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Green Synthesis and Characterization of Silver Nanoparticles from Randia dumetorum Roots for Drug Delivery Applications

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ABSTRACT
Nanoparticles derived from Randia Dumetorum Roots were successfully synthesized and thoroughly characterized to investigate their potential as innovative drug delivery systems. These nanoparticles demonstrated favorable characteristics, including an optimal particle size ranging between 1-100 nm, high entrapment efficiency (70–90%), and sustained drug release profiles, achieving 89–95% release within 60 minutes in phosphate-buffered saline (pH 7.4). Stability studies highlighted the robustness of the optimized formulation (NF4), which maintained consistent particle size, zeta potential, and entrapment efficiency over 12 weeks of storage at 4°C. Surface morphology analysis using Scanning Electron Microscopy (SEM) confirmed the spherical structure of the nanoparticles with minimal aggregation, aligning with particle size measurements obtained through light scattering techniques. Formulations designed for topical applications exhibited excellent performance, with suitable pH (6.2) for skin compatibility, enhanced spreadability (29±0.34 cm^2), and desirable viscosity (1248±0.632 cps), ensuring ease of application and patient compliance. The predictive accuracy of critical formulation parameters, such as pH and spreadability, was validated through statistical analysis using ANOVA, further strengthening the reliability of the study outcomes. The results underscore the promise of Randia Dumetorum-based nanoparticles as an effective platform for drug delivery, capable of improving therapeutic efficacy and patient outcomes. Future research directions include in vivo clinical validation to assess safety and bioavailability, exploration of molecular mechanisms underlying the therapeutic benefits, development of scalable production methods, and optimization for broader applications, such as oral or injectable dosage forms. These advancements will help unlock the full potential of Randia Dumetorum nanoparticles in modern medicine.

Keywords: Randia Dumetorum, roots, silver nanoparticles, nanogel, antimicrobial activity.

INTRODUCTION

Nanoparticles are solid colloidal particles composed of macromolecular substances, typically ranging in size from 10 nm to 1,000 nm. Therapeutic agents can be dissolved, entrapped, adsorbed, attached, or encapsulated within the nanoparticle matrix. Depending on the preparation method, nanoparticles, nanospheres, or nanocapsules with varying properties and release characteristics can be obtained. [1-3] Nanoparticulate drug-delivery systems (NPDDSs) have been extensively studied to address challenges in drug delivery. With diameters generally under 100 nm, these carriers can target and release therapeutic compounds in precise regions, offering significant advantages in drug distribution.

NPDDSs provide both hydrophobic and hydrophilic environments, aiding in drug solubility and reducing precipitation issues and toxicity associated with excipients designed to prevent drug aggregation. [4, 5] Furthermore, encapsulation enhances drug bioavailability by protecting drugs from rapid breakdown or clearance in vivo, enabling clinicians to prescribe lower doses. Advances in polymer and surface conjugation techniques and microfabrication methods have made NPDDSs a major focus in drug delivery technology. These submicron formulations range from simple metal–ceramic core structures to complex lipid–polymer matrices, functionalized to act as therapeutic vehicles for various conditions. Materials below 100 nm exhibit unique physical, chemical, and biological properties, making them particularly promising for addressing unmet therapeutic needs, especially in areas like CNS disorders.

The present research focuses on formulating, optimizing, and characterizing a herbal nanoparticulate drug-delivery system using pharmaceutical-grade polymers in varying concentrations [6].

MATERIALS AND METHODS

Plant Identification and Extraction: [7, 8]

Randia Dumetorum (Roots & leaves) collected from Regional Ayurvedic Research Institute C.C.R.A.S. Ministry of AYUSH Govt. of India, Nehru garden, Kothrud Pune, Maharashtra, India, in the month of January-February.The plant, was authenticated by Botanist of Botanical Survey of India, Pune by comparing morphological features. The herbarium of the plant specimen was deposited at Botanical Survey of India, Pune; with the Voucher specimen number MMDCS1 (Ref.No.BSI/WRC/Iden.Cer/2023/1103230002980 Dated 24/3/2023).

Plant Randia Dumetorum (Roots) were dried in the shade and pulverised. Each powdered component was passed through a 40# sieve. The roots were dried in sunlight separately and reduced to a coarse powder. Then the powder was subjected to Soxhlet extraction with methanol for 72 hours at a temperature of 50-60ºC. The extract was concentrated and the solvent was completely removed. Preliminary phytochemical screening was carried out to identify the chemical constituents**.**

Method of Preparation of Nanoparticles [9-13]

1. A 1 mM aqueous solution of AgNO3 was added drop wise to a specified quantity of plant extract in an Erlenmeyer flask for bio-reduction at room temperature.
2. The reaction mixture was stirred at 200 rpm using a magnetic stirrer until the solution changed color from yellow to dark brown, indicating the formation of silver nanoparticles (AgNPs).
3. The solution was centrifuged at 5,000 rpm for 30 minutes to separate the clear supernatant.
4. The nanoparticles were purified by repeatedly centrifuging the supernatant with distilled water.
5. Using Randia Dumetorum extracts (roots), six formulations each of silver nanoparticles (NF1-NF6) were prepared.
6. The nanoparticles were lyophilized and stored at 40°C until further use.

Table 1: Formula of Different Formulations of Randia Dumetorum (Roots) Silver Nanoparticles

S. No.	Name of Ingredients	NF1	NF2	NF3	NF4	NF5	NF6
1	Randia dumetorum (Roots)	10 mL	10 mL	10 mL	10 mL	10 mL	10 mL
2	AgNO3	98 mL	95 mL	90 mL	85 mL	80 mL	75 mL

Characterization of Nanoparticles [14-18]

1. Zeta Potential Study The surface charge of the silver nanoparticles was analyzed using a zeta sizer. Diluted nanoparticle formulations (NF1-NF6) were placed in an electrophoretic cell with an electric field of 15.5 V/cm, and the zeta potential was measured in triplicate.

2. Scanning Electron Microscopy (SEM) The morphology of silver nanoparticles was observed using SEM. Samples of nanoparticle formulations (NF1-NF6) were applied to glass slides, dried overnight in a vacuum desiccator, sputter-coated with gold, and analyzed at 15 kV under various magnifications.

3. Drug Entrapment Efficiency Entrapment efficiency was determined via ultracentrifugation at 10,000 rpm for 30 minutes. Pellets were re-dissolved in distilled water, and the supernatant's absorbance was measured at 418 nm using a UV-visible spectrophotometer. The entrapment efficiency was calculated as:

% Drug entrapment efficiency= experimental drug contentx100/Theoretical drug content

4. Production Yield of Nanoparticles The production yield was calculated by comparing the total weight of nanoparticles to the combined weight of the copolymer and drug:

% Yield calculation = Amount of drug X100 / Amount of drug +polymer

5. In-vitro Drug Release Study The drug release profile was assessed in phosphate-buffered saline (PBS, pH 7.4) at 37°C. Nanoparticles were dialyzed against 50 mL PBS with continuous shaking, and aliquots were periodically removed. The drug release was quantified spectrophotometrically at 418 nm.

6. Stability Study Nanoparticle stability was evaluated by storing the optimal formulation at 4°C for three months. Parameters such as particle size, zeta potential, entrapment efficiency, and physical appearance were analyzed monthly according to ICH Q1A guidelines.

A. Formulation of Polyhedral Gels [19-22]

Preparation Method

1. Gels were formulated using Carbopol 934, glycerin, methyl paraben, triethanolamine, and distilled water.
2. Water was divided into two portions (30:70). The plant extract was dissolved in the smaller portion, followed by the addition of glycerin and methyl paraben. Carbopol 934 was dissolved in the larger portion.
3. The two solutions were combined, and the pH was adjusted to 7.0 ± 0.5 using triethanolamine.
4. Control samples were prepared without plant extracts.

Table 2: Polyhedral Gel Formulation

Composition	Gel
Ethanolic Extract (Optimized Nanoparticle, NF4)	2.5%
Carbopol 934 (g)	0.5
Propylene Glycol (mL)	2.0
Methyl Paraben (mg)	0.2
Distilled Water (mL)	q.s.
Triethanolamine (mL)	q.s.

Experimental Design: BOX-Behnken Design

Response Surface Methodology (RSM) was employed using BOX-Behnken design (Design Expert®, Version 13.0). Three independent variables (Carbopol 934, propylene glycol, and methyl paraben) were evaluated, and dependent variables (pH and spreadability) were analyzed across 15 runs.

Table 3: DOE Suggested Table

Formulation Code	Carbopol 934 (%)	Propylene Glycol (mL)	Methyl Paraben (mL)
GR1	1.25	5.0	0.5
GR2	1.0	7.5	0.5
GR3	1.0	10.0	0.35
GR4	1.5	7.5	0.2
GR5	1.5	10.0	0.35
GR6	1.5	5	0.35
GR7	1.25	7.5	0.35
GR8	1.25	10	0.5
GR79	1.25	7.5	0.35
GR10	1.5	7.5	0.5
GR11	1.25	10	0.2
GR12	1	7.5	0.2
GR13	1.25	5	0.2
GR14	1.25	7.5	0.35
GR15	1	5	0.35

Evaluation Parameters for Gel [23-27]

1. Color, Appearance & Homogeneity Formulations were visually inspected for color, appearance, and homogeneity.

2. pH Measurement The pH was measured using a digital pH meter. Approximately 1 g of gel was dissolved in 10 mL of distilled water, and measurements were taken in triplicate.

3. Spreadability Spreadability was calculated using the formula:

$S = MxL/T$

where M is the applied weight, L is the distance, and T is the time taken.

4. Homogeneity Homogeneity was tested by visually inspecting the gels for aggregates after setting.

5. Viscosity Study Viscosity was determined using a Brookfield viscometer (spindle no. 64, 20 rpm, 25±2°C).

6. Extrudability Extrudability was evaluated by measuring the percentage of gel extruded from aluminum tubes under a 500 g load.

In-vitro Antimicrobial and Antifungal Activity of Polyherbal Gel Formulation GR8 Using Agar Well Diffusion Method [28-37]

Materials and Methods

The antimicrobial efficacy of the polyherbal gel formulation **GR8**, containing **Randia dumetorum root extract**, was evaluated using the **Agar Well Diffusion Method**. The study targeted both Gram-positive bacteria (**Bacillus subtilis**, **Staphylococcus aureus**) and Gram-negative bacteria (**Escherichia coli**, **Pseudomonas aeruginosa**) along with a fungal species (**Candida albicans**).

Culture Media and Conditions

Bacterial strains were cultivated on **Nutrient Agar** plates, while **Chloramphenicol Yeast Glucose Agar** was used for fungal cultures. Plates were inoculated with 0.2 mL of 24-hour-old microbial cultures using sterile swabs. The wells (8 mm diameter) were prepared in the agar using a cork borer.

Sample Preparation

A **100 mg/mL** stock solution of the GR8 gel was prepared in **Dimethyl Sulfoxide (DMSO)**. Each well was loaded with **50 µL** of this solution. Ciprofloxacin (**100 mg/mL**) was used as the standard for antibacterial activity, and fluconazole (**100 mg/mL**) was used as the standard for antifungal activity.

Incubation and Measurement

Plates were incubated at **37°C** for **24 hours**, and the **zone of inhibition (ZOI)** was measured in millimeters (mm) to evaluate antimicrobial and antifungal activity.

RESULTS AND DISCUSSION

Characterization of Nanoparticles

The prepared nanoparticles derived from the extract of Randia Dumetorum **Roots** were subjected to various evaluation parameters.

Particle Size Determination by Zeta Sizer

The particle size of nanoparticles (NF1-NF6) formulated from Randia Dumetorum **Roots** was determined to range between **1-100 nm**.

Table 4: Particle Size and Zeta Potential of Randia Dumetorum Roots Nanoparticles

Sr. No.	Sample	Nanoparticle Size (nm)	Zeta Potential (mV)
1	Extract of Randia Dumetorum Roots (NF1)	41.5 ±15	-24.0
2	Extract of Randia Dumetorum Roots (NF2)	42.1±17	-19.7
3	Extract of Randia Dumetorum Roots (NF3)	38.9±16	-25.2
4	Extract of Randia Dumetorum Roots (NF4)	41.5±18	-25.8
5	Extract of Randia Dumetorum Roots (NF5)	38.6±19	-19.0
6	Extract of Randia Dumetorum Roots (NF6)	38.2±15	-38.7

Values are shown as the mean ± standard deviation; n=5.

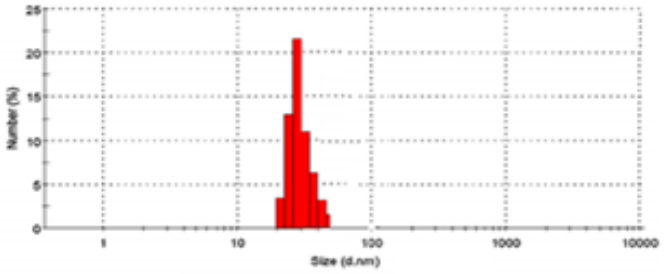

Figure 1: Results of Particle Density Index of extracts derived root extract of Randia Dumetorum loaded nanoparticles (NF4-Optimised).

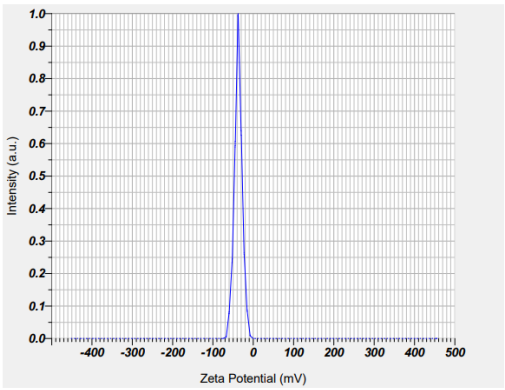

Figure 2: Zeta particle size distribution peak of nanoparticles of Leaves extract ofRandia Dumetorum (NF4-Optimised).

Scanning Electron Microscopy (SEM)

SEM was employed to evaluate the surface morphology of silver nanoparticles. The results revealed that the nanoparticles were predominantly **spherical**, with minimal aggregation. The average nanoparticle size from root extracts was approximately **55 nm**, corroborating the results from light scattering analysis.

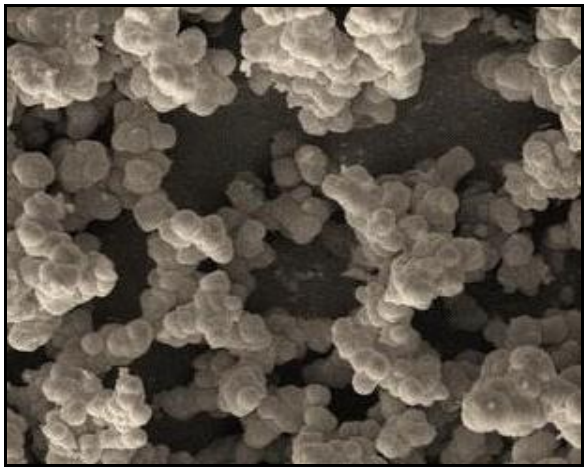

Figure 3: SEM of freeze-dried silver nanoparticles derived from root extracts of Randia Dumetorum (NF4-Optimized).

Drug Entrapment Efficiency

The entrapment efficiency for silver nanoparticles loaded with root extracts ranged from **70% to 90%**.

Table 5: Entrapment Efficiency of Formulations NF1-NF6

Formulations	Entrapment Efficiency (%)
NF1	91.25
NF2	90.46
NF3	89.97
NF4	96.56
NF5	87.86
NF6	88.94

Production Yield of Nanoparticles

Production yield was influenced by the concentration of **AgNO3**, with a consistent polymer concentration resulting in reliable yields.

Table 6: Production Yield of Formulations NF1-NF6

Formulation	Production Yield (%)
NF1	76.59
NF2	68.79
NF3	80.46
NF4	85.46
NF5	89.77
NF6	75.86

In-vitro Drug Release Study

Nanoparticles loaded withRandia Dumetorum extracts exhibited a drug release of **89-95%** in phosphate-buffered saline (pH 7.4) at **37°C**. Drug release was quantified using a UV-visible spectrophotometer at **418 nm**.

Table 7: Cumulative Drug Release (%) of Nanoparticles (NF1-NF6)

Time (min)	NF1	NF2	NF3	NF4	NF5	NF6
0	0	0	0	0	0	0
5	13.24	16.23	17.25	12.96	19.55	16.33
15	27.23	22.31	24.16	28.68	27.31	29.46
30	44.31	41.32	43.19	48.22	43.68	52.87
45	61.23	68.03	65.31	67.12	62.28	62.45
60	83.15	79.46	82.49	97.46	90.14	82.44

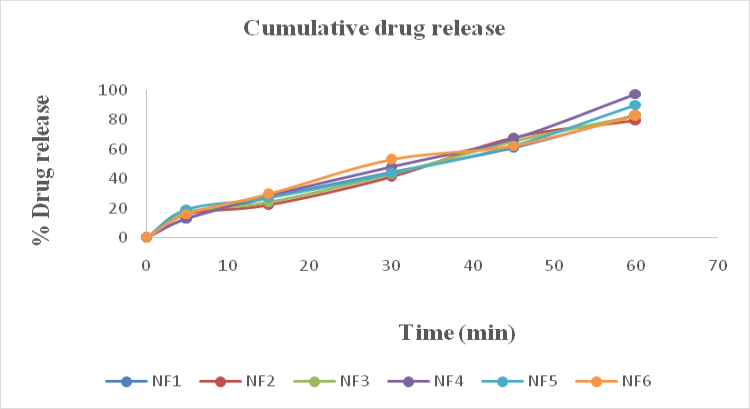

Figure 4: %Cumulative Drug Release (NF1-NF6).

Stability Studies

Optimized formulation **NF4** showed negligible changes after **12 weeks** of storage at **4°C**, indicating excellent stability.

Table 8: Effect of Storage on Particle Size, Zeta Potential, and Entrapment Efficiency (NF4)

Storage Time	Particle Size (nm)	Zeta Potential (mV)	Entrapment Efficiency (%)
"0" Month	48.7±21	-26.5	96.56±0.3
"1" Month	48.6±20	-26.4	96.24±0.7
"2" Month	46.5±23	-25.9	95.21±0.7
"3" Month	44.1±19	-25.8	95.54±0.08

Physicochemical Evaluation of Gel Formulations

Color: All formulations exhibited a **greenish** blue.

pH Measurements: The optimized batch **GR8** had a pH of **6.2**, suitable for topical application due to its compatibility with skin's natural pH.

Spreadability: GR8 demonstrated superior spreadability (**29±0.34**), indicating ease of application.

Viscosity: GR8 exhibited a viscosity of **1248±0.632 cps**, offering smooth texture and enhanced patient compliance.

Statistical Analysis

ANOVA Results: Significant model terms were identified, ensuring reliable prediction of responses for both pH and spreadability parameters. Adequate precision and R^2 values indicated robust models.

RESULTS

The antimicrobial activity of GR8 against each microorganism is presented in

Table 9. The results demonstrated that GR8 exhibited significant activity against all tested microbes.

Sample	Bacillus subtilis	Staphylococcus aureus	Escherichia coli	Pseudomonas aeruginosa	Candida albicans
GR8 Gel (100 mg/mL)	16 ± 0.5	14 ± 0.8	17 ± 0.6	18 ± 0.4	15 ± 0.7
Ciprofloxacin/Fluconazole	35 ± 0.3	35 ± 0.5	34 ± 0.2	35 ± 0.6	28 ± 0.5

The polyherbal gel formulation GR8 exhibited antimicrobial activity with ZOI values ranging from **14–18 mm** against bacterial strains and **15 mm** against fungal species. The antimicrobial activity of GR8 was notable but lower compared to the standard antibiotics. These results highlight the potential of GR8 gel as an effective natural antimicrobial agent with applications in managing microbial infections.

CONCLUSION

This study successfully synthesized and characterized nanoparticles derived from Randia Dumetorum **Roots**, demonstrating their potential as carriers for drug delivery. The nanoparticles displayed desirable properties, including optimal particle size, high entrapment efficiency, and sustained drug release. Stability studies confirmed the robustness of the formulations, particularly NF4, under storage conditions. Additionally, physicochemical evaluations of gel formulations revealed their suitability for topical applications, with favorable pH, spreadability, and viscosity parameters. The results underline the utility of Randia Dumetorum-

based nanoparticles as effective platforms for drug delivery, offering potential for enhanced therapeutic outcomes. Further studies should focus on the mechanisms underlying the antimicrobial activity and the synergistic effects of Randia dumetorum root extract with other bioactive compounds.

CONFLICT OF INTEREST

Nil

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