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Zinc Oxide Nanoparticles: A Comprehensive Review on Synthesis and Properties

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ABSTRACT: Zinc oxide nanoparticles (ZnO-NPs) are inorganic metal oxides extensively utilized as preservatives in packaging materials and as potent antibacterial agents with minimal associated risks. The physicochemical properties of ZnO-NPs, including antibacterial efficacy, are significantly influenced by parameters such as particle size, morphology, concentration, and duration of interaction with bacterial cells. Beyond their antimicrobial applications, ZnO-NPs have garnered interest in diverse fields such as food technology, agriculture, cosmetology, and optoelectronics. Green synthesis of ZnO-NPs mediated by plant extracts has demonstrated enhanced antibacterial activity against various bacterial and fungal pathogens. Several plant species, including Trifolium, Justicia adhatoda, Physalis alkekengi L., Cassia auriculata, Aloe barbadensis, Pongamia pinnata, Limonia acidissima, Plectranthus amboinicus, Sedum alfredii Hance, and Aspidoterys cordata, have been identified as effective bioresources for nanoparticle fabrication. The resultant ZnO-NPs exhibit desirable physicochemical characteristics that are largely dependent on synthesis conditions, including particle size, shape, and concentration. This review comprehensively summarizes various green synthesis methodologies and characterization techniques for ZnO-NPs, highlighting their potential applications across the food, pharmaceutical, and textile industries.

KEYWORDS: Antimicrobial activity, Biomedical applications Nanocomposites, Cytotoxicity, Characterization techniques, Green synthesis, Nanotechnology, Zinc oxide nanoparticles (ZnO-NPs).

1- INTRODUCTION

Nanotechnology has emerged as one of the most dynamic and interdisciplinary fields of scientific inquiry, enabling the fabrication and control of materials at the nanoscale (1–100 nm)[1]. The development of electron microscopy in the 20th century and Richard Feynman's visionary insights laid the foundation for the observation, characterization, and application of nanostructures across diverse domains such as biomedicine, electronics, and material sciences [2]. Among various nanomaterials, metal oxide nanoparticles—particularly zinc oxide nanoparticles (ZnO-NPs)—have gained significant attention due to their unique physicochemical, optical, and biological properties {REF}, and most importantly, their promising antiseptic activity[3]. ZnO-NPs possess a wide band gap (~3.37 eV), high excitonic binding energy (60 meV), excellent thermal and chemical stability, and natural n-type semiconducting behavior. These characteristics contribute to their broad application spectrum, ranging from optoelectronic devices, photocatalysis, and solar cells to cosmetics, food packaging, and biomedical fields. Furthermore, ZnO-NPs demonstrate potent antimicrobial activity against a variety of Gram-positive and Gram-negative bacteria and fungi—mediated by the generation of reactive oxygen species (ROS) and interaction with microbial membranes[1]. making them promising candidates for antiseptic and pharmaceutical applications.

The functionality and effectiveness of ZnO-NPs are highly dependent on their particle size, morphology, surface area, and synthesis method. Conventionally, ZnO-NPs have been synthesized through physical and chemical routes, including sol–gel, vapor deposition, and co-precipitation. However, these methods often involve high energy input, toxic chemicals, and environmentally hazardous by-products[4]. As an alternative, green synthesis approaches using biological systems—such as plant extracts, fungi, bacteria, and algae—have gained popularity due to their eco-friendliness, cost-effectiveness, and biocompatibility. Medicinal plants such as Aloe vera, Cassia auriculata, and Plectranthus amboinicus have been effectively employed in the biosynthesis of ZnO-NPs, producing nanoparticles with notable antimicrobial and anti-inflammatory properties[5]. There are two primary methods for producing nanoparticles (NPs): top-down and bottom-up approaches (Fig. 1). Mechanical milling, electroexplosion, ablation, and sputtering are examples of top-down techniques. On the other hand, bottom-up approaches incorporate biological, chemical, and physical processes all of which are essential to the creation of NP.

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High-quality nanoparticles can be produced efficiently using conventional methods. They can, however, produce dangerous byproducts that present risks in medical applications and are frequently expensive. These techniques also call for extra chemicals for stabilization and capping. Bottom-up green synthesis, which involves oxidation/reduction reactions, presents a significant challenge. By using algae, fungi, bacteria, plants, and microorganisms, green synthesis makes it possible to produce large amounts of pure ZnO-NPs. In order to facilitate NP synthesis, this process combines a number of components derived from medicinal plants (Fig. 1). In addition to antimicrobial effects, ZnO-NPs are known for their potential roles in drug delivery, bioimaging, UV protection, and environmental remediation[4]. Despite these promising applications, concerns remain about the cytotoxic and genotoxic effects of ZnO-NPs toward human cells, especially at higher concentrations[5].

Therefore, an in-depth understanding of their synthesis routes, physicochemical behavior, and biological interactions is essential for developing safe and effective antiseptic applications.

This review aims to comprehensively explore the synthesis techniques of ZnO-NPs (physical, chemical, and biological), describe their structural and functional properties, and examine their antiseptic activity in biomedical and industrial contexts. The paper also discusses current challenges and future prospects for ZnO-NPs as multifunctional nanomaterials in health and hygiene technologies[6].

2- MATERIAL AND METHOD

2-1- Chemical preparation

All chemicals used in this study, including starch, 3-ethyl-dimethylaminopropyl carbodiimide (EDC), sodium hydroxide (NaOH), zinc nitrate [$Zn(NO_3)_2$], and N-hydroxysuccinimide (NHS), were procured from Merck. Reagents and all serial dilutions were prepared using double-distilled water to ensure purity. Zinc oxide nanoparticles (ZnO-NPs) were synthesized via a chemical top-down approach under strongly alkaline conditions using a 0.2 M NaOH solution. Initially, 1000 mL of a 1% soluble starch solution was prepared and maintained at a temperature range of 40–45 °C. Subsequently, 14.47 grams of zinc nitrate [$Zn(NO_3)_2$] were dissolved into the starch solution with continuous stirring for 5 minutes to ensure homogeneity. Following this, 0.2 M NaOH was added dropwise to the mixture under constant agitation, and the reaction was maintained for 2 hours to complete the nanoparticle formation. The resulting suspension was centrifuged at 10,000 rpm for 10 minutes to collect the ZnO-NP pellets. These pellets were washed three to four times with deionized water to remove residual starch and any unreacted chemical species. After the water washes, the pellets were further rinsed with ethanol to eliminate any remaining impurities. The purified ZnO-NPs were then dried in a hot air oven at 80 °C for 2 hours. Finally, the dried materials were stored at 4 °C for subsequent characterization and analysis[7].

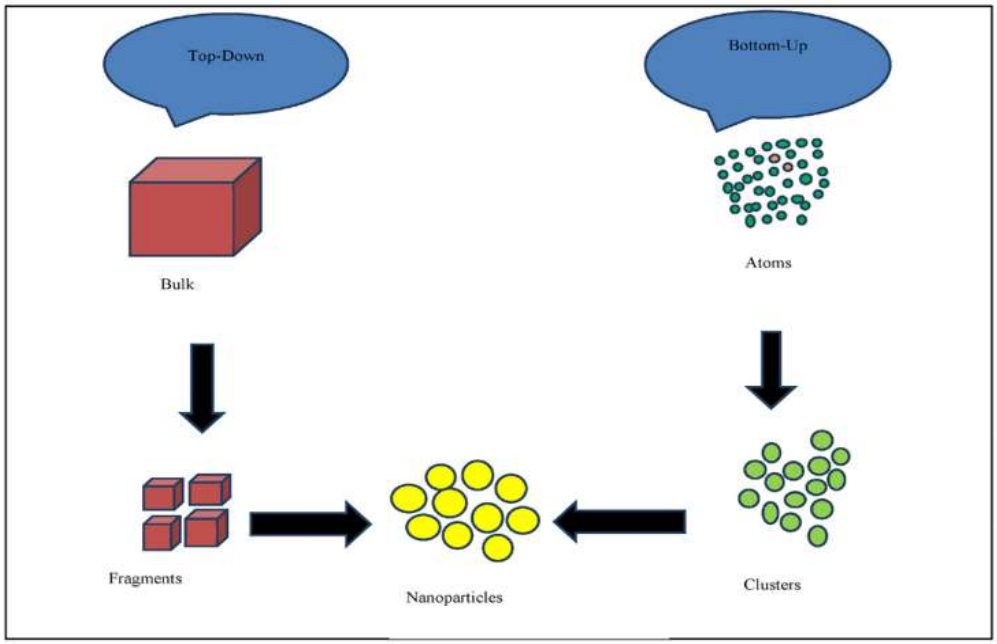

Fig 1- Techniques for producing zinc oxide nanoparticles both top-down and bottom-up

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3- SYNTHESIZING OF ZINC OXIDE NANOPARTICLES

Furthermore, this review outlines the various uses of zinc oxide nanoparticles and offers comprehensive scientific details on current developments in methods for synthesizing and characterizing zinc oxide nanoparticles from plant sources.

Traditional techniques to produce metallic NPs, such as ZnO-NPs, include physical and chemical processes. Traditional chemical synthesis processes include hydrothermal, sol-gel, co-precipitation, and microemulsion procedures. Physical methods include laser ablation, thermal evaporation, and high-energy ball milling. 24 There are a number of chemical, physical, and biological approaches used to generate ZnO-NPs. Every technique has unique requirements, benefits, and drawbacks[8].

3-1- Physical methods

This procedure creates stable nanoparticles with distinct characteristics, such as physical fragmentation, colloidal dispersion, amorphous crystallization, and vapor condensation, by drawing tiny particles together with physical forces. The drawbacks of physical techniques include high temperatures and pressures, costly equipment, and the need for a lot of area to set up apparatus. In order to produce nanoparticles, physical approaches entail physically manipulating materials. These techniques generally require high energy inputs and specialized equipment[9].

Three prominent top-down techniques for synthesizing zinc oxide nanoparticles (ZnO-NPs) include laser ablation**,** high-energy ball milling, and thermal evaporation. In the laser ablation method, bulk zinc metal is irradiated in a liquid medium such as NaOH, leading to the formation of high-purity ZnO-NPs. This method offers advantages such as chemical purity and controlled particle size and shape, producing spherical particles (80–102 nm) and rod-shaped particles with diameters around 30 nm[9]. However, in the presence of organic compounds, poorly understood pyrolysis by-products may form, which could limit biomedical applications[8]. High-energy ball milling, by contrast, is a mechanical process suitable for large-scale production, where ZnO powder is subjected to intense collisions inside a mill, reducing particle size over time[10]. Though particles around 30 nm can be produced, drawbacks include irregular morphologies and potential contamination from the milling media or environment. The third method, thermal evaporation, involves heating a condensed Zn source to high temperatures, allowing vapor to condense under controlled conditions to form ZnO nanostructures. This technique is catalyst-free, cost-effective, and capable of producing diverse morphologies such as nanorods, nanobelts, nanocombs, and nanorings. Owing to the strong photocatalytic activity of ZnO nanostructures, this method is also attractive for environmental applications like photocatalytic degradation[11].

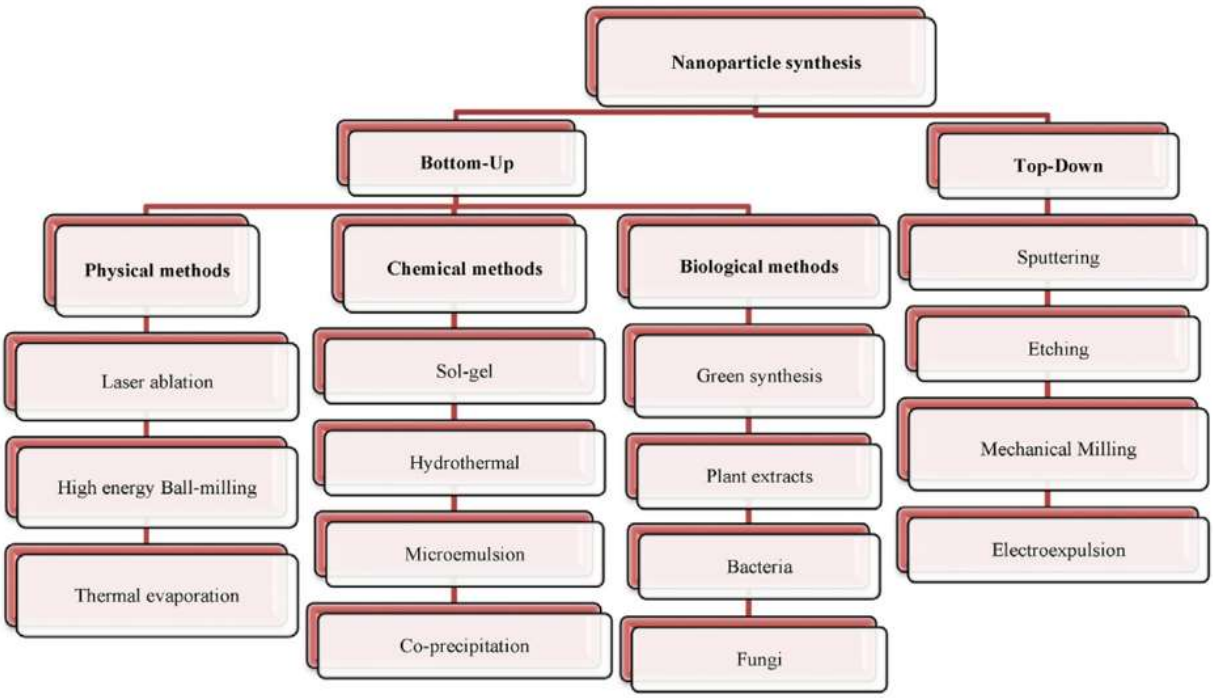

Fig 2- shows the several methods utilized to make zinc oxide nanoparticles.

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3-2- Chemical methods

Chemical synthesis methods for zinc nanocomposites are classified according to the physical state of the reaction medium: solid phase**,** liquid phase (commonly referred to as *wet chemical methods*), or vapor phase[12]. Among these, wet chemical methods are the most widely used due to their environmental friendliness, low cost, use of simple equipment, and low energy consumption. These methods also offer the advantage of precise control over the composition, morphology, and particle size of the resulting nanomaterials. Common wet chemical techniques include microemulsion**,** sol-gel synthesis, precipitation, and hydrothermal/solvothermal processes[13].

3-2-1- Sol-gel method

The sol-gel method involves the formation of a colloidal solution (sol) that undergoes hydrolysis, condensation, and polymerization reactions to form solid gels and nanoparticles. Common precursors include metal alkoxides or chlorides in alcohol-based media, and zinc acetate hydrate is widely used for the synthesis of ZnO nanoparticles. Key factors such as the type of solvent, temperature, and water-to-precursor ratio affect the growth and morphology of the nanoparticles. This method can produce ZnO particles in the range of 2–7 nm, and the addition of surfactants such as TEA or EDA allows for control of the shape and size, including spherical and rod-shaped structures. For example, TEA-enhanced synthesis improved the photoluminescence properties, while EDA affected the aspect ratio of the nanorods depending on its concentration. Other additives such as TMAH also allow the formation of nanocrystalline ZnO with average sizes between 20 and 50 nm. In general, sol-gel is valuable due to its scalability, control over morphology, and relatively fast nucleation, although it can be limited by the high cost of metal precursors[13].

3-2-2- Microemulsion

The microemulsion method involves a mixture of two immiscible liquids, usually water and oil, stabilized by surfactants. Two common types include oil-in-water (O/W) and water-in-oil (W/O) systems, with inverse microemulsion (W/O) being most commonly used for the synthesis of ZnO nanoparticles[14]. In this method, zinc salts are incorporated into the aqueous core of micelles and precipitate to form precursor particles. Surfactants such as AOT and Triton X-100 are commonly used. This method allows the synthesis of uniform ZnO nanoparticles (e.g., 10–20 nm), although aggregation may occur during extraction or calcination. Additives such as polyethylene glycols (PEGs) are used to adjust the size, shape, and optical properties of the particles, with different types and concentrations of PEG significantly affecting the morphology of the nanoparticles and their degree of aggregation[5].

3-3- Biological methods

Biological (green) synthesis of ZnO nanoparticles utilizes microorganisms, enzymes, or plant extracts as environmentally friendly alternatives to conventional chemical methods. Biological systems such as bacteria, fungi, yeasts, and plants act as reducing agents, enabling the controlled synthesis of nanoparticles without the use of toxic solvents. Parameters such as pH**,** temperature, culture medium**,** and type of organism significantly influence the size and shape of the resulting nanoparticles. This method is sustainable, cost-effective, and allows for precise control over nanoparticle morphology.

Green synthesis of zinc oxide nanoparticles (ZnO-NPs) is a simple, cost-effective, and environmentally friendly method for producing various types of nanoparticles with enhanced stability and reproducibility[5]. This emerging approach employs non-toxic, biocompatible reagents, typically derived from biological sources, to facilitate nanoparticle formation while minimizing the release of hazardous by-products. Utilizing biological systems like bacteria, fungi, or plant extracts to convert metal ions into nanoparticles is known as biosynthesis. This method is known for being economical and environmentally beneficial, providing a long-term substitute for traditional chemical techniques. Additionally, it minimizes the use of hazardous chemicals while enabling controlled synthesis, especially with regard to particle size and shape. This method's comparatively slow reaction rate and the need for meticulous parameter optimization to guarantee consistent results, however, are two of its biggest drawbacks.

Green synthesis of ZnO nanoparticles (ZnO-NPs) using plant extracts involves utilizing various plant parts—such as leaves, stems, bark, fruits, and seeds—to reduce zinc ions into nanoparticles[15].This approach is cost-effective, environmentally friendly, and requires minimal instrumentation, often resulting in high-quality, contaminant-free ZnO-NPs[14]. Prior to extraction, plant materials must be sterilized, typically using double-distilled water or mild surfactants like Tween 20, and then dried at room temperature[16]. To prepare the extract, a measured amount of powdered plant material is mixed with distilled water, heated under constant agitation, and subsequently filtered using Whatman filter paper[5]. The resulting extract is then combined with zinc precursors such as zinc nitrate ($Zn(NO_3)_2$), zinc acetate, zinc sulfate ($ZnSO_4$), or zinc chloride ($ZnCl_2$), and the mixture is stirred at elevated temperature. A visible color change typically indicates the formation of ZnO nanoparticles, which can be confirmed by

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UV–Vis spectroscopy[15]. Common characterization techniques include UV–Vis, SEM, TEM, XRD, and FTIR, which provide insights into the size, shape, crystal structure, composition, surface chemistry, and morphology of the synthesized nanoparticles. While this technique offers numerous advantages—including low cost, eco-friendliness, and reduced contamination risk—it also faces challenges such as inconsistent phytochemical composition of plant extracts, the need for careful sterilization, and potential difficulties in scaling up for industrial production, in addition to time-consuming extraction and synthesis steps[16].

Green synthesis of ZnO nanoparticles using bacteria involves employing microbial systems to reduce metal ions and generate nanoparticles either intracellularly—via ion transport into the cell—or extracellularly, through interactions with microbial biomolecules such as enzymes, polysaccharides, or glycoproteins[17]. This method is attractive because bacteria can be genetically engineered, allowing better control over nanoparticle size, shape, and synthesis efficiency [18]. However, challenges include the time-consuming screening of bacterial strains, the need for continuous culture maintenance, high costs of growth media, and difficulty in ensuring shape and size uniformity. Various strains like Bacillus licheniformis have been shown to produce ZnO nanoflowers with photocatalytic activity, while Aeromonas hydrophila has been used to synthesize spherical and oval-shaped ZnO-NPs (42–64 nm), as confirmed by AFM and XRD analyses. Moreover, probiotic strains such as Lactobacillus sporogens and Lactobacillus plantarum are widely used due to their non-toxic nature, easy preparation, and negative electrokinetic potential, which aids in Zn^{2+} ion attraction and nanoparticle formation[19].

Due to their high metal tolerance, efficient extracellular nanoparticle production, and strong commercial potential, fungi represent a promising biological agent for the green synthesis of ZnO nanoparticles (ZnO-NPs). They are often preferred over bacteria because of their superior ability to accumulate metals and produce larger quantities of nanoparticles with simplified downstream processing. Aspergillus fumigatus, for example, has been successfully used to synthesize spherical ZnO-NPs extracellularly, with particle sizes ranging from 1.2 to 6.8 nm as confirmed by dynamic light scattering (DLS) analysis [12]. This method offers advantages such as environmentally friendly conditions and scalability. However, its reproducibility and industrial feasibility may be limited by species-specific variability among fungi and the complexity involved in fungal cultivation and extraction[19].

Table1- Synthesis of zinc oxide nanoparticles mediated by plants

Source	Plant Parts Utilized	Nanoparticle Morphology	Size (nm)	Applications	References
Myristica fragrans	Fruit	Spherical and hexagonal	43–83	antibacterial activities and antioxidant	[20]
(Pachaiappan et al., 2021) Mussaenda frondosa	Leaf, stem, and callus	Hexagonal	5–20	Antibacterial, anti-inffammatory, anticancer	[21]
Jacaranda mimosifolia	ffower	Hexagonal wurtzite	2–4	Antimicrobial	[22]
grape	seed	hexagonal	15.86	antibacterial and antioxidant activities	[23]
Boerhavia diffusa linn	Leaf	hexagonal	23–32	antioxidant, antimicrobial, cytotoxic and anticancer	[24]
Beta vulgaris	Taproot	Spherical	20	antibacterial and antifungal	[25]
Cyathocline purpurea	Leaf	spherical	80-120	antimicrobial	[17]
Mangifera indica	Seed	Cylindrical	40–70	activities and antioxidant	[26]
Cissus quadrangularis	Stem	Spherical	75–90	Antibacterial and anticancer	[24]
Crotalaria verrucosa	Leaf	Hexagonal wurtzite	17.47	Antimicrobial and Anticancer Activity	[27]
Limonia acidissima	Leaf	Spherical	12–53	Antibacterial activity	[22]
Punica granatum	peel	Spherical	10–45	Antimicrobial	[28]
Sphagneticola trilobata	leaves	spherical	29.83	colon cancer and Antioxidant	[29]

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Sida rhombifolia linn	leaves	Spherica	30.23	Genotoxic and antibacterial	[30]
Oat biomass	Seeds	Wurtzite and hexagonal	17–52	antibacterial activities and antioxidant	[31]

4- CHARACTERIZATION OF ZnO NANOPARTICLES

4-1 X-ray diffraction

This rapid analytical method identifies the material type as well as its phase and crystalline properties by processing and analyzing X-rays reflected from the sample surface. Notably, it allows for the assessment of the purity of the produced CNOs. The crystallinity of zinc oxide nanoparticles can be evaluated using X-ray diffraction (XRD)[32].

4-2 Spectroscopy techniques

4-2-1 Fourier transform infrared spectroscopy

All infrared spectroscopy techniques are based on the principle that when infrared (IR) radiation passes through a material, some of the energy is absorbed. The radiation that passes through the sample is then recorded. The main difference between traditional IR and FTIR is that IR records a single spectrum using monochromatic light, while FTIR uses polychromatic light and scans up to 50 times per second, providing better resolution. This enhanced capability helps in identifying the functional groups involved in the reduction process[33].

4-2-2 UV–visible spectrophotometry

The analytical technique known as UV–visible spectroscopy compares a sample to a reference or blank to identify the specific wavelengths of ultraviolet or visible light absorbed or transmitted by the sample. The sample's composition influences its optical response, providing valuable information about its constituent components and their concentrations. By measuring the amount of light absorbed or scattered by the sample, the characteristic absorption wavelength of zinc oxide nanoparticles (ZnO-NPs) can be precisely determined[34].

4-3 Methods of microscopy

Microscopic techniques play a crucial role in the characterization and imaging of zinc oxide nanoparticles. These techniques primarily include scanning electron microscopy (SEM) and transmission electron microscopy (TEM)[33].

4-3-1 Scanning electron microscopy (SEM)

Scanning Electron Microscopy (SEM) is a surface imaging technique in which a focused electron beam interacts with the sample surface, generating backscattered and secondary electrons that are utilized to construct detailed images. This method produces high-resolution surface images, revealing nanoscale and microscale structural features of the specimen. SEM is commonly employed to determine the size and morphology of zinc oxide nanoparticles (ZnO-NPs)[35].

4-3-2 Transmission Electron Microscope (TEM)

Transmission Electron Microscopy (TEM) employs a focused electron beam to visualize samples at extremely high magnifications, capable of magnifying objects up to two million times. This characterization technique relies on the interaction between a thin specimen of zinc oxide nanoparticles and a high-intensity electron beam. TEM is widely used to analyze the size, shape, and dispersion of zinc oxide nanoparticles[32].

4-4 Size analysis

Particle size is a critical parameter in defining nanoparticles, particularly concerning drug release profiles and achieving uniform particle size distribution in formulations. The most commonly employed methods for nanoparticle size measurement include microscopic techniques and dynamic light scattering (DLS). Microscopic methods provide direct visualization and measurement of particle dimensions by analyzing images, allowing assessment of various size parameters. Dynamic light scattering (DLS), on the other hand, is widely used to evaluate the hydrodynamic diameter and size distribution of particles across a broad size range. Since the advent of coherent light sources in the 1970s, DLS has been extensively utilized to quantify macromolecules and nanoparticles in dilute solutions. Moreover, DLS is an effective tool for assessing nanoparticle stability in diverse environments such as buffer solutions and simulated biological fluids[36].

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4-5-Zeta potential

Accurately determining the surface charge of extremely small particles in a liquid remains challenging. The most common approach involves estimating the electric potential at a certain distance from the particle surface, typically within the diffusion layer. This

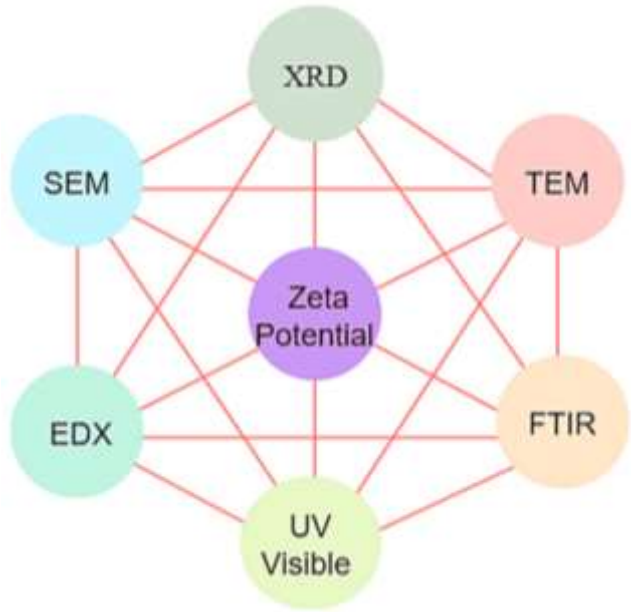

Fig 3- Characterization of ZnO nanoparticles

electrokinetic parameter, known as the zeta potential, is considered a practical indicator of the particle's surface charge. The zeta potential can significantly influence the pharmacokinetic behavior of biological nanosystems[37]. By applying an electric field to a particle dispersion, the zeta potential can be measured based on the velocity at which charged particles migrate toward oppositely charged electrodes; this velocity is directly proportional to the magnitude of the zeta potential[38].

5- PROPERTIES OF ZnO NANOPARTICLES

5-1- Antifungal activity

Numerous studies demonstrate that zinc oxide nanoparticles (ZnO-NPs) possess significant antifungal activity against various plant pathogens, including *Botrytis cinerea*, *Penicillium expansum*, and *Fusarium* species. The antifungal efficacy of ZnO-NPs strongly depends on their size and concentration. For example, nanoparticles around 32 nm exhibited higher inhibition rates compared to larger particles[39]. Increasing nanoparticle concentration generally enhances fungal growth inhibition, potentially due to membrane disruption and decreased enzymatic activity in fungi. Moreover, photoactivation of ZnO-NPs using visible light amplifies their antifungal effects, with up to 58% growth inhibition observed in *B. cinerea* at 5 mM concentration. Different fungi respond variably to ZnO treatment, likely because of morphological differences affecting exposure to nanoparticles. Conversely, larger ZnO particles (in micrometer scale) showed weak antifungal effects, underlining the importance of nanoparticle size in biological activity[39].

5-2- Cytotoxicity of (ZnO-NPs) on Normal and Tumor Cells

Zinc oxide nanoparticles (ZnO-NPs) are widely used in medicine for bioimaging, drug and gene delivery, and as effective antimicrobial agents. Due to their extensive use, humans are frequently exposed to ZnO-NPs, which can enter the body via respiratory, digestive, and parenteral routes. These nanoparticles have the potential to reach various organs and tissues, posing health risks. At the molecular level, ZnO-NPs can reduce cell viability, disrupt membrane integrity, and induce apoptosis[40]. Various in vitro assays are used to evaluate their cytotoxic effects, including MTT and NRU assays for cell viability, flow cytometry for nanoparticle uptake and cell cycle analysis, and lactate dehydrogenase (LDH) activity to assess membrane damage[18].

Two main mechanisms underlie the cytotoxicity of ZnO-NPs:

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1. Physical characteristics: such as size, shape, and surface composition influence toxicity. Studies show that spherical nanoparticles around 30–40 nm exhibit higher toxicity, with nanorods generally more toxic than nanospheres[41].
2. Release of zinc ions (Zn^{2+}): which contributes to the generation of reactive oxygen species (ROS), causing oxidative stress, DNA damage, and cell death[41].

ZnO-NPs exhibit differential toxicity toward normal and tumor cells. They induce higher ROS production and apoptosis in cancer cells, while normal cells are relatively less affected at lower concentrations. Notably, tumor cells can be up to 35 times more sensitive to ZnO-NPs than healthy cells[39]. Moreover, ZnO-NPs stimulate secretion of inflammatory cytokines such as IL-8, which plays a role in immune response and inflammation. Toxicity can occur even without nanoparticle internalization, mainly through extracellular release of Zn^{2+} ions. ZnO-NPs also affect cell cycle progression and induce apoptosis via both mitochondria-dependent and -independent pathways. Surface modifications like polyethylene glycol (PEG), silica (SiO_2), and aminopropyltriethoxysilane (APTES) coatings are used to reduce toxicity and improve biocompatibility by decreasing cellular uptake and aggregation. PEGylation, in particular, effectively lowers cytotoxicity. Despite these advances, further research is necessary to fully elucidate the mechanisms of ZnO-NP toxicity and to establish safety guidelines for their medical and industrial applications[12].

5-3- Antimicrobial activity

Investigations into antibacterial nanoagents are critical across multiple fields including medicine, food safety, textiles, packaging, and construction industries[42]. Compared to conventional antimicrobial compounds, metal oxide nanoparticles such as ZnO exhibit enhanced stability under extreme conditions, effective antimicrobial activity at low concentrations, and generally low toxicity to humans[39]. Among these, zinc oxide nanoparticles stand out due to their strong antibacterial efficacy and diverse morphologies, which contribute to significant growth inhibition across a broad spectrum of bacterial species. The antibacterial activity of ZnO-NPs is largely attributed to their high surface-to-volume ratio and unique physicochemical properties. While exact mechanisms remain under investigation, several have been proposed: electrostatic interactions disrupting bacterial cell walls, release of antimicrobial Zn^{2+} ions linked to nanoparticle accumulation inside bacterial cells, and the generation of reactive oxygen species (ROS) that induce oxidative stress damaging cellular components. These processes collectively compromise bacterial membrane integrity and metabolic functions[43].

For instance, ZnO-NPs induce electrostatic attraction to negatively charged bacterial surfaces, leading to membrane disruption and increased permeability. Concurrently, the liberation of Zn^{2+} ions interfere with active transport systems and enzymatic activities vital to bacterial survival[43]. The ROS generation mechanism involves photoexcitation of ZnO, creating electron-hole pairs that react with water and oxygen to produce hydroxyl radicals and superoxide ions, causing oxidative damage to bacterial cells. Comparative studies have demonstrated ZnO nanoparticles' superior antibacterial performance relative to other metal oxides such as MgO, TiO_2, Al_2O_3, CuO, and CeO_2[44]. Moreover, the size of ZnO-NPs critically influences their activity; smaller nanoparticles (~8 nm) achieve >95% inhibition at low concentrations, whereas larger particles (50–70 nm) exhibit substantially reduced effects. This size-dependent efficacy is hypothesized to result from enhanced cellular uptake and interaction with bacterial membranes in smaller NPs. ZnO-NPs effectively inhibit both Gram-positive and Gram-negative bacteria, though Gram-positive strains such as Staphylococcus aureus often show higher susceptibility due to differences in membrane charge and composition. For example, ZnO-NPs completely inhibited E. coli growth at 3.4 mM concentration and S. aureus at 1 mM, with S. aureus membranes allowing greater penetration of ROS and Zn^{2+} ions due to lower negative surface charge[44].

Additional mechanisms involving physical binding of nanoparticles to bacterial surfaces via electrostatic forces have been observed, facilitating membrane damage and bacterial aggregation[12]. Scanning electron microscopy confirms morphological damage to bacterial membranes post-exposure to ZnO-NPs, supporting these biochemical findings. While silica coatings and other surface modifications improve nanoparticle stability and dispersibility, their impact on antibacterial efficacy varies. For ZnO-NPs, surface modifications such as PEGylation may reduce cytotoxicity towards human cells without compromising antimicrobial effects, making them suitable for medical applications including ointments, lotions, mouthwashes, and antimicrobial surface coatings. In summary, ZnO nanoparticles demonstrate multifaceted antibacterial mechanisms—electrostatic disruption, ion release, and ROS generation—enabling potent inhibition of diverse bacterial strains. Their size-dependent activity and relatively low toxicity to humans make them promising candidates for various antimicrobial applications, though further studies are needed to optimize safety and efficacy profiles[7].

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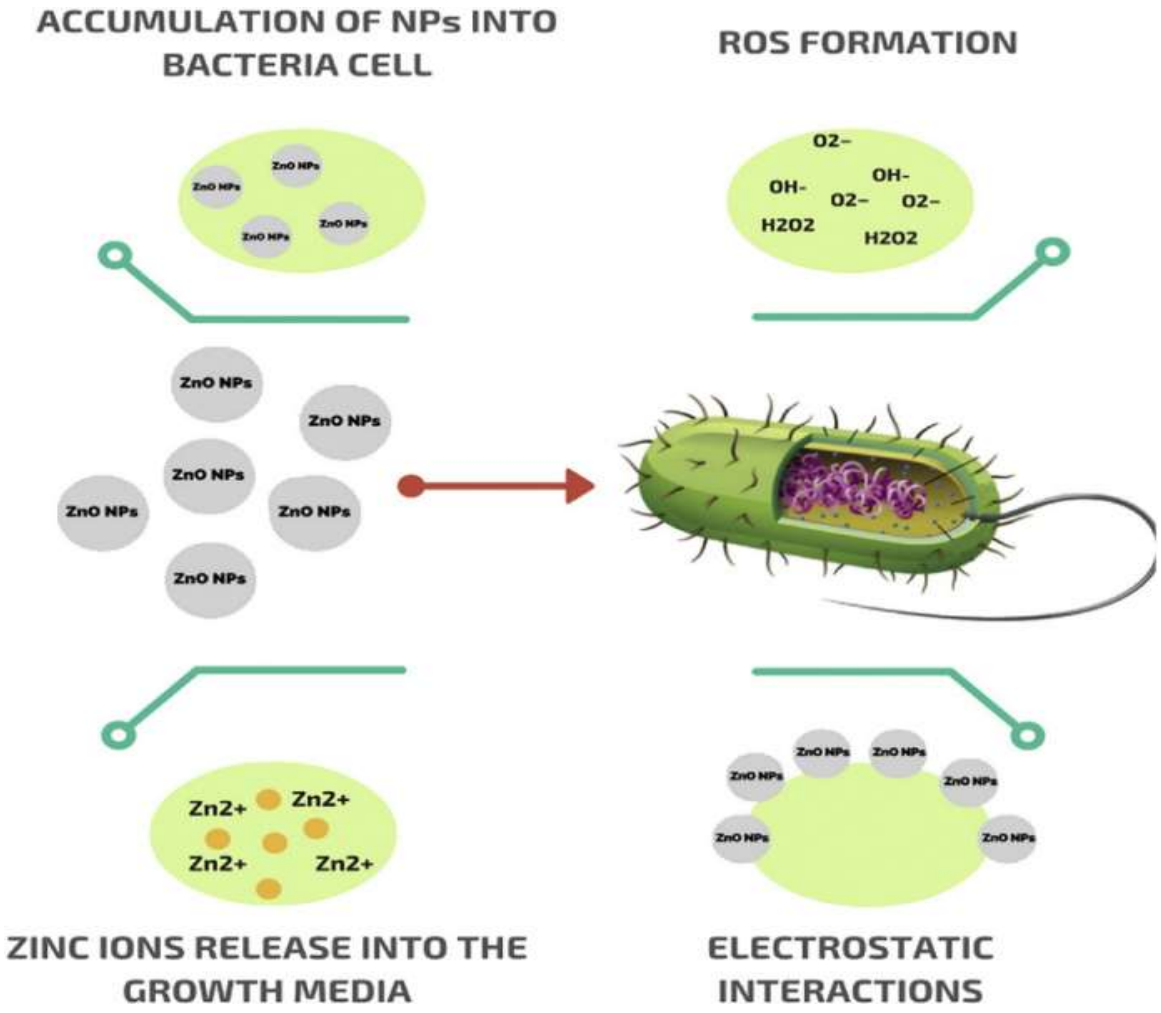

Fig. 4- Different possible mechanisms of antibacterial activity of ZnO NPs.

Table2- Antimicrobial activity of ZnO nanoparticles.

Bacteria	Size of NPs	Concentration of NPs	References
Staphylococcus aureus	13 nm	1 mM	[45]
	8 nm	1 mM	[28]
	50–70 nm	5 mM	[46]
	20–30 nm	15 µg/mL	[45]
Escherichia coli	13 nm	3.4 mM	[47]
Streptococcus agalactiae	150 nm	above 16 mM	[43]
Bacillus subtilis	8 nm	2 mM	[45]
Enterococcus faecalis	8 nm	2 mM	[45]
Vibrio fischeri	50–70 nm	160 mg/L	[41]
Klebsiella pneumoniae	20–30 nm	5 µg/mL	[44]

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6- ADVANTAGES & DISADVANTAGES OF ZnO-NPs

Potential advantages of Zinc oxide nanoparticles (ZnO-NPs) are enlisted in Fig 5[44].

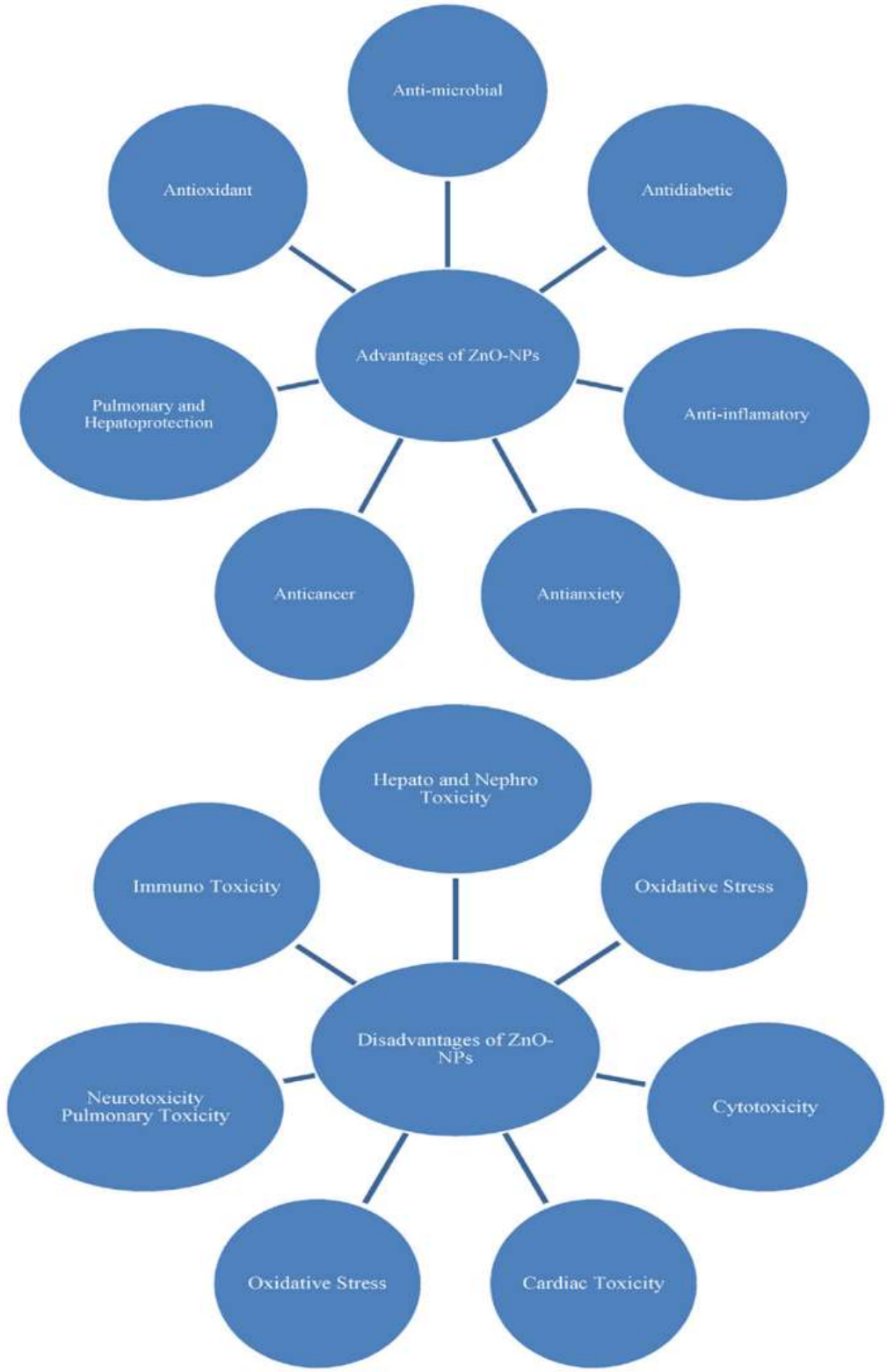

Fig. 5. Advantages & disadvantages of ZnO-NPs.

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7- CONCLUSION

This review has surveyed the principal synthesis routes, characterization methods, and sector-specific applications of biologically derived zinc oxide nanoparticles (ZnO-NPs) in food, pharmaceutical, and textile technologies. As nanotechnology has advanced, increasingly diverse applications for ZnO-NPs have emerged. Notably, green-synthesized ZnO-NPs—produced via plant or bacterial pathways—exhibit superior suitability for biomedical and pharmaceutical use, particularly as antimicrobial agents. The rapid, straightforward, environmentally benign, and cost-effective nature of these green methods constituted the focal point of the present analysis. By consolidating current knowledge, this review is expected to guide future investigations toward innovative characterization strategies and clinically relevant applications of ZnO-NPs.

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