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Review Article

ZINC OXIDE NANOPARTICLES OF HERBAL PLANTS FOR ANTIFUNGAL ACTIVITY: A REVIEW

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ABSTRACT

Zinc oxide nanoparticles (ZnO-NPs) have emerged as one of the most promising metal oxide nanomaterials owing to their unique physicochemical, optical, semiconducting, and biological properties. Their high surface area, wide band gap, excellent biocompatibility, photocatalytic activity, and antimicrobial potential have led to extensive applications in medicine, pharmaceuticals, agriculture, cosmetics, environmental remediation, and biosensing. Conventional methods for ZnO nanoparticle synthesis, including precipitation, sol-gel, microemulsion, and chemical vapor transport techniques, provide controlled particle characteristics but often require hazardous chemicals and energy-intensive processing. In contrast, green synthesis using plant extracts, microorganisms, and algae has gained considerable attention as an eco-friendly, cost-effective, and sustainable alternative. Plant-derived phytochemicals act as natural reducing and stabilizing agents, facilitating the synthesis of stable nanoparticles with enhanced biological activity. This review summarizes the physicochemical properties, synthesis approaches, and biomedical applications of ZnO nanoparticles, with particular emphasis on plant-mediated green synthesis. The advantages and limitations of conventional and biological synthesis methods are critically discussed. Furthermore, the review highlights the diverse therapeutic applications of ZnO nanoparticles, including antibacterial, antifungal, antimicrobial, anticancer, wound-healing, drug and gene delivery, biosensing, bioimaging, and cosmetic applications. Recent reports on the green synthesis of ZnO nanoparticles using various medicinal plant species and their enhanced biological activities are also summarized. The available evidence demonstrates that green-synthesized ZnO nanoparticles possess improved biocompatibility, stability, and therapeutic efficacy compared with conventionally synthesized nanoparticles. Despite significant advances, challenges related to large-scale production, reproducibility, long-term safety, and clinical translation remain. Future investigations should focus on standardized green synthesis protocols, detailed toxicity assessments, and clinical validation to facilitate the successful integration of ZnO nanoparticles into pharmaceutical and biomedical applications.

Keywords: Zinc oxide nanoparticles, Green synthesis, Plant-mediated synthesis, Nanotechnology, Biomedical applications, Antimicrobial activity, Antifungal activity, Drug delivery, Wound healing, Biosensors, Bioimaging, Medicinal plants.

INTRODUCTION

Zinc oxide (ZnO) is described as a functional, strategic, promising, and versatile inorganic material with a broad range of applications. It is known as II–VI semiconductor, since Zn and O are classified into groups two and six in the periodic table, respectively (Neumark, 2007). ZnO holds a unique optical, chemical sensing, semiconducting, electric conductivity, and piezoelectric properties (Fan and Lu, 2005). It is characterized by a direct wide band gap (3.3 eV) in the near-UV spectrum, a high excitonic binding energy (60 meV) at room temperature, and a natural n-type electrical conductivity. These characteristics enable ZnO to have remarkable applications in diverse fields (Wang, 2004). The wide band gap of ZnO has significant effect on its properties, such as the electrical conductivity and optical absorption.

The excitonic emission can persevere higher at room temperature and the conductivity increases when ZnO doped with other metals (Wang and Song, 2006). Though ZnO shows light covalent character, it has very strong ionic bonding in the Zn–O. Its longer durability, higher selectivity, and heat resistance are preceded than organic and inorganic materials. The synthesis of nano-sized ZnO has led to the investigation of its use as new antibacterial agent. In addition to its unique antibacterial and antifungal properties, ZnO-NPs possess high catalytic and high photochemical activities (Mende and Driscoll, 2007; Wellings *et al*., 2008). ZnO possesses high optical absorption in the UVA (315–400 nm) and UVB (280–315 nm) regions which is beneficial in antibacterial response and used as a UV protector in cosmetics (Song *et al*., 2011).

Advantages

I] Antimicrobial and Medical Strengths

Broad-spectrum action: Kills a wide range of bacteria, fungi, and microbes even at low concentrations.

Targeted therapy: Shows selective toxicity against cancer cells while remaining relatively safe for healthy biological tissues.

Wound healing: Accelerates tissue regeneration and fights infections when added to ointments or dental materials (Janotti and Van, 2009).

II] Optical and Electronic Properties

UV protection: Absorbs and reflects ultraviolet rays efficiently, making it a core ingredient in transparent sunscreens and cosmetics.

Wide bandgap: Possesses a high bandgap (~3.37 eV) ideal for advanced optoelectronic devices like solar cells, LEDs, and sensors.

III] Environmental and Agricultural Uses

Catalytic purification: Breaks down harmful organic dyes and water pollutants under light exposure via high photocatalytic activity.

Crop enhancement: Improves plant stress tolerance and acts as a safe nano-fertilizer to supply essential micronutrients (Zhang *et al*., 2012).

Synthesis of ZnO nanoparticles

Due to its unique optical and electrical properties, ZnO nanoparticles have attracted considerable attention with applications in optoelectronics, photocatalysis and biomedical engineering. Controlled synthesis of ZnO-NPs with desired size, shape and optoelectronic properties is crucial for their effective utilization in various technologies (Indhira *et al*., 2022; Ahmad *et al*., 2023).

I] Conventional Synthesis Methods

Precipitation Method

Precipitation is one of the simplest and most widely used wet chemical techniques for ZnO NP synthesis. It involves controlled addition of a base solution like sodium hydroxide or ammonium hydroxide to a zinc salt solution like zinc acetate or zinc nitrate under stirring.

The zinc hydroxide or zincate ions formed immediately precipitate as ZnO-NPs (Kavitha *et al*., 2023). The precipitation method for synthesizing ZnO-NPs offers several advantages. It is a simple one-step reaction that utilizes inexpensive precursors, allowing for cost-effective production on a large scale. The size of the nanoparticles can be easily controlled by adjusting parameters such as pH, concentrations, and temperature. However, this method has some drawbacks. The resulting nanoparticles often have a broad size distribution, which can limit their uniformity and application performance (Zhang *et al*., 2021).

Sol-gel Method

In this method, ZnO NPs are prepared by hydrolysis and condensation reactions of zinc-containing precursors like zinc acetate in alcohol solutions. Upon controlled addition of water and thermal treatment, the gel formed leads to crystalline ZnO-NPs. Variations involve using surfactants or polymers for shape and size control. The solgel method for synthesizing ZnO-NPs offers several advantages (Zhang *et al*., 2022).

It allows for homogeneous mixing at the molecular level, ensuring phase purity and uniform distribution of dopants or surface functionalization agents. This method provides flexibility for incorporating different materials and tailoring the properties of the nanoparticles (Tang *et al*., 2016). However, the sol-gel process can be lengthy and involve multiple steps, which may increase the complexity and time required for synthesis. It can also present challenges in terms of repeatability and scale-up due to the sensitivity of the process parameters (Wang *et al*., 2018).

Microemulsion Method

A microemulsion-based technique uses reverse micelles of surfactants in non-polar organic solvents to confine zinc salt hydrolysis. Nanoparticles nucleate and grow within the aqueous cores of inverse micelles (Guo *et al*., 2023). The microemulsion method for synthesizing ZnO-NPs offers several advantages. It allows for the synthesis of nanoparticles with a narrow size distribution, resulting in a more uniform product (Liu *et al*., 2023). The use of different surfactants in the microemulsion system provides the potential for shape-control, enabling the production of nanoparticles with specific morphologies. However, this method has some drawbacks. It often involves the use of toxic organic solvents, which can be a concern from both environmental and safety perspectives (Xie *et al*., 2023).

Chemical vapor transport method

In this method, the powder is heated to a high temperature in the presence of a transport agent such as graphite or iodine, then transported to a cooler region, where it condenses to form nanoparticles (Xue *et al*., 2015). Bunsen initially introduced this technique in 1852. Heterogeneous reactions that have a common characteristic are referred to as “Chemical Vapor Transfer”. ZnO nanostructures are formed as a result of the process that results from the vapors of oxygen

and zinc or oxygen mixture being transported and reacting with one zone after another (Colibaba, 2019). That was a straightforward, simple, and easy way to obtain the ZnO decomposition. It also required heating the zinc powder while the oxygen was flowing, which required careful control of the oxygen pressure to zinc vapor pressure ratio in order to produce suitable ZnO nanostructures. Changes in this ratio led to significant variations in the morphology of ZnO, including the size and geometry of nanostructures, which have been observed (Guell *et al*., 2021).

II] Biological/Green Synthesis Methods

Plant-mediated synthesis

An interesting alternative to traditional chemical approaches is the production of ZnO-NP using plants and plant extracts. The use of plants and plant extracts is an appealing, innovative, and safe method choice. For the synthesis of ZnO-NPs, we have a variety of plants and processes at our disposal. 200 mL of water was extracted for 4 h at 60–70 °C from powdered ground leaves, flowers, and fruits. The collected plant extracts and ZnO were then mixed in a separate flask for the synthesis of ZnO-NPs (Dixon *et al*., 2016). The mixture was stirred for 4 h at 100 rpm under the heating condition. The reaction solution was centrifuged at 10,000× g for 20 min, the supernatant was discarded, and the precipitation was collected. The precipitate obtained was washed with distilled water and freeze-dried to obtain ZnO NP (Paul *et al*., 2019).

Microorganisms-mediated synthesis

There has been a lot of interest in employing microbes, and numerous studies have been done using various models of microorganisms. However, maintaining certain processes, such as cell cultures, intracellular synthesis, and multiple purification steps, made microbially assisted nanoparticle synthesis somewhat challenging, and the mechanism of biological synthesis of ZnO-NP using microbes is not yet fully understood.

Many studies have been conducted on biologically mediated production of ZnO-NP using microorganisms such as fungus, bacteria, yeast, algae, and phage (Muhammad *et al*., 2019). The choices of microorganisms, ideal cell growth conditions, and the route of biosynthesis, intracellular or extracellular, are the primary requirements for the production of ZnO-NPs. Most of the time, Sphingobacterium thalpophilum, Staphylococcus aureus, and Bacillus megaterium NCIM2326 were used to produce rod/cubic, multiform, triangular, and acicular ZnO-NP with a particle size of 10–95 nm (Reghioua *et al*., 2021).

Algae-mediated synthesis

As it reduces the toxicity of the chemical ingredients used to produce the nanoparticles, algae are one of the safest and most stable natural materials used in the green synthesis of nanoparticles. According to reports, ZnO-NPs can be produced using a variety of marine macro- and microalgae, including chlorella, brown *Sargassum muticum*, green *caulerpa peltata*, and red *gracilaria gracilis* (Rudramurthy *et al*., 2016; Sanaeimehr *et al*., 2018).

Applications of ZnO-NPs in biomedicine

Antibacterial activity

The synthesised green ZnO-NPsare effective antibacterial agents for both Gm(+ve)&Gm(-

ve) bacteria, such as Mycobacterium tuberculosis, Bacillus subtilis, Salmonella typhimurium, Staphylococcusaureus, *Streptoc occus pyogenes*, *Escherichiacoli*, *Klebsiellapn eumonia*. The usage of antibacterial materials including ZnO-NPs in dental composites and common goods like mouthwash, diapers, and shampoo demonstrates the antibacterial property of ZnO-NPs (Butsele *et al*., 2009).

Antifungal activity

ZnO NPs have been demonstrated to possess antifungal activities against a variety of pathogenic yeasts and fungi, which is why they are widely used as antifungal additives in the food business. ZnO NPs were made from Lycopersicon esculentum leaf extract, and Vijaya kumar *et al* showed that at concentrations of 100 g/ml, it was effective against the most prevalent fungus, Candida albicans (Islam *et al*., 2022).

Antimicrobial activity

ZnO-NPs made from Azadirachtaindica's aqueous leaf extract have demonstrated antibacterial efficacy against yeast and Gm(+ve) and Gm(-ve) bacteria.Because ZnO-NPs produce reactive oxygen species from water and oxygen, their antibacterial properties compromise the integrity of bacterial membranes. Significant antimicrobial activity, including both antibacterial and antifungal properties, has been shown by ZnO-NPs. ZnO-NPs made from the aqueous leaf extract of Azadirachta indica, or neem, are one prominent example. The effectiveness of these nanoparticles against a variety of microorganisms, such as yeast and Gram-positive (Gm(+ve)) and Gram-negative (Gm(-ve)) bacteria, has been shown. This broad-spectrum antibacterial activity demonstrates how adaptable and potent ZnO-NPs are against a range of infections (Khan *et al*., 2023).

Drug and gene delivery

ZnO-NPsare frequently employed in drug delivery where the pharmaceuticals are loaded with NPs to ensure sufficient drug delivery to the target. Additionally, the duration of medication delivery to the target location is prolonged when biodegradable materials are utilised to create NPs.

For the treatment of numerous fatal clinical disorders, including cancer and neurodegeneration, gene therapy is a promising area. Creating a suitable vector that retains the DNA and allows for efficient delivery is one of the industry's biggest difficulties (Anjum *et al*., 2021).

Anticancer activity

One of the main functions of the mineral zinc is to keep the tumor suppressor gene p53 operating properly. P53 controls apoptosis by activating the caspase-6 enzyme. Furthermore, ZnO-NPs' superior electrostatic property makes it easier to destroy cancer cells one at a time. A number of malignant cell lines, including Human Colon Adenocarcinoma (Caco2), Pancreatic Adenocarcinoma (PANC-1), Ovarian Adenocarcinoma (CaOV-3), and Colonic Adenocarcinoma, have been shown to be sensitive to ZnO-NPs produced using the green synthesis method (COLO205). ZnO-NPs are able to target and kill cancer cells through a variety of mechanisms, showing a promising future in anticancer therapy. Zinc has many important functions in the body, one of which is to keep the tumour suppressor gene p53 intact. This gene is essential for controlling the cell cycle and triggering

apoptosis in DNA-damaged cells (Mierke, 2020).

Biosensor

Zinc oxide (ZnO) nanoparticles (NPs) are widely utilized in biosensor applications because to their optical characteristics, polymorphic nature, ease of manufacturing, and high electron mobility. Additionally, the high isoelectric pH of 9.5 of ZnO-NPs allows for protein adsorption by electrostatic contact. A highly effective platform for high-performance biosensors can be created using ZnO-NPs and adsorbed biomolecules (Naik, 2022).

Wound healing

Numerous studies have shown that ZnO-NPs may be used as an efficient wound healing agent. ZnO-NPs made by green synthesis have wound-healing properties. Khatami *et al* saturated the cotton with coffee grounds to create cotton wound dressings and evaluate the antibacterial capabilities of ZnO-NPs. ZnO-NPs, have shown plenty of potential as useful agents in the healing of wounds because of their unique properties. Numerous studies that show their capacity to encourage wound closure and improve healing processes lend credence to their use in wound care.

In this particular context, ZnO-NPs have a number of benefits, such as their antibacterial activity, anti-inflammatory effects, and capacity to promote tissue regeneration. ZnO-NPs' strong antibacterial activity is one of the main elements influencing their ability to heal wounds. It has been demonstrated that a wide range of bacterial and fungal infections that can impede wound healing are inhibited by ZnO-NPs (Iqbal *et al*., 2021).

Bio imaging

Another well-known semiconductor that has the potential to replace the conventional Cod-related species employed in biology and optical landscapes is ZnO. It's intriguing how ZnO-NPs are used for bio-imaging. This feature has applications in biology and medicine that can be employed at different levels. In biomedical applications like medication delivery and gene transfer including cellular imaging, bio imaging is commonly used as a vital supplement for human systems. ZnO-NPs, are showing promise as an alternative for traditional semiconductor materials based on cadmium that are employed in optical and bio imaging applications. Because of their distinct optical characteristics, such as their high luminescence and wide band gap, ZnO-NPs are a good choice for bioimaging (Mirzaei, and Darroudi, 2017).

Pharmaceutical and cosmetics

ZnO-NPs have an anti-inflammatory tendency and hasten the healing of wounds. They are utilised as a bone substitute in dentistry as well as in dermatological applications like wound dressings and ointments. ZnO-NPs is transparent to light as opposed to the white colour that bulk ZnO emits. This has raised consumer interest in sunscreens based on nanotechnology. ZnO-NPs are also viewed as typical examples of conventional physical sunblocks that cover pigments and other elements that must be free of irritants, allergies, and acne-causing properties (Raina *et al*., 2022).

Table 1: ZnO nanoparticles of herbal plants

S. No.	Plant and Plant Part	Extraction of Phytochemicals	Zn Salt Precursor	Reference
1.	*Agathosma betulina* Leaf	Deionised water as solvent, ~100 ℃ for 1 h, pH 5	$Zn(NO_3)_2 \cdot 6H_2O$	Thema et al., (2015)
2.	*Plumbago auriculata* Aerial parts	Ethanol as solvent, evaporation under reduced pressure using Buchi rotary evaporator	$Zn(CH3COO)_2 \cdot 2H_2O$	Melk et al., (2021)
3.	*Monsomia burkeana* plant	Deionised water as solvent, 80 ℃ for 1 h	$ZnCl_2 \cdot 6H_2O$	Ngoepe et al., (2018)
4.	*Lessertia montana* Leaf	Distilled water as solvent, 65 ℃ for 4 h	ZnO	Balogun and Ashafa, (2021)
5.	*Lessertia frutescens* Leaf	Deionised water as solvent, 80 ℃ for 15 min	$Zn(NO)_3 \cdot 6H_2O$	Mahlaule et al., (2019)
6.	*Tulbaghia violacea* Bulb	Distilled water as solvent, 80 ℃ for 1 h	$Zn(CH_3COO)_2 \cdot 2H_2O$	Mbenga et al., (2022)
7.	*Aspalathus linearis* Leaf	Deionised water as solvent, 25 ℃ for 48 h	$Zn(NO_3)_2 \cdot 6H_2O$	Diallo et al., (2015)
8.	*Dovyalis caffra Leaf*	Deionised water as solvent, 80 ℃ for 2 h	$Zn(CH_3CO_2)_2 \cdot 2H_2O$	Adeyemi et al., (2022)
9.	*Dovyalis caffra Fruit*	Distilled water as solvent, boiled for 20 min	$Zn(CH_3CO_2)_2$	Elemike et al., (2019)
10.	*Athrixia phylicoides DC Leaf*	Deionised water as solvent, 60 ℃ until water turned dark green in colour	$Zn(NO_3)_2 \cdot 6H_2O$	Kaningini et al., (2022)

CONCLUSION

Green-synthesized zinc oxide nanoparticles have emerged as promising nanomaterials due to their eco-friendly synthesis, excellent biocompatibility, and broad biomedical applications. Plant-mediated synthesis offers a simple, cost-effective, and sustainable approach for producing stable ZnO nanoparticles with enhanced biological activity. These nanoparticles exhibit significant antibacterial, antifungal, anticancer, wound-healing, drug delivery, and biosensing potential. Although further studies are required to standardize large-scale production and evaluate long-term safety, green-synthesized ZnO nanoparticles

represent a promising platform for future pharmaceutical and biomedical applications.

DECLARATION OF INTEREST

The authors declare no conflicts of interests. The authors alone are responsible for the content and writing of this article.

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