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Eco-friendly Synthesis of Zinc Oxide Nanoparticles Utilizing Plant Extracts for Multifaceted Biomedical Applications

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Abstract: The biogenic preparation of ZnO nanoparticles (ZnO NPs) utilizing aqueous plant extracts has gained more attention for environmental advantage and cost-effectiveness. Plant leaf extract containing phytochemicals such as terpenoids and flavonoids act as a sustain property and reducing agent in this process. This review mainly focuses on synthesizing, characterizing, and exploring the pharmaceutical activity of ZnO NPs. Characterization methods, such as SEM, FTIR, TEM, UV-Vis, and XRD, confirmed nanoparticle formation, crystalline nature, surface chemistry, and morphology. The ZnO NPs demonstrated significant antibacterial, anticancer, antidiabetic, and antioxidant properties, along with potential applications in healthcare products.

Keywords: Antimicrobial, Antifungal, Anti-inflammatory, Antiviral, Antidiabetic

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Introduction

Nanotechnology involves manipulating substances at the supramolecular level, molecular and atom. The particular properties of nanoscale matter make them suitable for applications in environmental remediation, electronics, energy, and medicine (Ahire *et al*., 2022). This dynamic field of material science has seen significant global advancements in nanoparticle (NP) synthesis (Joseph *et al*., 2023). Nanoparticles exhibit novel or enhanced properties due to their specific characteristics, such as size (1–100 nm), structure, and shape, distinguishing them from bulk materials (Joudeh *et al*., 2022). Nanoparticles can be classified into two type: organic and inorganic (Sajid and Płotka-Wasylka, 2020). Organic NPs encompass carbon-based NPs, like fullerenes, carbon nano-tubes and quantum dots.

Zinc oxide nanoparticles have attracted attention across various sectors including optics, electronics, medicine, and packaged foods, due to their own cost-effectiveness, low cytotoxicity, and bio-compatibility. ZnO NPs can induce cellular death by facilitating reactive oxygen species manufacture and issuingzinc ions (Zn^{2+}), in particular, which have chemotherapeutic properties (Wei *et al*., 2023). Additionally, zinc, an essential trace element in the human body, contributes to ZnO NPs' biocompatibility due to its high biodegradability and very low toxicity, attributed to the solubility of Zn^{2+} ions (Bhatia *et al*., 2024). However, the therapeutical use ofchemically synthesized ZnO nanoparticles is limited due to the dangerous nature of the chemicals involved in their production (Raha and Ahmaruzzaman, 2022).

This limitation has led to a growing interest in environmental friendly method for ZnO NPs. Recent improvements have highlighted exploi-tation using plant section as a reducing factor in synthesizing ZnO nanoparticles. Green synthesis technologies offer numerous advantages over traditional methods, characterized by greater sustainability, an ecologically conscious approach, enhanced safety, and simplicity (Verma *et al*., 2024). Biologically synthesized ZnO nanoparticles possess significant biological properties, making them appropriate for versatile biomedical applications (Al-darwesh *et al*., 2024). For instance, ZnO nanoparticles synthesized using plant extracts exhibit superior antibacterial activities compared to conventional medications in combating infections (Xu *et al*., 2021). Additionally, nanoparticles demonstrate malignant tumor properties and potential as factors that scavenge free radicals (Mohammed *et al*., 2024).

Green plant-mediated synthesis shows promise in processing advanced therapeutics for ill health, such as urinary tract infections and malaria (Al-darwesh *et al*., 2024). Furthermore, green-synthesized ZnO NPs have shown appreciable potential for wound healing, with their antibacterial drug properties being particularly effective when incorporated into nanoscale and microscale formulations (Islam *et al*., 2022). These nanoparticles also have potential as biosensors for detecting and characterizing biomarkers related to versatile clinical states (Yang *et al*., 2024). Compared to conventionally manufactured ZnO nanoparticles, those produced through green methods exhibit enhanced biomedical properties and superior biocompa-tibility, making them moreappropriate as antibacterial agents and pharmaceuticals for malignant tumor treatment. Additionally, these nanoparticles have been effective in drug delivery and sensing use (Fakayode *et al*., 2024).

The emergence of nano-biotechnology has revolutionized the production of metallic oxide nanostructure. Plant-based methods in green analysis processes offer a sustainable and biocompatible alternative for various biomedical applications (Vijayaram *et al*., 2024). Exploitation of botanical components as a reduction factor in fabricating ZnO NPs has shown significant expectation across various biomedical fields, including wound healing, antibacterial, anti-oxidant, biosensing functionalities, and anticancer (Vagena *et al*., 2024). Green-synthesized nano-particles present a bright pathway for advancing efficacious therapeutic and environ-mental approaches within medicine (Osman *et al*., 2024). However, the potential ecological ramifications of nanoparticles, regardless of their synthesis technique, have raised concerns. Their small size and unique characteristics may lead to varied interactions with organisms and environ-ments (Benson *et al*., 2022). These interactions require careful consideration and additional research to interpret and mitigate any adverse effects while maximizing the benefits of nanoparticles in the biomedical approach (Villanueva-Flores *et al*., 2020).

Top-Down and Bottom-Up Methods in Synthesis

The chemical process of nanoparticles (NPs) involves two important approaches: bottom-up and top-down (Abid *et al*., 2022). The top-down method breaks down larger-volume materials into smaller particles throughmethods such as ball milling, evaporation-condensation, pulse wire discharge, and pulse laser ablation (Fazio *et al*., 2020). The bottom-up method synthesizes nanoparticles from atomic or molecular components, resulting in the self-assembly of these units into nanoscale particles (Borah *et al*., 2023). Evaporation-condensation, a commonly employed top-down technique, is particularly effective for synthesizing metal nanoparticles (Harish *et al*., 2022). This process involves vaporizing the base material, usually placed inside a boat within a furnace, into a carrier gas. Carbon and zinc oxide nanoparticles have been successfully produced using this technique (Sen *et al*., 2023).

Drawbacks of Tube Furnace in the Top-Down Approach

Using a tube furnace in the top-down approach has limitations, including significant space requirements, high energy consumption (Pham *et al*., 2024), and the lengthy time needed to achieve thermal stability. These factor cause defects in the external structure adversely affecting the physical characteristics of the nanostructure and synthesized products (Mohite *et al*., 2024).

Advantages of Chemical Step-down in the Bottom-Up Formulation

Chemical reaction is the common method to analyze ZnO nanoparticles in the bottom-up approach (Jamkhande *et al*., 2019). This method utilizes various inorganic and organic reducing agents in non-aqueous or aqueous method, along with capping agents to stabilize the size of the NPs (Farooqi *et al*., 2021).

Green Synthesis as an Eco-Friendly Alternative

There is a growing shift towards green synthesis as environmental friendly alternate to traditional chemical and physical methods. This approach uses biological entities such as microorganisms, plant biomass and plant extracts for NP generation (Samuel *et al*., 2022), avoiding toxic chemicals and harmful byproducts.

Benefits of Green Synthesis

Green synthesis offers respective benefit, including environmental cost-effectiveness, friendliness, scalability for extensive nanoparticle production and absence of pressure, energy consumption, harmful chemicals and high temperatures typically related to traditional methods (Ying *et al*., 2022).

Potency Green-Inspired Synthesis of ZnO-NPs

Green-inspired analysis of ZnO-NPs have numerous benefits over chemical methods, making it fit for several use and advancing nanotechnology in an eco-friendly manner (Elsakhawy *et al*., 2022).

Bottom-up Approaches, Top-down, and Comparison

Table 1 compares approach, techniques, advantages and drawbacks of bottom-up and top-down approaches. Table 2 compares synthesis of nanoparticles of bottom-up and top-down approaches.

Synthesis of Zinc Oxide Nanoparticles

The analysis of ZnO nanoparticles utilizes different techniques, including biological, physical, and chemical methods. Chemical methods encompass sol-gel processing, polyol methods, precipitation, water-oil micro-emulsion, colloidal processes, Sono chemical methods, hydrothermal synthesis, cellulothermal techniques, and co-precipitation (Al-darwesh *et al*., 2024). Physical methods include ultrasonic irradiation, arc plasma, physical vapor deposition, laser ablation, and thermal evaporation (Sarma *et al*., 2024). These conventional procedures often have significant drawbacks, including high costs, contamination, instability, and limited repeatability and reliability. Moreover, they frequently require hazardous chemicals, posing substantial risks to environmental and medical applications (Rathi *et al*., 2021). Researchers have increasingly turned to alternative, economic, and environmental approaches for synthesizing ZnO nanoparticles. The green synthesis technique, a biologic

Table 1: Comparison of approach, techniques, advantages and drawbacks of bottom-up and top-down approaches

Approach	Techniques	Advantages	Drawbacks
Top-Down	Pulse laser ablation, evaporation-condensation, ball milling, pulse wire discharge	Effective for large-scale production, controllable particle size	High energy consumption, space requirements, surface defects
Bottom-Up	Chemical reduction, green synthesis	Environmentally friendly, cost-effective, scalable	Dependent on suitable biological entities for green synthesis

Table 2: Comparison of synthesis of nanoparticles of bottom-up and top-down approaches

Synthesis of Nanoparticles	Bottom-up Approach	Top-down Approach
Green Methods (Non-toxic)	Chemical Methods (Toxic)	Physical Methods (Toxic)
- Using bacteria	- Chemical reduction	- Pulsed laser ablation
- Using fungi	- Sonochemical	- Evaporation–condensation
- Using plants and their extracts	- Microemulsion	- Arc discharge
- Using yeast	- Photochemical	- Spray pyrolysis
- Using enzymes and biomolecules	- Electrochemical	- Ball milling
- Using microorganisms	- Pyrolysis	- Vapor and gas phase
	- Microwave	- Pulse wire discharge
	- Solvothermal	- Lithography
	- Coprecipitation	

approach utilizing plant-mediated extracts, offers different advantages ofconventional methods like cost efficiency, replicability, environmental sustainability, and simplicity (Ahmed *et al.*, 2022). Green technique reduces the harmful byproducts and minimizes the certainty on dangerous solution or chemical agents typically needed in conventional synthesis methodological analysis (Clarke *et al.*, 2018). Additionally, manipulating temperature during the green synthesis process can control and enhance the morphological characteristics of the nanoparticles (Jafarzadeh *et al.*, 2024).

Furthermore, ZnO semiconductors have intrinsic defects, including zinc and oxygen vacancies, as well as oxygen and zinc interstitials, which can significantly impact their properties and potential applications (Gurylev *et al.*, 2021). Calcination temperatures, also known as annealing temperatures, can possibly activate dopant atoms, repair defects, eliminate impurities, and enhance optical and electrical ZnO nanoparticles (Nwanna *et al.*, 2024). These properties improvements can vary based on the intended applications. The environment-friendly synthesis of zinc oxide nanoparticles was carried out using varied plant extracts (Fig. 1), such as *Melia azedarach*, *Limonium brunneri*, *Cassia fistula*, and royal jelly (Naseer *et al.*, 2020). The size and morphology of the analyzed of ZnO NPs vary depending on the specific plant extract used, demonstrating the influence of the biological source on nanoparticle characteristics (Xu *et al.*, 2021).

Synthesis of ZnO nanoparticles for biomedical innovations

The sustainable and environmentally friendly manufacturing of zinc oxide nanoparticles using plant extracts known as green synthesis has acquired significant involvement within the technology-based community (Bhattacharjee *et al.*, 2024). Plant extracts, which contain compounds such as amino acids, polysaccharides, proteins, alkaloids, enzymes, serve as both capping and reducing agents. This dual functionality simplifies the synthesis activity while enhancing its sustainability, eco-friendliness, and safety compared to traditional chemical and physical methods

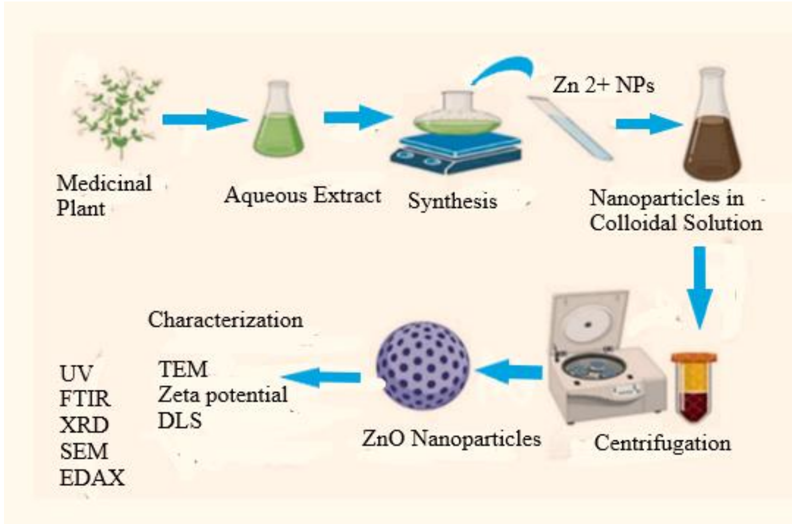

Fig 1: Production of ZnO NPs from plant solution.

(Osman *et al*., 2024). Zinc oxide nanoparticles are recognized for their potential in different biomedical applications because oftheir low toxicity, cost-effectiveness, and biocompatibility. These nanoparticles exhibit strong biological properties and have been explored for their antioxidant, anti-inflammatory, antibacterial, wound-healing, and anticancer capabilities (Nandhini *et al*., 2024).

Green synthesis techniques utilize versatile plant parts, including flowers, stems, leaves, roots, rhizomes, bark, seeds, and fruits. These solutions contain phytochemicals like anthocyanins, oleanolic acid, proanthocyanidins, sitosterol, rutin, ursolic acid, lupeol, quercetin, glycosides, and leucocyanidin of kaempferol (Rajendram *et al*., 2023), which are essential for reducing nanoparticle synthesis. Plant-based methods offer several advantages over traditional physic-chemical approaches, notably reducing the use of hazardous substances that pose health risks to ecosystems and individuals (Ahmed *et al*., 2023).

Temperature plays an important part in the emergence and size of ZnO nanoparticles during green analysis. Higher temperatures increase ZnO NP production but result in slower particle growth and smaller sizes due to shorter reaction times (Islam *et al*., 2022). While green synthesis primarily relies on biological substrates for nanoparticle biosynthesis, microbial-mediated synthesis, particularly using lactic acid-generating bacteria, has also gained interest due to the bacteria's ability to produce enzymes and their non-pathogenic nature (Al-darwesh *et al*., 2024). However, microbial-mediated synthesis faces challenges such as time-consuming isolation and screening of microorganisms, stringent aseptic conditions, potential genetic changes affecting nanoparticle production, and the usage of chemicals as growth media (Murali *et al*., 2023).

The choice between plant-mediated and microbial-mediated analysis depends on the desirable nanoparticle properties and specific application. Researchers and industries are required to evaluate drawbacks and benefits based on requirements when choosing between these synthesis methods (Ahmad *et al*., 2024).

Characterisation Method for ZnO NPs Synthesized with Green Synthesis

Characterization methods are essential for assessing the potential applications and properties of zinc oxide nanoparticles synthesized through the green method (Hussain *et al*., 2024). Various techniques were used to examine ZnO nanoparticles produced by using plant-based extract. Green synthesis technology offers significant advantages due to its environmentally friendly and potential biomedical use (Vadakkan *et al.*, 2024). Plant extracts contain metabolites with capping and reducing properties that analyze bio-based ZnO nanoparticles (Nguyen *et al.*, 2022). The fundamental interchange between various components in extracts can promote the fabrication of ZnO NPs. Sustainably factory-made nanoparticles can be evaluated for their propertiess through various description techniques (Vieira *et al.*, 2024).

UV - Visible spectrophotometry

UV-visible spectrophotometry is widely used and cost-efficient technique for confirming the creation of zinc oxide nanoparticles. This method involves scanning and analyzing ZnO NPs with UV light in the 200 to 700 nm range (Bloch *et al.*, 2024). The interaction between surface electrons and light on ZnO NPs results in surface plasmon resonance (SPR). Studies have identified peaks between 289 and 386 nm as characteristic of ZnO NPs' SPR (Kumar *et al.*, 2021). The SPR band's shape can be influenced by the density of plant extract and another reaction component. UV spectroscopy is extensively used to verify ZnO NP synthesis (Jayaseelan *et al.*, 2024).

Fourier Transform-Infrared Spectroscopy (FTIR)

Fourier Transform Infrared Spectroscopy involves the absorptionon of electromagnetic radiation between 400 to 4000 cm^{-1}, enabling the collection of spectra over a broad range (Zhang *et al.*, 2024). This technique characterizes the functional groups and chemical structures of ZnO nanoparticles by examining their ability to acquire electromagnetic waves of various intensities and frequencies (Carnival *et al.*, 2024). The unique arrangement and shape of ZnO nanostructures make them identifiable among different clusters and structures (Debnath *et al.*, 2024).

X-ray Diffraction

X-ray diffraction was crucial in determining the purity ofthe hexagonal wurtzite structure of ZnO samples. XRD is effective in nanostructure analysis, as the breadth and shape of reflections reveal structural details such as crystallite sizes (Shitu *et al.*, 2024). For ZnO, the reflection values for planes 100, 002, 101, 103, 110, 112, and 201 are 31.84, 34.52, 36.33, 47.63, 56.71, 69.18, and 72.36, respectively (Almoneef *et al.*, 2024). X-ray diffraction has been used to attribute peaks observed in microemulsion and calcinations (Georgieva *et al.*, 2019).

Zeta Potential

Zeta potential quantifies the external interchange of nanoparticles in colloidal solution, representing electric potency, the boundary of the counter ion dual layer formed around nanoparticles due to their surface charge (Matyushov, 2024). Factors such as solvent, particle size, temperature, ionic strength, and concentration influence the Zeta potential. Values between 25 and 40 mV are considered stable.While above 60 mV indicates high stability in nanoparticles. For ZnO NPs synthesized with *T. grandis* extract, a Zeta potential of 25 mV was observed, indicating stability (Daneshfar *et al.*, 2024). The phenolic compounds in *T. grandis* extract contribute to this stability (Quan *et al.*, 2021). Thermogravimetric analysis (TGA) assessed the thermal stability of green plant-mediated ZnO NPs, and Brunauer-Emmett-Teller (BET), along with X-ray photoelectron spectroscopy (XPS), was utilized to analyze their atomic structure (Mutukwa *et al.*, 2022). Chromatography techniques like GC-MS, HPLC-MS, and LC-MS analyze plant extracts before and after synthesis, providing insights into the involved biomolecules (Ilyas *et al.*, 2024).

Scanning Electron Microscopy (SEM)

Scanning electron microscopy is higher-resolution imaging technique used to examine the nano and microscale structures of objects through an electron beam (Wacker *et al.*, 2024). SEM images, with their high magnification and broad field of view, allow for a detailed evaluation of the surface topology of ZnO nanoparticles. The method depends on visual view for morphological identification (Ismail *et al.*, 2024). When ZnO NPs are capable of electron beams, the detector produces and records signals that can infer the nanoparticles' shape, orientation, and crystalline

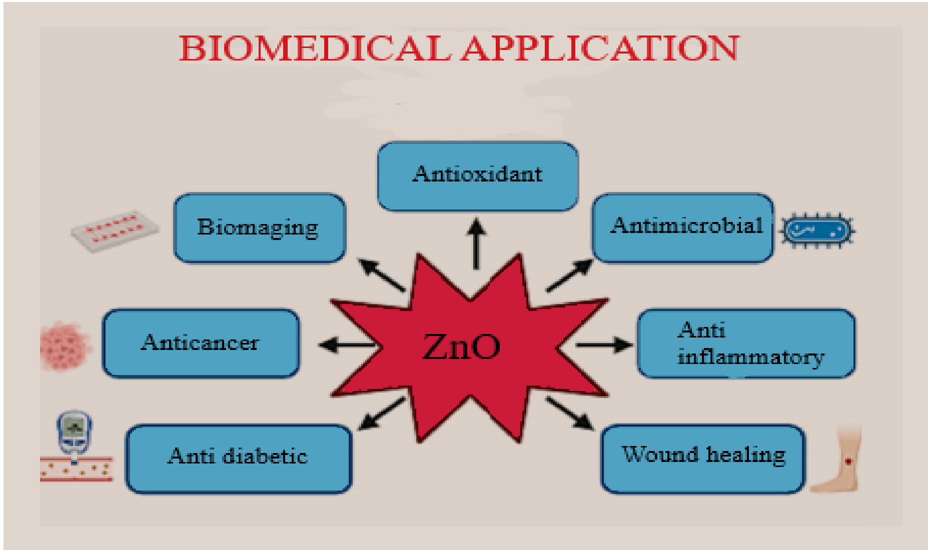

Fig. 2: Biomedical applications of ZnO NPS.

structure (Goel *et al.*, 2024). Data obtained from SEM is crucial for characterizing the size and shape of biosynthesized ZnO NPs.

Energy Dispersive X-ray (EDX) Spectroscopy

Energy Dispersive X-ray spectroscopy is analytical method used to examine the chemical composition and purity of nanoparticles. By measuring the X-rays expelled when nanoparticles are bombarded with an energetic electromagnetic radiation, EDX can identify the elements present in the sample (Prasad *et al.*, 2024). Each element's atomic structure produces characteristic peaks in the X-ray spectrum. For instance, ZnO NPs synthesized using *P. amboinicus* extract contained 23.55% oxygen and 75.12% zinc and a subsidiary peak attributed to bonds bio-compounds of extract (Al-darwesh *et al.*, 2024). ZnO NPs analyzed using *S. baicalensis* extract were found to contain 34.58% zinc and 63.5% oxygen, with a minor peak of 2.08% traced to biomolecules from the extract (Mutukwa *et al.*, 2022).

Transmission Electron Microscopy (TEM)

TEM is extensively used to qualify physical propertyy of nanoparticle providing high-resolution images that clearly depict sizes and shapes (Modena *et al.*, 2019). TEM is valuable for nanoparticle characterization, showing that synthesized ZnO had medium size of 7.4 ± 1.2 nm. The results confirmed the thermal analysis process narrow statistical distribution of ZnO NPs (Verma *et al.*, 2021).

Biomedical application - ZnO NPs

The distinct characteristics of Zinc had sparked significant interest in their biomedical applications lately (Cruz *et al.*, 2020). This discussion delves into their roles in cancer treatment, inflammation reduction, antioxidation, and antibacterial action (Fig. 2).

Anti-inflammation

The swelling is a complex instinctive response of body tissues to deadly stimuli like bacteria or damage, which has been elucidated by the natural properties, showcasing zinc oxide nanoparticles' anti-inflammatory potential (Kallungal *et al.*, 2024). Atopic dermatitis (AD), a chronic instigative epidermic condition, involves a compromised skin barrier, influenced by genetic and environmental factors (Luger *et al.*, 2021). Textiles, in close contact with skin, are explored for mitigating oxidative stress in AD through ZnO-functionalized fibers (Raha and Ahmaruzzaman, 2022). Studies on ZnO-functionalized fibers *in vivo* and *in vitro* demonstrate efficacy in allergic skin and wound penetration in mouse AD models (Nozari *et al*., 2021). Nano-sized ZnO significantly reduces pro-inflammatory cytokines in AD models, suggesting its role in alleviating skin inflammation (Raha and Ahmaruzzaman, 2022).

Antimicrobial Properties

ZnO nanostructures exhibit superior antibacterial properties compared to other oxides, leveraging reactive oxygen species (ROS) production to combat bacterial cells (Cruz *et al*., 2020). ROS technology, environmentally benign and cost-effective, enhances ZnO nanostructures' antibacterial efficacy (Li *et al*., 2022). Biologically analyzed ZnO, especially using *Azadirachta indica* (L.) leaves, displays significant inhibitory effects against various bacteria (Ijaz *et al*., 2020). ZnO nanostructures synthesized from *Camelia sinensis* leaf extract are effective against certain bacteria, showcasing potential as antibacterial agents (Panda *et al*., 2021). ZnO's antibacterial activity varies with the extract used, as demonstrated by its effectiveness against different strains (Arumugam *et al*., 2021).

Anticancer Activity

Cancer, characterized by abnormal cell proliferation, presents challenges in treatment efficacy and side effects (Abdel-Razeq and Hashem, 2020). Nanoparticles, especially ZnO NPs, offer targeted delivery and cytotoxicity against cancer cells, showing promise in cancer therapy (Raj *et al*., 2021). Phytofabricated ZnO NPs exhibit dose-dependent cytotoxicity against cancer cells, highlight its potency as therapeutic factor (Chandrababu *et al*., 2023). ZnO NPs derived from plant extracts show cytotoxic effects on various cancer cell lines, suggesting their role in tumor suppression (Anjum *et al*., 2021). However, careful consideration of toxicity and interactions is essential for their therapeutic use (Naser *et al*., 2023).

Antioxidant Properties

ZnO NPs possess significant antioxidant properties, enhancing cellular defense mechanisms against oxidative stress (Madkour *et al*., 2020). They protect cells by neutralizing free radicals, though higher doses can induce oxidative stress (Attia *et al*., 2018). ZnO NPs synthesized from *Artocarpus gomezianus* and other extracts demonstrate potent antioxidant activity, influenced by size and charge density (Chanda *et al*., 2020). Studies indicate their potential in managing diseases caused by oxidative stress (Zhang *et al*., 2023).

Antifungal Activity

ZnO NPs exhibit antifungal efficacy against various pathogens, including *Candida albicans*, suggesting applications in agriculture and food industries (Ali *et al*., 2020). Combined with light, itincreases yeast cell death, indicating their potential as antifungal agents (Youssef *et al*., 2024).

Antiviral Activity

Zinc, known for its antiviral properties, stimulates immune responses and disrupts viral infectivity (Root-Bernstein, 2024). ZnO NPs show promise in preventing and treating viral infections, although further studies are needed to assess their risks and benefits (Sarkar *et al*., 2022).

Anti-Diabetic Activity

Zinc oxide nanoparticles studied for anti-diabetic properties due to zinc's crucial role in secretion, creation, and insulin storage. ZnO NPs have shown superior anti-diabetic efficacy compared to $ZnSO_4$, improving insulin levels, glucose elimination, and zinc status (Alkazazz *et al*., 2021). Studies have demonstrated that ZnO NPs can normalize serum insulin and blood sugar levels, indicating their effectiveness in treating diabetes and related pancreatic diseases. Combining ZnO NPs with diabetes medications like red sandalwood and vildagliptin enhances their effectiveness (San Tang *et al*., 2019).

ZnO NPs inhibit pancreatic amylase and colonic glucosidase enzymes, which are responsible for breaking down oligosaccharides and disaccharides into glucose. Inhibiting these enzymes helps manage blood glucose levels in diabetic patients (Bhatnagar *et al*., 2022). ZnO NPs have shown inhibition percentages of 20% to 74% for amylase and 36% to 82% for glucosidase, with glucosidase inhibition being higher (Vinotha *et al*., 2019). The trace metal zinc, essential for insulin release and structural integrity, has been incorporated into ZnO NPs to develop innovative anti-diabetic treatments (Ruan *et al*., 2023). ZnO NPs combined with red sandalwood extract (RSW) showed significant inhibition of pancreatic glucosidase and amylase, demonstrating enhanced antidiabetic efficacy compared to each component alone (Sahoo *et al*., 2021).

Drug Delivery

Nanotechnology offers promising applications for drug delivery, particularly in treating diseases like cancer. Nanoparticles (NPs) are one of the most important systems for delivering pharmaceuticals (Zahin *et al*., 2020). Researchers have used zinc oxide nanoparticles (ZnO NPs) to deliver drugs for various ailments (Anjum *et al*., 2021). For instance, ZnO quantum dots were used to specifically target doxorubicin in HeLa cells, enhancing drug stability by coating the nanoparticles with chitosan (Singh *et al*., 2020). This method successfully administered doxorubicin to cancer cells, demonstrating the potential of drug delivery technology (Szuplewska et al., 2019). Additionally, NPs can serve as gene delivery systems for various cells, including malignant cells, offering benefits like safe and efficient plasmid gene transfer to recipient tissues (Duan *et al*., 2021).

Conclusion

The environment-friendly synthesis of ZnO nanoparticles can significantly boost their medicinal applications. Green synthesis, valued for its eco-friendliness and cost-effectiveness, is preferred over chemical and physical methods. Plant extracts rich in photochemicals like tannins, terpenoids, flavonoids, polyphenols,and alkaloids are good resources of ZnO NP products. This method not only stabilizes ZnO NPs but also unveils novel physicochemical properties. Studies show that green-synthesized ZnO NPs possess particular bio-processes because of diverse flavonoids on their surfaces. These nanoparticles display potent antibacterial properties, offering a viable option against drug-resistant bacteria. They also act against cancer cells by penetrating and accumulating within them, inducing cell death via Zn^{2+} ions or ROS production, making them effective anticancer agents for targeted therapy.

Green synthesis of ZnO NPs also exhibit potential as antidiabetic causal agent and potent antioxidants, scavenging radicals effectively. They inhibit fungi, viruses, parasites, and inflammation, expanding their utility in healthcare products like sunscreens, acne treatments, and UV protection. However, their potential toxicity and biological effects require empirical studies for validation. While promising, green-synthesized ZnO NPs await commercialization and clinical studies, necessitating further *in vivo* research for future clinical applications.

Author Contributions

Sampath Saranya: Conceptualization, literature survey, data curation, and manuscript drafting; *Janarthanam Hemapriya*: Supervision, critical review of the manuscript, and final editing; *Rajinikanth Kamali*: Data analysis, preparation of tables and figures, and manuscript refinement; *Girirajan Reshma*: Literature collection, data interpretation, and manuscript writing; *Balaji Rajalakshmi*: Assisted in manuscript writing, proofreading, and technical validation; *Selvaraj Vijayanand*: Overall project supervision, manuscript review, and approval for publication. All authors have read and agreed to the published version of the manuscript.

Conflict of Interest

The authors declare no conflicts of interest.

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