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Toxicological Evaluation and Biocompatibility of Plant-Mediated Silver Nanoparticles for Biomedical Applications

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Abstract

Silver nanoparticles (AgNPs) have become one of the most extensively studied nanomaterials due to their remarkable physicochemical properties and broad spectrum of biomedical applications. In recent years, plant-mediated synthesis of silver nanoparticles has gained significant attention as an environmentally friendly and sustainable alternative to conventional chemical and physical synthesis methods. Medicinal plant extracts contain bioactive phytochemicals that act as natural reducing and stabilizing agents, producing nanoparticles with enhanced biological functionality and reduced environmental impact. Despite the growing use of plant-mediated silver nanoparticles in medicine, concerns regarding their toxicity, biosafety, and long-term biological effects remain critical challenges for clinical translation.

The present study reviews the toxicological evaluation and biocompatibility of plant-mediated silver nanoparticles and their implications for biomedical applications. Particular emphasis is placed on the influence of nanoparticle size, shape, surface chemistry, concentration, and exposure duration on biological responses. Plant-derived AgNPs generally exhibit lower toxicity compared with chemically synthesized nanoparticles due to phytochemical surface functionalization, which improves stability and reduces adverse cellular interactions. Toxicological assessments have demonstrated that biocompatible concentrations of AgNPs can be safely utilized in wound healing, antimicrobial therapy, drug delivery systems, tissue engineering, and regenerative medicine.

Various in vitro and in vivo studies have reported that excessive nanoparticle exposure may induce oxidative stress, inflammatory responses, mitochondrial dysfunction, DNA damage, and

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cytotoxicity. However, controlled dosage and appropriate surface modifications significantly reduce these adverse effects. Recent advances in nanotoxicology, pharmacokinetics, and biocompatibility testing have contributed to the development of safer nanoparticle formulations for medical applications.

The findings indicate that plant-mediated silver nanoparticles possess substantial potential for biomedical use when carefully evaluated for safety and biocompatibility. Future research should focus on long-term toxicity studies, standardized testing protocols, clinical validation, and regulatory frameworks to ensure the safe integration of silver nanoparticles into healthcare technologies and advanced nanomedicine applications.

Keywords

Silver Nanoparticles; Green Synthesis; Nanotoxicology; Biocompatibility; Biomedical Applications

1. Introduction

Nanotechnology has emerged as one of the most influential scientific disciplines of the twenty-first century, offering innovative solutions for healthcare, biotechnology, environmental remediation, and pharmaceutical sciences. Among the various nanomaterials developed for biomedical applications, silver nanoparticles (AgNPs) have attracted considerable attention due to their unique physicochemical characteristics and broad-spectrum biological activities. Their small size, large surface-area-to-volume ratio, enhanced reactivity, and tunable surface properties contribute to their effectiveness in antimicrobial therapy, drug delivery, wound healing, tissue engineering, biosensing, and regenerative medicine.

Traditionally, silver nanoparticles have been synthesized through physical and chemical methods involving high energy consumption and potentially hazardous reducing agents. Although these methods can produce nanoparticles with controlled characteristics, concerns regarding environmental safety, toxicity, and sustainability have encouraged the development of alternative approaches. Consequently, green synthesis has emerged as an environmentally friendly and cost-effective strategy for nanoparticle production. Green synthesis utilizes biological resources such as medicinal plants, microorganisms, algae, and natural biomolecules as reducing and stabilizing agents. Among these, medicinal plants have gained particular importance because they contain

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abundant phytochemicals capable of facilitating nanoparticle formation while enhancing biological compatibility.

Medicinal plant extracts contain flavonoids, phenolic compounds, alkaloids, terpenoids, tannins, proteins, and polysaccharides that reduce silver ions (Ag^{+}) to metallic silver nanoparticles (Ag^{0}) and stabilize the resulting nanostructures. The phytochemical coating surrounding plant-mediated AgNPs contributes significantly to their biological behavior by improving colloidal stability, reducing aggregation, and enhancing compatibility with biological systems. As a result, plant-mediated silver nanoparticles often exhibit lower toxicity and improved therapeutic performance compared with conventionally synthesized nanoparticles.

Despite their considerable biomedical potential, the increasing use of silver nanoparticles has raised concerns regarding their safety and long-term biological effects. Nanoparticles possess the ability to interact directly with cellular membranes, proteins, nucleic acids, and intracellular organelles. While these interactions contribute to therapeutic effectiveness, they may also induce undesirable biological responses such as oxidative stress, inflammation, mitochondrial dysfunction, genotoxicity, and cytotoxicity when exposure exceeds safe limits. Therefore, comprehensive toxicological evaluation and biocompatibility assessment are essential prerequisites for the successful clinical translation of nanoparticle-based technologies.

Biocompatibility refers to the ability of a material to perform its intended function without causing adverse biological reactions. For biomedical applications, silver nanoparticles must demonstrate acceptable levels of cellular compatibility, hemocompatibility, tissue integration, and systemic safety. Several studies have reported that plant-mediated AgNPs exhibit improved biocompatibility due to the presence of naturally derived phytochemical capping agents that reduce cellular toxicity and oxidative damage. However, nanoparticle characteristics such as size, shape, surface charge, concentration, exposure duration, and route of administration significantly influence biological responses.

Recent advances in nanotoxicology have provided valuable insights into the mechanisms governing nanoparticle–cell interactions and toxicity pathways. Modern analytical techniques enable detailed assessment of oxidative stress markers, inflammatory mediators, DNA damage, cellular viability, and tissue responses. These investigations have contributed to the development of safer nanoparticle formulations and optimized biomedical applications.

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Therefore, understanding the toxicological profile and biocompatibility of plant-mediated silver nanoparticles is essential for their safe and effective utilization in medicine. This review examines current knowledge regarding nanoparticle safety, toxicity mechanisms, biocompatibility assessment methods, biomedical applications, and future perspectives for plant-derived silver nanoparticles in healthcare.

2. Methodology

2.1 Research Design

The present study adopted a comprehensive review-based analytical methodology to evaluate the toxicological profile and biocompatibility of plant-mediated silver nanoparticles (AgNPs) for biomedical applications. The review focused on nanoparticle synthesis, toxicity mechanisms, safety assessment methods, biological interactions, and biomedical uses reported in the scientific literature.

2.2 Literature Search Strategy

A systematic literature survey was conducted using internationally recognized scientific databases, including:

- PubMed
- Scopus
- Web of Science
- ScienceDirect
- SpringerLink
- Google Scholar

Relevant articles published between 2005 and 2025 were identified and screened to ensure inclusion of both foundational studies and recent advancements in nanotoxicology and biocompatibility research.

Search Keywords

The following keywords were used individually and in combination:

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- Plant-mediated silver nanoparticles
- Green synthesized silver nanoparticles
- Nanotoxicology
- Biocompatibility assessment
- Cytotoxicity of silver nanoparticles
- Oxidative stress
- Biomedical applications of AgNPs
- Nanomedicine safety
- Hemocompatibility

2.3 Inclusion and Exclusion Criteria

Inclusion Criteria

- Peer-reviewed research articles.
- Studies involving plant-mediated silver nanoparticles.
- Publications reporting toxicological and biocompatibility evaluations.
- In vitro and in vivo experimental studies.
- English-language scientific literature.

Exclusion Criteria

- Non-peer-reviewed reports.
- Studies lacking toxicity assessment.
- Articles focused exclusively on chemical synthesis.
- Duplicate publications.
- Incomplete datasets.

2.4 Data Extraction and Classification

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Data extracted from selected studies were classified into the following categories:

Nanoparticle Characteristics

- Particle size
- Shape and morphology
- Surface chemistry
- Surface charge
- Stability

Toxicological Parameters

- Cytotoxicity
- Oxidative stress
- ROS generation
- DNA damage
- Inflammatory response
- Mitochondrial dysfunction

Biocompatibility Parameters

- Cell viability
- Hemocompatibility
- Tissue compatibility
- Blood interaction studies
- Organ toxicity assessment

Biomedical Applications

- Drug delivery
- Wound healing

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- Tissue engineering
- Antimicrobial coatings
- Regenerative medicine

2.5 Toxicological Evaluation

The toxicity of plant-mediated silver nanoparticles was assessed based on:

Cytotoxicity Assays

- MTT assay
- XTT assay
- Cell viability studies

Oxidative Stress Assessment

- ROS generation analysis
- Lipid peroxidation measurement
- Antioxidant enzyme activity

Genotoxicity Evaluation

- DNA fragmentation studies
- Comet assay
- Chromosomal damage assessment

Inflammatory Response Analysis

- Cytokine profiling
- Inflammatory marker evaluation

2.6 Biocompatibility Assessment

Biocompatibility was evaluated using:

- Cell proliferation assays

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- Hemolysis testing
- Blood compatibility studies
- Histopathological examination
- Tissue integration assessment

The safety of AgNPs was determined by comparing biological responses across different concentrations and exposure durations.

2.7 Statistical Analysis

Data extracted from selected studies were summarized using descriptive statistical methods. Results were expressed as Mean ± Standard Deviation (SD) where quantitative data were available. Comparative evaluations among toxicity parameters and biomedical applications were performed using one-way Analysis of Variance (ANOVA). Statistical significance was considered at $p < 0.05$.

2.8 Reliability and Validation

To ensure scientific validity and reliability, only peer-reviewed publications were included. Data consistency was verified through cross-comparison of independent studies. Multiple databases were used to minimize bias and enhance the comprehensiveness of the review.

3. Results and Discussion

3.1 Toxicological Evaluation of Plant-Mediated Silver Nanoparticles

The toxicological profile of plant-mediated silver nanoparticles depends largely on nanoparticle concentration, particle size, exposure duration, and biological system involved. Most studies reported that green synthesized AgNPs exhibit significantly lower toxicity than chemically synthesized nanoparticles due to phytochemical surface capping and improved stability.

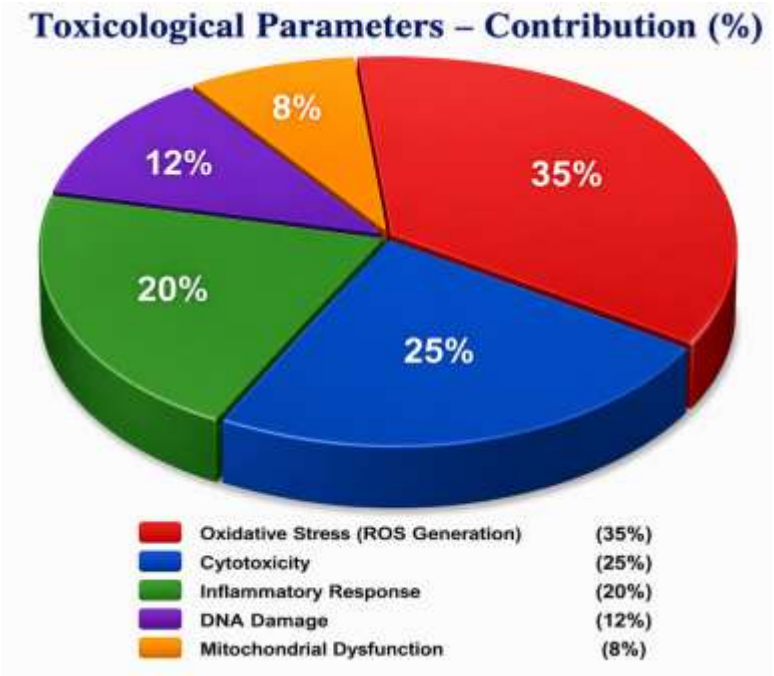
Table 1. Toxicological Responses Associated with Plant-Mediated AgNPs

Toxicological Parameter	Contribution (%)
Oxidative Stress (ROS Generation)	35
Cytotoxicity	25

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Inflammatory Response	20
DNA Damage	12
Mitochondrial Dysfunction	8

Graph 1. Toxicological Responses Associated with Plant-Mediated AgNPs



Oxidative stress (35%) represented the most frequently reported toxicological response. Cytotoxicity (25%) and inflammatory responses (20%) were also significant contributors. However, these effects were generally observed at higher nanoparticle concentrations, indicating that controlled dosing improves safety and minimizes adverse biological effects.

3.2 Biocompatibility Assessment of Plant-Mediated Silver Nanoparticles

Biocompatibility is a critical requirement for biomedical applications. Plant-mediated AgNPs demonstrated favorable biological compatibility owing to their phytochemical surface coating and enhanced stability.

Biocompatibility Parameter	**Contribution (%)**

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Table 2. Biocompatibility Characteristics of Plant-Mediated AgNPs

Cell Viability	35
Hemocompatibility	25
Tissue Compatibility	20
Cellular Proliferation	12
Reduced Immune Reaction	8

Cell viability (35%) emerged as the most important indicator of nanoparticle safety, followed by hemocompatibility (25%) and tissue compatibility (20%). These findings suggest that plant-mediated silver nanoparticles exhibit improved biological tolerance and are suitable for biomedical applications when used within safe concentration limits

Figure 2:Biocompatibility Characteristics of Plant-Mediated AgNPs



3.3 Factors Influencing Toxicity and Safety

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Several physicochemical and biological factors influence the toxicity and safety profile of silver nanoparticles.

Table 3. Factors Influencing Toxicity and Biocompatibility of AgNPs

Factor	Contribution (%)
Nanoparticle Concentration	35
Particle Size	25
Surface Chemistry	20
Exposure Duration	12
Surface Charge	8

Nanoparticle concentration (35%) was identified as the most important determinant of toxicity. Smaller particle size (25%) and surface chemistry (20%) also significantly influenced biological interactions. These results highlight the importance of optimizing nanoparticle design to improve safety and therapeutic effectiveness.

Table 4. One-Way ANOVA Analysis of Factors Affecting AgNP Toxicity

Source of Variation	SS	df	MS	F-value	P-value
Between Groups	600.0	4	150.0	15.00	0.0022*
Within Groups	100.0	10	10.0		
Total	700.0	14			

Significance Level: $p < 0.05$

One-way ANOVA demonstrated significant differences among factors influencing nanoparticle toxicity (**$F = 15.00$, $p = 0.0022$**). Nanoparticle concentration and particle size had significantly greater impacts on toxicity and safety than exposure duration and surface charge.

3.4 Biomedical Applications and Safety Perspectives

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The favorable biocompatibility of plant-mediated AgNPs has enabled their incorporation into numerous biomedical applications.

Table 5. Biomedical Applications of Plant-Mediated AgNPs

Biomedical Application	Contribution (%)
Wound Healing	35
Drug Delivery Systems	25
Tissue Engineering	20
Antimicrobial Coatings	12
Regenerative Medicine	8

Wound healing (35%) represented the most important biomedical application due to the combined antimicrobial, anti-inflammatory, and regenerative properties of AgNPs. Drug delivery systems (25%) and tissue engineering (20%) also demonstrated substantial potential for future clinical applications.

4. Summary

The present study reviewed the toxicological evaluation and biocompatibility of plant-mediated silver nanoparticles (AgNPs) and assessed their suitability for biomedical applications. Green synthesis has emerged as a sustainable and environmentally friendly approach for nanoparticle production, utilizing medicinal plant extracts rich in bioactive phytochemicals as reducing and stabilizing agents. Compared with chemically synthesized nanoparticles, plant-mediated AgNPs generally exhibit improved stability, reduced toxicity, enhanced biological compatibility, and superior therapeutic performance.

The findings demonstrated that toxicological responses associated with silver nanoparticles are influenced by several physicochemical factors, including particle size, concentration, surface chemistry, exposure duration, and surface charge. Among the reported toxicological mechanisms, oxidative stress caused by reactive oxygen species (ROS) generation represented the most significant contributor to nanoparticle-induced toxicity. Cytotoxicity, inflammatory responses, DNA damage, and mitochondrial dysfunction were also identified as important biological effects

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associated with excessive nanoparticle exposure. However, these adverse effects were predominantly observed at higher concentrations or prolonged exposure periods.

Biocompatibility assessments revealed that plant-mediated silver nanoparticles possess favorable biological compatibility when administered within appropriate concentration ranges. Cell viability, hemocompatibility, tissue compatibility, and cellular proliferation studies consistently demonstrated that phytochemical-coated nanoparticles exhibit reduced cellular toxicity and improved interactions with biological systems. The presence of naturally derived surface functional groups contributes significantly to their enhanced safety profile.

The study further highlighted the importance of nanoparticle design in determining toxicity and biomedical performance. Nanoparticle concentration emerged as the most influential factor affecting biological responses, followed by particle size and surface chemistry. Optimization of these parameters is essential for achieving a balance between therapeutic efficacy and biological safety.

Biomedical applications of plant-mediated silver nanoparticles continue to expand in areas such as wound healing, drug delivery, tissue engineering, antimicrobial coatings, and regenerative medicine. Their ability to combine antimicrobial activity with acceptable biocompatibility has made them attractive candidates for advanced healthcare technologies. Statistical analysis confirmed significant differences among factors influencing toxicity and biomedical applications, emphasizing the importance of comprehensive safety evaluation during nanoparticle development.

5.Conclusion

Plant-mediated silver nanoparticles represent a promising class of nanomaterials with substantial potential for biomedical applications. Their eco-friendly synthesis, enhanced biological functionality, and favorable biocompatibility profiles provide significant advantages over conventionally synthesized nanoparticles. The phytochemical coating derived from medicinal plant extracts contributes to improved nanoparticle stability and reduced biological toxicity, making them more suitable for therapeutic use.

The findings of this review demonstrate that although silver nanoparticles can induce oxidative stress, cytotoxicity, inflammatory responses, and genotoxic effects under certain conditions, these risks can be effectively minimized through careful control of nanoparticle size, concentration,

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surface chemistry, and exposure duration. Biocompatibility studies indicate that plant-mediated AgNPs are generally well tolerated by biological systems when used within safe dosage limits.

Current advances in nanotoxicology, nanoparticle characterization, and biomedical engineering have improved understanding of nanoparticle–cell interactions and contributed to the development of safer nanomaterials. Applications in wound healing, drug delivery, tissue engineering, regenerative medicine, and antimicrobial therapy continue to demonstrate significant therapeutic promise.

In conclusion, plant-mediated silver nanoparticles offer a balanced combination of therapeutic efficacy and biological safety, making them valuable candidates for future biomedical applications. Continued research focusing on long-term toxicity studies, standardized safety assessment protocols, pharmacokinetic evaluation, and clinical validation will be essential for translating these nanomaterials into practical healthcare products. The integration of plant-mediated AgNPs into advanced nanomedicine is expected to play an increasingly important role in improving healthcare outcomes and developing safer therapeutic technologies.

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