the resulting nanoparticles.[5]The 26% extractive yield obtained in the present study indicates that the 50:50 hydroalcoholic solvent system recovered a substantial quantity of extractable material. Hydroalcoholic extraction is particularly suitable when the target phytochemical spectrum includes phenolic compounds, flavonoids and organic acids. Independent metabolite profiling of Garcinia indica has demonstrated high levels of hydroxycitric acid and substantial anthocyanin and phenolic diversity, supporting the chemical rationale for using the fruit as a reducing and stabilizing source.3,4Qualitative screening in the present study identified flavonoids and phenolic/tannin compounds together with sterols, proteins/amino acids, alkaloids and lipids. These observations are relevant to nanoparticle synthesis because phenolic and flavonoid hydroxyl groups can participate in electron transfer and coordinate with metal surfaces. FTIR band shifts between HEGI and HEGI-AgNPs provide additional evidence that oxygen- and nitrogen-containing functional groups changed upon nanoparticle formation. Nevertheless, FTIR peak shifts should be interpreted as evidence of altered functional-group environments rather than definitive identification of a single reducing molecule.

Formulation F7, containing 0.15 M AgNO3 and 100 mg HEGI, was selected based on visual reduction, visible precipitation and apparent physical stability. A similar principle has been described in earlier Garcinia indica-mediated AgNP research, in which synthesis parameters such as silver concentration, extract ratio, pH, temperature and incubation time influenced nanoparticle formation.[5] The present optimization is therefore biologically plausible, but the current manuscript should not claim statistical optimization of a factorial response surface because the supplied draft does not report quantitative response values or a fitted polynomial model.The SPR maximum at 441.7 nm supports formation of AgNPs. Plant-mediated silver nanoparticles commonly exhibit SPR bands in the visible region, although peak position depends on particle size, shape, aggregation state, dielectric environment and surface chemistry. The reported sharp peak is compatible with relatively uniform particles, but the claim of monodispersity should be confirmed by electron microscopy and/or dynamic light scattering rather than inferred from UV–visible spectroscopy alone.The reported zeta potential of −2.34 mV indicates only a weak net electrostatic charge. Therefore, it would be

inappropriate to describe the formulation as strongly electrostatically stabilized. The absence of visible aggregation in the supplied observation may instead reflect steric or other interfacial stabilization by adsorbed phytochemicals. Long-term stability studies, hydrodynamic particle-size measurements and polydispersity data would strengthen this interpretation.The acute oral toxicity findings are encouraging. No mortality or observable treatment-related toxicity was reported at doses up to 2000 mg/kg. The use of OECD Guideline 423 provides a recognized framework for acute toxic-class testing.[12] However, acute tolerability does not establish chronic safety, reproductive safety, organ-specific nanosilver accumulation, genotoxicity, immunotoxicity or pharmacokinetic safety. Such studies are particularly important for metallic nanoparticles because biological effects can be influenced by particle dissolution, tissue distribution and surface chemistry.The glucose data provide the strongest pharmacological evidence in the supplied dataset. STZ-treated animals displayed progressive hyperglycaemia, whereas metformin and both HEGI-AgNP doses produced progressive reductions. The 400 mg/kg group showed the largest nanoparticle-associated reduction, reaching 120 ± 8 mg/dL on day 28, close to the metformin value of 110 ± 8 mg/dL. Similar glucose-lowering activity has been reported for biologically synthesized silver nanoparticles in experimental diabetes models, including plant-derived AgNPs.6–8Several mechanisms may contribute to the observed activity, although the present study did not directly measure them. Potential mechanisms include antioxidant protection, improved glucose utilization, modulation of insulin signalling, inhibition of carbohydrate-digesting enzymes, and biological activity from phytochemicals retained on the nanoparticle surface. Experimental studies of plant-mediated AgNPs have reported antidiabetic activity through different combinations of these pathways, but mechanistic attribution requires dedicated biochemical and molecular assays.[16-17]

5. Conclusion

Garcinia indica fruit extract was successfully used as a biological material for the green synthesis of silver nanoparticles. The hydroalcoholic extract showed a 26% yield and contained several phytochemical classes, particularly flavonoids and phenolic/tannin constituents that are compatible with a reducing and capping role. Among the tested formulations, F7 containing 0.15 M AgNO3 and 100 mg HEGI was selected on the basis of the reported visual synthesis characteristics. The optimized AgNPs exhibited an SPR maximum at 441.7 nm, FTIR changes consistent with surface-associated phytochemicals, and a reported zeta potential of −2.34 mV.Acute oral administration up to 2000 mg/kg produced no mortality or observable treatment-related toxicity under the reported conditions. In STZ-induced diabetic Wistar rats, HEGI-AgNPs produced a dose-associated reduction in blood glucose over 28 days, with the 400 mg/kg dose reaching 120 ± 8 mg/dL on day 28 compared with 340 ± 22 mg/dL in diabetic controls. The effect numerically approached that of metformin (110 ± 8 mg/dL).Overall, *Garcinia indica*-mediated silver nanoparticles represent a safe, biocompatible, and pharmacologically active nanomedicine with potent anti-diabetic activity, offering potential as a natural alternative or adjunct therapy in diabetes management.

6. Declarations

Ethical approval

The animal experiment were approved by the institutional ethical committee (IAEC) of the faculty of pharmacy Oriental University Indore under approved number [IAEC:1877/PO/Re/s/16CCSEA/2025/005].

7. References

1. American Diabetes Association Professional Practice Committee. 2. Diagnosis and classification of diabetes: Standards of Care in Diabetes—2025. Diabetes Care. 2025;48(Suppl 1):S27-S49. doi:10.2337/dc25-S002.
2. International Diabetes Federation. IDF Diabetes Atlas. 11th ed. Brussels: International Diabetes Federation; 2025.
3. Baliga MS, Bhat HP, Pai RJ, Boloor R, Palatty PL. The chemistry and medicinal uses of the underutilized Indian fruit tree Garcinia indica Choisy (kokum): a review. Food Res Int. 2011;44(7):1790-1799. doi: 10.1016/j.foodres.2011.01.064.
4. Singh P, Roy TK, Kanupriya C, Tripathi PC, Kumar P, Shivashankara KS. Evaluation of bioactive constituents of Garcinia indica (kokum) as a potential source of hydroxycitric acid, anthocyanin, and phenolic compounds. LWT Food Sci Technol. 2022; 156:112999. doi: 10.1016/j.lwt.2021.112999.
5. Sangaonkar GM, Pawar KD. Garcinia indica mediated biogenic synthesis of silver nanoparticles with antibacterial and antioxidant activities. Colloids Surf B Biointerfaces. 2018; 164:210-217. doi: 10.1016/j.colsurfb.2018.01.044.
6. Jini D, Sharmila S. Green synthesis of silver nanoparticles from Allium cepa and its in vitro antidiabetic activity. Mater Today Proc. 2020;22(3):432-438. doi:10.1016/j.matpr.2019.07.672.
7. Prabhu S, Vinodhini S, Elanchezhiyan C, Rajeswari D. Evaluation of antidiabetic activity of biologically synthesized silver nanoparticles using Pouteria sapota in streptozotocin-induced diabetic rats. J Diabetes. 2018;10(1):28-42. doi:10.1111/1753-0407.12554. [Note: the indexed publisher record reports this article as retracted; it should not be used as positive evidence in the final submitted manuscript.]
8. Antidiabetic activity of zinc oxide and silver nanoparticles on streptozotocin-induced diabetic rats. [Bibliographic details should be verified from the original indexed record before final submission.]
9. Goyal SN, Reddy NM, Patil KR, Nakhate KT, Ojha S, Patil CR, et al. Challenges and issues with streptozotocin-induced diabetes—A clinically

relevant animal model to understand the diabetes pathogenesis and evaluate therapeutics. Chem Biol Interact. 2016; 244:49-63. doi: 10.1016/j.cbi.2015.11.032.

10. Ghasemi A, Jeddi S. Streptozotocin as a tool for induction of rat models of diabetes: a practical guide. EXCLI J. 2023; 22:274-294. doi:10.17179/excli2022-5720.
11. Organisation for Economic Co-operation and Development. Test No. 423: Acute oral toxicity—Acute toxic class method. OECD Guidelines for the Testing of Chemicals, Section 4. Paris: OECD Publishing; 2002. doi:10.1787/9789264071001-en.
12. World Health Organization. Quality control methods for herbal materials. Geneva: World Health Organization; 2011.
13. Nguyen DH, Nguyen MD, Huong LM, Tai LT, Thinh DB, Nam NTH, et al. Phytosynthesis of silver nanoparticles using Mangifera indica leaves extract at room temperature: formation mechanism, catalytic reduction, colorimetric sensing, and antimicrobial activity. Colloids Surf B Biointerfaces. 2022; 220:112974. doi: 10.1016/j.colsurfb.2022.112974.
14. Nguyen TLC, Narayanan M, Chinnathambi A, Govindasamy C, Subramani B, Brindhadevi K, et al. Fabrication, characterization, anti-inflammatory, and anti-diabetic activity of silver nanoparticles synthesized from Azadirachta indica kernel aqueous extract. Environ Res. 2022; 208:112684. doi: 10.1016/j.envres.2022.112684.
15. Yadav, Yashraj and DeshrajShyamkant Chumbhale. "DMBA induced mammary tumor study of Phyto-fabricated sliver nanoparticles from Russelia Equisetiformis flower extract in rat." *International journal of health sciences* (2022): page.
16. Kumaravelu P, Shanmugam R, Jayakodi S. Advancements in medicinal plant-derived trace element nanoparticles for diabetes mellitus therapy. BioNanoScience. 2025 Sep;15(3):429.
17. Khan, H. A., Ghufran, M., Shams, S., Jamal, A., Khan, A., Abdullah, Awan, Z. A., & Khan, M. I. (2023). Green synthesis of silver nanoparticles from plant Fagoniacretica and evaluating its anti-diabetic activity through indepth in-vitro and in-vivo analysis. *Frontiers in Pharmacology*, *14*. https://doi.org/10.3389/fphar.2023.1194809