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A REVIEW ON NANOTECHNOLOGY-DRIVEN GREEN SYNTHESIS OF SILVER NANOPARTICLES USING NIGELLA SATIVA

Narrative Review

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ABSTRACT

Background: Nanotechnology has revolutionized modern science by enabling the synthesis of nanoparticles with unique physicochemical properties. Among these advancements, green synthesis using plant-based resources has gained significant attention for being eco-friendly and cost-effective. *Nigella sativa* (black seed), known for its rich bioactive compounds like alkaloids, flavonoids, and phenolics, has traditionally been used for treating various ailments.

Body: This review focuses on the green synthesis of silver nanoparticles (AgNPs) using *Nigella sativa* as a nanotechnology-driven resource. The process leverages plant extracts to produce AgNPs, showcasing reduced toxicity and environmental impact compared to conventional physical and chemical methods. Key topics include the historical evolution of nanotechnology, top-down and bottom-up synthesis approaches, and the superior antimicrobial and biomedical applications of AgNPs due to their high surface area to volume ratio. The potential of *N. sativa* in producing nanomaterials highlights its importance in sustainable nanotechnology for diagnostics, antimicrobial therapies, and other applications.

Conclusion: The incorporation of nanotechnology and green synthesis has positioned *Nigella sativa* as a promising resource for environmentally safe and biocompatible nanoparticle synthesis. Its role in modern science underscores its potential in addressing global challenges in medicine and environmental management.

Keywords: Antimicrobial therapies, Green synthesis, Nanotechnology, *Nigella sativa*, Phenolic compounds, Silver nanoparticles, Sustainable nanotechnology.

INTRODUCTION

The exploration of medicinal plants has been integral to healthcare systems for centuries, providing a natural reservoir of therapeutic agents. Historically, numerous drugs have been derived from botanical sources, particularly those containing secondary metabolites such as alkaloids, flavonoids, saponins, and terpenoids. These bioactive compounds exhibit significant activity against a broad spectrum of microorganisms, making them essential in combating infectious diseases (1). Among these plants, *Nigella sativa*—commonly known as black seed—has garnered substantial attention for its extensive therapeutic potential(2, 3).

Nigella sativa, belonging to the family Ranunculaceae, is often referred to as a "miracle plant" due to its diverse medicinal properties and strong historical, cultural, and religious significance. Its therapeutic importance is emphasized in Islamic traditions, where it is hailed as a remedy for all ailments except death, as highlighted in a prophetic hadith (4). The black seeds of *N. sativa*, frequently mentioned in traditional medicine, are lauded for their remarkable healing attributes and are an integral part of Tibbe-Nabwi practices. These seeds, often termed "blessing seeds," are rich in bioactive compounds such as polyunsaturated fatty acids (PUFA), alkaloids, and phenolics, contributing to their potent antioxidant properties(5, 6).

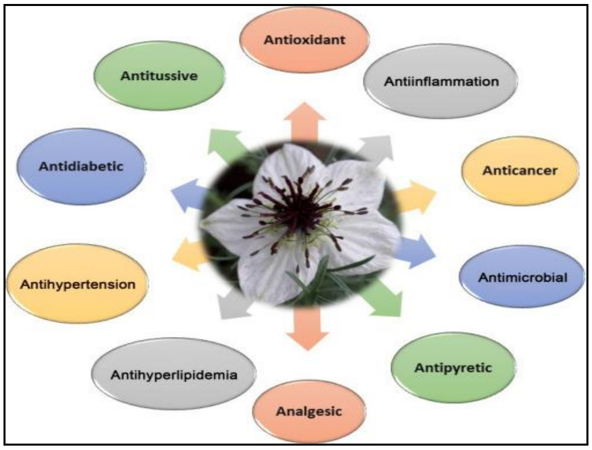
Globally, the reliance on medicinal plants for healthcare remains significant, with the World Health Organization estimating that up to 80% of the population depends on conventional herbal remedies. Plants like *N. sativa* not only serve as rich biosources of therapeutic agents but also play a vital role as pharmaceutical intermediates and nutritional supplements. The historical use of *N. sativa* is well-documented; for instance, Pliny the Elder noted its use in treating snake and scorpion bites as early as the first century A.D. (7). Modern pharmacopoeias also recognize its potential, recommending powdered *N. sativa* for alleviating gastrointestinal issues and improving digestion. Additionally, the seeds are widely employed in folk medicine across regions like Algeria for managing hyperglycemia and hypertension (8-10).

Contemporary research underscores the pharmacological versatility of *N. sativa*, demonstrating efficacy against a range of pathogens, including bacteria, viruses, fungi, and parasites. Its antioxidant and anti-inflammatory properties further enhance its reputation as a therapeutic agent. This makes *N. sativa* particularly relevant in addressing the growing challenge of microbial resistance, where advanced microorganisms have outpaced traditional antibiotics. The increasing prevalence of drug-resistant infections underscores the need for alternative antimicrobial agents derived from plants(11-13).

The wide-ranging uses of *N. sativa* extend beyond antimicrobial activity. Its wooden stem is employed in jaundice treatments, while its seeds are utilized for managing cardiovascular, gastrointestinal, and lactation-related issues. Traditional applications also include its use as herbal tea, porridge, or even a painkiller, demonstrating its adaptability and significance in diverse healthcare systems. The seeds and leaves, enriched with alkaloids, terpenes, and phenolics, remain the most studied components of the plant due to their extensive therapeutic potential. However, variability in the bioactive compound composition has been observed across different *N. sativa* samples, attributed to factors such as geographic location, cultivation conditions, plant part, and extraction techniques(13-15).

Despite a surge in studies exploring the pharmacological properties and chemical composition of *N. sativa*, gaps remain in standardizing its therapeutic applications. Variations in bioactive compound concentrations and extraction methods pose challenges in fully harnessing its potential. Nevertheless, the increased focus on medicinal plants as alternative therapeutic agents makes this an opportune time to review the advancements in *N. sativa* research. By synthesizing current findings, this review aims to highlight the plant's significance and pave the way for its further integration into modern medicine(15, 16).

Thus, the growing interest in nanotechnology-driven applications, including green synthesis of silver nanoparticles using *N. sativa*, represents a promising frontier. These approaches leverage the plant's bioactive compounds for innovative solutions in healthcare, particularly in combating antimicrobial resistance. By examining these advancements, this review seeks to provide valuable insights into the multifaceted applications of *N. sativa*, emphasizing its role in bridging traditional and modern therapeutic practices(17, 18).



BODY

Nanotechnology and Its Evolution

Nanotechnology, an interdisciplinary field that bridges physics, chemistry, biology, and material sciences, has revolutionized various industries, including pharmaceuticals, biotechnology, and materials engineering. By manipulating materials at the molecular level, nanotechnology facilitates the creation of novel nanostructures with unique properties that offer wide-ranging applications. These include advancements in medicine, energy, agriculture, and environmental management (19). As a burgeoning discipline, nanotechnology has shown immense potential for addressing complex challenges in healthcare and diagnostics, thus paving the way for futuristic treatment strategies(20, 21).

The foundation of nanotechnology lies in its nanoscale precision, where materials are manipulated at dimensions as small as 1 to 100 nanometers. The term "nanotechnology" was first introduced by Professor Norio Taniguchi in 1974, referring to the precise fabrication of substances at the nanoscale. Later, Eric Drexler popularized the concept in his seminal work *Engines of Creation: The Coming Era of Nanotechnology* (1986), which envisioned a transformative role for nanotechnology in science and society(22, 23).

Despite being hailed as a contemporary breakthrough, nanotechnology's principles can be traced back to antiquity. Mesopotamian craftsmen applied nanoscale techniques in the ninth century to create shimmering effects on pottery. In 1857, Michael Faraday provided the first scientific description of the optical properties of nanometric metals, marking a milestone in the formal understanding of nanomaterials. Modern developments in nanotechnology have garnered significant global attention, with nations like Japan and the United States investing heavily in research and development programs to explore its vast potential(24, 25).

Role of Nanotechnology in Green Synthesis

Nanotechnology plays a pivotal role in the green synthesis of nanoparticles, offering eco-friendly and cost-effective alternatives to traditional methods. Conventional chemical and physical synthesis techniques for nanoparticles, although efficient in producing large quantities, often involve toxic chemicals and are resource-intensive. Green synthesis methods, in contrast, utilize biological resources such as plant extracts, fungi, and bacteria, thus mitigating environmental hazards (26, 27).

Goyal (2017) highlighted that nanotechnology enables the creation of nanoscale materials for disease diagnosis, treatment, and monitoring, while also being instrumental in the fabrication of nanosensors. Biologically mediated nanoparticle synthesis is considered a safer and more sustainable approach compared to chemically derived nanoparticles, which often have associated side effects. This has led to a surge in interest in biogenic synthesis techniques, particularly for producing metal nanoparticles like silver (Ag) and gold (Au), which are widely regarded as biocompatible and effective (28, 29).

Plant-Mediated Synthesis of Nanoparticles

Among biological methods, plant-mediated synthesis has emerged as a prominent technique for nanoparticle production. Plants are non-pathogenic, readily available, and inherently sustainable, making them ideal for large-scale nanoparticle synthesis. Abdelghany et al. (2018) emphasized that biogenic synthesis using plants offers advantages such as reduced failure rates and simpler characterization processes compared to chemical and physical methods. Additionally, plant-based synthesis requires fewer hazardous reagents and produces nanoparticles in an environmentally friendly manner(30, 31).

Various medicinal plants have been used for synthesizing metallic nanoparticles. For example, silver nanoparticles (AgNPs) synthesized using plant extracts exhibit exceptional antibacterial and antifungal properties, making them highly desirable for biomedical applications. The green synthesis process typically involves reacting a metal salt solution with a specific aqueous plant extract under controlled conditions, allowing nanoparticle formation within minutes or hours. This process not only minimizes chemical waste but also enhances the stability of the synthesized nanoparticles (32, 33).

Metallic Nanoparticles

Metal nanoparticles, particularly those composed of silver, gold, platinum, and copper, have garnered attention for their unique physicochemical properties and wide applicability in bio-nanomaterial production. Silver nanoparticles (AgNPs) stand out among these due to their remarkable antimicrobial activity, even at low concentrations, and their biocompatibility (34). McGillicuddy et al. (2017) estimated that approximately 320 tonnes of silver nanoparticles are produced annually for applications ranging from medical imaging to biosensors and food packaging(33, 35).

The nanoscale size of AgNPs results in a high surface-to-volume ratio, enhancing their reactivity and enabling their use in diverse medical practices. AgNPs have been extensively studied for their roles in drug delivery, diagnostic imaging, molecular diagnostics, wound healing, and surgical applications. Their relatively low cytotoxicity and immunogenicity further solidify their position as a preferred nanomaterial for therapeutic purposes(34, 36).

Approaches and Methods for Nanoparticle Synthesis

Nanoparticles can be synthesized through two primary approaches: the top-down approach and the bottom-up approach. The top-down approach involves physically breaking down bulk materials into nanoscale particles using techniques such as ball milling, laser ablation, and evaporation-condensation. While effective, these methods often generate significant waste and are less environmentally friendly(37, 38).

The bottom-up approach, on the other hand, involves assembling nanoparticles from atomic or molecular precursors. This method includes chemical reduction, photochemical synthesis, and biogenic synthesis using biological entities such as plants, fungi, or enzymes. The bottom-up approach is widely favored for its ability to produce uniform nanoparticles with minimal waste and greater control over size and shape (29, 39).

Methods for Nanoparticle Synthesis

Nanoparticle synthesis can be broadly categorized into physical, chemical, and biological methods:

1. **Physical Methods**
   Physical techniques rely on processes such as material erosion, evaporation, and condensation to produce nanoparticles. These methods often yield uniform-sized particles with narrow size distributions but are associated with high energy consumption and significant waste production, making them less sustainable.
2. **Chemical Methods**
   Chemical methods involve the reduction of metal ions into nanoparticles using chemical reagents. While these methods are efficient, they often require toxic substances that pose environmental and biological risks. Moreover, the high costs associated with chemical reagents limit their scalability.
3. **Biological Methods (Green Approach)**
   Green synthesis methods utilize biological entities like plants, fungi, bacteria, and enzymes to produce nanoparticles. These methods are gaining prominence for their eco-friendliness, cost-effectiveness, and ability to produce biocompatible nanoparticles. For instance, plant extracts act as both reducing and stabilizing agents, eliminating the need for hazardous chemicals. This approach has shown promise in producing silver and gold nanoparticles, which are widely used in biomedical and environmental applications (24, 40).

Silver Nanoparticles

Silver nanoparticles (AgNPs) are among the most widely studied and utilized nanomaterials due to their exceptional antimicrobial properties and biocompatibility. Their high surface-to-volume ratio enhances their reactivity, allowing effective interaction with bacterial membranes and inhibiting microbial growth, even at low concentrations. AgNPs are also economically viable, with minimal cytotoxic effects, making them suitable for medical and industrial applications(37).

In healthcare, AgNPs have been employed in wound dressings, surgical meshes, and drug delivery systems. Their potential in diagnostic imaging and molecular testing has further expanded their applications. Beyond medicine, AgNPs are utilized in the food industry for packaging and preservation, highlighting their versatility as a nanomaterial(37).

Emerging Trends and Challenges

While the potential of nanotechnology in green synthesis is vast, several challenges remain. The variability in plant-based synthesis, influenced by factors such as plant species, growth conditions, and extraction methods, can lead to inconsistencies in nanoparticle properties. Additionally, the scalability of green synthesis methods and their integration into industrial applications require further research. Nevertheless, the growing emphasis on eco-friendly and sustainable technologies continues to drive innovation in nanotechnology. By combining advancements in green synthesis with a deeper understanding of plant-mediated processes, researchers can unlock new possibilities for developing biocompatible and environmentally friendly nanomaterials(34, 36).

Nanotechnology has established itself as a transformative force in science and medicine. Its integration with green synthesis techniques not only addresses environmental concerns but also opens new avenues for innovation in healthcare, diagnostics, and beyond. Silver nanoparticles, in particular, exemplify the immense potential of nanotechnology in addressing global challenges, from antimicrobial resistance to sustainable development(33).

Table: Methods for Synthesis of Nanoparticles

Synthesis of Nanoparticle

Bottom-up approach		**Top-down approach**
Green method	**Chemical method**	**Physical method**
Bacteria	Chemical reduction	Evaporation condensation
Fungi	Photochemical	Ball milling
Plants and their extracts	Electrochemical	Pulse laser ablation
Yeast	Sonochemical	Pulse wire discharge
Enzymes and biomolecules	Microemulsion	Lithography

CONCLUSION

In conclusion, nanotechnology, particularly green synthesis, has revolutionized biomedical and environmental applications. Plant-mediated methods, like those using *Nigella sativa*, offer eco-friendly, cost-effective solutions for synthesizing nanoparticles such as silver. With immense potential in medicine and industry, continued research into sustainable nanotechnological approaches will drive innovation and address global challenges effectively.

Authors' Contribution

Author	Contribution
Fiza Perveen	Substantial Contribution to study design, analysis, acquisition of Data Manuscript Writing Has given Final Approval of the version to be published
Asad Rehman	Substantial Contribution to study design, acquisition and interpretation of Data Critical Review and Manuscript Writing Has given Final Approval of the version to be published
Farmn Ullah	Substantial Contribution to acquisition and interpretation of Data Has given Final Approval of the version to be published
Haidar Zaman	Contributed to Data Collection and Analysis Has given Final Approval of the version to be published
Waseem Abbas	Contributed to Data Collection and Analysis Has given Final Approval of the version to be published

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