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REVIEW ARTICLE

Current Investigations on the Eco-friendly Production and Medical Implementations of Zinc Oxide Nanoparticles

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Abstract

Nanoparticles (NPs) have numerous applications in nanotechnology. NPs range in diameter from 1 to 100 nanometers (10^{-9} m) and are used in various fields such as engineering, energy science, electronics, mechanics, food and cosmetics production, healthcare, environmental protection, chemical industries, drug development, pharmaceuticals, biomedical science, painting, and pottery. Green synthetic approaches to obtain metal and metal oxide NPs from plant extracts have been a focus of research because they are simple, economical and biocompatible compared to traditional chemical and physical synthetic methods. Zinc oxide NPs (ZnO NPs) have been investigated in recent studies because of their excellent semiconducting properties, energy bandwidth of 3.37 eV, and exciton binding energy of 60 meV. This timely review article presents a comprehensive study of the synthesis and characterization methods used for the green synthesis of ZnO NPs using different biological sources, with a special emphasis on the antibacterial, antifungal, anticancer, and antioxidant properties of ZnO NPs.

Keywords: Antibacterial, Anticancer, Antifungal, Antioxidant, Antioxidant, Green synthesis, Zinc oxide nanoparticle

Introduction

Nanotechnology refers to the scientific study of developing and altering materials and equipment at the nanoscale level, which ranges from 1 to 100 nanometers (10^{-9} m). In 1960, Richard P. Feynman introduced the idea of nanotechnology in his presentation "There's Plenty of Room at the Bottom" at the California Institute of Technology. In his wide vision, machines could be deployed to build smaller machines, which could ultimately build even smaller machines at a molecular level (Feynman, 1960). To the best of our knowledge, Japanese scientist Norio Taniguchi originally elucidated the term “nanotechnology” in 1974. He stated “Nanotechnology mainly consists of the processing of separation, consolidation, and deformation of materials by one atom or molecule” (Taniguchi, 1974). Since then the field of nanotechnology has seen significant advancements, leading to a wide range of applications in various fields such as engineering, energy science, electronics, mechanics, food and cosmetics production, healthcare, environmental protection, chemical industries, drug development, pharmaceuticals, biomedical science, painting, and pottery (Chausov *et al.*, 2022; Rakesh *et al.*, 2022).

Methods of Nanoparticle Synthesis

There are two main methods of producing NPs: the top-down approach and the bottom-up approach (Fig.1). The top-down method implies cutting and mechanically grinding voluminous particles until they reach the nanoscale level through plastic deformation. However, this approach is unsuitable for large-scale production due to its slow and expensive nature (Ijaz *et al.*, 2020). On the other hand, the bottom-up approach involves the green synthesis of NPs, where metal atoms cluster together to form NPs of various sizes and shapes that can be utilized for different applications. This method is more affordable and quicker than the top-down approach. The approach and technique of synthesis mostly depend on the type of nanomaterials, materials of interest, quantity, and their application (Jamkhande *et al.*, 2019).

Physical and Chemical Method of Nanoparticle Synthesis

Since the discovery, various physical, chemical, and biological methods have been developed to synthesize NPs (Fig.2). Physical methods include powder ball milling, electron arc deposition, laser ablation, physical

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*Corresponding Author Email: ronakchetani2196@gmail.com vapour deposition, and sputtering (Aref and Salem, 2020). Chemical processes such as precipitation, hydrothermal procedures, microemulsion, and sol-gel synthesis commonly produce NPs (Zamarchi and Vieira, 2021). However, these methods have several disadvantages. Physical methods require expensive equipment, specific laboratory conditions, and high energy consumption during synthesis. Chemical methods require stabilizers, capping, and reducing agents like sodium borohydride ($NaBH_4$), sodium citrate ($Na_3C_6H_5O_7$), alcohols (-OH), and radiation that can be toxic and limit the use of NPs in clinical and biomedical applications (Alrajhi *et al.,* 2021;Abdelmoneim *et al.,* 2022). Therefore, it is necessary to develop reliable, clean, biologically appropriate, and environmentally friendly techniques for NPs synthesis.

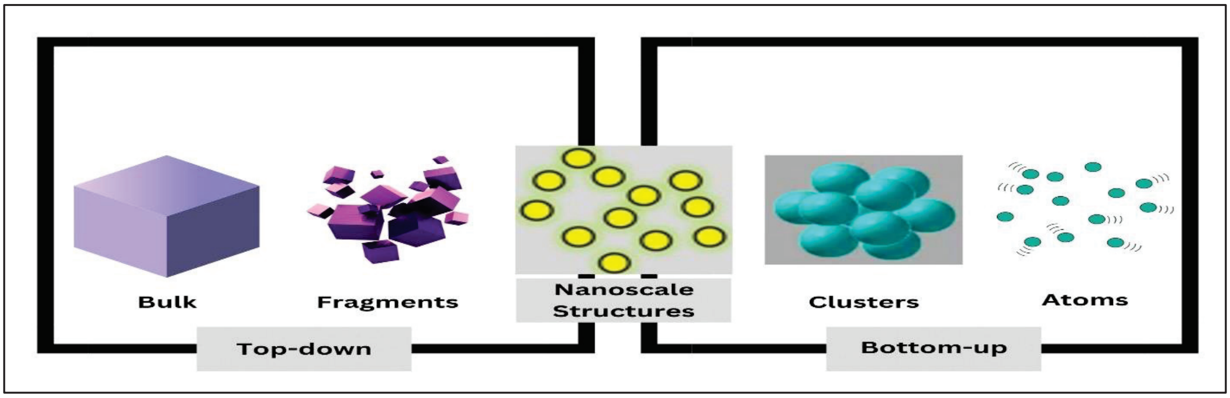

Fig. 1. The schematic representation of the top-down and bottom-up approaches for the NP synthesis

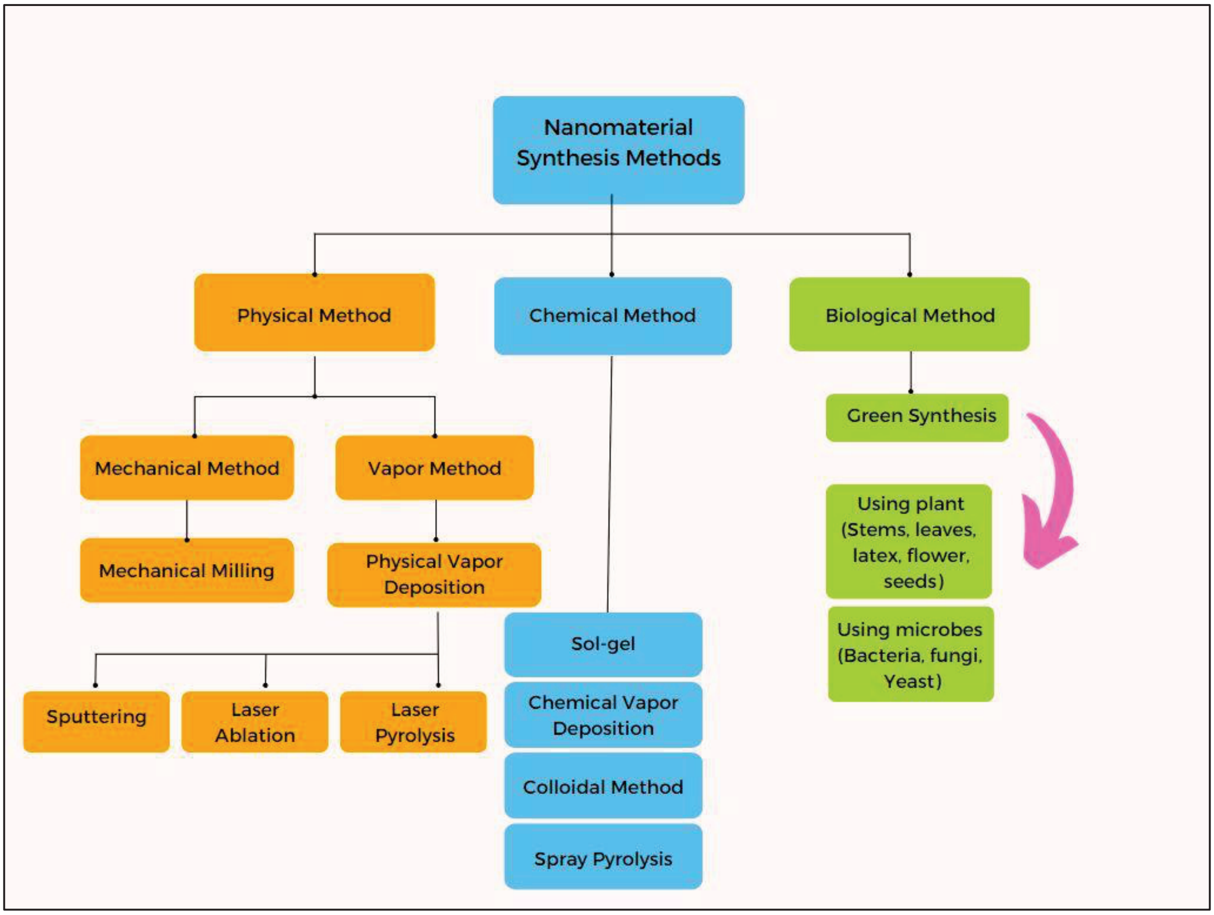

Fig. 2. Synthesis approaches for NPs Synthesis

Biological Method

Green chemistry has emerged as a viable alternative for NP synthesis, utilizing biological entities namely fungi (Sharma *et al.*, 2021), viruses (Attia *et al.*, 2021), yeast (Hassabo *et al.*, 2022), bacteria (Ijaz *et al.*, 2022), algae (Hameed *et al.*, 2023), diatoms (Saadattalab *et al.*, 2023), actinomycetes (Chackaravarthi *et al.*, 2023), and plants (Momeni *et al.*, 2023) having biomedical applications. Among the biological methods for nanoparticle formation, microbe-mediated formation is unsuitable for industrial use because of the need for extremely sterile surroundings and maintenance.

Unequivocally, plant extracts are the ultimate solution for mass production of NPs (Table 1). Plant extracts contain secondary metabolites and phytochemical compounds, such as proteins, tannins, amino acids, enzymes, vitamins, polysaccharides, phenolic acids, flavonoids, alkaloids, saponins, and terpenoids, which are excellent reducing, and stabilizing agents for NP synthesis. Flavonoids and phenolic acids are powerful hydrogen donors because of their functional groups that are responsible for various antimicrobial, anticancer, and antioxidant activities(Abdelbaky *et al.*, 2022). Owing to these molecules, no further chemical reducing or capping substances are required for the capping of NPs, which is crucial for their stability and biocompatibility (Murali *et al.*, 2021). This approach does not involve extreme temperatures pressures, expensive machinery, or hazardous substances. To compose NPs of various shapes and sizes, researchers have used distinct parts of plants such as leaves, roots, seeds, shoots, flowers, bark, calli, stems, and fruits (Aref and Salem, 2020; Abdelghany *et al.*, 2022(a); Al-Zahrani *et al.*, 2022). When plants are used for biosynthesis, several aspects influence the synthesis, characterization, and application of NPs. These factors include temperature, pH, reaction duration, plant extracts, and substrate concentration (Alshameri and Owais, 2022).

ZnO NPs

Extensive research on NPs has conclusively revealed that metallic NPs, including gold, silver, copper, zinc, titanium, magnesium, and, iron are the typically employed materials for synthesizing NPs (Aboyewa *et al.*, 2021). Researchers have extensively used these NPs owing to their unique properties (Fig. 3). ZnO NPs are of particular interest to researchers owing to their substantial semiconducting properties, 3.37eV of energy bandwidth, and remarkable exciton binding energy of 60 meV, making them well suited for optical systems at or above room temperature (Liu *et al.*, 2023). ZnO NPs generally possess hexagonal wurtzite structure with a P63MC space symmetry (Chen *et al.*, 2019). Their

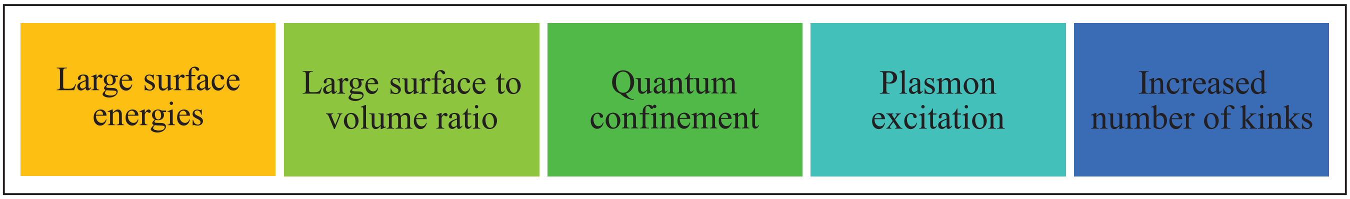

Fig. 3. Characteristics of Metallic NPs

Table 1. Comparison between the microorganisms and plant extract-mediated nanoparticle synthesis

S. No.	Microorganisms-mediated synthesis of NPs	Plant-mediated synthesis of NPs
1	Enzymes or proteins secreted by microorganisms are chargeable for metal NP synthesis.	Phytochemicals secreted by plants are chargeable for metal NP synthesis.
2	The NPs synthesize either intercellularly or extracellularly.	The NPs synthesize either intercellularly or extracellularly, but the intracellular process is expensive.
3	Low yield	High yield
4	Less economical	More economical
5	Complicated method of NP synthesis	One-pot synthesis process
6	Preparation time Longer than plant due to incubation time	Short preparation time

different shapes are flower-like (Vinayagam *et al.,* 2021), rod-like (Ata *et al.,* 2019), flake-shaped (Nataraj *et al.,* 2022), belt and wire (Wang *et al.,* 2023), and a wide range of size distribution (30-150 nm), making them an ideal choice for research. Additionally, the soluble form of ZnO, Zn ion (Zn^{2+}), is an indispensable trace element available in human physiological tissues, such as the brain, bone, skin, muscles, and enzymes (Choi *et al.,* 2020). Additionally, it plays a pivotal role in the synthesis of proteins and nucleic acids (Li *et al.,* 2022). ZnO NPs also have a hydroxyl (-OH) group on their surface, which enables them to diffuse slowly in a strong basic and acidic environment such as cancer cells, establishing them as an eligible material for biomedical applications (Selim *et al.,* 2020). In addition, it possesses high luminescence properties, making it useful for bioimaging (Sharma *et al.,* 2022).

ZnO NPs are widely used in various applications, such as environmental pollutants, photocatalytic degradation (Utaiyachandran *et al.,* 2023), nano-fertilizers (Soltani *et al.,* 2023), water purification (Ashar *et al.,* 2021), meat packaging (Smaoui *et al.,* 2023), and food supplements in animal husbandry (Yusof *et al.,* 2019). Due to its ability to screen UV rays, it is widely used in paints, coatings, and personal care products such as sunscreens and lotions (Abdulazeem *et al.,* 2023; Porrawatkul *et al.,* 2023). The Food and Drug Administration (FDA) recommended ZnO NPs as Generally Recognized As Safe (GRAS) metal oxides that can be used in the food industry as an additive (Zhou *et al.,* 2023). Furthermore, it has a broad array of biogenic applications, including drug delivery(Kadhim *et al.,* 2023), anticarcinogenic (Manimegalai *et al.,* 2023), antidiabetic (Masud *et al.,* 2023), antiviral (Wolfgruber *et al.,* 2023), antibacterial, and antifungal properties (Sharma *et al.,* 2023). Extracts of a diverse range of plant species have been successfully used to synthesize ZnO NPs, including *Pinusbrutia* (Ismail *et al.,* 2023), *Pelargonium odoratissimum* (Abdelbaky *et al.,* 2022), *Brassica oleracea var.* (Utaiyachandran *et al.,* 2023), *Chrysanthemum spp.* (Nguyen *et al.,* 2023) ,*Zingiber officinale, Allium sativum* (Urge *et al.,* 2023) ,and *Ailanthus altissima* (Awan *et al.,* 2023). Table 2 presents therecent studies on ZnO NPs using plant extracts.

Method of green synthesis of ZnO NPs

ZnO NPs are conceivably produced employing various approaches and the preparation choice relies on the demand of the application. The plant material was carefully washed and sterilized with double-distilled water to eliminate unwanted substances. The washed plant parts were then shade-dried at room temperature and ground into a fine powder using an electric grinder (Fig. 4). The aqueous extract was prepared by mixing the plant powder with double-distilled water at the desired concentration and incubating the mixture overnight in a mechanical shaker. The resulting solution was filtered and used for the green synthesis of ZnO NPs.

To create the metal precursor, zinc salts, such as zinc nitrate (Zn(NO)), zinc sulfate heptahydrate ($ZnSO_4 \cdot 7H_2O$), and zinc acetate dihydrate ($Zn(CH_3CO_2)_2 \cdot 2H_2O$), were mixed in distilled water to a specific amount. The filtered plant extract was then added to the zinc solution and NaOH was added dropwise as a precipitating agent to reach pH 12 under magnetic stirring at room temperature for 1 h. The process was optimized by monitoring the temperature, pH, concentration of plant extracts, and time. The resulting white-to-yellowish-white crystalline precipitate was separated by centrifugation, dried at 60°C in a hot-air oven for 2 h, and mashed using a mortar and pestle. The final product (i.e., ZnO Nps) was a white powder that was preserved in an airtight brown reagent bottle for further experimentation. The general chemical mechanism for forming ZnO NPs from zinc acetate is as follows:

$$Zn\ (CH_3COO)_2\ .2H_2O\ +\ 2NaOH \xrightarrow{\qquad} Zn(OH)_2 + 2CH_3COONa + 2H_2O\ \ldots\ldots(1)$$

$$Zn\ (OH)_2 + 2H_2O \xrightarrow{\qquad} Zn\ (OH)_4^{2-} + 2H^+ \ldots\ldots\ldots\ldots\ldots\ (2)$$

$$Zn\ (OH)_4^{2-} \longleftrightarrow ZnO + 2OH + 2H_2O \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots(3)$$

Methods employed to characterize NPs

Researchers have utilized different methodologies to precisely measure and comprehend the structure, dimensions, surface area, and dispersion of ZnO NPs which is pivotal for understanding their varied physicochemical properties (Ibrahim *et al.,* 2021) (Table 3).

These techniques include UV-visible spectroscopy (UV-Vis), fourier transform infrared spectroscopy (FTIR), atomic force microscopy (AFM), thermal gravimetric analysis (TGA), dynamic light scattering (DLS), scanning electron microscopy (SEM), transmission electron microscopy (TEM), x-ray diffraction (XRD),

Table 2. Overview of recent research on the synthesis of ZnO NPs using plant extracts.

S. No.	Plant Used	Part used	Zinc Precursor Used	SPR peak (nm)	Shape	Size (nm)	Functional group identified	Applications	References
1	*Lycopersicon esculentum M.*	fruits	Zinc oxide	386	Cubic	65.6 to 133	-OH, CH3, C=O, C -O-H, C-N	Antibacterial Activity	Ogunyemi *et al.,* 2019
2	*Matricaria Chamomilla L.*	flower	Zinc oxide	384	Cubic	49.8 to 191.0	-OH, CH3, C=O, C -O-H, C-N	Antibacterial Activity	Ogunyemi *et al.,* 2019
3	*Olea europaea*	leaves	Zinc oxide	380	Cubic	40.5 to 124	-OH, CH3, C=O, C -O-H, C-N	Antibacterial Activity	Ogunyemi *et al.,* 2019
4	*Punica grantum*	Fruit peel	Zinc nitrate	370 and 378	Spherical and hexagonal	32.98 to 81.84	C=O, C –O-H, C –O-C, carboxylic groups, and aromatic rings	Potential uses in the biomedical field	Sukri *et al.,* 2019
5	*Strawberry*	leaves	Zinc acetate	393	Quasi-spherical	30-40	NA	Antibacterial and antifungal applications	Bayat *et al.,* 2019
6	*Azadirachta indica*	leaves	Zinc sulfate	NA	irregular	20	-COOH, -CONH2 and-OH group	multifarious biomedical applications	Sohail *et al.,* 2020
7	*Brassica oleracea var.*	Whole plant	Zinc nitrate		spherical	47±2	Proteins, secondary alcohols, and alkene	Water Remediation	Pillai *et al.,* 2020
8	*Lippia adoensis (Koseret)*	leaves	Zinc acetate	360-363	Spherical and hexagonal	19.78	aldehydes, ketones, alcohols, and phenols	Antibacterial Activity	Demissie *et al.,* 2020
9	*Mussaenda frondosa*	callus	Zinc nitrate	373	spherical	NA	$-CONH_2$, -COOH, aliphatic and aromatic amines	Industrial and biomedical application	Jayappa *et al.,* 2020
10	*Orange*	Peels of fruit	Zinc acetate	NA	Spherical	35 to 60 and 70 to 100	C=C, C=O	Biomedical field application	Thi *et al.,* 2020
11	*Pineapple*	Peels of fruit	Zinc nitrate	NA	Spherical and rod - shaped	8-46	Carboxylic acid and amine groups	Biomedical application	Basri *et al.,* 2020

12	*Becium grandiforum*	Leaves	Zinc acetate	315	hexagonal wurtzite	2.07	OH, C–H, C=C group, O –N=O nitro group, C –O stretching, C–N stretching, meta disubstituted ring, and Zn–O stretching	Antibacterial and photocatalytic activity	Kahsay, 2021
13	*Eriobotrya japonica*	leaves	Zinc nitrate	375	Irregular platelets	13	aliphatic amine, aromatic,	Antibacterial applications	Nazir *et al.*, 2021
14	*Jute*	stick	Zinc acetate	373	hexagonal wurtzite, flower-like, irregular	29.04	C-O, -C-C, -OH, CO_2, C - H,-C=C	Antibacterial and photocatalytic activity	Nayem *et al.*, 2022
15	*Phoenix roebelenii*	Leaves	Zinc nitrate		Spherical	8-25	Amines, alcohols, and phenols	Wastewater treatment and bacterial inactivation	Aldeen *et al.*, 2022
16	*Ailanthus altissima*	Leaf	Zinc sulfate	327	Spherical	13.27	Phenol, amides, C -O-H, Alkanes	Antibacterial and antioxidant activity	Awan *et al.*, 2023
17	*Capparis spinosa L.*	fruit	Zinc acetate	366	Spherical	37.49	C=O, C=C, C -O-H, C -H and Phenolic group	Cytotoxic and antioxidant activity	Neamah *et al.*, 2023
18	*Cassia siamea*	Leaf	Zinc nitrate	384	spherical	13	C-O and Phenolic O -H groups, alkanes	Antibacterial, MIC, and MBC	Khan *et al.*, 2023
19	*Cassia sieberiana*	Root bark	Zinc acetate	377	spherical	12.9±3.1	-OH, -NH, -CH, and C=C	Antimicrobial, Anti-inflammatory, Antioxidant	Kyene *et al.*, 2023
20	*Lentinula edodes*	Whole plant	Zinc nitrate	363	Hexagonal, spherical	90-148	OH group, C=O group	Antioxidant, antimicrobial, antipyretic, antidiabetic, and anti-inflammatory	Amin *et al.*, 2023

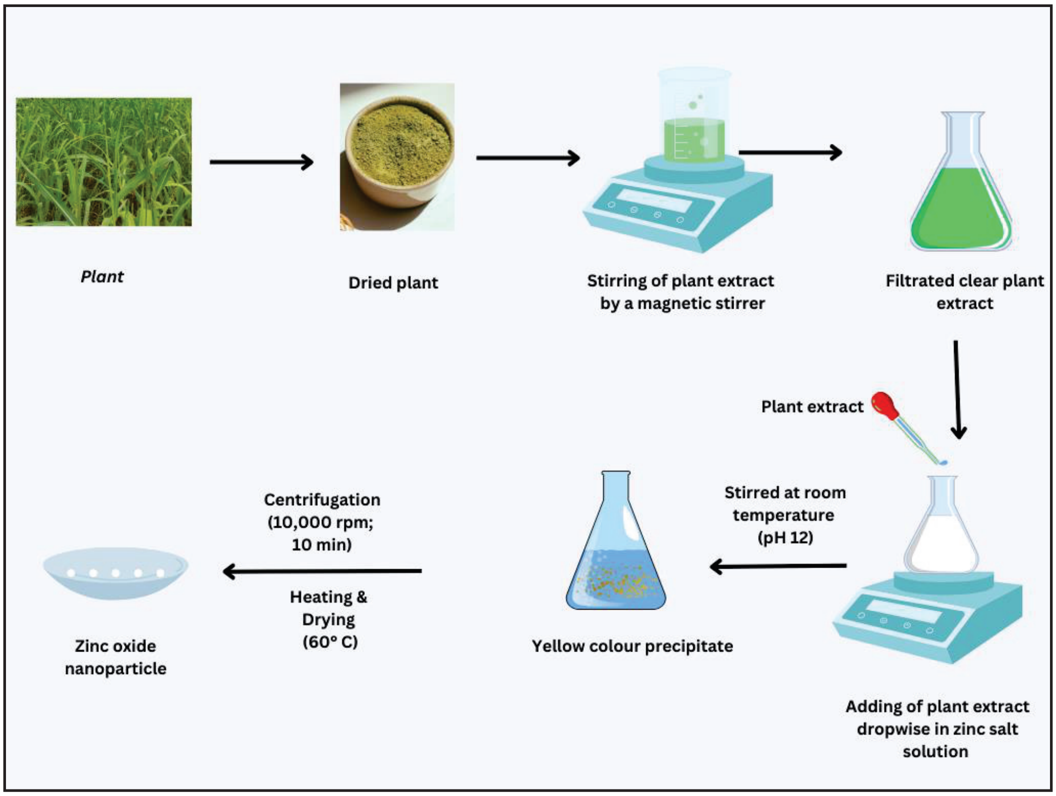

Fig. 4. Schematic Representation for the biosynthesis of ZnONPs

energy dispersive x-ray spectroscopy (EDX), and photoluminescence (PL).

Bio-medical Applications of ZnO NPs

The application of nanotechnology to medical research has opened up research opportunities and expanded our understanding of molecular biology. Several researchers have focused are on the usefulness of ZnO NPs, and we have included a number of their most recent uses.

Anticancer activity

Cancer is a deadly disease prompted by the uncontrolled growth of cells in the body. Sadly, it is anticipated that by 2040, there will be a considerable increase in the number of new cancer cases and fatalities, with a projected 29.5 million new cases and 16.4 million deaths annually (Bray *et al.*, 2021). Vomiting, baldness, stiffness, and nausea, are some of the unfavorable responses to conventional treatment of cancer like surgery, chemotherapy, and radiation. Combinational chemo-immunotherapies have been developed using nanotechnology to successfully treat several cancer cell types. The incorporation of NPs into cancer treatment aims to enable targeted drug delivery to overcome the drawbacks of traditional therapies. The size, shape, and concentration of NPs play significant roles in their ability to combat cancer cells. Studies have indicated that smaller NPs and higher concentrations result in greater anticancer activity (Motazedi *et al.*, 2020). By releasing dissolved zinc ions into cells, ZnO NPs aid in boosting ROS activity and triggering the apoptotic signaling pathway (Sana *et al.*, 2020). Additionally, ZnO NPs can effectively target cancer cells due to electrostatic attraction caused by anionic phospholipids found in cancer cells (Zhang *et al.*, 2020).

Several studies have shown that ZnO NPs are effective at killing MCF-7 cell lines, and MDA-MB 134 breast cancer through the process of apoptosis (Shandiz *et al.*, 2021; Dhayalan *et al.*, 2021). Other research demonstrated that ZnO NPs generated by cell biomass and supernatant of *Lactobacillus plantarum* TA4 had a dose-dependent harmful effect on the Vero cell line (Yusof *et al.*, 2020). ZnO NPs derived from *Raphanus sativus* var. Longipinnatus leaves demonstrated anticancer activity against A549 lung cancer cells. The increased cytotoxic activity could be attributed to a larger surface area-to-volume ratio. Furthermore, phytoconstituents found in plant ethanolic extracts, such as anthraquinones and saponins, are thought to target several cancer-related proteins (Umamaheshwari *et al.*, 2021). In recent work, ZnO NPs were generated utilizing the combustion

Table 3. A List of major Techniques and their Role in the Characterization of ZnONPs

S.No	Technique	Role	Reference
1.	UV-vis spectroscopy	A UV-Vis spectrophotometer is used to scan ZnNPsin the UV region (200-800 nm) to confirm their initial formation. The interaction between light and surface electrons produces Surface Plasmon Resonance (SPR), which determines the NPs' morphological properties.	Fakhari *et al.,* 2019
2.	SEM	Use for high-resolution surface topological assessment of nanoparticle	Rajeshkumar *et al.,* 2023
3.	DLS	It is a non -destructive approach that uses a monochromatic laser to characterize these compounds in the liquid solution phase.	Naseer *et al.,* 2020
4.	TEM	It is used for the determination of the size, morphology, aggregation state, and distribution of NPs in high resolution which is based on the interaction of high-density electron beam and nanomaterials.	Demissie *et al.,* 2020
5.	PL	It tells us about the band gap and crystalline purity of NPs	Galdámez-Martinez *et al.,* 2020
6.	XRD	It characterizes the surface chemistry, bioactive surface, and morphology of NPs.	Awwad *et al.,* 2020
7.	FTIR	It is an easy and non-destructive technique that determines the functional group and various photochemical constituents.	Chinnapaiyan *et al.,* 2022
8.	EDX	It helps in identifying the elemental composition and also functions as a tool for the examination of the extent of ZnO NP purity.	Abdelbaky *et al.,* 2022
9.	AFM	Use to determine the volume and height of synthesized NPs.	Ho *et al.,* 2022
10.	TGA	It determines the amount of coating on the surface of the NP	Worku *et al.,* 2021

method from zinc nitrate hexahydrate and fungal filtrate to explore their anticancer effect against Human MDA-MB 134 mammary gland carcinoma cells. The findings revealed that at a concentration of 1 g/mL, the produced ZnO NPs demonstrated considerable anticancer action without disrupting cancer cell morphology (Sumanth *et al.,* 2020).

As a result of their capacity to cause apoptosis of various cell lines, ZnO NPs have proven to hold promise as a selective and efficient treatment for cancer cells. They present a potentially fruitful route for additional studies and advancements in the realm of cancer treatment.

Antibacterial activity

Bacterial infections are a growing concern, with an annual death rate of up to 700,000 worldwide, and this number is expected to rise to 10 million by 2050 (Vassallo *et al.,* 2020). Researchers are currently seeking new and effective antimicrobial drugs to combat multidrug-resistant bacteria such as *Enterococcus faecium*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, and *Enterococcus spp*., which are the leading causes of hospital-acquired infections worldwide (Mitevska *et al.,* 2021; Sarshar *et al.,* 2021). Nanotechnology is a reliable alternative to traditional antibacterial agents (Mthana *et al.,* 2022). NPs are named as "a wonder of modern medicine" (Joseph *et al.,* 2023). The antibacterial activity of green-synthesized ZnO NPs runs by binding to functional groups in respiratory enzymes, which ultimately leads to cell death. Other scientists have reported that suspensions of ZnO NPs produce an enhanced level of reactive oxygen species (ROS), such as superoxide anion (O^{-2}), hydrogen peroxide (H_2O_2), and hydroxide (OH^-). ROS formation is the primary mechanism behind the antibacterial activity of ZnO NPs (Khan *et al.,* 2023).

Sukri *et al.,* (2019) synthesized NPs using *Punica granatum* plant extract found that biogenic ZnO NPs exhibited good antibacterial activity against gram-negative bacteria *Escherichia coli* and gram-positive bacteria *Enterococcus faecalis.* ZnO NPs derived from *Pelargonium odoratissimum* (L.) showed significant antibacterial activity against *S. aureus*, *P. aeruginosa*, and *E. coli*, whereas minimum sensitivity was shown by *Bacillus cereus* (Abdelbaky *et al.,* 2022). Spherical-shaped and 44.5 nm diameter long NPs showed antimicrobial activity against*, Pseudomonas otitis, Pseudomonas oleovorans, B. cereus, E. faecalis,* and, *A. baumannii* (Jayabalan *et al.,* 2019). Similarly, high antibacterial activity was observed with ZnO NPs formed using the leaf extract of *Acalypha fruticosa* (Bhavaniramya *et al.,* 2019). Additionally, kappa-carrageenan-wrapped ZnO NPs (KC-ZNONPs) showed increased antibacterial activity against Methicillin resistant *S. aureus* (MRSA) strains and were compatible with human RBCs (Vijaykumar *et al.,* 2020).

Tyagi *et al.,* (2020) demonstrated that ZnO NPs chemically coupled with ciprofloxacin had increased antibacterial activity against *E. coli* by 2.9 times and against *Streptococcus spp*. by 2.8 times. Similarly, ZnO NPs conjugated with ceftriaxone and ampicillin demonstrated significant antibacterial activity against both gram-positive and gram-negative bacteria, including *Staphylococcus. aureus*, *Escherichia. coli* K1, *Pseudomonas. aeruginosa, Streptococcus pneumoniae*, *Serratia marcescens,* and *Streptococcus pyogenes* (Akbar *et al.,* 2021). Recently, it was found that ZnO NPs formed using *Cassia siamea* L. act as anti-quorum sensing molecules for the laboratory strain *P. aeruginosa* PA01, reducing the virulence of various virulence factors like pyochelin, pyocyanin, and PQS signals (Khan *et al.,* 2023). Amin *et al.,* (2023) biologically synthesized ZnO NPs using methanolic extract of plant *Lentinula edodes.* According to the data obtained by HPLC analysis, flavonoids and phenolic compounds like quercetin, m-coumaric acid, benzoic acid, and sinapic acid are mainly accountable for the bio-reduction of metal salts into ZnO particles. The prepared ZnO NPs showed remarkable antibacterial activity against *K. pneumoniae*, *S. aureus*, and *E. coli*.

Biogenic ZnO NPs, which are produced using plant extracts like *Phoenix roebelenii*, and *Ailanthus altissima*, exhibit impressive antibacterial properties against various bacterial strains (Aldeen *et al.,* 2022). These recent discoveries hold great promise for the development of alternative antibacterial agents.

Antifungal activity

The antifungal efficacy of bio-fabricated ZnO NPs against *Candida albicans* isolates has been uncovered in numerous studies, which proved to be more efficient against drug-resistant strains. *Galleria mellonella* has been demonstrated to protect against *C. albicans* infection through prophylactic treatment with lower doses of ZnO NPs (Abomuti *et al.,* 2021; Xu *et al.,* 2021). Additionally, a nanocomposite film consisting of soy protein isolate (SPI), cinnamaldehyde (CIN), and ZnO NPs showed stronger *antifungal* activity compared to SPI-CIN and SPI-ZnO films (Wu *et al.,* 2019).

Furthermore, ZnO NPs derived from *Prosopis farcta* extract displayed antifungal activity against *C. albicans*, with MIC and MFC values of 128 and 256 g/ml, respectively (Miri *et al.,* 2019). Also, a synergistic antifungal effect was observed when ZnO NPs were combined with fluconazole against *C. albicans* strains (Hajar *et al.,* 2020).

Antioxidant activity

Through numerous metabolic processes in the body, cosmetics, smoking, contaminated products, and radiation exposure, reactive oxygen species (ROS) can lead to the generation of free radicals such as nitric oxide, hydroxyl radicals, and superoxide anions. The accumulation of these free radicals causes oxidative stress leading to chronic diseases like cancer, Alzheimer's disease, diabetes, cardiovascular diseases, skin inflammation, premature aging, degenerative eye disorders, Parkinson's disease, and neurodegenerative diseases. Polyphenols, flavonoids, and vitamin C, which are abundant in fruits and vegetables, can help to restrict the generation of free radicals. Quercetin, a flavonoid, exhibits significant antioxidant potential and pharmacological activity. Scientists have discovered that ZnO NPs have excellent antioxidant properties (Abdelghany *et al.,* 2023).

H_2O_2 free radical scavenging activity was used to test the antioxidant activities of ZnO NPs generated using *Albizia lebbeck* stem bark. The results indicated high IC_{50} values of 48.5, 48.7, and 60.2 g/mL for 0.1M, 0.05M, and 0.01M ZnO NPs, respectively(Umar *et al.,* 2019).The antioxidant activity of ZnO NPs produced using the leaf extract of *Aquilegia pubiflora* was evaluated using several assays, including total antioxidant capacity (TAC), total reducing power (TRP), free radical scavenging activity (FRSA), and 2, 2'-azino-bis (3-ethylbenzothiazoline-6-sulfonic acid) (ABTS) assays. Five different concentrations ranging from 12.5 to 200 µg/ml were employed for these assays, and the results were found to be extremely significant (Jan *et al.,* 2021). *Knoxia sumatrensis* leaf extract ZnO NPs were also investigated for their antioxidant activity using DPPH, ABTS, and H_2O_2 tests. Among them, the DPPH assay results were dependent upon dose, with IC_{50} values of95.80 µg/ml and 87.62 µg/ml for ZnO NPs and standard ascorbic acid, respectively (Loganathan *et al.,* 2021).Additionally, several plant sources such as *Salvia hispanica* (Rabiee *et al.,* 2020), *Punica granatum* (Abdelghany *et al.,* 2022(b)), and *Borassus flabellifer* (Kalaimurugan *et al.,* 2022) have been utilized to evaluate the antioxidant activity of ZnO NPs.

Conclusion

NPs have numerous applications in nanotechnology. This review highlights the biogenic synthesis of ZnO NPs. ZnO as an eco-friendly alternative to traditional chemical and physical synthesis methods. ZnO NPs have gained popularity because of their easy, economical, and biocompatible nature and have been studied in various fields, including healthcare, energy, engineering, and cosmetics. This review emphasizes the antibacterial, antifungal, anticancer, and antioxidant properties of ZnO NPs. However, the exact mechanism underlying their synthesis remains unclear. Future research should focus on elucidating the phytochemicals involved in the synthesis of NPs, the expansion of laboratory research to fields and industries, exploring the long-term impact of ZnO NPs on the environment, and understanding the factors that affect their size and shape.

Conflict of Interest

The Authors declare no conflict of interest.

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