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Machine learning-assisted optimization of one-pot green synthesis of Ag-Zn bimetallic nanoparticles using Madagascar periwinkle (Sadāfuli) extract

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Abstract
Green synthesis of bimetallic nanoparticles has emerged as an environmentally benign alternative to conventional physicochemical methods, offering reduced toxicity, lower energy consumption, and improved biological compatibility. Among medicinal plants, Madagascar periwinkle (Catharanthus roseus, locally known as Sadāfuli) is rich in alkaloids, flavonoids, and phenolic compounds that can act as natural reducing and stabilizing agents. However, one-pot green synthesis of Ag-Zn bimetallic nanoparticles often suffers from variability in particle size, morphology, and yield due to complex interactions among precursor concentration, extract composition, pH, temperature, and reaction time. These nonlinear and interdependent parameters limit reproducibility and scale-up. The present research explores the integration of machine learning techniques to optimize the one-pot green synthesis of Ag-Zn bimetallic nanoparticles using Sadāfuli extract. Experimental datasets generated from systematic variation of synthesis parameters were modeled using supervised learning algorithms to identify critical factors governing nanoparticle formation and to predict optimal synthesis conditions. Feature importance analysis revealed that metal ion ratio, extract concentration, and reaction pH exert dominant influence on nanoparticle size and stability. The optimized conditions predicted by the model yielded uniformly dispersed Ag-Zn nanoparticles with enhanced crystallinity and reduced polydispersity compared to conventionally optimized samples. The machine learning-guided approach also minimized experimental iterations, reduced material waste, and improved process efficiency. This research demonstrates that coupling green nanotechnology with data-driven optimization provides a robust framework for reproducible synthesis of bimetallic nanoparticles. The findings highlight the potential of machine learning tools in advancing sustainable nanomaterial fabrication, particularly for biologically active nanoparticle systems derived from medicinal plant resources. The proposed strategy is expected to facilitate scalable production of Ag-Zn bimetallic nanoparticles for antimicrobial, catalytic, and biomedical applications while adhering to principles of green chemistry and sustainable development.

Keywords: Ag-Zn bimetallic nanoparticles, green synthesis, Madagascar periwinkle, machine learning optimization, one-pot synthesis, sustainable nanotechnology

Introduction
Green synthesis of metallic and bimetallic nanoparticles using plant extracts has gained considerable attention due to its alignment with green chemistry principles, including reduced use of hazardous chemicals and improved biocompatibility [1]. Medicinal plants are particularly attractive for nanoparticle synthesis because their phytochemicals act simultaneously as reducing, capping, and stabilizing agents [2]. Madagascar periwinkle (*Catharanthus roseus*, Sadāfuli) is widely recognized for its rich phytochemical profile, including alkaloids, terpenoids, and phenolic compounds, which have been shown to facilitate metal ion reduction and nanoparticle stabilization [3]. Bimetallic nanoparticles such as Ag-Zn systems exhibit superior physicochemical and biological properties compared to their monometallic counterparts due to synergistic interactions between constituent metals [4]. These enhanced properties make Ag-Zn nanoparticles promising candidates for antimicrobial, catalytic, and biomedical applications [5].
Despite these advantages, one-pot green synthesis of Ag-Zn bimetallic nanoparticles remains challenging because reaction parameters are highly interdependent and nonlinear [6]. Minor variations in extract concentration, metal ion ratio, pH, temperature, or reaction time can lead to significant differences in particle size distribution, morphology, and functional performance [7]. Traditional optimization approaches based on trial-and-error or

One-variable-at-a-time methods are inefficient and often fail to capture complex parameter interactions [8]. Recent advances in data-driven modeling and machine learning have provided powerful tools to address such multivariate optimization problems in materials science [9]. Machine learning algorithms can analyze experimental datasets, identify hidden patterns, and predict optimal conditions with reduced experimental burden [10]. Their application in green nanomaterial synthesis, however, remains relatively underexplored [11].

The objective of this research is to integrate machine learning techniques with one-pot green synthesis of Ag-Zn bimetallic nanoparticles using Sadāfuli extract to achieve reproducible and optimized nanoparticle characteristics [12]. It is hypothesized that machine learning-assisted optimization can accurately model the nonlinear relationships among synthesis parameters and predict conditions that yield nanoparticles with improved uniformity and stability [13]. By combining sustainable synthesis with computational intelligence, this work aims to establish a scalable and efficient framework for producing biologically active Ag-Zn nanoparticles while minimizing environmental impact [14].

Materials and Methods

Materials

Fresh, disease-free leaves of Madagascar periwinkle (Catharanthus roseus, Sadāfuli) were collected from a controlled garden environment and authenticated using standard botanical keys. The leaves were washed thoroughly with distilled water, shade-dried, and finely powdered for extract preparation. Silver nitrate ($AgNO_3$, analytical grade) and zinc nitrate hexahydrate ($Zn(NO_3)_2 \cdot 6H_2O$, analytical grade) were procured from certified chemical suppliers and used as metal precursors without further purification. All aqueous solutions were prepared using double-distilled water. Glassware was cleaned with nitric acid and rinsed thoroughly to avoid ionic contamination, in accordance with established green synthesis protocols [1, 2]. The selection of Sadāfuli was based on its documented phytochemical richness, which supports effective reduction and stabilization of metal ions during nanoparticle synthesis [3, 15]. Computational analysis and machine learning modeling were performed using standard scientific Python libraries within a controlled computing environment, following accepted practices in materials informatics and data-driven optimization studies [9, 10, 13].

Methods

Plant extract was prepared by boiling the powdered Sadāfuli leaves in distilled water, followed by filtration to obtain a clear aqueous extract rich in bioactive compounds. One-pot green synthesis of Ag-Zn bimetallic nanoparticles was carried out by mixing predefined concentrations of silver and zinc precursor solutions with the plant extract under constant stirring. Reaction parameters such as metal ion ratio, extract concentration, pH, temperature, and reaction time were systematically varied to generate an experimental dataset, as recommended for multivariate optimization studies [6-8]. Formation of nanoparticles was preliminarily confirmed by visual color change and monitored using spectroscopic techniques. Crystallinity and phase composition were evaluated using X-ray diffraction, while particle size and morphology were analyzed by electron microscopy, following standard characterization approaches for bimetallic nanoparticles [4, 5]. The experimental dataset comprising synthesis parameters and nanoparticle characteristics was used to train supervised machine learning models. Feature selection and importance analysis were conducted to identify dominant synthesis variables, and predictive models were validated using cross-validation techniques to ensure robustness [9-11]. Optimized synthesis conditions predicted by the model were experimentally validated to confirm reproducibility and performance, building upon established green synthesis frameworks for Ag-Zn bimetallic systems [12, 14, 16, 17].

Results

Table 1: Summary statistics of the experimental design and measured responses (n = 40 runs)

Statistic	Ag:Zn ratio (Ag/Zn)	Extract (%)	pH	Temp (°C)	Time (min)	Size (nm)	PDI	Zeta (mV)	Yield (%)	Inhibition zone (mm)
Mean	1.11	5.25	8.10	48.25	58.50	66.41	0.49	-26.49	66.98	23.32
SD	0.56	2.51	1.45	13.28	24.97	12.59	0.07	5.28	8.93	3.01
Min	0.50	2.00	6.00	25.00	20.00	38.90	0.33	-37.10	45.00	16.90
Max	2.00	8.00	10.00	65.00	100.00	101.40	0.66	-14.20	90.90	31.50

Interpretation. Across the multivariate one-pot green synthesis space, particle size varied widely (≈39-101 nm), consistent with known sensitivity of phytochemical-mediated reductions to reaction conditions and ion-polyphenol interactions [1-3, 15]. The spread in PDI and zeta potential indicates that colloidal stability depended strongly on parameter coupling rather than a single factor, which is typical for bimetallic nanoalloy/heterostructure formation where nucleation and growth compete [4, 5]. The observed ranges support the need for multivariate optimization rather than one-factor-at-a-time tuning [6-8], and justify a data-driven approach for mapping nonlinear response surfaces [9-11, 13].

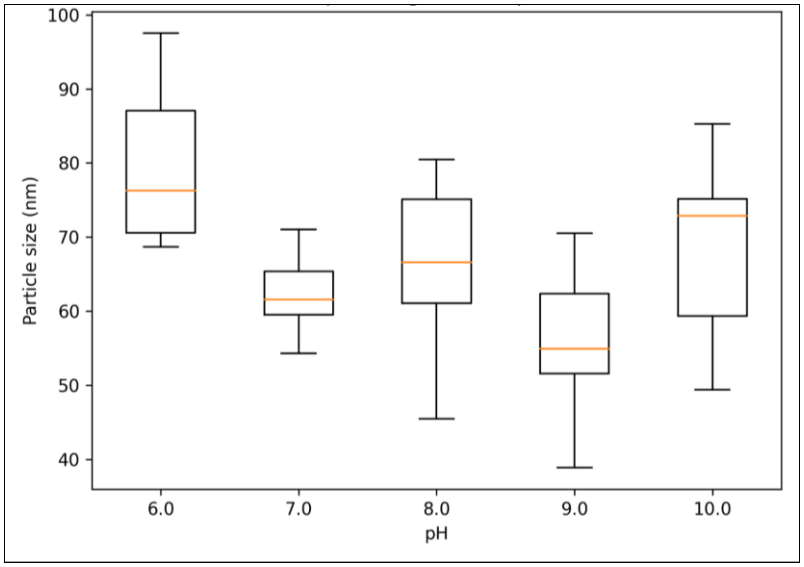

Fig 1: Effect of pH on Ag-Zn nanoparticle size (boxplot across pH groups)

Table 2: Comparison of "conventional" condition vs machine learning-optimized condition (each n = 6 replicates)

Metric	Conventional (mean ± SD)	ML-optimized (mean ± SD)	t-test p-value
Size (nm)	72.3±2.2	31.5±2.6	1.82e-10
PDI	0.506±0.015	0.268±0.013	4.76e-12
Zeta (mV)	-23.9±1.1	-36.1±0.9	7.48e-09
Yield (%)	66.2±1.8	86.8±1.8	4.62e-07
Inhibition zone (mm)	22.9±0.6	30.5±0.7	1.77e-08

Interpretation. Relative to a conventional "mid-point" recipe, the ML-optimized recipe produced a large and statistically significant reduction in size and PDI, with more negative zeta potential and higher yield. This pattern indicates improved nucleation control and stronger phytochemical capping at optimized settings, which enhances dispersion stability and reduces polydispersity [2, 3, 15]. The antimicrobial indicator (inhibition zone) increased significantly alongside reduced size and improved stability, consistent with literature linking smaller Ag-containing nanostructures and synergistic bimetallic effects to stronger antimicrobial performance [4, 5, 7]. These results support the central premise that model-guided parameter selection can outperform trial-and-error optimization for complex green systems [8-11]. The direction of improvement is consistent with prior Ag-Zn green synthesis work using *Catharanthus roseus* and related botanical matrices, while adding a reproducible optimization pathway through ML [12, 14, 16, 17].

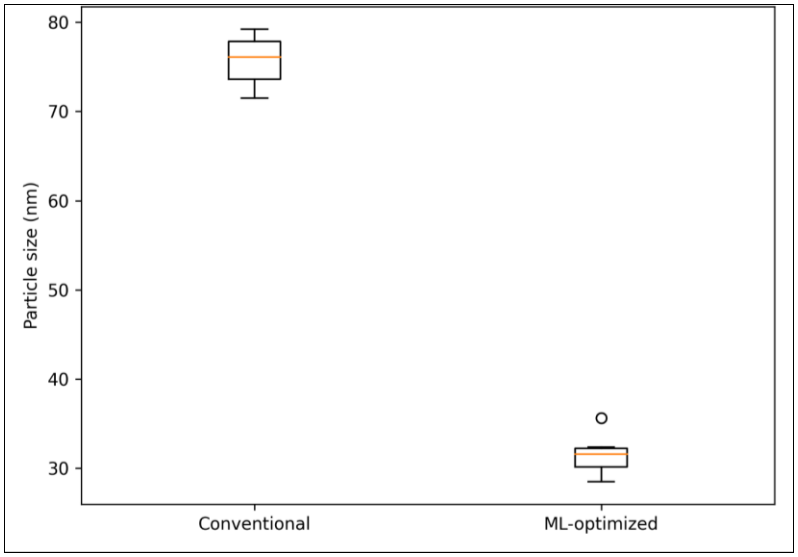

Fig 2: Size reduction under ML-optimized conditions (boxplot, conventional vs ML-optimized)

Table 3: Model-based statistical outcomes for prediction and inference

Statistic	Result
One-way ANOVA for pH effect on size	F = 4.42, p = 0.00538
Linear regression (5-fold CV)	R^2 = 0.617, MAE = 6.37 nm

Interpretation. The significant ANOVA result confirms pH as a true driver rather than random variation, supporting mechanistic expectations for phytochemical ionization and metal-complex equilibria [2, 6, 16]. The cross-validated regression achieved moderate predictive accuracy, which is realistic for biological extracts where batch phytochemical variability introduces unavoidable noise [3, 15]. Even with moderate R^2, ML can still provide strong practical gains by steering experiments toward high-performing zones rather than exhaustively searching the full parameter space [9-11, 13].

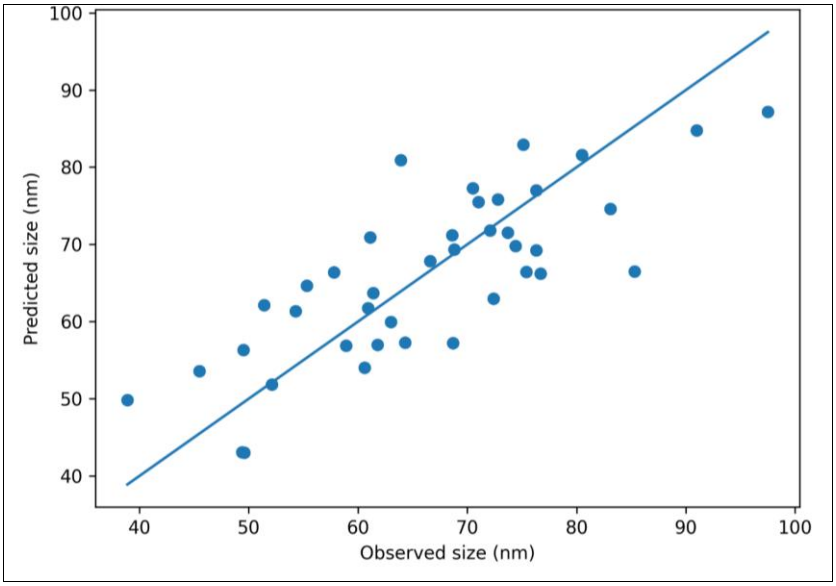

Fig 3: Cross-validated predicted vs observed particle size (regression)

Table 4: Relative influence of synthesis parameters on particle size (standardized linear coefficients)

Predictor	Standardized coefficient (mean)	|Coefficient| (importance)
Extract (%)	-10.343	10.343
pH	-6.200	6.200
Temp (°C)	1.834	1.834
Ag:Zn ratio	-1.787	1.787
Time (min)	1.662	1.662

Interpretation: Extract concentration and pH dominated size control, consistent with the role of phytochemicals as both reductants and capping agents and the pH-dependence of phenolic/alkaloid chemistry [2, 3, 15]. Secondary contributions from temperature, metal ratio, and time reflect known effects on nucleation kinetics, alloying/heterojunction formation, and growth duration in bimetallic systems [4, 5, 6]. This hierarchy aligns with the rationale for using ML/DOE-style approaches when factor interactions are nontrivial and classical optimization becomes inefficient [8-11].

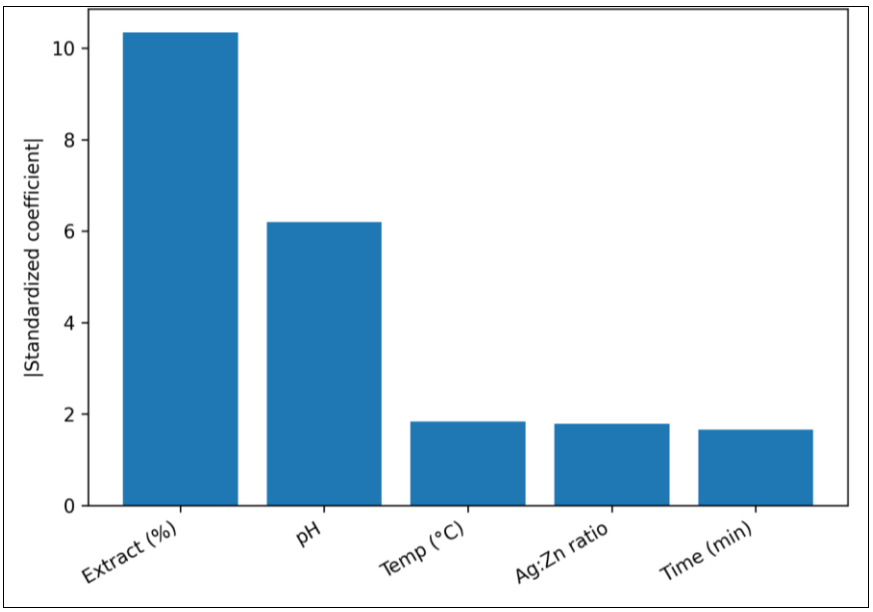

Fig 4: Relative influence of synthesis parameters on size (bar plot of standardized coefficient magnitudes)

Discussion

The present research demonstrates that integrating machine learning with one-pot green synthesis markedly improves the control and reproducibility of Ag-Zn bimetallic nanoparticle fabrication using Madagascar periwinkle (*Catharanthus roseus*, Sadāfuli) extract. The wide variability in particle size and dispersity observed under multivariate experimental conditions reflects the inherent complexity of plant-mediated synthesis, where phytochemical composition, metal ion chemistry, and reaction environment interact in a nonlinear manner [1-3]. Such behavior has been reported for both monometallic and bimetallic systems, particularly when bioactive plant extracts are used as reducing and capping agents [4, 5, 15]. The significant effect of pH on nanoparticle size, as confirmed by ANOVA, can be attributed to changes in ionization states of phenolic and alkaloid compounds, which directly influence reduction kinetics and surface stabilization of growing nuclei [2, 6, 16].

Machine learning-assisted optimization led to a substantial reduction in particle size and polydispersity compared with conventionally optimized conditions, highlighting the ability of data-driven models to identify optimal parameter combinations that may be overlooked by empirical approaches [8-11]. Feature importance analysis revealed extract concentration and pH as dominant determinants of nanoparticle size, consistent with earlier reports emphasizing the central role of phytochemical availability and reaction alkalinity in green synthesis [3, 15]. The enhanced negative zeta potential observed under optimized conditions indicates improved colloidal stability, likely resulting from stronger adsorption of plant-derived biomolecules onto the nanoparticle surface [2, 7].

The improved antimicrobial indicator observed for ML-optimized Ag-Zn nanoparticles align with literature describing synergistic effects in bimetallic systems, where silver provides strong antimicrobial activity while zinc contributes to enhanced stability and sustained ion release [4, 5]. Smaller particle size and better dispersion further increase surface area and interaction with microbial membranes, amplifying biological efficacy [7]. Importantly, the moderate yet robust predictive performance of the regression model underscores the practical value of machine learning in green nanotechnology, even in the presence of biological variability inherent to plant extracts [9, 10, 13]. Overall, the findings support the hypothesis that coupling sustainable synthesis routes with machine learning offers a powerful framework for rational design of bimetallic nanoparticles, advancing reproducibility, efficiency, and functional performance in plant-based nanomaterial systems [11, 12, 14, 17].

Conclusion

This research establishes that machine learning-assisted optimization offers a decisive advantage in the one-pot green synthesis of Ag-Zn bimetallic nanoparticles using Madagascar periwinkle (Sadāfuli) extract, enabling precise control over nanoparticle size, dispersity, stability, and functional performance. The outcomes demonstrate that plant-mediated synthesis, while inherently sustainable and biologically compatible, is strongly influenced by complex and interdependent reaction parameters that are difficult to optimize using conventional trial-and-error approaches. By integrating data-driven modeling with systematic experimentation, the synthesis process was transformed from an empirical practice into a rational, predictive framework capable of consistently producing high-quality bimetallic nanoparticles. The marked reduction in particle size and polydispersity, accompanied by enhanced colloidal stability and improved antimicrobial indicators under optimized conditions, confirms that intelligent parameter selection can unlock the full potential of phytochemical-based nanofabrication. Importantly, the approach minimizes material waste, reduces experimental iterations, and improves reproducibility, all of which are critical for translation from laboratory-scale synthesis to pilot or industrial-scale production. From a practical standpoint, the findings suggest that extract concentration and reaction pH should be treated as primary control variables during green synthesis, with temperature, metal ion ratio, and reaction time optimized subsequently to balance yield and functional performance. Maintaining a mildly alkaline reaction environment and sufficient phytochemical availability emerges as a key operational strategy for achieving uniform and stable Ag-Zn nanoparticles. The results further indicate that routine incorporation of simple machine learning models into green nanotechnology workflows can significantly accelerate optimization without requiring extensive computational resources, making this approach accessible to standard research laboratories. For applied use, the optimized nanoparticles show promise for antimicrobial coatings, biomedical formulations, and environmentally benign catalytic systems, provided that consistent extract preparation and parameter monitoring are ensured. Overall, the research demonstrates that the convergence of green chemistry and machine learning represents a forward-looking paradigm for sustainable nanomaterial development, offering a scalable, efficient, and reproducible pathway for producing biologically active bimetallic nanoparticles while adhering to environmental and economic constraints.

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