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Green Synthesis of Nanoparticles Using Ayurvedic Medicinal Plants and their Endophytes: Bridging Ayurveda, Crop Protection, and Nanomedicine

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Abstract

Biogenic synthesis of nanoparticles (NPs) for therapeutic and agricultural applications is a newly emerging field of research called "Nano Ayurveda,"which has developed by the convergence of Ayurveda—the traditional Indian system of medicine—and modern nanotechnology. This review focuses on the green synthesis of metallic and metal oxide nanoparticles (Ag, Au, Cu, ZnO, and Se) using Ayurvedic medicinal plants— *Azadirachta indica*, *Ocimum sanctum*, *Tinospora cordifolia*, and *Phyllanthus emblica*—as well as their endophytes. The paper also highlights the detailed explanation of the biochemical pathways of synthesis, focusing how secondary metabolites (flavonoids, alkaloids, polyphenols, enzymes) acts as reducing and stabilising agents. The two main uses of green nano particles have been discussed. First in plant care where these nano wonders, act as safe nanopesticides, nanofertilisers, and growth boosters to help crops grow better become more resilient. Second, in medicine, they demonstrate powerful, anti cancer, microbial and targeted drug delivery properties (against A549, HeLa, MCF-7 lines). Finally, the critical aspects of safety, cytotoxicity, and the regulatory landscape, outlining future perspectives for the integration of green nanotechnology into sustainable global health and agriculture has been addressed.

Keywords: *Nano Ayurveda; green synthesis; biogenic nanoparticles; Ayurvedic medicinal plants; endophytic microorganisms; nanomedicine; nanopesticides; plant growth promotion; anticancer activity; antimicrobial activity; biosafety.*

1. Introduction

The emerging discipline of Nano Ayurveda merges centuries-old Ayurvedic herbal practices with modern nanotechnology, utilizing engineering techniques to create highly potent, targeted herbal treatments which can meet contemporary healthcare demands [25], [33]. For thousands of years, the traditional Indian medical system of Ayurveda depended on medicinal plants to treat various human illnesses. These traditional medicinal plants are now serving as sustainable biological machines that synthesize nanoparticles naturally, thus providing an eco-friendly alternative to hazardous chemical and physical synthesis methods [23], [35]. (Figure:1)

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Green nanotechnology harnesses the complex plethora of phytochemical matrices of prominent ayurvedic herbs such as *Azadirachta indica*, *Ocimum sanctum*, and *Tinospora cordifolia*, employing their natural molecular profiles for chemical reduction and structural stabilization of metallic ions into functional nanoparticles without relying on toxic synthetic additives [1], [11], [24]. This cost-effective and non-polluting green approach pathway produces nanoparticles with natural biocompatibility and distinctive biological activities [23], [34]. Both nanomedicine and agriculture are showing vast transformation due to synergistic association of ancient botanical knowledge and nanomaterial science. While in agriculture, nanotechnology furnish eco-friendly solutions for crop protection and nutrition, in medicine, it increases the efficacy and bioavailability of therapeutic agents [18], [28], [38].

Recent research has emphasized that the plant microbiome, particularly endophytes, plays a crucial role in nanoparticle synthesis [15], [26]. Endophytes are microorganisms which are the natural bio factories that are present within the plant tissues producing metallic and metal oxide nanoparticles with specific functionalities and great stability [9], [21] This review provides a detailed overview of the mechanisms, characterization, and diverse applications of green nanoparticles derived from Ayurvedic plants and their endophytes.

2. Synthesis Mechanisms: Plant-mediated vs. Endophyte-mediated

In the green synthesis of nanoparticles, biological agents like plant, fungus and bacteria transform metal ions (e.g., Ag^{+}, Au^{3+}, Zn^{2+}) solid, zero-valent metal particles. This is a more ecofriendly approach and the biochemical compounds inside these organisms drive the reaction which directly alter the size, shape, and medical or biological strength of the final nanoparticles.

2.1 Plant-mediated Synthesis

The most widely explored green approach is the Plant-mediated synthesis (phytosynthesis) utilising aqueous or organic extracts from various plant parts [22], [37]

Plant secondary metabolites like flavonoids, alkaloids, terpenoids, polyphenols, phenolic acids, tannins, and proteins act as “Phytochemical Reducers” that facilitate the bioreduction of metallic salts [7], [24]. Ayurvedic plants like *Adhatoda vasica* containing alkaloids and terpenoids act as both reducing and capping agents [2].

Polyphenolic chemicals like quercetin are found in the fruit extracts of *Phyllanthus emblica* (Amla) and *Vaccinium oxycoccos* which provide electrons for reduction [20]. Similarly, rapid and green synthesis of metallic and bimetallic nanoparticles has been generated using classic Ayurvedic formulation- Triphala [12]. Methanolic root extracts of *Valeriana wallichii* contain polyphenols capable of generating nanoconjugates without chemical additives [5].

Due to high reduction rates in photosynthesis, plant mediated synthesis of nanoparticles is a preferable method over the microbial methods for large scale, production [18].

2.2 Endophyte-mediated Synthesis

One of the novel and sustainable sources for nanoparticle synthesis is Endophytic microorganisms, including bacteria and fungi which acts through enzymatic reduction and metabolite-based bio-capping mechanisms [48], [51]. These organisms have attracted significant interest in recent years due to their ability to produce massive diversity of bioactive secondary metabolites and these "biofactories" have the ability to synthesis metal-based nanoparticles [43], [45]. Endophyte-mediated nanotechnology is a convergence of green chemistry, microbiology and material science creating nanostructures through sustainable and eco-friendly systems [44], [46]. The technique has successfully bypassed the usage of hazardous chemicals, high energy utilization and extreme physical conditions required for nanoparticle synthesis which are toxic to the biological systems [48], [49]. In contrast, the endophyte mediated particles utilize the natural reduction capacity of microorganisms to convert metal ions into elemental forms [1], [5] and display high stability, biocompatibility and unique biological activities, largely due to the presence of a natural capping layer comprised of proteins and metabolites from the source organism [42], [46], [15].

Several species have been successfully employed in nanoparticle synthesis (Table 1)

Table 1. Species utilised for nanoparticle synthesis.

Category	Organism	Source Plant	Nanoparticle generated	Reference
Fungal Endophytes	*Penicillium* sp.	*Curcuma longa* & *Centella asiatica*	Silver (Ag)	**[6], [9]**
	Aspergillus terreus	Various host plants	Silver (Ag) / Gold (Au)	**[9], [10], [17]**
	Aspergillus versicolor	Various host plants	Metallic Nanoparticles	**[10], [17]**
	Colletotrichum sp.	Host plant tissues	Metallic / Silver (Ag)	**[9], [10]**
	Paecilomyces sinensis	Host plant tissues	Metallic / Silver (Ag)	**[10], [17]**
	Fusarium species	Various host plants	Silver (Ag), Gold (Au), etc.	**[9], [10], [14]**
Bacterial Endophytes	*Sphingobacterium thalpophilum*	Host plant tissues	Zinc Oxide (ZnO)	**[15], [21]**
	Pantoea anthophila	*Waltheria indica* (Stem)	Silver (Ag)	**[19]**

2.2.1 Biosynthetic pathways

Endophytic synthesis can be categorized under two broad categories -intracellular and extracellular [17], [21]. (Figure: 2)

Extracellular Synthesis:

This process involves the secretion of functional enzymes and metabolic compounds into their surrounding environment. For instance, the endophytic bacterium *Pantoea anthophila* synthesizes silver nanoparticles (Pa-AgNPs) by secreting a mixture of proteins, quinones, vitamins and enzymes that facilitate both nanoparticle formation and stabilization. Researchers frequently prefer this method due to the ease of downstream purification [19].

Intracellular Synthesis:

In this method cytoplasmic enzymes and redox-active metabolites carryout the reduction of metal ions within the cell [17], [21]. Fungal endophytes like *Aspergillus and Penicillium* shows NADH-dependent nitrate reductase activity [21]. Study reveals the utilization of nitrate reductase enzymes, naphthoquinones, and anthraquinones by endophytes for the reduction of silver ions and proteins and peptides stabilize the resulting nanoparticles [17]. Secretion of bioactive compound dimethylsulfoxonium formylmethylide has been reported in *Corynespora smithii* an endophyte from *Bergenia ciliata* [6]

2.3 Secondary Metabolites as Capping Agents

Biological molecules are the naturally derived capping agents that creates a stable nanoparticle surface, regulating their growth, aggregation and biological reactivity. Phytochemicals like flavonoids, terpenoids and proteins prevents the aggregation of nanoparticles thereby increasing their stability in aqueous solutions [1], [11]. Apart from this, these biomolecules also regulate the overall biological activity of the nanoparticles. For instance, metal nanoparticles conjugated with plant polyphenols from *Valeriana wallichii* extracts exhibits enhanced therapeutic properties [5].

3. Characterization Techniques for Green Nanoparticles

To confirm the successful synthesis and to access the physical properties of the nanoparticles, accurate characterisation is essential using various techniques – Table 2.

Table 2- Techniques for characterization of nanoparticles.

Characterization Technique	Primary Function	Key findings	Reference(s)
UV-Visible Spectroscopy	Surface Plasmon Resonance (SPR) peak identification	Confirmation of metallic nanoparticle synthesis	[19], [37]
(FTIR) Fourier Transform Infrared Spectroscopy	Detects functional group	Phytochemicals and microbial metabolites involved in reduction and capping	[11], [19], [37]

(XRD) X-Ray Diffraction	Examines crystal structure	Crystalline nature, phase, and purity of nanoparticles	[36], [37]
(TEM/SEM) Electron Microscopy	Helps in High-resolution structural imaging	Size, shape and morphology (e.g., spherical, hexagonal)	[19], [37]
(DLS) Dynamic Light Scattering	Quantification of hydrodynamic diameter and surface charge	Size distribution and colloidal stability	[15], [37]

4. Applications in Nanomedicine

Nanoparticles derived from Ayurvedic plants and their endophytes offer solutions for infectious diseases, cancer, and targeted therapy.

4.1 Antimicrobial and Antibiofilm Activity: Silver nanoparticles (AgNPs) are well known for their robust, broad-spectrum antimicrobial effects.

Pathogen inhibition

AgNPs produced using *Ocimum sanctum* (Tulsi) and *Azadirachta indica* (Neem) show remarkable activity against *Staphylococcus aureus* and *Escherichia coli* [3,11]. Polyherbal combination of Tulsi, Neem, and Giloy extracts yield AgNPs that are effective against *Proteus vulgaris* and *Bacillus subtilis* [11].

Endophytic Sources

P. aeruginosa, S. aureus, and *Candida albicans* has been reported to be inhibited by AgNPs from the endophytic fungus *Calonectria eucalypti* found in *Saxifraga stolonifera* [4] while in another study 26 mm zone of inhibition against *E. coli* has been demonstrated by AgNPs from Talaromyces funiculosus [21]. Green synthesis of silver nanoparticles (AgNPs) from *Phyllanthus emblica* are highly stable, biocompatible and active nanostructures for dental applications particularly against *Streptococcus mutans* [20]. Antifungal activity against human and plant pathogens like *Aspergillus niger* and *Fusarium oxysporum* is shown by copper oxide nanoparticles from *Brevibacillus brevis* [16].

Green synthesis of silver nanoparticles (AgNPs) using *Phyllanthus emblica* (Indian Gooseberry/Amla) fruit extract yields highly stable, biocompatible, and active nanostructures for dental applications. Phytochemicals of *P. emblica,* such as polyphenols, ascorbic acid, tannins, and flavonoids not only act as reducing agents but also display capping agents that prevent nanoparticle aggregation (Ajintha et al., 2023)

4.2 Anticancer and Cytotoxic Properties

Fungal-mediated nanoparticles exhibit strong anticancer selectivity. For instance, AgNPs produced by *C. smithii* inhibited A549 cell growth (IC50 = 10.46 µg/mL) [6], whereas nanoparticles synthesized from *Cladosporium cladosporioides* (AgNPs) and SeNPs from *P. verhagenii successfully* triggered apoptosis in lung carcinoma lines [21]. These green-synthesized nanoparticles exhibit minimal cytotoxicity toward healthy human cells, including HFB4 and L929 fibroblast lineages [5], [16].

4.3 Precision Therapeutics and Site-Specific Drug Delivery.

Research shows that the therapeutic index of drugs is enhanced by providing targeted delivery and increasing stability [8], [23]. Nanoparticles like AgNPs synthesized from neem leaf extract act as drug carrier and are packed with paclitaxel, exhibiting enhanced anticancer activity against MCF-7 breast cancer cells [8], [21].

Various other therapeutic areas like cognitive enhancement, antidiabetic treatment (e.g., Tulsi leaf extracts stimulating insulin secretion), immune modulation and heart protection have been addressed using modern nanoformulations [3], [25]. Neurological and Anti-inflammatory actions of Neem-based metallic nanoparticles have also great prospects in treating anti-inflammatory conditions and neurological diseases [1], [25].

5. Plant Protection methods and application

Green nanotechnology is rapidly transforming the modern agricultural practices and providing a more ecofriendly and sustainable alternative by substituting noxious and detrimental chemical treatments. These green farming practices have boost the crop yield and ecosystem resilience [10], [30], [40].

Let's have a deeper look at how these nanoparticles work and why they are shaping the future of sustainable farming:

5.1 Nano-pesticides and Biocontrol Agents

Green nanoparticles can efficiently control agricultural pests and diseases.

AgNPs derived from *Nyctanthes arbor-tristis* harbouring endophytes like *Bacillus cereus* display strong Antifungal activities against *Penicillium janthinellum*, a phytopathogenic fungus [13]. These *Bacillus*-mediated AgNPs can also target the rice blast fungus *Magnaporthe oryza* [21]. High level larvicidal activity have been reported by the copper oxide nanoparticles from *Brevibacillus brevis* and mosquito larvae such as *Culex quinquefasciatus* are effectively controlld by the silver nanoparticles from *Adhatoda vasica* [2], [16]. Apart from these, broad-spectrum Protection is ensured by the phytosynthesized nanomaterials from *Azadirachta indica* and *Ocimum sanctum* in various crops [18].

5.2 Nano-Fertilizers for Enhanced Nutrient Delivery

Nano- formulations and "nano-fertilizers" enhances the crop productivity by providing better targeted and effective nutrient delivery system [18]. As a result, there is improved nutrient uptake and enhanced biological processes. AgNPs from teak leaves (*Tectona grandis*) and *Bacillus cereus* endophytes promotes the seedling growth of green gram *(Vigna radiata)* [13], [27] whereas, nanoparticles like ZnO NPs and SiNPs facilitates the nutrient uptake and growth of tea and soyabean plants [14], [21].

5.3 Stress management and increased resilience.

Green nanoparticles from endophytic fungi- silver (Ag), zinc oxide (ZnO), copper (Cu), and silicon (Si) can enhance physiological tolerance in plants against different biotic and abiotic environmental stresses (drought, salinity and pathogen attacks) [14], [26], [29].These biogenic microwonders improve crop resilience and productivity by promoting sustainable agriculture and minimization of chemical usage in agricultural practices [10], [14], [39]. Integration of endophytic nanoparticles has given a sustainable alternative in the form of eco-friendly farming system and has elevated the stress tolerance and crop yield by minimizing agrochemical usage [10, 14, 39].

6. Safety, Toxicity and policy hurdles.

For widespread adoption, understanding and assessment of biocompatibility of green nanoparticles is of utmost importance [31]. Evidence from multiple studies like haemolytic assays and *in vitro* cytotoxicity tests indicate minimal toxicity at therapeutic concentrations [7], [16], [22]. For instance, AgNPs generated from *Terminalia arjuna* demonstrated decent antibacterial activity with minor cytotoxicity [7]. Although the eco-friendly aspect of these green “nanowonders” is very important and desirable for the ecosystem resilience, careful monitoring of its long-term impact on the environment and potential entry into the food chain demands critical vigilance [31]. For "Nano Ayurveda" one of the most significant challenges is the lack of consistent and standardized legal frameworks [25]. Hence, for commercialisation of Nano Ayurveda, one of the greatest responsibilities will be the development of a consistent protocol for characterization, safety, and clinical validation [25], [32].

7. Future Perspectives and Conclusion

A harmonious amalgamation of ancient knowledge and the modern green nanotechnology can offer a sturdy system for future innovations. By utilizing the power of plant secondary metabolites and its endophytes as “green bio-factories” will be a sustainable, extendable and eco-friendly approach.

Future directions should include, elucidation of the precise Molecular Mechanisms involved in nanoparticle synthesis, optimization of synthesis parameters so that consistent nanoparticle sizes and shapes can be achieved are essential. Further, rigorous field applications in agriculture and clinical trials in medicine are essential for assessing the effectiveness of the system. Also, establishment of international standards for the safety and quality of these biogenic nanoparticles are of absolute necessity.

In conclusion, this eco-friendly nanosynthesis technique using medicinal plants and their endophytes marks a pivotal advancement in both nanomedicine and plant protection. By incorporating ancient knowledge with modern science, we can achieve a more effective, sustainable solutions for human health and agricultural resilience [23], [33], [34].

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