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Advances in green chemistry: plant and microbial processes for sustainable nanoparticle synthesis, and their antimicrobial and anticancer applications

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ABSTRACT

Nanotechnology is a rapidly evolving field providing crucial solutions for human well-being. Recently, biogenic nanoparticles from natural sources have garnered significant interest for their health and environmental benefits. These nanoparticles are synthesized through green synthesis techniques, using microorganisms and plant extracts as bio-capping and bio-reducing agents, functioning as bio-nanofactories for nanoscale material production. This method is environmentally friendly, biocompatible, non-toxic, and cost-effective, aligning with green chemistry principles. In light of recent research, we explore the latest advancements in the eco-friendly synthesis of nanomaterials using plants and microbes, and their various biomedical applications.

1. Introduction

Protecting our planet is now second nature. Global warming, melting glaciers, and pollution are ongoing threats due to interconnected factors. Ignoring these issues exacerbates our situation, endangering all life with heightened risks and toxicity. Scientists focus on eco-sustainability and green chemistry to foster safer practices and safeguard our environment. Green chemistry is all about finding innovative ways to reduce or eliminate the use and generation of hazardous substances in the design, manufacture, and application of chemical products [1–3].

Green chemistry provides a safe and environmentally friendly way to produce valuable natural molecules [4,5]. These natural molecules, abundant in plants, animals, and even microscopic organisms, offer a wealth of useful products like medications, fragrances, and flavorings [6,7]. Combining natural products with green chemistry principles is a major step towards sustainable chemical practices [8–10]. By utilizing the potential of natural resources like plants and microbes, scientists have made significant progress in various fields [11–13].

Several research studies have demonstrated the efficacy of green synthesis techniques in creating nanoparticles with favorable characteristics [14–16]. Microbial-assisted synthesis has displayed considerable potential as microorganisms are capable of reducing metal ions and generating nanoparticles [17,18]. Additionally, fungal and algal-mediated synthesis have emerged as feasible options, presenting sustainable and scalable approaches for nanoparticle manufacturing [19,20]. The utilization of plant-mediated synthesis has garnered considerable interest due to the abundance and variety of plant species, offering a diverse pool of bioactive compounds [21,22]. This review is notable for its extensive analysis of green synthesis methods employing plants and microbes. Its key focus is to underscore the importance of green chemistry in promoting sustainability. Moreover, it highlights the use of nanoparticles produced through eco-friendly processes in medical applications.

2. Green chemistry and It's importance

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Green chemistry plays a pivotal role in promoting sustainable development by prioritizing the reduction of environmental harm caused by chemical processes and products. Its objectives include decreasing carbon emissions, mitigating the creation of harmful byproducts, and optimizing the efficiency of chemical production [23–28]. The origins of green chemistry can be traced to the enactment of the Pollution Prevention Act of 1990 in the United States, which prompted a transition towards minimizing waste directly at its source rather than solely focusing on waste treatment [29,30]. By prioritizing the principles of green chemistry, such as waste prevention, atom economy, and energy efficiency, researchers and industries can develop sustainable solutions that not only benefit the environment but also contribute to human health and well-being [31–36]. This approach combines reducing waste, saving resources, and minimizing environmental harm, all while being profitable. It encourages using renewable materials, creating closed-loop systems, and developing products that break down naturally. This tackles problems like resource depletion, pollution, and climate change. By combining these ideas in research, we can create a future that's good for both the environment and the economy [37–42]. The significance of green chemistry lies in its capacity to develop chemicals and procedures that pose fewer risks to human health and the environment. Its goal is to curb pollution and hazardous practices [5,43]. By adhering to the Twelve Principles of Green Chemistry (Table 1), scientists can pursue a more sustainable and eco-friendly approach to chemical processes [44].

Table 1. Basic Principles of green chemistry.

Principle	Description
Prevention	It's better to prevent waste than to clean it up after it's formed. Design processes to maximize efficiency and minimize waste generation.
Atomic economy	Design synthetic methods to maximize the incorporation of all materials used in the process into the final product, minimizing the generation of waste.
Safer chemical synthesis	Design synthetic methods to use and generate substances with little or no toxicity to humans and the environment.
Safer chemicals design	Design chemical products to be effective, yet have minimal toxicity and be safe for humans and the environment.
Use of safer solvents and auxiliaries	Minimize the use of auxiliary substances (solvents, separation agents, etc.) and use safer, less hazardous alternatives wherever possible.
Energy efficiency	Minimize energy usage during the synthesis of chemicals and the products themselves, aiming for processes that are both environmentally benign and economical.
Renewable Feedstocks	Use renewable feedstocks and raw materials whenever possible to reduce dependence on fossil fuels and decrease the environmental impact of chemical production.
Reduction of derivatives	It's best to steer clear of or reduce unnecessary derivatization processes since they involve using extra reagents, which ultimately leads to waste generation.
Catalysis	Design catalytic processes to maximize the efficiency of chemical reactions while minimizing waste generation and energy consumption.
Degradation products design	Design chemical products so that at the end of their function, they break down into innocuous substances and do not persist in the environment.
Real-time analysis for pollution prevention	Develop analytical methodologies to allow for real-time monitoring and control of chemical processes to minimize the formation of hazardous substances.
Accidents prevention	The selection of both materials and their application in a chemical procedure should prioritize the reduction of possible mishaps like leaks, explosions, and fires, with the goal of enhancing safety for both workers and the environment.

This approach prioritizes waste minimization, the use of safer chemicals, energy conservation, and renewable resources. Overall, green chemistry plays a crucial role in advancing sustainable development by promoting cleaner production methods, fostering innovation, and supporting the transition to a more environmentally responsible economy. It represents a fundamental shift in the way we approach chemistry and industrial processes, emphasizing the importance of sustainability and long-term thinking in scientific and technological innovation [45–47].

3. Green synthesis of nanoparticles

Green nanoparticle synthesis offers advantages over traditional chemical methods, being eco-friendly, non-toxic, and sustainable for large-scale production. Anastats (1999) explores utilizing green synthesis to develop durable and safe processes for ecological sustainability. Unlike conventional approaches using hazardous chemicals, green synthesis employs renewable natural resources with minimal environmental impact [48]. By adhering to green chemistry principles, these methods ensure safety, effectiveness, and economic viability, fostering sustainable technologies. Using natural reagents like herbs, microorganisms, and agricultural waste [49], it offers a cost-effective and environmentally friendly route for synthesis, yielding biogenic nanomaterials via reduction processes facilitated by biological components [50]. Green synthesis, utilizing plant extracts, bacteria, fungi, and enzymes, is simple, cost-effective, and scalable for industrial production [51–57].

4. Biological components for synthesis

Green synthesis employs substances sourced from nature such as plant extracts, fungi, bacteria, algae, and other living organisms to create nanomaterials, thereby decreasing reliance on harmful chemicals and lessening environmental impact17,58. This method is non-toxic, pollution-free, and offers eco-friendly and sustainable production of nanoparticles, making it a crucial approach in nanotechnology due to its numerous benefits (Table 2).

4.1. Synthesis of Plant-Mediated

Across time, plants and their derivatives have been profoundly meaningful to humans, tapping into both ancient wisdom and practical knowledge. The observation of animals consuming plants has served as a treasure trove of information, enabling humans to link plant consumption with its outcomes. Plants are deemed "medicinal" when they exhibit notable effectiveness in healing or managing illnesses [58–60].

Table 2. Benefits for eco-friendly and sustainable synthesis of nanoparticles.

Advantages	Description
Environmentally friendly	Most of the approaches rely on natural sources and processes, using harsh chemicals for longer durations, thus leaving less impact on the environment.
Sustainability	Since these methods are almost always based on biological entities, such as plants, microbial, or enzymatic, are dependent on a growing phenomenon. The latter promotes sustainability since hardly any physical resources are utilized except for the nanoparticles.
Cost-effectiveness	Some of the traditional chemical methods entail costly reagents, and most of the processes involve energy-intensive, limitations, where most of plant-facilitated, microbial, and enzymatic-assisted processes are somewhat less expensive due to the availability of the biological material used and the reaction conditions being less harsh.
Controlled synthesis	Biological systems substantially alleviate the size and shape of the nanoparticles and help maintain consistent nanoparticle composition, leading to more uniform and tailored nanoparticles with specific properties.
Biocompatibility	Nanoparticles produced via biological processes typically exhibit higher biocompatibility, rendering them suitable for a range of applications in biomedicine and environmental contexts.

Eco-friendly nanoparticle production relies on plant-based derivatives, which are trusted for their safety. The green synthesis of nanomaterials from plant extracts is gaining popularity due to its flexibility and cost-effectiveness. These extracts can come from various plant parts, including leaves, fruits, seeds, roots, stems, and flowers, each containing unique structural components like essential oils, carotenoids, and phenolics that play a crucial role in the green synthesis process [61–63]. Extracts from various plant parts are added to metal ion solutions to initiate production. Phytochemicals like sugars, flavonoids, proteins, enzymes, polymers, and organic acids in these extracts act as both reducing and stabilizing agents. Alkaloids, polyphenols, terpenoids, polysaccharides, amino acids, organic acids, vitamins, and heterocyclic compounds participate in bio-reduction and contribute to capping and stabilizing the bio-synthesized nanoparticles [64–66].

Nanoparticles derived from medicinal plants exhibit a spectrum of features dependent on factors such as the bioactive molecules present in the plant, its composition, and the processing variables like pH and temperature [67–70]. These distinctions yield a wide array of nanoparticle traits, significantly influenced by the plant's phytochemical properties. Often, nanoparticles inherit the medicinal properties of the plant, showcasing improved efficacy compared to extracts alone. They present an exciting avenue for molecular diagnosis and targeted drug delivery, overcoming the limitations of traditional medicinal approaches and potentially integrating more swiftly into conventional treatments [71,72].

Silver and gold were the initial nanoparticles examined through this synthesis method. Numerous widely recognized and easily accessible plants, including aloe vera, margousier, and Luzerne (Figure 1), can be utilized to produce nanoparticles of different metals such as silver, copper, cobalt, zinc, and others.

Aloe vera — *Azadirachta indica* (margousier) — *Medicago sativa* L. (Luzerne)

Fig. 1. Plants used in the biogenic synthesis of nanoparticles

4.2. Synthesis of microorganisms-Mediated

Microbes like bacteria, fungi, and algae are crucial for making metal nanoparticles through biogenic synthesis, an eco-friendly method. By using enzymes and biological components, this approach reduces materials, offering a sustainable alternative to traditional chemical methods [73,74]. Table 3 lists the microorganism strains used for the synthesis of metal nanoparticles.

Microbial enzymes act as effective reducing agents, allowing efficient nanoparticle synthesis while cutting energy and chemical costs. Extremophilic microbes, like thermophiles and haloalkaliphiles, are being studied for nanoparticle production, especially for silver and selenium, showcasing their potential. These biogenic nanoparticles, coated in proteins, possess antimicrobial properties against various pathogens, emphasizing their practical benefits [75–77].

The literature indicates that *Actinobacter* spp., *Escherichia coli*, *Klebsiella pneumonia*, *Lactobacillus* spp., *Bacillus cereus*, *Corynebacterium* spp., *Pseudomonas* spp., and *Enterobacter cloacae* can generate metallic nanoparticles by converting metallic ions into nanoparticles [78–80].

Actinomycetes, a diverse group of Gram-positive bacteria, have garnered attention due to their commercial significance and superior intracellular production capabilities compared to other contenders in biosynthesis [81,82]. *Streptomyces*, *Rhodococcus*, and *Nocardia* are acknowledged for their involvement in the production of gold nanoparticles [83]. Cyanobacteria, the most prevalent photosynthetic bacteria, primarily contribute to the stabilization of nanoparticles. Notably, *Oscillatoria limnetica*, a cyanobacterium, has been effectively employed in the synthesis and stabilization of silver nanoparticles. However, bacterial synthesis of nanosystems encounters challenges in purification and the precise control of particle size and shape [84].

Yeast releases enzymes to reduce metal ions at a fast pace, making them easily collectible in labs due to their quick multiplication. Yeast generates more nanoparticles than bacteria. Research has shown that silver nanoparticles can be produced from various yeast strains like *Pichia capsulata*, *Candida utilis*, *Rhodotorula glutinis*, and a silver-tolerant *Saccharomyces cerevisiae* strain. *Hansenula anomala* shows potential as a catalyst for biofuel production [85–88].

5. Anticancer application of green-nanoparticles

Nanotechnology, offer promising avenues for various medical purposes, with medicine being particularly prominent [96-98]. Metal nanoparticles produced through phytochemical reduction have recently gained attention for their significant applications. The increasing attention on research in phytonanotechnology arises from its promising benefits compared to conventional physicochemical approaches (Figure 2).

In a research endeavor led by Maheswari and colleagues in 2021, developed Titanium dioxide (TiO_2) nanoparticles using extracts from *Plectranthus amboinicus*, *Phyllanthus niruri*, and *Euphorbia hirta* plants. These modified nanoparticles showed promising anticancer effects against oral cancer cells.

Table 3. List of microorganisms for synthesis of nanoparticles.

Metal	Microorganism	Classification	References
Silver	*Lactobacillus delbrueckii*	Bacteria	[89]
Silver	*Fusarium oxysporum*	Fungi	[90]
Silver	*Escherichia coli*	Bacteria	[91]
Cadmium Sulfide	*Lactobacillus* sp	Bacteria	[78]
Cadmium Sulfide	*Sachharomyces cerevisae*	Bacteria	
Cadmium Sulfide	*Escherichia coli*	Bacteria	[92]
Cadmium Selenide	*Saccharomyces cerevisiae*	Fungi	[93]
Cadmium Selenide	*Fusarium oxysporum*	Fungi	[94]
Cadmium Selenide	*Pseudomonas aeruginosa*	Bacteria	[95]

Especially notable was the combination of *P. amboinicus* and *P. niruri* extracts, which significantly enhanced the nanoparticles' anticancer efficacy. *Artemisia turcomanica* leaf extract is employed in the eco-friendly synthesis of silver nanoparticles (AgNPs), and researchers are investigating its impact on inhibiting gastric cancer cell growth and promoting apoptosis [99]. Compared to commercially available nanoparticles, AgNPs produced through photosynthesis required a smaller dosage to effectively inhibit cell proliferation. Studies suggest that silver nanoparticles disrupt signaling pathways and interact with membrane proteins to impede cell growth [100]. Research presents the creation of silver palladium bimetallic nanoparticles (AgPd NPs) using water-based extract from *Terminalia chebula* fruit. These nanoparticles exhibit notable effectiveness in combating lung cancer cells. The fruit extract comprises various compounds such as phenols, flavonoids, saponins, proteins, and others. These compounds serve crucial roles as capping and reducing agents during the synthesis of AgPd NPs [101]. In 2021, Wang et al. synthesized gold nanoparticles (AuNPs) from *Phyllanthus emblica* fruit extract. These AuNPs showed significant concentration-dependent reduction in AGS cancer cell viability, with IC50 values of 80 µg/mL and 100 µg/mL. Microscopy revealed reduced colony formation in cells treated with 100 µg/mL of AuNPs compared to cisplatin, suggesting anticancer activity without normal cell toxicity [102].

6. Antimicrobial application of green-nanoparticles

Scientists are improving antimicrobial agents due to rising antibiotic resistance. Metal nanoparticles show promise by disrupting microorganisms' resistance mechanisms and preventing biofilm formation. They can alter microbial genetics, though multiple changes in a single cell are rare. Gold nanoparticles (AuNPs) possess biocompatibility and antimicrobial properties but need interaction with biomolecules for full antimicrobial effect. Cross-linking with substances like gelatin, collagen, or chitosan enhances bonding, integrating AuNPs with macromolecules, boosting antimicrobial efficacy for biomedical applications [103–106].

Cinnamon tamala leaf extract was tested for antimicrobial potential, determining its minimum inhibitory concentration (MIC). Biologically synthesized silver nanoparticles (AgNPs) were then assessed for their antimicrobial activity against multidrug-resistant *E. coli*, *K. pneumoniae*, and Gram-positive *Staphylococcus aureus*. AgNPs showed concentration-dependent bacteriostatic effects against all strains and inhibited biofilm formation, with various plant extracts, phytochemicals, and proteins acting as capping agents in this nanocomposite. AgNPs also exhibited time-dependent reduction in bacterial growth [107]. Silver nanoparticles derived from *Cola nitida* demonstrated antimicrobial efficacy against *E. coli*, *P. aeruginosa, Aspergillus niger*, *Aspergillus fumigatus*, and *Aspergillus flavus*. The incorporation of advanced nanomaterials like silver nanoparticles in the paint sector could enhance paint quality by imparting antimicrobial properties. This potential is highlighted by the prospect of utilizing nanoparticles as supplements in paint formulations [108]. Zinc oxide nanoparticles have potent antibacterial and antifungal properties due to their photo-oxidizing and photocatalytic nature. Their small size allows them to penetrate bacterial cells, disrupting internal processes effectively [103].

Iron nanoparticles demonstrate strong antimicrobial properties. Studies reveal that these nanoparticles, sourced from various origins, show significant effectiveness against a variety of diseases. Extensive research has investigated how different types of iron nanoparticle extracts affect specific bacterial strains. Utilizing iron-based nanosystems in medical equipment effectively hampers microbial growth. Notably, applying iron nanoparticles combined with essential oils on catheter surfaces reduces biofilm formation by *S. aureus* and *K. pneumonia*. However, their efficacy declines as biofilm formation progresses. Moreover, integrating patchouli oil infused with iron nanoparticles into wound dressing fibers has been proven to curb the growth of *S. aureus* biofilms [109–111].

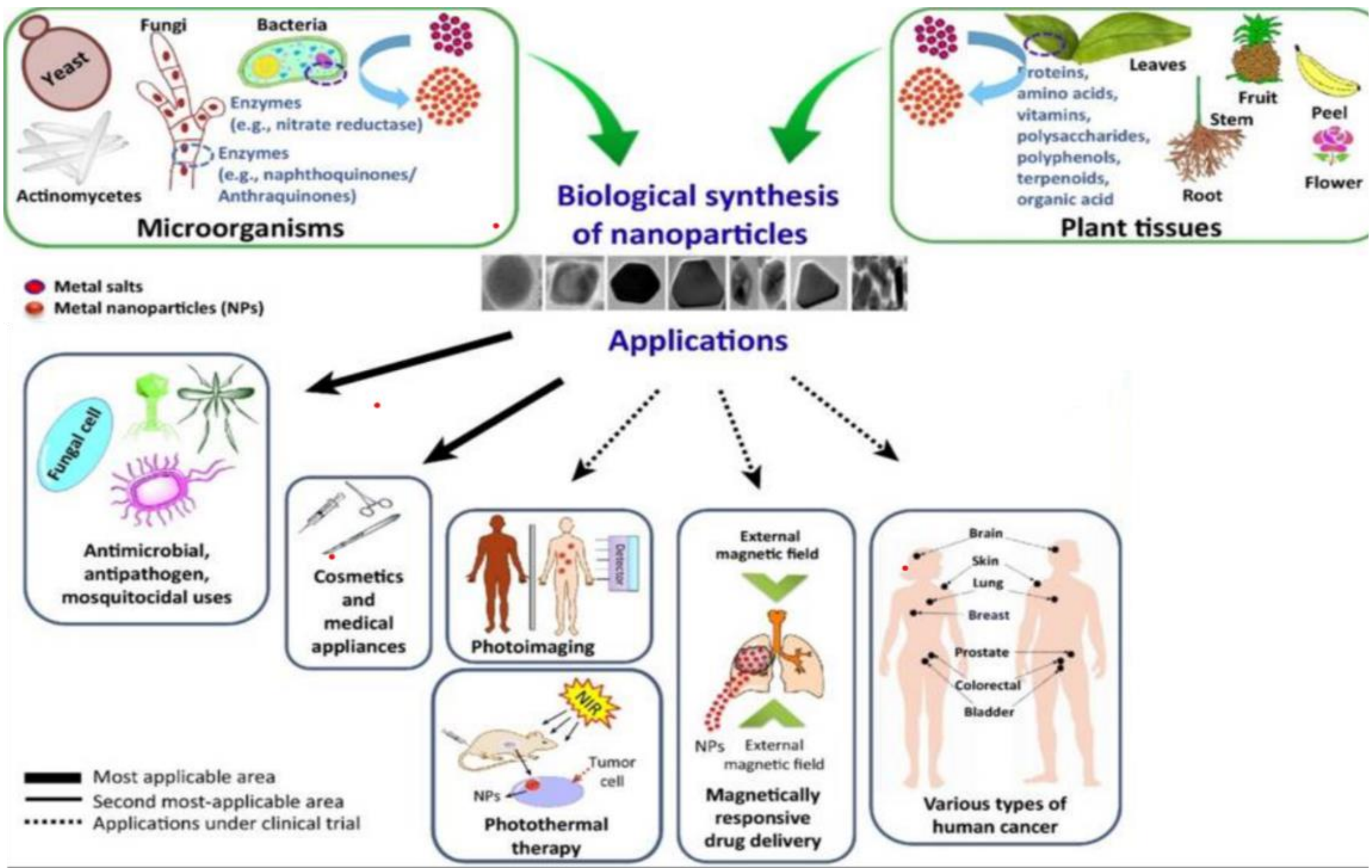

Fig. 2. Applications of nanoparticles in biomedical fields (Adapted from[53])

7. Conclusion

This review examines the environmentally friendly creation of metallic nanoparticles using biological methods, with a specific focus on understanding the underlying processes involved in their biosynthesis. It emphasizes the importance of biomolecules found in plant extracts and microorganisms and their potential applications in medicine. The review also highlights the significance of phytonanotechnology as a complementary approach for developing nanoparticles with bioactive properties. Additionally, it underscores the importance of green synthesis as an alternative method for producing phytonanoparticles with enhanced antimicrobial and anticancer activities. Biosynthesis methods are praised for their speed, simplicity, cost-effectiveness, environmental sustainability, and safety in producing nanoparticles that are highly stable and effective. These eco-friendly nanoparticles, known as green nanoparticles, have the potential to promote sustainable development by utilizing renewable resources in their production and facilitating easy recycling, thereby reducing the environmental impact of nanoparticle manufacturing and waste. Scientists are now exploring natural resources for their abundance, compatibility with the environment, scalability, and affordability.

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