

Zinc Oxide Nanoparticles from *Murayya Koenigii*: Antibacterial Potential Review

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Abstract

Nanoparticles (NPs) display unique characteristics in contrast to conventional physico-chemical synthesis methods, and they are utilized in various life science fields including surface coating, catalysis, food packaging, corrosion prevention, environmental cleanup, electronics, biomedical applications, and antimicrobial purposes. Metal NPs synthesized through green methods, particularly from plant origins, have garnered significant interest because of their inherent traits such as environmental friendliness, quick production, and cost efficiency. Over the past few years, there has been a remarkable surge in the interest surrounding zinc oxide nanoparticles (ZnOs) owing to their distinct properties. These nanostructures are widely regarded as the most desirable group, exhibiting exceptional characteristics in terms of both structure and properties. Addressing the rise of antibiotic resistance in bacteria is a top priority in global health care. Metal nanoparticles and their oxides present an encouraging approach to tackle microbial resistance to antibiotics. This review introduces a sustainable method for synthesizing ZnO nanoparticles with plant extracts, delving into their antibacterial properties and the mechanisms by which they exert antibacterial action. ZnO is characterised as an inorganic material with a wide range of applications that is practical, strategic, promising, and versatile. To produce selective nanostructured ZnO for the antibacterial tests, many researchers have been driven. They were successful in creating morphologies that complemented the antibacterial activity very well. ZnO-NPs were created using a non-hydrolytic solution process and zinc acetate dehydrate. This method has been applied to various unicellular and multicellular organisms, including bacteria, fungi, actinomycetes, yeasts, viruses, and plants. Numerous life forms possess this capability, which can be exploited to their disadvantage. This method favours the synthesis of metallic nanoparticles in a quick, inexpensive, clean, non-toxic, and environmentally friendly manner. The main drawback of this strategy is that it involves challenging processes like sampling, isolation, culturing, and storage. Aside from that, downstream processing is necessary for the recovery of MnPs produced using this method.

Keywords: *Murayya koenigii*, nanoparticles, ZnO nanoparticles, green synthesis, antibacterial action

INTRODUCTION

A growing field of science called nanoscience examines materials at extremely small scales. The nanoscale is the range of dimensions between 1 and 100 nanometers. Nanotechnology focuses on the creation, management, and manipulation of nanoparticles, which are microscopic particles. The concept of nanotechnology, as articulated by Nobel laureate Richard P. Feynman, is characterized by "plenty of room at the bottom," showcasing its elevated surface area to volume ratio. They may bond with a variety of molecules thanks to this property, which also increases their chemical stability, thermal conductivity, catalytic reactivity, and nonlinear optical performance.

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The components, origin, dimension, and structural makeup of nanoparticles, as well as their size and other physical characteristics, can all be used to categorise them. The classification of nanoparticles as organic or inorganic is determined by the composition of their constituent parts, offering a way to differentiate between the two types. Inorganic nanoparticles like magnetic nanoparticles (MNPs) and carbon nanoparticles (fullerenes) are examples of inorganic nanoparticles. MNPs' super paramagnetic behaviour is an advantage. They can be either natural or artificial nanoparticles, depending on their source. In the realm of nanoparticles, they can take on different dimensions such as zero-dimensional (0D), one-dimensional (1D), two-dimensional (2D), or three-dimensional (3D). Zero dimensional nanoparticles have nano-dimensions in each of the three dimensions, whereas one-dimensional nanoparticles have just one exterior nanometer-range dimension, two-dimensional nanoparticles have two exterior nanometer-range dimensions, and three-dimensional nanoparticles have all exterior nanometer-range dimensions. Nanoparticles can be dispersed and amalgamated based on their structural makeup.

For the synthesis of nanoparticles, numerous conventional approaches, including physical and chemical ones, have been applied. Physical and chemical procedures are quick and efficient, but they can contaminate the environment by using harsh chemicals and radiation. Therefore, the environmentally beneficial method of creating nanoparticles through biological processes is gaining prominence today. The biological creation of different metal oxide and metal nanoparticles is utilised to control chemical toxicity in the environment. Organisms have acclimated by creating defense mechanisms to endure in habitats rich in metals. As a result of a resistance mechanism against a particular metal, the generation of nanoparticles can be employed as an alternative method for their production. One significant and intensively researched class of materials that exhibits great diversity and has a wide range of applications is metallic nanoparticles. The partnership between science and biology has enabled the eco-friendly production of metal nanoparticles. Various bacteria, fungi, and plants have exhibited the capacity to create metallic nanoparticles. Plant extracts are rich in active bio molecules that aid in reducing and maintaining the stability of nanoparticles [1,2]

The special attributes and multiple applications of zinc oxide (ZnO) have sparked the interest of researchers in recent times [3-6]. ZnO-based nanomaterials are being considered for a wide range of applications, including energy storage, nanosensors, personal care products, nano-optical devices, and nanoelectronic devices [7-12]. One of ZnO nanomaterials' most significant properties is biodegradability and low toxicity. Zn²⁺ is a crucial trace element for adults and is incorporated into many aspects of metabolism. ZnO NPs could slowly dissolve in acidic and strongly basic environments. Zn²⁺ ion release has been shown on stress cells and have negative effects on various organisms by solubilized ZnO nanoparticles [13]. Concern over the necessary ZnO nanomaterial properties for biomedical applications has grown [14]. The toxic properties of ZnO nanoparticles result from their solubility. ZnO nanoparticles are dissolved in the extracellular spaces, which gradually increases the intracellular [Zn²⁺] level. The factors contributing to the rise in intracellular [Zn²⁺] concentration and the dispersion of ZnO nanoparticles in the solution have not been identified [15].

The synthesis of ZnO nanoparticles has been explored in previous literature using a range of plant extracts, including *Azadirachta indica* [16,17], *Passiflora caerulea* [18], *Aloe vera* [19,20], *Vitex trifolia* [21], and *Trifolium pratense* [22], *Bauhinia tomentosa* [23], *Cinnamomum verum* [24], *Camelliasinensis* [25], *Artocarpus gomezianus* [26], *Duranta erecta* [27], *Moringa oleifera* [28], *Matricaria chamomilla*, *Olea europaea*, and *Lycopersicon esculentum* [29], and their antimicrobial activities were also reported.

This research delved into the utilization of *Murayya koenigii* leaf extract as both a capping and reducing agent in the synthesis of ZnO NPs. The antibacterial efficacy of the synthesized ZnO NPs against pathogenic organisms was evaluated through the disc diffusion method. The confirmation of

nanoparticle synthesis was accomplished using UV-Vis spectroscopy, which verified the purity of the synthesized NPs by exhibiting a single absorption peak in the spectra. To identify the constituents of the samples, FT-IR analysis was conducted, employing infrared light to detect organic, inorganic, and polymeric materials. Changes in the typical pattern of absorption bands unmistakably point to a modification in the composition of the material.

Various other methods can be applied in the to characterise nanoparticles. Information about the crystalline structure is provided by XRD. It is a sophisticated method for analysing samples of nanoparticles of different sizes. The examination of nanoparticles' shape and size involves the use of scanning electron microscopy, commonly referred to as SEM, EDAX, or electron dispersive X-ray analysis, is used to identify the elements in the compound.

Synthesis of Nanoparticles

The three main steps in the synthesis of nanoparticles—solvent used, eco-friendly reducing agent, and non-toxic stabilizer—must be taken into account when applying the principles of green chemistry [30]. There are numerous organisms that alter, reduce, or eliminate the toxic effects of metals. There are two types of natural biological metallic nanoparticle synthesis: (a) Bioreduction:- Oxidation-reduction is a component of bioreduction. Here, the enzyme is oxidised while the metal ion is reduced. As a result, contaminated sample can be cleaned up of metallic nanoparticles, (b) Biosorption:- A metal ion binds to the sample in this process.

Metallic Nanoparticles

When metals have dimensions (length, width, or thickness) between 1 and 100 nm, they are classified as metal nanoparticles. These nanoparticles are composed of metal precursors and possess remarkable opto-electric properties, primarily attributed to their localized surface Plasmon resonance (LSPR) characteristics. They are readily observable in the visible region of the solar spectrum and have a wide absorption band, making them noble metal NPs like gold, silver, and copper.

Metal nanoparticles found use in a variety of research fields, including conductors, catalysis, quantum dots, quantum devices, and electronics, thanks to their superior optical properties. The reason that essential metal nanoparticles were chosen is that they are nontoxic at a wide range of concentrations and are essential metals for plants. Nanoparticles made of Zn, Cu, Fe, Mn, and their oxides make up this group of metals.

Zinc Oxide Nanoparticles

Since it has strong reduction properties, zinc is an active element. Zinc oxide is a simple byproduct of the oxidation of zinc. A substance that is inorganic is zinc oxide. It has a white colour and a variety of nanostructures. Its chemical formula is ZnO.

ZnONPs have the most extensive and significant range of applications of any synthesised nanoparticles, including antimicrobial, antibiotic, and antifungal agents that are used in paint, dressing materials, nanofibers, plastics, and textiles [31]. Additionally, ZnO NPs are frequently used in personal care items like lipsticks, sunscreen, cosmetics, textiles, and hair dyes. They are utilised in industrial products such as floor coatings, solar cells, antibacterial agents, optical and electronic materials, and floor coatings [32–34]. Promising anticancer agents include ZnONPs. They aid in the apoptosis of cancer cells, making them effective in the treatment of cancer. It only exhibits selective toxicity against tumour T cells and does not harm any normal cells. Because it is dose dependent, ZnONPs only work as an anticancer agent at higher doses.

Due to its biodegradable qualities and low toxicity, cancer treatment based on drug delivery to the target organ reduces both the amount of medication needed and the severity of side effects. PEG

functionalized ZnONPs possess anticancer properties as a result of the generation of ROS, or "reactive oxygen species." ROS prevent the DNA repair process, which pushes cells into apoptosis.

Crystal Structure of ZnO

A hexagonal unit cell of ZnO is crystalline. Each anion in this hexagonal structure is surrounded by four cations at the tetrahedron's corners, demonstrating tetrahedral coordination and exhibiting sp^3 covalent bonding. ZnO's tetrahedral structure results in a noncentro symmetric structure [35–37]. ZnO's tetrahedral structure results in a noncentro symmetric structure as shown in Figure 1

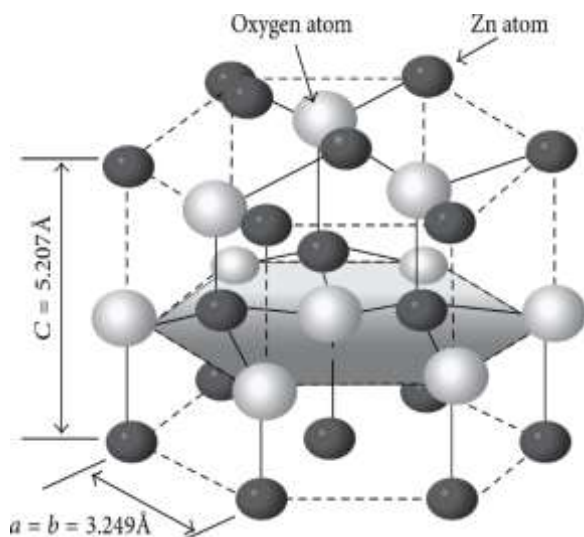


Figure 1. Tetrahedral structure of ZnO.

Synthesis of Nanoparticles

There are several chemical processes that can be used to create ZnONPs, including the hydrothermal technique, the chemical reaction of zinc metal with alcohol, the vapour transport synthesis, and the precipitation method. However, these techniques leave some toxic chemicals adsorbed on the surface that might have negative effects. Nanoparticle stabilisation and synthesis are performed using toxic chemicals that produce unfriendly byproducts [38].

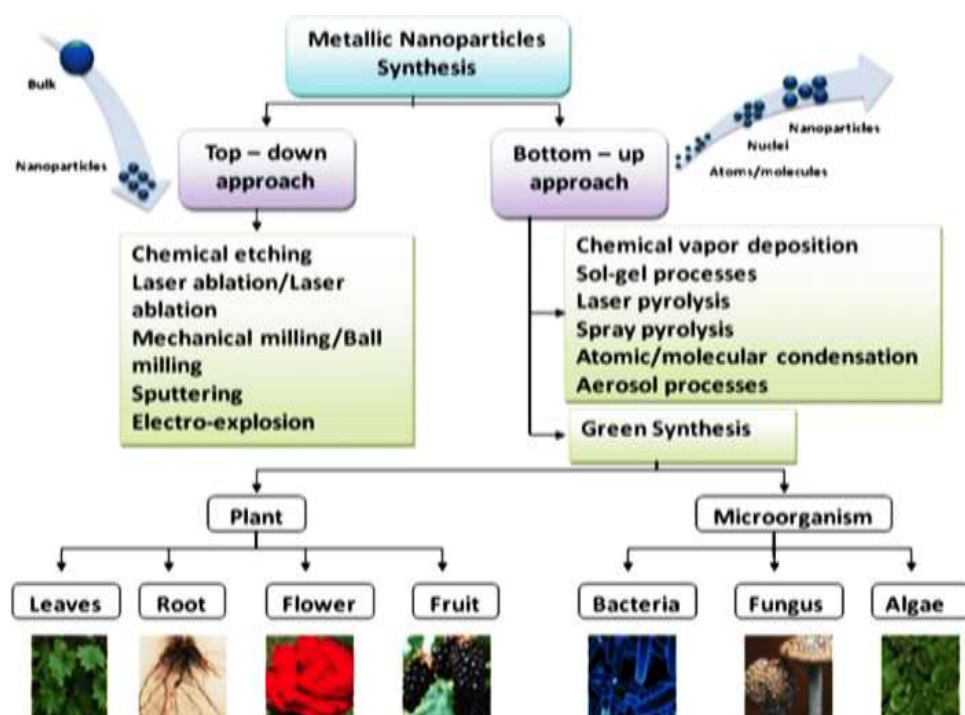


Figure 2. Preparation of metal nanoparticles by different approaches.

There are 2 approaches in the synthesis of nanoparticles:- (a)Top-Down Approach, (b)Bottom-Up Approach (Figure 2).

In the Bottom-Up approach, materials are created at the atomic level to create large nanostructures using physical, chemical, and biological materials, whereas in the Top-Down approach, a larger substance is divided into smaller pieces using a variety of processes.

Biosynthesis Using Microorganisms and their Characterization

Nanoparticle synthesis using biological components, such as plants or microorganisms, is referred to as biological synthesis. The use of microorganisms has drawn the most attention among all biological methods for the synthesis of NPs due to their rapid growth rates, ease of cultivation, and propensity to grow in natural environments with respect to pressure, pH, and temperature [39]. This mechanism involves capturing microorganisms from the environment and reducing them using enzymes, as described in a reduction mechanism [40]. Because this synthesis also depends on the microorganisms' capacity to tolerate heavy metals, not all microorganisms can produce MtNPs. Therefore, high metal stresses can impact microbial activity and convert metal ions to metals. Typically, microbes living in environments rich in metal are resistant to those metals. The cell wall plays a crucial role in intracellular synthesis because of its negative charge. Electrostatic interactions cause the positively charged metal ions to cling to the cell wall. MtNPs are created inside of the cell from ions by enzymes like nitrate reductase. Now, these MtNPs can penetrate the cell wall. Microbes possess cell walls that are comprised of a wide variety of polysaccharides and proteins. These components play a crucial role as active sites for the attachment of metal ions [41]. This phenomenon arises due to the affinity of metal ions towards the negatively charged carboxylate groups present in the cell wall, which encompass cysteine, polypeptides, and specific enzymes [42]. The mechanisms of ZnO NPs' intracellular synthesis by microbes has been depicted in Figure 3.

In the extracellular synthesis pathway (Figure 4), enzyme-mediated synthesis can take place on the cell membrane or the enzyme can be released as an extracellular enzyme into the growth medium. Nitrate reductase, an enzyme involved in the nitrogen cycle, plays a crucial role in converting nitrate to nitrite. For instance, the NADH-dependent reductase, functioning as an electron carrier, transfers an

electron from NADH to initiate the bioreduction of Zn^{2+} [43]. As a result, Zn^{2+} received an electron and was reduced to ZnO. ZnO NPs were subsequently created as a result of this.

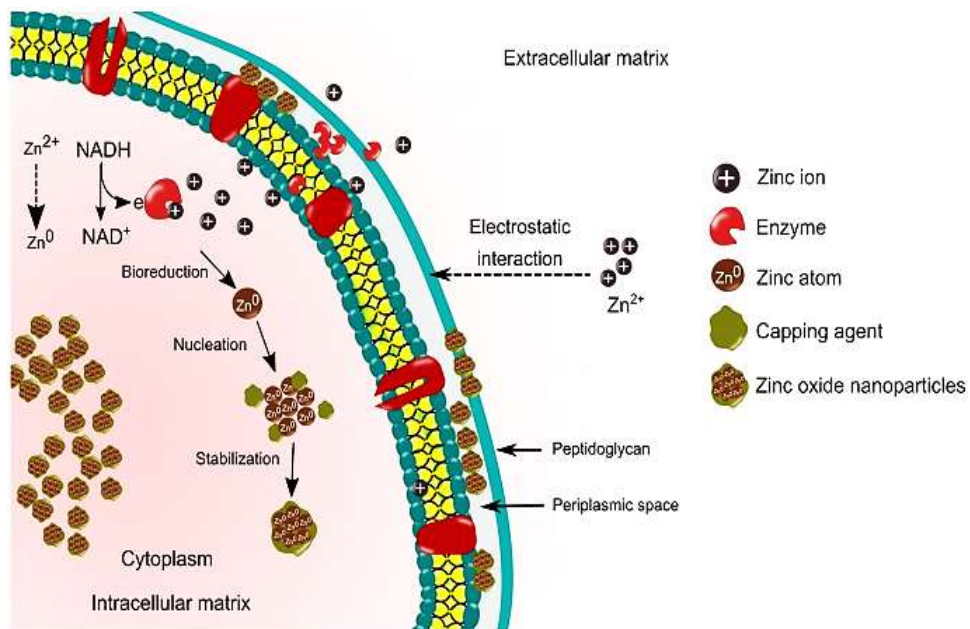


Figure 3. Schematic Representation of the intracellular synthesis of ZnO NPs.

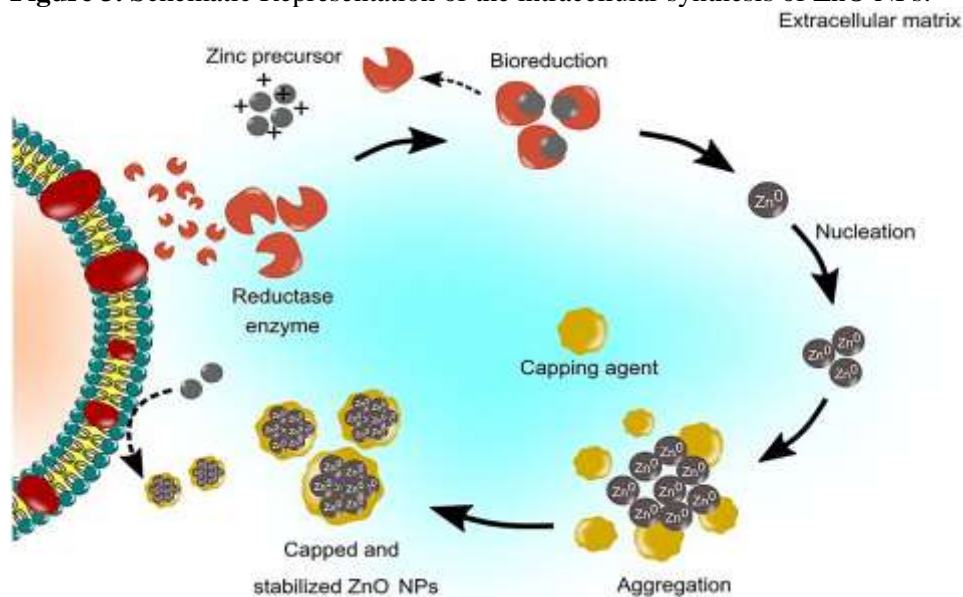


Figure 4. Schematic Representation of extracellular synthesis mechanism of ZnO NPs.

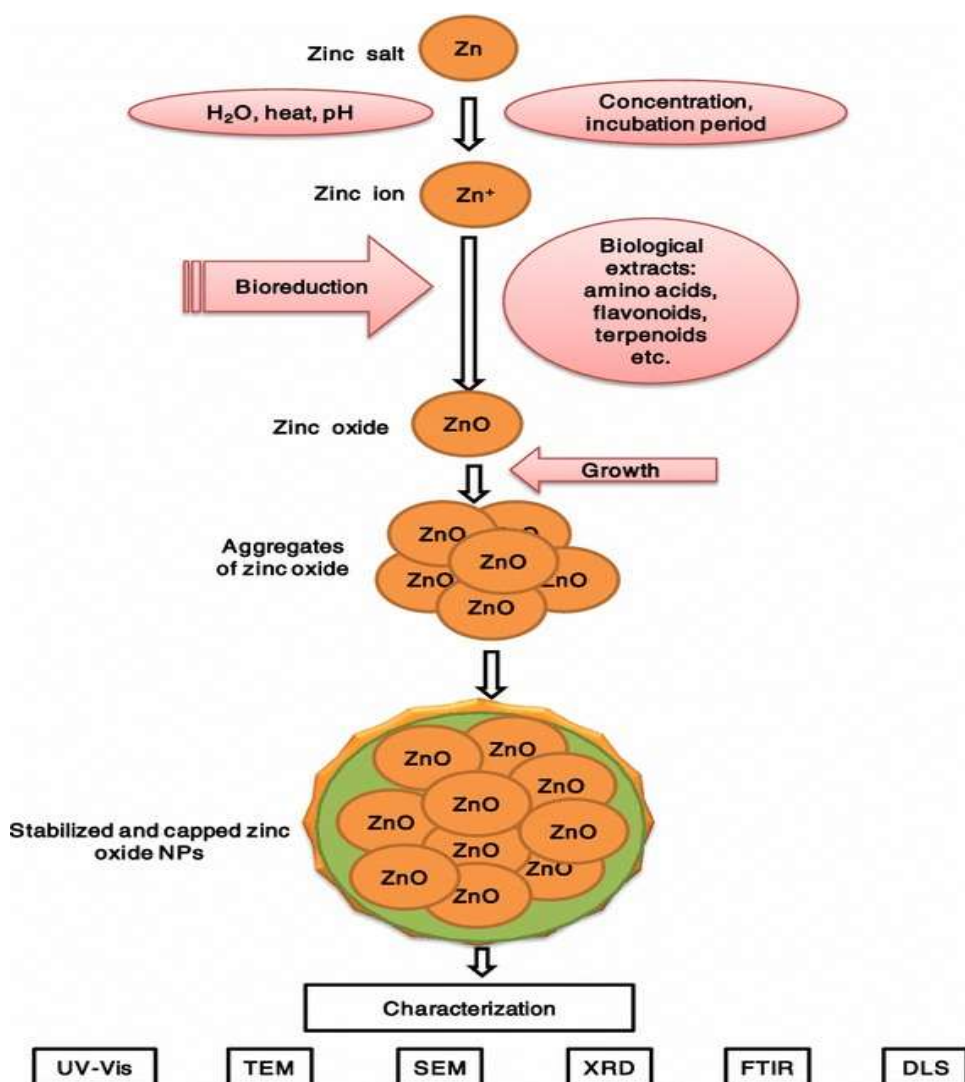


Figure 5. Schematic Representation of steps in synthesis of ZnO NPs and characterization.

The technology listed below can be used to characterise synthesised MtNPs. MtNPs are typically tested for stability and synthesis using UV-visible spectroscopy. The utilization of transmission electron microscopy (TEM), scanning electron microscopy (SEM), and atomic force microscopy (AFM) allows for the observation of the location, size, and morphology of MtNPs. Fourier-transform infrared (FTIR) spectroscopy is employed to measure various properties of MtNPs, including chemical concentration, surface chemistry, surface functional groups, and atomic arrangement [44]. The crystallographic structure of MtNPs is determined through X-ray powder diffraction (XRD) [44]. Energy dispersive x-ray spectroscopy (EDS) is commonly utilized to analyze the elemental composition of MtNPs [45]. The dynamic light scattering (DLS) method is primarily used to assess the size and surface charge of MtNPs [44]. The steps for the synthesis of ZnO nanoparticles and their characterization has been shown in Figure 5.

ZnO Nanoparticle Synthesis Using Bacteria

Prokaryotic organisms include bacteria, and current research is more heavily focused on using prokaryotes to synthesise nanoparticles. Bacteria are remarkable for being simple to grow, quick to multiply, simple to manipulate, and simple to handle. Various bacteria, including *Aeromonas hydrophila*, are known to withstand high zinc ion concentrations and can produce ZnO NPs [46]. Table 1 presents a compilation of bacteria known for their capability to synthesize zinc oxide (ZnO) nanoparticles.

Table 1. Bacteria Known for the Production of Zinc Oxide (ZnO) Nanoparticles.

Bacteria	Size	Shape	Reference
<i>Aeromonas hydrophila</i>	57.7	Spherical	46
<i>Bacillus licheniformis</i> MTCC9555	250	Flower	47
<i>Bacillus megaterium</i> (NCIM2326)	45-95	Rod and cubic	48
<i>Staphylococcus aureus</i>	10-50	Acicular	49
<i>Streptomyces</i> sp.	20-50	Spherical	49
<i>Pseudomonas aeruginosa</i>	35-80	Spherical	50
<i>Lactobacillus sporogens</i>	145.7	Hexagonal	51

ZnO Nanoparticle synthesis using Fungi

Fungi have been utilized in the synthesis of nanoparticles because of their ability to secrete significant amount of proteins than bacteria. Table 2 presents a compilation of fungal species known for their capability to synthesize zinc oxide (ZnO) nanoparticles.

Table 2. Fungi known for the Production of Zinc Oxide (ZnO) Nanoparticles.

Fungi	Size	Shape	Reference
<i>Aspergillus aeneus</i>	100-140	Spherical	52
<i>Aspergillus niger</i>	~61	Spherical	53
<i>Aspergillus terreus</i>	54.8~82.6	Spherical	54
<i>Candida albicans</i>	25	Quasi-spherical	55
<i>Fusarium</i> spp.	>100	Triangle	56
<i>Aspergillus fumigatus</i> JCF	60~80	Spherical	57

ZnO Nanoparticle synthesis using Yeast

Yeast cells can also be used for the synthesis of nanoparticles of ZnO such as., *Pichia kudriavzevii* [58] and *Pichia fermentas* JA2 [59].

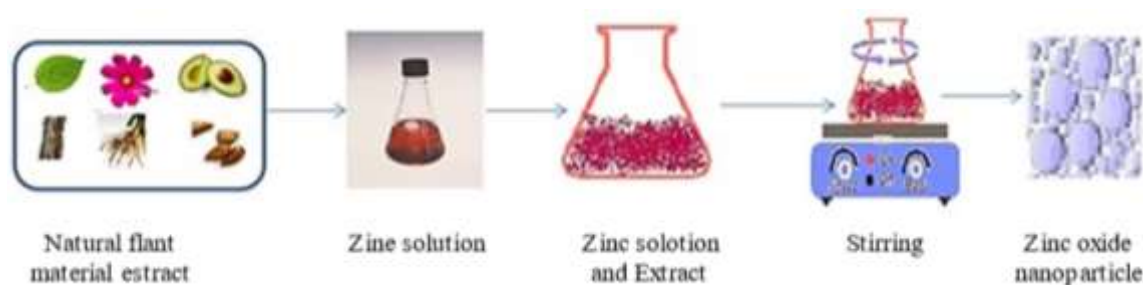
ZnO Nanoparticle Synthesis Using Microalgae

Many species of algae are involved in the biosynthesis of ZnO nanoparticles including brown *Sargassum muticum* [60], green *Caulerpa peltata*, and red *Gracilariagracilis* with various size, shape, and morphology [61].

Green Synthesis of nanoparticles

Using plant extracts to create nanoparticles is known as "green synthesis." Throughout history, plants have shown less emphasis on the synthesis of nanoparticles.

However, in recent years, plants rather than microbes have been the primary candidates for synthesis because they are non-pathogenic and the NPs they produce are found to be more stable.

**Figure 6.** Synthesis of ZnO Nanoparticles.

The appropriate plant extract is chosen, and the prepared salt solution of the desired nanoparticle is

then added. Nanoparticles are created after stirring as represented in Figure 6. The green synthesis of nanoparticles can be achieved by harnessing the potential of medicinal plants, which provide a wide range of usable parts such as leaves, roots, stems, and more. This approach is better and more environmentally friendly because it eliminates pollution at the source. Other benefits of using green synthesis include reduced time requirements, non-toxic byproducts, and most importantly, the ease with which large-scale synthesis can be accomplished. Since there are no requirements for high pressure, toxic chemicals, temperature, or energy, many researchers are turning their focus to green methods. The green method makes it simple to scale up and produces more stable nanoparticles with little contamination. Therefore, creating nanoparticles from plants and their components is a preferable alternative method. Much research is being done using plants and their parts because it is simple to scale up the synthesised nanoparticles. The table 3 given below lists various ZnO nanoparticles produced by different plants.

Table 3. Diversity of Zinc Oxide Nanoparticles Produced by Various Bacteria.

Plant	Reference
<i>Abutilon indicum</i>	62
<i>Aloe barbadensis</i>	63
<i>Melia azedarach</i>	64
<i>Pidium guajava</i>	65
<i>Mangifera indica</i>	66
<i>Nigella sativa</i>	67
<i>Monsoniaborkeana</i>	68

MURAYYA KOENIGII

A tropical to subtropical tree is the Murayya. It is a member of the Rutaceae family and is indigenous to Asia. "Curry leaves" is the common name for *Murraya koenigii*. Various components of *M. koenigii*, including its leaves, roots, bark, and fruit, have been recognized for their ability to support a range of biological functions. The leaves of *M. koenigii* are characterized by a slightly bitter taste, a pungent aroma, and a mild acidity. These leaves are commonly utilized in Indian cuisine as antihelmintics, analgesics, digestives, and appetizers. In traditional medicine, the green leaves of *M. koenigii* are employed to address various health issues such as piles, inflammation, itching, cuts, dysentery, bruises, and edema. The roots of this plant have purgative properties and are often used to alleviate general body aches. Additionally, the bark of *M. koenigii* is known for its effectiveness in treating snakebites. Furthermore, the essential oil extracted from the leaves of *M. koenigii* has been found to exhibit antioxidant, hepatoprotective, antimicrobial, antifungal, anti-inflammatory, and nephroprotective properties in animal studies.

The leaves, roots, and stem bark of *M. koenigii* have yielded a broad spectrum of phytochemicals through isolation. The composition of the plant leaves is characterized by notable proportions. The moisture content stands at 63.2%, protein content at 8.8%, carbohydrate content at 39.4%, total nitrogen content at 1.15%, fat content at 6.15%, total sugars content at 18.92%, starch content at 14.6%, and crude fiber content at 6.8%. Moreover, these leaves have been acknowledged as a significant source of various vitamins. An extensive assortment of carbazole alkaloids, essential oils, terpenoids, and flavonoids play a significant role in providing numerous benefits.

This study set out to look into the antibacterial properties of curry leaves. Most of the pharmacological activities of this plant have been illustrated in Figure 7.



Figure7. Pharmacological activities of *Murayya koenigii* [78].

Anti-bacterial Activity of *Murayya Koenigii* Mediated ZnO NPs

Cell wall, cytoplasm, and cell membrane serve as the main characteristics of bacteria. Situated outside the cell membrane, the cell wall contains a homogeneous peptidoglycan layer composed of amino acids and sugars. This layer constitutes most of the material in the cell wall. The osmotic pressure in the cytoplasm as well as the distinctive cell shape are both maintained by the cell wall. The cell wall of gram-positive bacteria is thicker, measuring between 20 to 80 nm, and consists of a single cytoplasmic membrane with several layers of peptidoglycan polymer [69]. On the other hand, gram-negative bacteria have a wall made up of two cell membranes: an outer membrane and a plasma membrane with a thin layer of peptidoglycan that is 7-8 nm thick [69].

For the analysis and investigation of antibacterial activity in vitro, various techniques have been used. These techniques include microtiter plate-based analysis, broth dilution, agar dilution, and disc diffusion [70]. Numerous studies [71] have investigated the antibacterial efficacy of ZnO-NPs by assessing bacterial growth through culture turbidity and determining the percentage of viable cells using the colony counts test.

Murraya koenigii has been linked to antibacterial activity in the ancient times. Most common conventional antibiotics are ineffective against pathogenic mycobacterial strains. ZnO and *Murayya koenigii*'s antibacterial properties combined to make them toxic to bacteria. Therefore, ZnO nanoparticles mediated by *Murayya koenigii* can be used in order to eradicate the coliform bacteria found in wastewater.

MECHANISM OF ANTI-BACTERIAL ACTION

The following distinct mechanisms have been proposed in the literature: direct ZnO-NP contact with cell walls, which results in bacterial cell integrity destruction [72–74], liberation of antimicrobial ions, primarily Zn^{2+} ions [75–77], and ROS formation [78,79]. Nonetheless, the toxicity mechanism varies depending on the medium due to the potential alteration of dissolved Zn species, alongside the physicochemical characteristics of ZnO-NPs [77]. When combined with other nanomaterials, zinc oxide nanoparticles change the physical and morphological properties of nanoparticles, which enhances their antibacterial effects. It can be regarded as a promising new generation antimicrobial agent that is being used effectively in the food industry for the packaging of food materials, effectively utilising its antimicrobial activity by preventing the growth of microorganisms, protecting food from spoilage, and in the prevention of many food-borne diseases. By incorporating ZnO

nanoparticles into the medical dressing material, ZnO nanoparticles can be used in the medical field to avoid microbial contamination of wounds [80].

CONCLUSION

Studies found that ZnO nanoparticles had greater bactericidal activity against Gram-positive bacteria than Gram-negative bacteria [81]. The variation in morphological composition of these microorganisms could potentially explain the contrasting sensitivity observed between Gram-positive and Gram-negative bacteria. Gram-negative bacteria possess an outer lipopolysaccharide membrane that hinders the passage of chemical antibacterial agents through the cell wall. Conversely, gram-positive bacteria are more susceptible due to their sole outer layer of peptidoglycan, which lacks effectiveness as a permeability barrier. Consequently, Gram-negative bacteria exhibit more intricate cell walls compared to Gram-positive bacteria, acting as a diffusion barrier and diminishing their vulnerability to antibacterial agents. There are a few potential bactericidal mechanisms that could explain how ZnO NPs interact with bacteria. Some claimed that smaller NPs released Zn²⁺ because of their easier cell penetration and higher surface reactivity. The release of Zn²⁺ from ZnO NPs constitutes a pivotal aspect of antibacterial mechanisms. This phenomenon is renowned for its capacity to hinder multiple functions within bacterial cells, encompassing active transport, bacterial metabolism, and enzyme activity. As a result, it culminates in the demise of bacterial cells [82]. The formation of reactive oxygen species (ROS), which results in oxidative stress and subsequent cell damage or death, is the source of the other proposed antibacterial activity. ZnO NPs frequently use the formation of ROS as an antibacterial strategy [83]. Through electrostatic forces, ZnO NPs can attach to the bacterial cell membrane, offering another potential mechanism for their antimicrobial activity. This interaction may alter the structure of the membrane plasma and harm the integrity of the bacterial cell, leading to the leakage of intracellular materials and ultimately to cell death [84].

Zinc is used as an antimicrobial, and it has been added to toothpaste and mouthwash to reduce halitosis, inhibit the growth of calculus, and control dental plaque. An effective antimicrobial agent against pathogenic microorganisms is ZnO nanoparticles. Basically, the main mechanism of these metal oxide particles' antibacterial activity may be the detected active oxygen species they produce.

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