Review Paper:

Green-Synthesized Nanoparticles of Catharanthus Roseus: A Review of Synthesis, Characterization and Biomedical Applications

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Abstract

Catharanthus roseus, a medicinal plant rich in bioactive compounds like alkaloids, flavonoids and terpenoids, has gained prominence in green nanoparticle synthesis. This review highlights its role as a reducing and stabilizing agent in the eco-friendly production of nanoparticles such as silver (AgNPs), gold (AuNPs), zinc oxide (ZnO-NPs) and iron oxide (Fe_2O_3-NPs). Characterization techniques including UV-Vis spectroscopy, FTIR and SEM, confirm their stability and functionality. These nanoparticles demonstrate significant biomedical applications including antimicrobial, antioxidant, anticancer and anti-inflammatory activities.

AgNPs and ZnO-NPs exhibit strong pathogen disruption and oxidative stress reduction while AuNPs show targeted cytotoxicity against cancer cells. Challenges such as scalability and reproducibility persist, but interdisciplinary research and clinical validation can unlock their full potential. This review underscores the promise of C. roseus-derived nanoparticles in sustainable nanotechnology for health and environmental solutions.

Keywords: Anticancer, Antioxidant, *Catharanthus roseus*, Nanoparticles, Phytochemicals.

Introduction

Nanotechnology has revolutionized multiple fields including medicine, agriculture and materials science due to its ability to manipulate materials at the nanoscale.[38] Nanoparticles (NPs), measuring 1–100 nm, are the cornerstone of this technology, offering unique properties such as high surface area and tuneable physical and chemical characteristics.[59] However, conventional NP synthesis methods, chemical and physical, pose significant limitations including high energy requirements, toxic reagents and environmental hazards.[3] These drawbacks necessitate the development of sustainable alternatives like green synthesis, which leverages biological resources to produce NPs in an eco-friendly and cost-effective manner.[13] Green synthesis has gained prominence as a viable alternative to traditional approaches. It utilizes natural reducing and stabilizing agents from biological systems including plants, fungi, bacteria and algae. Unlike chemical methods that rely on hazardous chemicals, green synthesis is environmentally benign and biocompatible, producing NPs with enhanced functional properties.[40] Plant-mediated synthesis, in particular, is highly advantageous due to the abundance of phytochemicals such as phenolics, flavonoids, alkaloids and terpenoids. These secondary metabolites not only facilitate NP formation but also confer intrinsic biological activities, making them highly relevant for biomedical applications.[60]

Among the various plants utilized, *Catharanthus roseus* (Madagascar periwinkle) stands out for its phytochemical richness and medicinal significance. Belonging to the Apocynaceae family, *C. roseus* is a known source of terpenoid indole alkaloids like vincristine and vinblastine, which are extensively used in cancer therapy.[22] Additionally, the plant contains phenolics, flavonoids and tannins, which act as efficient reducing and capping agents in NP synthesis. These bioactive compounds impart stability and functionality to the synthesized NPs, enhancing their biomedical potential for applications such as anticancer, antimicrobial and antioxidant therapies.[9]

The widespread availability and adaptability of *C. roseus* make it a sustainable choice for green NP synthesis. Its ability to stabilize nanoparticles ensures high yield and stability, addressing critical challenges in NP production.[41] This review explores the synthesis, characterization and biomedical applications of *C. roseus*-derived NPs, highlighting the plant's dual role as a reducing and capping agent. By integrating green chemistry and nanotechnology, *C. roseus* exemplifies the advancements in eco-friendly NP synthesis and its potential to address pressing challenges in medicine and beyond.

Synthesis of Nanoparticles using *Catharanthus roseus*

The use of *Catharanthus roseus* in nanoparticle synthesis represents a sustainable and eco-friendly approach, leveraging the plant's abundant phytochemicals to produce diverse nanoparticles.[37] The process begins with the preparation of plant extracts, typically using aqueous or ethanolic methods. For aqueous extraction, fresh or dried plant material is boiled in distilled water, facilitating the release of bioactive compounds such as alkaloids, flavonoids and terpenoids.[14] Ethanol extraction, on the other hand, enhances the solubility of a broader range of secondary metabolites, allowing for the efficient recovery of bioactive constituents. The extracts are filtered to remove plant debris,

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creating a solution rich in phytochemicals that serve as reducing and stabilizing agents.

The phytochemicals in *Catharanthus roseus* play a dual role in nanoparticle synthesis. Compounds like flavonoids, tannins and phenolic acids reduce metal salts to their respective nanoparticles by donating electrons during the redox reaction.[53] For instance, silver nitrate ($AgNO_3$) is reduced to silver nanoparticles (AgNPs), while gold chloride ($HAuCl_4$) is reduced to gold nanoparticles (AuNPs). In addition to reduction, these bioactive compounds stabilize the nanoparticles by capping their surfaces, which prevent aggregation and ensures uniform size distribution. This stabilization is attributed to the functional groups, such as hydroxyl and carboxyl groups, present in the phytochemicals, which interact with the nanoparticle surfaces.[64]

Different types of nanoparticles have been synthesized using *Catharanthus roseus*. AgNPs exhibit potent antimicrobial and antioxidant activities, making them suitable for biomedical and environmental applications.[31] AuNPs are valued for their use in cancer therapy, bioimaging and drug delivery due to their biocompatibility and tunable surface properties.[12] Zinc oxide nanoparticles (ZnO-NPs) demonstrate strong antibacterial, antifungal and photocatalytic properties, making them useful in wastewater treatment and antibacterial coatings.[2,56] Iron oxide nanoparticles (Fe_2O_3-NPs) are extensively studied for their applications in magnetic resonance imaging, targeted drug delivery and hyperthermia therapy.[42] The synthesis process is optimized by controlling parameters such as pH, temperature, metal salt concentration and reaction time.

Optimal conditions ensure high yield, narrow size distribution and enhanced stability of the nanoparticles.[44,63] For example, slightly alkaline pH and moderate temperatures (around 50–70°C) are often ideal for nanoparticle formation.[47] Thus, the utilization of *Catharanthus roseus* not only underscores the potential of green nanotechnology but also provides a cost-effective and sustainable pathway for synthesizing functional nanoparticles.

Characterization of Synthesized Nanoparticles from *Catharanthus roseus*: Nanoparticles synthesized using *Catharanthus roseus* extracts including silver (AgNPs), gold (AuNPs), zinc oxide (ZnO-NPs) and iron oxide (Fe_2O_3-NPs), exhibit diverse properties and applications. Characterization of these nanoparticles is essential for confirming synthesis, analysing structural and morphological features and assessing stability and biocompatibility. Advanced analytical techniques provide detailed insights into their properties.[16] UV-Vis spectroscopy is a primary tool used to monitor nanoparticle synthesis. Silver nanoparticles exhibit a characteristic surface plasmon resonance (SPR) peak in the range of 400–450 nm while gold nanoparticles show SPR peaks around 520–570 nm.[8,36] These optical features provide information about nanoparticle size and aggregation.

Zinc oxide nanoparticles absorb strongly in the UV range of 300–380 nm due to their wide bandgap while iron oxide nanoparticles display unique absorption features associated with electronic transitions of iron ions, confirming their synthesis.[4] These spectral properties also highlight the effectiveness of phytochemicals in the nanoparticle synthesis process. Fourier-transform infrared (FTIR) spectroscopy plays a pivotal role in identifying functional groups in *Catharanthus roseus* extracts responsible for reducing and stabilizing nanoparticles.[29] Peaks corresponding to hydroxyl (-OH), carbonyl (-C=O) and carboxyl (-COOH) groups confirm the involvement of phytochemicals such as alkaloids, flavonoids and terpenoids.[61] These biomolecules not only reduce metal ions to their respective nanoparticles but also form a capping layer, ensuring colloidal stability.[52]

For ZnO-NPs and Fe_2O_3-NPs, FTIR analysis further validates the presence of metal-oxygen bonds, indicative of successful nanoparticle formation. X-ray diffraction (XRD) analysis provides information about the crystalline nature of nanoparticles. The face-centered cubic (FCC) structure is observed for both silver and gold nanoparticles, while zinc oxide nanoparticles display a hexagonal wurtzite pattern and iron oxide nanoparticles exhibit characteristic peaks of their spinel structure. The average crystallite size is determined using the Debye-Scherrer equation, providing quantitative data on nanoparticle dimensions and confirming their crystalline integrity.[6]

Microscopy techniques like Scanning electron microscopy (SEM) and Transmission electron microscopy (TEM) are indispensable for understanding the morphology of nanoparticles.[15] SEM reveals surface characteristics and shapes, such as spherical structures for AgNPs and AuNPs, rod-like configurations for ZnO-NPs and cubic morphologies for Fe_2O_3-NPs.[1] TEM offers high-resolution imaging, enabling precise measurement of nanoparticle size and observation of uniformity.[55] Additionally, TEM can reveal the phytochemical capping layer, demonstrating the stabilization provided by *Catharanthus roseus* extracts. Dynamic light scattering (DLS) complements TEM by providing information on the hydrodynamic size and zeta potential of nanoparticles.[45]

The hydrodynamic sizes are typically larger than TEM-measured sizes due to solvation layers. High zeta potential values, often above ±30 mV, indicate strong electrostatic stabilization, ensuring colloidal stability. For iron oxide nanoparticles, magnetic properties are also assessed to confirm their potential for applications like drug delivery and magnetic imaging. The stability and biocompatibility of nanoparticles synthesized using *Catharanthus roseus* extracts are primarily attributed to the phytochemical content.[31] Compounds such as flavonoids, alkaloids and terpenoids act as natural capping agents, preventing aggregation and oxidative degradation. This natural coating enhances the antimicrobial and anticancer efficacy of AgNPs and AuNPs respectively, improves the photocatalytic activity of ZnO-NPs and supports the biocompatibility of Fe_2O_3-NPs, making them suitable for biomedical applications.[7]

Characterization of nanoparticles synthesized from *Catharanthus roseus* ensures a thorough understanding of their optical, structural and morphological features. These analyses validate their potential for diverse applications including antimicrobial treatments, cancer therapy, photocatalysis and targeted drug delivery. The role of phytochemicals in stabilization and biocompatibility further enhances their utility, marking these nanoparticles as versatile agents in biomedical and environmental sciences.

Biomedical Applications of Catharanthus roseus derived Nanoparticles: The antimicrobial activity of *Catharanthus roseus* derived nanoparticles, particularly silver (AgNPs) and zinc oxide nanoparticles (ZnO-NPs), has been extensively documented. These nanoparticles exhibit broad-spectrum efficacy against pathogenic bacteria, fungi and viruses. Studies reveal potent antibacterial activity against Gram-positive bacteria like *Staphylococcus aureus* and Gram-negative strains such as *Escherichia coli* and *Pseudomonas aeruginosa*.[9,30] The mechanism primarily involves the disruption of bacterial cell membranes, leading to leakage of cellular contents and eventual cell death. AgNPs also generate reactive oxygen species (ROS), further amplifying their bactericidal effects.[39]

Against fungal pathogens like *Candida albicans* and *Aspergillus niger*, nanoparticles disrupt fungal hyphae and inhibit spore germination.[27] Moreover, *Catharanthus roseus* derived AgNPs and AuNPs have shown antiviral properties, inhibiting the replication of viruses such as herpes simplex virus (HSV) and influenza.[21,46] This is achieved by binding to viral envelope proteins, thereby preventing viral entry into host cells. The antioxidant potential of *Catharanthus roseus*-mediated nanoparticles is another significant attribute. These nanoparticles effectively combat oxidative stress by scavenging free radicals and reducing the levels of reactive oxygen species.[18]

For instance, gold nanoparticles (AuNPs) synthesized from *Catharanthus roseus* extract have demonstrated robust antioxidant activity in DPPH and ABTS assays, with IC50 values indicating high radical-scavenging efficiency.[20] Zinc oxide nanoparticles also show notable antioxidant capabilities, attributed to their interaction with reactive species and stabilization by plant-derived phytochemicals like flavonoids and alkaloids.[5] This antioxidant activity has profound implications in preventing cellular damage caused by oxidative stress, thereby reducing the risk of chronic diseases such as cardiovascular disorders and neurodegenerative conditions.[26] One of the most promising applications of *Catharanthus roseus* derived nanoparticles is their anticancer activity. Silver and gold nanoparticles exhibit potent cytotoxic effects against various cancer cell lines including lung (A549) and (HeLa229) cancers.[23,28] The mechanisms involve multiple pathways, such as the induction of apoptosis, generation of reactive oxygen species and disruption of mitochondrial membrane potential. Studies have demonstrated that these nanoparticles upregulate pro-apoptotic proteins like Bax and downregulate anti-apoptotic proteins such as Bcl-2, triggering programmed cell death.[17] Additionally, nanoparticles enhance the production of ROS within cancer cells, leading to oxidative damage and cell cycle arrest.

The selective toxicity of these nanoparticles towards cancer cells while sparing normal cells underscores their potential as effective and biocompatible anticancer agents.[25] The anti-inflammatory properties of *Catharanthus roseus*-mediated nanoparticles further enhance their biomedical relevance. These nanoparticles mitigate inflammation by downregulating pro-inflammatory cytokines such as TNF-α, IL-6 and IL-1β and upregulating anti-inflammatory markers like IL-10.[43] Zinc oxide and iron oxide nanoparticles synthesized using *Catharanthus roseus* extracts have been shown to reduce inflammation in animal models of arthritis and colitis.[58] The anti-inflammatory effects are attributed to the suppression of NF-κB signalling pathways, which play a critical role in the inflammatory response. This makes these nanoparticles valuable in managing inflammatory diseases and associated conditions.[24]

Beyond these primary biomedical applications, *Catharanthus roseus* derived nanoparticles find utility in drug delivery, imaging and environmental remediation. Gold and iron oxide nanoparticles have been extensively studied as drug delivery vehicles, capable of targeting specific tissues and releasing therapeutic agents in a controlled manner. For example, AuNPs functionalized with tumour-specific ligands have demonstrated effective delivery of chemotherapeutic drugs to cancer cells, minimizing off-target effects.[62] Magnetic iron oxide nanoparticles (Fe_2O_3-NPs) synthesized from *Catharanthus roseus* are used in magnetic resonance imaging (MRI), offering enhanced contrast for better visualization of pathological conditions.[42] Furthermore, the photocatalytic activity of zinc oxide nanoparticles has been harnessed for environmental remediation, such as the degradation of organic pollutants in wastewater.

Challenges and Future Perspectives

The green synthesis of nanoparticles using *Catharanthus roseus* and other plant-based systems has garnered significant attention due to its eco-friendliness, cost-effectiveness and biocompatibility. However, several challenges persist, limiting its large-scale application and clinical translation. Addressing these limitations while leveraging future opportunities is critical for advancing this field. One of the primary challenges in green synthesis is

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scalability. While laboratory-scale synthesis methods have been extensively optimized, replicating these processes on an industrial scale remains difficult.[54]

Variations in the phytochemical composition of plant extracts, influenced by factors such as plant age, geographical location and seasonal changes, often result in inconsistencies in nanoparticle characteristics such as size, shape and stability. This lack of uniformity is particularly problematic for biomedical applications where strict regulatory standards demand reproducibility and consistency.[33] Moreover, green synthesis methods typically yield nanoparticles in smaller quantities compared to conventional chemical or physical methods, necessitating the development of techniques that can increase production volumes without compromising the quality and eco-friendly nature of the process.[10]

Reproducibility is another significant limitation. The inherent complexity of plant-based extracts, which often contain a mixture of bioactive compounds such as flavonoids, alkaloids and phenolics, poses challenges in standardizing the synthesis process.[57] Each bioactive compound can influence the reduction and stabilization of metal salts differently, making it difficult to achieve a predictable and reproducible outcome. In addition, reaction parameters such as pH, temperature and extract concentration require precise control and even minor deviations can lead to significant variations in nanoparticle properties.[11] Despite these challenges, the future of green synthesis holds immense promise. Interdisciplinary approaches combining nanotechnology, biochemistry and computational modelling could pave the way for more robust and efficient synthesis methods.[3]

For example, integrating omics technologies such as metabolomics and proteomics, can help to identify the specific phytochemicals responsible for nanoparticle synthesis and their precise mechanisms of action. This knowledge can be used to engineer plant extracts or mimic their bioactive components for more controlled and reproducible synthesis.[19] Exploring novel applications of *Catharanthus roseus* derived nanoparticles is another promising direction. While current research predominantly focuses on antimicrobial, antioxidant, anticancer and anti-inflammatory properties, these nanoparticles have untapped potential in areas like regenerative medicine, biosensing and advanced drug delivery systems.

Developing hybrid nanoparticles, where plant-derived nanoparticles are combined with synthetic materials, could further enhance their functionality and expand their application spectrum.[32] Conducting preclinical and clinical trials is essential for translating these nanoparticles from the laboratory to real-world applications. Rigorous *in vivo* studies are required to evaluate their pharmacokinetics, toxicity and therapeutic efficacy in human models.[34] Regulatory pathways for green-synthesized nanoparticles must also be streamlined to address the unique challenges associated with their complexity and variability. Collaboration between academia, industry and regulatory agencies will be critical in overcoming these challenges.[48] Industry partnerships can facilitate the development of scalable synthesis technologies, while regulatory agencies can provide guidelines for standardization and approval. Public and private funding will also be vital to support large-scale studies and commercialization efforts.[35]

Conclusion

The synthesis of nanoparticles using *Catharanthus roseus* represents a promising, sustainable and versatile approach in nanotechnology, combining the rich phytochemical diversity of this medicinal plant with cutting-edge advancements in material science. These nanoparticles exhibit remarkable biological properties including antimicrobial, antioxidant, anticancer and anti-inflammatory activities, underscoring their potential for diverse biomedical applications.

Despite the significant progress achieved in understanding their synthesis mechanisms, characterization techniques and applications, challenges such as scalability, reproducibility and clinical translation remain key hurdles. To fully harness the potential of *Catharanthus roseus*-derived nanoparticles, interdisciplinary collaborations are essential for optimizing green synthesis methods and addressing these limitations. Furthermore, expanding their applications into emerging fields such as regenerative medicine, targeted drug delivery and environmental remediation can provide transformative solutions to global health and environmental challenges.

Rigorous preclinical and clinical evaluations will play a pivotal role in ensuring the safety, efficacy and standardization of these nanomaterials for practical applications. *Catharanthus roseus* mediated nanoparticles can become a cornerstone in sustainable nanotechnology, bridging traditional knowledge with modern science to improve health outcomes and contribute to a more eco-friendly future.

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