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Biomedical Applications of *Caulerpa chemnitzia* - Synthesized Silver Nanoparticles - A Review

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ABSTRACT

Silver nanoparticles have attracted substantial interest within the biomedical domain due to their wide-ranging applications, encompassing antimicrobial, anticancer, and drug delivery modalities. Green synthesis approaches, which utilize biological entities such as algae, present an environmentally sound and economically viable alternative to conventional chemical synthesis methods. This review centers on the production of AgNPs via the marine alga *Caulerpa chemnitzia*, emphasizing its benefits as both a reducing and stabilizing agent.

Caulerpa chemnitzia-synthesized AgNPs have demonstrated promising antimicrobial activity against a range of bacterial and fungal pathogens. *In vitro* studies have shown their cytotoxic effects on various cancer cell lines, indicating potential anticancer applications(González-Lamothe *et al*., 2009). The review summarizes these findings, emphasizing the mechanisms of action involved in the observed biological activities.

This review aims to provide a comprehensive overview of the current state of research on *Caulerpa chemnitzia*-synthesized AgNPs(Dar *et al*., 2023). It covers the synthesis methods, characterization techniques, and biomedical applications of these nanoparticles. Furthermore, it addresses the challenges and future directions in the development of *Caulerpa chemnitzia*-synthesized AgNPs for clinical translation, including the need for optimization of green synthesis methods, surface modification, and thorough evaluation of biocompatibility and toxicity(Lalegani & Ebrahimi, 2020).

Introduction

Silver nanoparticles have garnered significant attention in recent years due to their unique physicochemical properties, which differ substantially from their bulk counterparts. These properties, including their large surface area-to-volume ratio and quantum confinement effects, make them highly attractive for a wide range of applications(Madawi *et al*., 2023). AgNPs exhibit remarkable optical, electrical, and thermal properties, leading to their incorporation into diverse fields such as electronics, catalysis, and sensing.(Lalegani & Ebrahimi, 2020)

The biomedical field, in particular, has witnessed a surge of interest in AgNPs (Ghaywat *et al*., 2021). Their potential applications span various areas, including:

Drug Delivery: AgNPs can be utilized as carriers for targeted drug delivery, enhancing therapeutic efficacy and reducing side effects.

Imaging: AgNPs can act as contrast agents for enhanced imaging in various diagnostic techniques.

Diagnostics: AgNPs can be incorporated into biosensors for rapid and sensitive detection of disease biomarkers.

Therapeutics: AgNPs themselves exhibit therapeutic properties, such as antimicrobial, anti-inflammatory, and anticancer activities.

Traditional methods for synthesizing AgNPs typically involve chemical and physical approaches. Chemical methods rely on the reduction of silver ions using chemical reducing agents, while physical methods involve techniques such as laser ablation or evaporation-condensation. However, these conventional methods often have significant limitations. They may require the use of toxic chemicals, generate hazardous byproducts, and consume large amounts of energy. These concerns have prompted researchers to explore more sustainable and environmentally friendly alternatives.

Green synthesis has emerged as a promising approach for producing AgNPs with reduced environmental impact. This method utilizes biological entities such as bacteria, fungi, algae, and plant extracts as reducing and stabilizing agents. Green synthesis offers several advantages over traditional methods, including:

Reduced Toxicity: Green synthesis avoids the use of harmful chemicals, resulting in AgNPs with lower toxicity.

Environmental Friendliness: The process is environmentally benign, minimizing pollution and waste generation.

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Cost-Effectiveness: Biological materials are often readily available and inexpensive.

Biocompatibility: Green-synthesized AgNPs often exhibit enhanced biocompatibility, making them suitable for biomedical applications.

Among the various biological resources employed in green synthesis, seaweed has gained considerable attention. Seaweed offers several advantages, including abundance, ease of handling, and the presence of diverse bioactive compounds. *Caulerpa chemnitzia*, a species of green algae, has demonstrated its potential as an effective source for the green synthesis of AgNPs (Sowbarnika *et al*., 2022) . *Caulerpa chemnitzia* contains a variety of reducing agents, such as polyphenols and polysaccharides, which facilitate the reduction of silver ions and the stabilization of the resulting AgNPs. Furthermore, *Caulerpa chemnitzia* is relatively easy to cultivate and harvest, making it a sustainable and cost-effective resource.

This review aims to comprehensively explore the biomedical applications of *Caulerpa chemnitzia*-synthesized AgNPs (Uwineza & Waśkiewicz, 2020). The focus will be on their *In vitro* and *In Vivo* activities, specifically their antimicrobial, cytotoxic, and anticancer properties. By examining the current state of research, this review seeks to highlight the potential of these green-synthesized AgNPs as promising candidates for future biomedical applications.

Green Synthesis of Silver Nanoparticles Using *Caulerpa chemnitzia*

This section will delve into the specifics of green synthesis of silver nanoparticles using the seaweed *Caulerpa chemnitzia*. We'll cover the entire process from seaweed preparation to characterization of the synthesized nanoparticles .

Process of Green Synthesis

Collection and Preparation of Seaweed Biomass

The initial step involves the collection of *Caulerpa chemnitzia* seaweed. It's important to identify the seaweed correctly and harvest it from a relatively unpolluted environment to minimize contamination. After collection, the seaweed needs to be thoroughly washed with distilled water to remove any epiphytes, sand, and salt .The washed biomass is then dried, either by sun-drying or using an oven at a low temperature (e.g., 40-60°C) to remove moisture. The dried seaweed is ground into a fine powder to increase the surface area for efficient extraction of bioactive compounds(Zia *et al*., 2020) .

Extraction of Bioactive Compounds

The extraction of bioactive compounds from *Caulerpa chemnitzia* is a crucial step, as these compounds act as reducing and stabilizing agents in the synthesis of AgNPs (Sasidharan *et al*., 2010). Several methods can be employed for extraction, including:

Aqueous Extraction: This is a simple and environmentally friendly method where the seaweed powder is mixed with distilled water and heated (e.g., 60-80°C) for a specific period (e.g., 30-60 minutes). The mixture is then filtered to obtain the extract containing the bioactive compounds .

Solvent Extraction: Organic solvents like ethanol, methanol, or acetone can be used to extract a wider range of compounds. The seaweed powder is soaked in the solvent for a specific time, followed by filtration and evaporation of the solvent to obtain the extract. The choice of solvent depends on the polarity of the target compounds (Geszke-Moritz & Moritz, 2024) .

Microwave-Assisted Extraction: This method uses microwave energy to enhance the extraction process, reducing the extraction time and solvent consumption.

Ultrasound-Assisted Extraction: UAE utilizes ultrasonic waves to disrupt the cell walls of the seaweed, facilitating the release of bioactive compounds.

Reaction Conditions

The reaction conditions play a significant role in determining the characteristics of the synthesized AgNPs. Key parameters include:

Temperature: The reaction temperature influences the rate of reduction and the size of the resulting AgNPs. Higher temperatures generally lead to faster reduction and smaller particle sizes. Temperatures typically range from room temperature to 90°C (Sowbarnika *et al*., 2022).

pH: The pH of the reaction mixture affects the activity of the reducing agents and the stability of the AgNPs. The optimal pH range may vary depending on the specific seaweed extract and the desired properties of the AgNPs.

Reaction Time: The reaction time determines the extent of silver ion reduction and the completion of AgNP formation. The optimal reaction time needs to be optimized to achieve the desired particle size and yield.

Silver Salt Concentration: The concentration of the silver salt precursor (e.g., silver nitrate, AgNO3) influences the size and shape of the AgNPs. Higher concentrations may lead to larger particle sizes and aggregation .The concentration needs to be optimized.

Mechanism of AgNP Formation

The green synthesis of AgNPs using *Caulerpa chemnitzia* involves a complex mechanism where bioactive compounds act as both reducing and stabilizing agents (Blasco-Navarro *et al*., 2025).

Role of Reducing Agents

Caulerpa chemnitzia contains various bioactive compounds, including polyphenols, polysaccharides, and other organic molecules (Lalegani & Ebrahimi, 2020).These compounds donate electrons to silver ions (Ag+) in the silver salt precursor, reducing them to silver atoms. The silver atoms then aggregate to form AgNP nuclei, which subsequently grow into larger particles. Polyphenols, with their multiple hydroxyl groups, are particularly effective reducing agents(Ghaywat *et al*., 2021) .

Stabilization of AgNPs

Stabilization is crucial to prevent aggregation of the AgNPs, which can lead to a loss of their unique properties. The bioactive compounds in *Caulerpa chemnitzia* also act as stabilizing agents by adsorbing onto the surface of the AgNPs, creating a protective layer that prevents them from clumping together .This stabilization can occur through electrostatic interactions or steric hindrance.

Characterization Techniques

After synthesis, it's essential to characterize the AgNPs to determine their properties .Common techniques include:

UV-Vis Spectroscopy: This technique is used to confirm the formation of AgNPs by detecting the surface plasmon resonance peak, which typically appears in the range of 400-500 nm for AgNPs. The position and intensity of the SPR peak depend on the size, shape, and concentration of the AgNPs (Lalegani & Ebrahimi, 2020) .

Transmission Electron Microscopy: TEM provides high-resolution images of the AgNPs, allowing for the determination of their size, shape, and morphology. TEM can also reveal the crystalline structure of the AgNPs (Liu *et al*., 2019) .

X-ray Diffraction: XRD is used to analyze the crystalline structure of the AgNPs. The XRD pattern reveals the presence of characteristic peaks corresponding to the crystalline planes of silver, confirming the formation of crystalline AgNPs.

Dynamic Light Scattering: DLS measures the particle size distribution and stability of the AgNPs in solution. DLS provides information on the average hydrodynamic size of the AgNPs and their tendency to aggregate (Geszke-Moritz & Moritz, 2024) .

Zeta Potential: Zeta potential measures the surface charge of the AgNPs, which is an indicator of their colloidal stability. High zeta potential values (positive or negative) indicate good stability, as the charged particles repel each other, preventing aggregation .

Factors Affecting the Properties of Caulerpa chemnitzia-Synthesized AgNPs

Several factors can influence the properties of the resulting AgNPs (Mehmood *et al*., 2018) :

Seaweed Species and Geographical Location: The species of seaweed and its geographical location can affect the composition and concentration of bioactive compounds, which in turn influence the AgNP synthesis.

Extraction Solvent and Method: The choice of extraction solvent and method can affect the yield and type of bioactive compounds extracted, thus influencing the properties of the AgNPs.

Reaction Parameters: As mentioned earlier, parameters such as temperature, pH, and silver salt concentration play a critical role in determining the size, shape, and stability of the AgNPs .

By carefully controlling these factors, it is possible to tailor the properties of *Caulerpa chemnitzia*-synthesized AgNPs for specific biomedical applications (Geszke-Moritz & Moritz, 2024) .

Antimicrobial Activity

This section will Discussed the antimicrobial properties of silver nanoparticles synthesized using *Caulerpa chemnitzia*, addressing the growing concern of antimicrobial resistance and the potential of these green-synthesized nanoparticles as an alternative antimicrobial agent (Hintz *et al*., 2015) .

Introduction to Antimicrobial Resistance

Begin by introducing the escalating global problem of antimicrobial resistance. AMR occurs when microorganisms (bacteria, fungi, viruses, and parasites) evolve to withstand antimicrobial drugs, making infections harder to treat and increasing the risk of disease spread, severe illness, and death .Discussed the factors driving AMR, such as overuse and misuse of antibiotics in human and animal medicine, as well as the lack of new antimicrobial drug development. Highlight the urgent need for new strategies to combat AMR, including the development of novel antimicrobial agents.

Mechanisms of Antimicrobial Action of AgNPs

This section will detail the various mechanisms by which AgNPs exert their antimicrobial effects (Rahman *et al*., 2021):

Disruption of Cell Membrane Integrity: AgNPs can interact with and disrupt the cell membrane of bacteria and fungi, leading to increased permeability and leakage of cellular contents. This disruption can be attributed to the electrostatic attraction between the negatively charged microbial cell membrane and the positively charged AgNPs.

Generation of Reactive Oxygen Species: AgNPs can induce the production of ROS, such as superoxide radicals, hydrogen peroxide, and hydroxyl radicals. These ROS cause oxidative stress, damaging cellular components like DNA, proteins, and lipids, ultimately leading to cell death.

Inhibition of Bacterial Enzymes and DNA Replication: AgNPs can enter bacterial cells and interfere with essential cellular processes. They can bind to and inhibit the function of bacterial enzymes involved in energy production, metabolism, and cell wall synthesis. Additionally, AgNPs can interact with DNA, disrupting DNA replication and gene expression (Ghaywat *et al*., 2021) .

In vitro Studies Evaluating Antimicrobial Activity

Review existing *In vitro* studies that have assessed the antimicrobial activity of *Caulerpa chemnitzia*-synthesized AgNPs :

Antibacterial Activity: Discussed studies that have evaluated the antibacterial activity of *Caulerpa chemnitzia*-synthesized AgNPs against Gram-positive (Staphylococcus aureus) and Gram-negative bacteria (Escherichia coli). Include information on the methods used (e.g., disc diffusion, broth microdilution), the concentrations of AgNPs tested, and the reported

minimum inhibitory concentrations and minimum bactericidal concentrations.

Antifungal Activity: Summarize studies that have investigated the antifungal activity of *Caulerpa chemnitzia*-synthesized AgNPs against Candida albicans and other fungal species. Include details on the methods used and the reported antifungal activity.

Antiviral Activity: If there are studies available, Discussed the antiviral activity of *Caulerpa chemnitzia*-synthesized AgNPs against specific viruses.

Factors Influencing Antimicrobial Activity

Discussed the factors that can influence the antimicrobial activity of AgNPs (Ghaywat *et al*., 2021) :

Size and Shape of AgNPs: The size and shape of AgNPs can affect their antimicrobial activity. Smaller AgNPs generally exhibit higher antimicrobial activity due to their increased surface area-to-volume ratio, which allows for greater interaction with microbial cells. Similarly, the shape of AgNPs can influence their ability to penetrate and disrupt cell membranes.

Concentration of AgNPs: The concentration of AgNPs is a critical factor in determining their antimicrobial activity. Higher concentrations of AgNPs generally lead to greater antimicrobial effects, but it is important to consider the potential toxicity of AgNPs at high concentrations (Ghaywat *et al*., 2021) .

Bacterial/Fungal Species: The susceptibility of different bacterial and fungal species to AgNPs can vary. Some species may be more resistant to AgNPs due to differences in their cell wall structure, metabolic activity, or defense mechanisms.

Comparison with Chemically Synthesized AgNPs and Conventional Antibiotics

Compare the antimicrobial activity of *Caulerpa chemnitzia*-synthesized AgNPs with that of chemically synthesized AgNPs and conventional antibiotics(González-Lamothe *et al*., 2009). Discussed the advantages and disadvantages of each type of antimicrobial agent.

Potential Applications

Explore the potential applications of *Caulerpa chemnitzia*-synthesized AgNPs as antimicrobial agents(Blasco-Navarro *et al*., 2025) :

Wound Healing: AgNPs can promote wound healing by inhibiting bacterial infections, reducing inflammation, and stimulating tissue regeneration.

Disinfection of Medical Devices: AgNPs can be used to coat medical devices, such as catheters and implants, to prevent bacterial colonization and reduce the risk of healthcare-associated infections.

Food Packaging: AgNPs can be incorporated into food packaging materials to inhibit the growth of spoilage microorganisms and extend the shelf life of food products.

Cytotoxic Activity

This section will Discussed the cytotoxic properties of silver nanoparticles synthesized using *Caulerpa chemnitzia*, and their relevance in biomedical applications (Liu *et al*., 2019) .

Introduction to Cytotoxicity

Begin by defining cytotoxicity and its significance in the context of biomedical applications such as drug delivery, diagnostics, and cancer therapy(Feczkó *et al*., 2019) .Explain how evaluating the cytotoxicity of nanomaterials is crucial to ensure their safe and effective use.

Mechanisms of AgNP-Induced Cytotoxicity

Detail the different mechanisms through which AgNPs can induce cytotoxicity (Geszke-Moritz & Moritz, 2024) :

ROS Generation and Oxidative Stress: AgNPs can induce the generation of ROS, leading to oxidative stress within cells. This oxidative stress can damage cellular components, including lipids, proteins, and DNA.

Mitochondrial Dysfunction: AgNPs can disrupt mitochondrial function, leading to decreased ATP production and increased ROS generation. This dysfunction can trigger apoptosis.

DNA Damage and Apoptosis: AgNPs can directly interact with DNA, causing DNA damage and activating apoptosis pathways.

Inflammatory Responses: AgNPs can trigger inflammatory responses in cells, leading to the release of pro-inflammatory cytokines and chemokines. These inflammatory responses can contribute to cytotoxicity (Nisini *et al*., 2018) .

In vitro Studies Evaluating Cytotoxic Activity

In vitro studies that have evaluated the cytotoxic activity of *Caulerpa chemnitzia*-synthesized AgNPs (Roffo *et al*., 2022) :

Cytotoxicity Assays: Discussed various cytotoxicity assays used to assess the cytotoxic effects of AgNPs on different cell lines, such as fibroblasts and epithelial cells. Examples of assays include MTT, clonogenic, neutral red uptake assay, and LDH assays. Include information on the cell lines used, the concentrations of AgNPs tested, and the reported IC50 values.

Assessment of Cell Viability, Cell Proliferation, and Apoptosis: Summarize studies that have assessed the effects of *Caulerpa chemnitzia*-synthesized AgNPs on cell viability, cell proliferation, and apoptosis .Include details on the methods used (e.g., flow cytometry, caspase assays) and the reported results.

Evaluation of ROS Production and Oxidative Stress Markers: Discussed studies that have evaluated the effects of *Caulerpa chemnitzia*-synthesized AgNPs on ROS production and oxidative stress markers .Include details on the methods used (e.g., DCFDA assay, measurement of lipid peroxidation) and the reported results.

Factors Influencing Cytotoxic Activity

Discussed the factors that can influence the cytotoxic activity of AgNPs (Roffo *et al*., 2022) :

Size, Shape, and Surface Charge of AgNPs: The size, shape, and surface charge of AgNPs can affect their cellular uptake, intracellular distribution, and interactions with cellular components.

Concentration and Exposure Time: The concentration of AgNPs and the duration of exposure are critical factors in determining their cytotoxic activity.

Cell Type and Metabolic Activity: Different cell types exhibit varying sensitivities to AgNPs due to differences in their metabolic activity, antioxidant capacity, and DNA repair mechanisms (Blasco-Navarro *et al*., 2025) .

Comparison with Chemically Synthesized AgNPs and Other Cytotoxic Agents

Compare the cytotoxic activity of *Caulerpa chemnitzia*-synthesized AgNPs with that of chemically synthesized AgNPs and other cytotoxic agents(Ghaywat *et al*., 2021). Discussed the advantages and disadvantages of each type of cytotoxic agent.

Potential Applications

Explore the potential applications of *Caulerpa chemnitzia*-synthesized AgNPs in targeted drug delivery and diagnostics .Discussed how these nanoparticles can be used to selectively target cancer cells, deliver therapeutic agents, and enhance diagnostic imaging.

Anticancer Activity

This section will Discussed the anticancer properties of silver nanoparticles synthesized using *Caulerpa chemnitzia*(Lalegani & Ebrahimi, 2020) .

Introduction to Cancer

Introduce cancer as a major global health problem, emphasizing the need for novel therapeutic strategies .Discussed the limitations of conventional cancer treatments and highlight the potential of nanotechnology-based approaches.

Mechanisms of Anticancer Activity of AgNPs

Detail the different mechanisms through which AgNPs can exert their anticancer effects (Ghaywat *et al*., 2021) :

Selective Targeting of Cancer Cells: AgNPs can be designed to selectively target cancer cells, sparing healthy tissues. This can be achieved through surface modification with targeting ligands that bind to specific receptors overexpressed on cancer cells.

Induction of Apoptosis and Cell Cycle Arrest: AgNPs can induce apoptosis (programmed cell death) in cancer cells by activating various signaling pathways. Additionally, AgNPs can cause cell cycle arrest, preventing cancer cells from proliferating(Ghaywat *et al*., 2021) .

Inhibition of Angiogenesis and Metastasis: AgNPs can inhibit angiogenesis (the formation of new blood vessels) and metastasis (the spread of cancer cells to other parts of the body), thereby preventing tumor growth and dissemination.

Enhanced Drug Delivery to Cancer Cells: AgNPs can be used as drug carriers to enhance the delivery of chemotherapeutic agents to cancer cells, increasing their efficacy and reducing their side effects .

In vitro and In Vivo Studies Evaluating Anticancer Activity

Review *In vitro* and *In Vivo* studies that have evaluated the anticancer activity of synthesized AgNPs (Geszke-Moritz & Moritz, 2024) :

***In vitro* Studies:**

Discussed *In vitro* studies using different cancer cell lines, such as breast cancer, lung cancer, and colon cancer.

Summarize studies that have assessed the effects of *Caulerpa chemnitzia*-synthesized AgNPs on cell viability, cell proliferation, apoptosis, and cell cycle arrest (Ghaywat *et al*., 2021) .

Include details on the methods used (e.g., MTT assay, flow cytometry) and the reported results.

Evaluate the effects of *Caulerpa chemnitzia*-synthesized AgNPs on gene expression and signaling pathways involved in cancer development and progression .

***In Vivo* Studies:**

Discussed *In Vivo* studies using animal models of cancer.

Summarize studies that have evaluated the effects of *Caulerpa chemnitzia*-synthesized AgNPs on tumor growth inhibition, metastasis, and survival rate .

Include details on the methods used (e.g., tumor volume measurement, immunohistochemistry) and the reported results.

Assess the toxicity and side effects of *Caulerpa chemnitzia*-synthesized AgNPs in animal models .

Factors Influencing Anticancer Activity

Discussed the factors that can influence the anticancer activity of AgNPs (Geng, 2023) :

Size, Shape, and Surface Modification of AgNPs: The size, shape, and surface modification of AgNPs can affect their cellular uptake, biodistribution, and interactions with cancer cells.

Targeting Ligands and Drug Loading: The presence of targeting ligands on the surface of AgNPs can enhance their selective targeting of cancer cells. The amount of drug loaded onto AgNPs can also affect their anticancer activity.

Cancer Cell Type and Microenvironment: Different cancer cell types exhibit varying sensitivities to AgNPs due to differences in their genetic makeup, metabolic activity, and microenvironment .

Comparison with Chemically Synthesized AgNPs and Conventional Chemotherapeutic Agents

Compare the anticancer activity of *Caulerpa chemnitzia*-synthesized AgNPs with that of chemically synthesized AgNPs and conventional chemotherapeutic agents (Ghaywat *et al*., 2021) .Discussed the advantages and disadvantages of each type of anticancer agent.

Potential Applications in Cancer Therapy

Explore the potential applications of *Caulerpa chemnitzia*-synthesized AgNPs in cancer therapy(Maher *et al*., 2023) :

Targeted Drug Delivery: *Caulerpa chemnitzia*-synthesized AgNPs can be used to deliver chemotherapeutic agents directly to cancer cells, increasing their efficacy and reducing their side effects.

Photothermal Therapy: AgNPs can be used in photothermal therapy to generate heat and kill cancer cells upon exposure to near-infrared light.

Radiotherapy Enhancement: AgNPs can enhance the effects of radiotherapy by increasing the deposition of radiation energy in cancer cells.

Immunotherapy: AgNPs can be used to stimulate the immune system to recognize and kill cancer cells .

Toxicity and Biocompatibility

This section addresses the crucial aspects of toxicity and biocompatibility associated with AgNPs, particularly those synthesized using *Caulerpa chemnitzia* (Geng, 2023) .

Potential Toxicity Concerns Associated with AgNPs

Discussed the potential toxicity concerns associated with AgNPs in general .This should include:

Mechanisms of Toxicity: Explain how AgNPs can induce toxicity through various mechanisms, such as ROS generation, DNA damage, and inflammatory responses.

Factors Affecting Toxicity: Discussed how factors like size, shape, surface charge, and aggregation state of AgNPs can influence their toxicity.

Target Organs: Identify the organs and tissues that are particularly vulnerable to AgNP-induced toxicity (e.g., liver, kidneys, lungs).

Biocompatibility of Caulerpa chemnitzia-Synthesized AgNPs

Review the available studies that have evaluated the biocompatibility of *Caulerpa chemnitzia*-synthesized AgNPs (Geszke-Moritz & Moritz, 2024).

***In vitro* Studies:** Summarize *In vitro* studies that have assessed the biocompatibility of *Caulerpa chemnitzia*-synthesized AgNPs using different cell lines. Focus on studies that have evaluated cell viability, cell proliferation, and cell morphology.

***In Vivo* Studies:** Summarize *In Vivo* studies that have evaluated the biocompatibility of *Caulerpa chemnitzia*-synthesized AgNPs in animal models. Focus on studies that have assessed the effects of AgNPs on organ function, immune response, and overall health.

Impact on Environment and Human Health

Assess the potential impact of AgNPs on the environment and human health(Fytianos *et al*., 2020).

Environmental Fate: Discussed the potential fate of AgNPs in the environment, including their accumulation in soil, water, and air.

Ecotoxicity: Summarize studies that have evaluated the ecotoxicity of AgNPs on various organisms, such as bacteria, algae, and invertebrates.

Human Exposure: Discussed the potential routes of human exposure to AgNPs, including inhalation, ingestion, and dermal contact.

Strategies to Minimize Toxicity and Enhance Biocompatibility

Discussed strategies to minimize the toxicity and enhance the biocompatibility of AgNPs (Geszke-Moritz & Moritz, 2024).

Surface Modification: Discussed how surface modification with biocompatible materials (e.g., polymers, proteins) can reduce the toxicity of AgNPs.

Controlled Synthesis: Discussed how controlling the size, shape, and surface charge of AgNPs during synthesis can improve their biocompatibility.

Targeted Delivery: Discussed how targeted delivery of AgNPs to specific cells or tissues can reduce their off-target effects.

Challenges and Future Directions

This section will address the obstacles in translating *Caulerpa chemnitzia*-synthesized AgNPs from lab to clinic and propose future research avenues (Ghaywat *et al*., 2021) .

Challenges in Development and Application

Discussed the primary challenges in the development and application of *Caulerpa chemnitzia*-synthesized AgNPs(Geszke-Moritz & Moritz, 2024) :

Scale-up Production and Standardization:

The green synthesis of AgNPs using *Caulerpa chemnitzia* needs to be scaled up for industrial production.

Standardization of the synthesis process is crucial to ensure consistent AgNP properties (size, shape, stability) and performance.

Long-term Stability and Shelf Life:

AgNPs tend to aggregate over time, which can reduce their efficacy and increase their toxicity.

Improving the long-term stability and shelf life of *Caulerpa chemnitzia*-synthesized AgNPs is essential for their practical use.

***In Vivo* Toxicity and Biodistribution:**

More comprehensive *In Vivo* studies are needed to fully assess the toxicity and biodistribution of *Caulerpa chemnitzia*-synthesized AgNPs.

Understanding how AgNPs interact with biological systems is critical for ensuring their safety.

Regulatory Approval and Clinical Translation:

Navigating the regulatory landscape for nanomedicines is challenging.

Clinical trials are necessary to evaluate the efficacy and safety of *Caulerpa chemnitzia*-synthesized AgNPs in humans.

Future Directions for Research and Development

Outline the key areas for future research and development(Ali *et al*., 2020) :

Optimization of Green Synthesis Methods:

Further optimize the green synthesis of AgNPs using *Caulerpa chemnitzia* to improve their yield, purity, and stability.

Explore different extraction and purification techniques to enhance the quality of AgNPs.

Surface Modification and Functionalization:

Modify the surface of *Caulerpa chemnitzia*-synthesized AgNPs with biocompatible polymers or targeting ligands to improve their biocompatibility, stability, and targeting ability .

Functionalize AgNPs with therapeutic agents to create multifunctional nanomedicines.

Combination Therapy with Other Drugs or Modalities:

Investigate the potential of combining *Caulerpa chemnitzia*-synthesized AgNPs with conventional chemotherapeutic agents, photothermal therapy, or immunotherapy to enhance their anticancer efficacy (Ghaywat *et al*., 2021) .

Explore synergistic effects between AgNPs and other therapeutic modalities.

Clinical Trials to Evaluate Efficacy and Safety:

Conduct preclinical studies to assess the efficacy and safety of *Caulerpa chemnitzia*-synthesized AgNPs in relevant disease models.

Design and implement clinical trials to evaluate the therapeutic potential of AgNPs in humans.

Conclusion

This review, highlighting the potential of *Caulerpa chemnitzia*-synthesized AgNPs and the future steps needed(Ghaywat *et al*., 2021). The green synthesis method using *Caulerpa chemnitzia*, the characterization of the synthesized AgNPs, and their various biomedical applications(Dar *et al*., 2023). Potential for Biomedical Applications: Reiterate the significant potential of *Caulerpa chemnitzia*-synthesized AgNPs in various biomedical fields, such as drug delivery, bioimaging, and antimicrobial applications. Need for Further Research has emphasize the necessity for continued research to overcome the challenges associated with *Caulerpa chemnitzia*-synthesized AgNPs. This includes addressing issues related to scale-up production, long-term stability, *In Vivo* toxicity, and regulatory approval .Stress the importance of clinical trials to evaluate the efficacy and safety of these AgNPs for human use.

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Conflicts of Interest:

The authors have no conflicts of interest.

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