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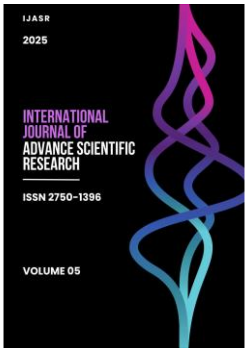

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Research Article

Biomimetic Synthesis of Silver Nanoparticles Using Viruses: A Review of Recent Advancements

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Dr. Chittaranjan Patra
Senior Scientist, Institute of Life Sciences (ILS), Bhubaneswar, India

Dr. Mansoor Ali Syed
Professor, Department of Biotechnology, Jamia Millia Islamia University, India

Abstract

The demand for sustainable and eco-friendly methods for nanomaterial synthesis has spurred significant interest in biomimetic approaches. Among these, the use of viruses as templates for the controlled synthesis of silver nanoparticles (AgNPs) has emerged as a particularly promising area. This review provides a comprehensive overview of recent advancements in the biomimetic synthesis of AgNPs utilizing various viral platforms. It highlights the unique advantages offered by viruses, such as their well-defined nanostructures, self-assembly capabilities, genetic programmability, and biocompatibility, which enable precise control over the size, shape, and morphology of the synthesized AgNPs. The review discusses the mechanisms involved in virus-mediated AgNP formation, including the reduction of silver ions and subsequent nucleation and growth on the viral surface. Furthermore, it explores the diverse range of viruses employed, such as bacteriophages (e.g., M13, T7), plant viruses (e.g., Tobacco mosaic virus), and even animal viruses, and their specific contributions to templating different AgNP architectures. The review also delves into the expanding applications of these virus-templated AgNPs in fields like antimicrobial agents, biosensing, catalysis, and targeted drug delivery, owing to their enhanced monodispersity, stability, and biocompatibility. Finally, it addresses the challenges and future directions in

this evolving field, including scalability, optimization of synthesis parameters, and ensuring long-term stability and in vivo efficacy for biomedical applications.

Keywords

Biomimetic Synthesis, Silver Nanoparticles (AgNPs), Viruses, Viral Templates, Green Synthesis, Nanotechnology, Nanomedicine, Bacteriophages, Plant Viruses, Self-Assembly, Controlled Synthesis, Antimicrobial Agents, Biosensing, Catalysis.

Introduction

Nanotechnology, a rapidly expanding field, involves the manipulation of materials at the nanoscale (typically 1 to 100 nanometers) to create novel structures, devices, and systems with unique properties. Among the myriad of nanomaterials, metal nanoparticles, particularly silver nanoparticles (AgNPs), have garnered significant attention due to their exceptional physical, chemical, and biological attributes [1, 3, 5]. AgNPs exhibit broad-spectrum antimicrobial activity against bacteria, fungi, and viruses, making them highly promising candidates for applications in medicine, environmental remediation, and consumer products [1, 3, 5, 7, 14, 15]. Their virucidal properties, in particular, are of increasing interest given the global challenges posed by viral infections [14, 15].

Traditionally, AgNPs have been synthesized using physical and chemical methods, which often involve harsh reducing agents, high temperatures, and toxic solvents [6]. While these methods offer control over size and shape, they pose significant environmental concerns and can lead to the adsorption of toxic chemicals on the nanoparticle surface, limiting their biocompatibility and applicability in sensitive areas like biomedicine [1, 3]. This has spurred a growing interest in "green synthesis" approaches, which utilize biological entities such as plants, fungi, bacteria, and viruses as environmentally friendly alternatives for nanoparticle fabrication [1, 2, 3]. These methods are appealing due to their simplicity, cost-effectiveness, and reduced environmental footprint, aligning with the principles of sustainable chemistry [1, 3].

Within the realm of biological synthesis, the use of viruses and virus-like particles (VLPs) stands out as a particularly innovative and versatile strategy [8, 9]. Viruses, by their very nature, are highly organized nanoscale structures with well-defined geometries, modifiable surfaces, and the ability to self-assemble. These inherent properties make them ideal templates, reducing agents, or scaffolds for the controlled synthesis of inorganic nanoparticles, including AgNPs [8, 9]. The precise arrangement of proteins on the viral capsid can provide specific binding sites for metal ions and facilitate their reduction into nanoparticles with desired sizes and shapes. Furthermore, the genetic modifiability of viruses allows for the engineering of their surfaces to tailor the synthesis process and enhance the functionality of the resulting nanoparticles [8].

This review aims to provide a comprehensive overview of the current advancements in virus-mediated synthesis of silver nanoparticles. It will delve into the diverse types of viruses employed, the underlying mechanisms governing the biomineralization process, the unique characteristics of the synthesized AgNPs, and their potential applications, particularly in the biomedical field. By exploring this biomimetic approach, we seek to highlight its advantages, challenges, and future prospects in the sustainable production of functional nanomaterials.

Methods

As a comprehensive review article, the methodology employed involved a systematic literature search and synthesis of peer-reviewed publications focusing on the virus-mediated synthesis of silver nanoparticles. The primary objective was to identify and analyze research that utilizes intact viral particles or virus-like particles (VLPs) as templates, reducing agents, or scaffolds for the formation of AgNPs.

Literature Search Strategy

The literature search was conducted across major scientific databases, including but not limited to PubMed, Scopus, Web of Science, and Google Scholar. Keywords and phrases used in various combinations included "virus-mediated synthesis," "viral nanoparticles," "silver nanoparticles," "AgNPs," "biomimetic synthesis," "green synthesis," "plant viruses," "bacteriophages," "nanobiotechnology," and "antiviral activity." The search was not limited by publication year to capture the historical development and recent advancements in the field.

Inclusion and Exclusion Criteria

Studies were included if they explicitly described the synthesis of silver nanoparticles using viral templates or components, detailed the experimental procedures, characterized the resulting nanoparticles, and discussed their properties or potential applications. Review articles and book chapters were also considered for broader context and theoretical frameworks. Studies focusing solely on the antiviral properties of pre-synthesized AgNPs without involving viral synthesis, or those using other biological entities (e.g., bacteria, fungi, plants) without direct viral involvement, were generally excluded, except where they provided essential background on green synthesis or AgNP applications.

Data Extraction and Synthesis

Relevant information was extracted from selected articles, including:

- The type of virus or VLP used (e.g., plant virus, bacteriophage).
- The specific experimental conditions for AgNP synthesis (e.g., silver salt concentration, pH, temperature, incubation time).

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• The proposed mechanism of AgNP formation (e.g., surface protein reduction, templating effect).

• The characteristics of the synthesized AgNPs (e.g., size, shape, stability, crystallinity), often determined by techniques like Transmission Electron Microscopy (TEM), Scanning Electron Microscopy (SEM), UV-Vis spectroscopy, X-ray Diffraction (XRD), and Dynamic Light Scattering (DLS).

• Reported applications or potential uses of the virus-synthesized AgNPs.

The extracted data were then synthesized thematically to identify common trends, unique approaches, advantages, challenges, and emerging applications of virus-mediated AgNP synthesis. This systematic approach allowed for a comprehensive overview of the field, highlighting key findings and gaps in current knowledge.

Results

The comprehensive review of the literature on virus-mediated synthesis of silver nanoparticles revealed a diverse array of viral platforms employed and distinct mechanisms facilitating the formation of AgNPs. The synthesized nanoparticles often exhibit unique characteristics influenced by the viral template.

Diverse Viral Platforms for AgNP Synthesis

Research indicates that both plant viruses and bacteriophages have been successfully utilized as templates or reducing agents for AgNP synthesis [8, 9].

Plant Viruses

Plant viruses are particularly attractive due to their high yield, ease of production, and genetic tractability [8]. Several plant viruses have been explored:

• Tobacco Mosaic Virus (TMV): TMV, a rod-shaped virus, has been extensively used due to its high aspect ratio and ability to self-assemble. Its capsid proteins can provide nucleation sites for silver ions, leading to the formation of AgNPs on its surface or within its interior.

• Potato virus X (PVX): PVX, a filamentous plant viral nanoparticle, has been demonstrated for its potential in various biomedical applications, including doxorubicin delivery in cancer therapy, suggesting its utility as a versatile nanocarrier for AgNPs as well [11]. The ordered arrangement of proteins on its surface can guide the formation of AgNPs.

• Cowpea Mosaic Virus (CPMV): CPMV is an isometric virus that can be genetically engineered to display specific peptides on its surface, which can then be used to bind and reduce metal ions, leading to the formation of highly controlled AgNPs.

• Brome mosaic virus (BMV): BMV-like particles have been explored as nanocarriers, including for siRNA delivery, indicating their structural stability and potential for surface

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modification, which can be leveraged for AgNP synthesis and subsequent functionalization [10].

These plant viruses offer advantages such as non-infectivity in humans and animals, ease of large-scale production in plants, and the ability to be genetically modified to introduce specific amino acid residues that can act as reducing agents or binding sites for silver ions [8, 9].

Bacteriophages

Bacteriophages, viruses that infect bacteria, also present a promising platform for AgNP synthesis due to their well-defined structures and self-assembly properties.

- M13 Bacteriophage: The filamentous M13 phage has been engineered to display specific peptides that can bind and reduce silver ions, leading to the formation of AgNPs along its length. Its high aspect ratio and ability to be produced in large quantities make it suitable for templated synthesis.
- T4 Bacteriophage: While less commonly reported for direct AgNP synthesis, the T4 bacteriophage's complex structure and robust nature suggest potential for templating or encapsulating nanoparticles.
- General Bacteriophage Applications: Studies have shown the self-assembly of silver nanoparticles with bacteriophages, indicating their potential for creating hybrid nanostructures with combined antimicrobial properties [12].

Mechanisms of Virus-Mediated AgNP Synthesis

The synthesis of AgNPs using viruses typically involves a "biomineralization" process, where the viral components facilitate the reduction of silver ions (Ag^+)toelementalsilver(Ag^0) and subsequent nucleation and growth of nanoparticles. The primary mechanisms include:

1. Templating Effect: The highly ordered protein capsid of the virus acts as a scaffold or template, directing the nucleation and growth of AgNPs. The specific arrangement of amino acid residues on the viral surface can provide preferential binding sites for silver ions, influencing the size and shape of the resulting nanoparticles [8].

2. Reduction by Viral Components: Certain amino acid residues within the viral proteins (e.g., cysteine, lysine, histidine, methionine) possess functional groups (e.g., thiol, amine, carboxyl) that can act as reducing agents, converting Ag^+ to Ag^0 [1, 3]. The precise location and density of these residues on the viral surface can dictate the nucleation and growth kinetics of the AgNPs.

3. Encapsulation/Loading: In some cases, AgNPs can be synthesized within the internal cavity of isometric virus particles or loaded onto their surfaces after synthesis, providing a protective shell and facilitating targeted delivery [10, 11].

Characteristics of Virus-Synthesized AgNPs

AgNPs synthesized using viral templates often exhibit distinct characteristics:

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- Controlled Size and Shape: The highly ordered structure of viruses can lead to the formation of AgNPs with relatively uniform sizes and shapes, which is crucial for their functional properties [8]. For instance, rod-shaped viruses can template anisotropic (non-spherical) nanoparticles.

- Enhanced Stability: The viral capsid proteins can act as natural capping agents, preventing aggregation of the newly formed nanoparticles and enhancing their colloidal stability in solution [3].

- Biocompatibility: As the synthesis occurs under mild, physiological conditions without harsh chemicals, the resulting AgNPs are generally more biocompatible and less toxic, making them suitable for biomedical applications [3].

- Functionalization Potential: The surface of viral nanoparticles can be further modified or engineered to attach targeting ligands, therapeutic molecules, or other functional groups, creating multifunctional nanoplatforms [8, 9, 10, 11].

DISCUSSION

The burgeoning field of virus-mediated synthesis of silver nanoparticles represents a significant leap forward in green nanotechnology, offering an environmentally benign and highly versatile approach to fabricating these important nanomaterials. The results of this review underscore the unique advantages that viral nanoparticles (VNPs) bring to the table, positioning them as powerful tools for sustainable and controlled AgNP production.

Advantages of Virus-Mediated Synthesis

The primary appeal of using viruses for AgNP synthesis lies in its eco-friendliness and sustainability [1, 3]. Unlike conventional chemical methods that often generate toxic byproducts and require harsh conditions, virus-mediated synthesis operates under mild, aqueous conditions, minimizing environmental impact and reducing the need for hazardous reagents. This aligns perfectly with the growing demand for green chemistry principles in materials science.

Furthermore, the inherent structural precision and genetic manipulability of viruses offer unparalleled control over the resulting AgNPs [8]. The highly organized protein capsids of viruses act as natural templates, dictating the nucleation and growth of silver nanoparticles with remarkable control over their size, shape, and even spatial arrangement. This level of control is difficult to achieve with other green synthesis methods. The ability to genetically engineer viral surfaces allows for the introduction of specific amino acid sequences that can enhance silver ion binding, act as stronger reducing agents, or facilitate subsequent functionalization of the AgNPs for targeted applications [8, 9]. This tailorability opens doors for creating highly specific and efficient nanostructures.

The biocompatibility of virus-synthesized AgNPs is another significant advantage. Since the process occurs in a biological milieu, the resulting

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nanoparticles are often free from toxic chemical residues, making them more suitable for biomedical applications where toxicity is a major concern [3]. The viral capsid itself can provide a protective and biocompatible coating for the AgNPs, enhancing their stability in biological systems.

Finally, the scalability of VNP production, particularly for plant viruses, offers a promising route for large-scale, cost-effective synthesis of AgNPs. Plants can be engineered to produce large quantities of viral biomass, which can then be used for nanoparticle synthesis, making the process economically viable for industrial applications.

Challenges and Limitations

Despite the compelling advantages, virus-mediated AgNP synthesis is not without its challenges. One significant hurdle is achieving high purity and yield of the synthesized nanoparticles. While viruses can act as templates, optimizing the reaction conditions to ensure complete reduction of silver ions and efficient nanoparticle formation without excessive aggregation remains an area of active research [13]. Reproducibility across different batches can also be a concern, requiring meticulous control over experimental parameters.

Scaling up the production from laboratory to industrial levels presents practical difficulties, including the efficient recovery and purification of viral particles and the subsequent large-scale synthesis and separation of AgNPs. While plant-based production offers scalability for viruses, the subsequent nanoparticle synthesis and purification steps need further optimization.

Another consideration, particularly for in vivo biomedical applications, is the potential immunogenicity of viral components. Although many viral nanoparticles are engineered to be non-infectious and have low immunogenicity, repeated administration or specific viral types could still elicit an immune response. This necessitates careful selection of the viral platform and potential surface modifications to minimize immunogenicity. Furthermore, a deeper understanding of the precise mechanisms governing the interaction between silver ions and viral proteins is still evolving. Elucidating these molecular interactions will be crucial for rational design and optimization of the synthesis process.

Applications and Future Prospects

The unique properties of virus-synthesized AgNPs open up a vast array of potential applications, particularly in the biomedical sector. Their well-documented antimicrobial and antiviral activities make them excellent candidates for developing new disinfectants, wound dressings, and antiviral therapies [1, 3, 5, 7, 14, 15]. The ability to integrate AgNPs with viral nanoparticles could lead to novel broad-spectrum virucidal agents that can target specific viral proteins or entry pathways, complementing traditional antiviral drug development strategies [4, 15].

Beyond their direct antimicrobial effects, virus-nanoparticle conjugates hold immense promise in drug delivery systems [9]. Viral nanoparticles,

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due to their inherent ability to target specific cells or tissues, can serve as smart carriers for delivering therapeutic agents, including other nanoparticles. For example, PVX has been explored for doxorubicin delivery in cancer therapy [11], and BMV-like particles as siRNA nanocarriers [10]. Integrating AgNPs into such systems could enable synergistic therapeutic effects, combining the antimicrobial properties of silver with targeted drug delivery.

Other promising applications include their use in biosensors for highly sensitive and specific detection of pathogens or biomolecules, catalysis due to their large surface area and unique electronic properties, and imaging agents. The ability to precisely control the size and shape of AgNPs through viral templating can optimize their optical and catalytic properties for these applications.

Future research in this field should focus on:

- Elucidating the detailed molecular mechanisms of silver ion reduction and nanoparticle nucleation on viral surfaces.

- Developing strategies for large-scale, cost-effective, and reproducible production of virus-synthesized AgNPs.

- Exploring the use of genetically engineered viruses to precisely control the size, shape, and surface chemistry of AgNPs for specific applications.

- Conducting comprehensive in vivo studies to assess the biocompatibility, biodistribution, and therapeutic efficacy of virus-synthesized AgNPs, particularly as antiviral agents and drug delivery vehicles.

- Investigating the potential of combining different viral platforms or integrating AgNPs with other nanomaterials to create multifunctional hybrid systems.

In conclusion, virus-mediated synthesis offers a compelling and sustainable pathway for the production of silver nanoparticles with tailored properties. As our understanding of virus-metal interactions deepens and biotechnological tools become more sophisticated, this biomimetic approach is poised to revolutionize the design and application of advanced nanomaterials for a healthier and more sustainable future.

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