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Study of biogenic fabrication of zinc oxide nanoparticles and their applications: A review

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ABSTRACT

Nanotechnology offers the synthesis and utilization of matter with Nano-scale size. The Nanoscale dimension gives nanoparticles a high SA/V (Surface area to Volume) proportion and because of this, it shows remarkable properties. Nowadays tremendous research is carried out on zinc oxide nanoparticles (ZnO NPs) because of their high bandwidth and maximum binding energy. ZnO NPs have different biological applications such as antimicrobial, antioxidant, photocatalytic, anti-diabetic, anti-inflammatory, wound healing, and optic properties. In the physical and chemical method of synthesis of ZnO NPs, there is the use of different toxic chemicals which is harmful and also causes deterioration of the environment over these conventional methods, green synthesis approach utilizes bacteria, algae, fungus, and plants. This review is a complete investigation of the use of different biological sources utilized for the synthesis of ZnO NPs and characterization studies of ZnO NPs and their potential applications.

1. Introduction

Nanotechnology has impacted every corner of the applied research field so it came to fame in the last 10 to 15 years. The field of nanoparticles is a branch of nanotechnology that specifically deals with materials with significantly small particles ranging from 1 to 100 nm in size. Due to the small size of a nanoparticle, it bears a maximum surface area to volume ratio, NPs exhibit unique qualities that have been attributed to the critical variations in attributes between them and their mass counterparts [\[1\].](#page-5-0) Titanium dioxide (TiO2), indium (III) oxide (In2O3), zinc oxide (ZnO), tin (IV) oxide (SnO2), and silicon dioxide (SiO2) are examples of metal oxides, with ZnO being one of the most founding metal oxides followed by SiO2 and TiO2 [\[2\]](#page-5-0). A ZnO nanoparticle possesses unique and different properties such as a piezoelectric, pyroelectric, and semiconductor, and has high synergist development [\[3\].](#page-5-0) Furthermore, due to their non-harmful qualities [\[5\]](#page-5-0), ZnO nanoparticles come under the GRAS (Generally Recognized as Safe) as clas-sified by US FDA [\[4\].](#page-5-0) As a result, it is safe to use on both humans and animals. Zinc oxide nanoparticles have attracted a lot of attention in recent years (ZnO NPs). The main reason is that they have the smallest particle size possible, increasing their chemical reactivity. As a result, this has increased the widespread utilization of ZnO NPs in machinery, optics, medical, agriculture, and horticulture [6–[9\]](#page-5-0).

Zinc is a significant supplement in living organisms as it plays an important role as a micronutrient in biological entities [9–[11,19\]](#page-5-0). ZnO NPs have tremendous prospective applications, particularly as the antibacterial and antifungal activity has been shown by evidence [\[12,13,51\].](#page-5-0) Furthermore, numerous studies have been done to determine how well ZnO NPs work at preventing the growth of a variety of bacteria and fungi $[14–16]$; this may be able to replace the use of traditional antibiotics. Furthermore, zinc is a vital microelement that is responsible for a variety of metabolic bodily functions [\[9,11,17,18\].](#page-5-0)

1.1. Zinc oxide nanoparticles

ZnO is a semiconductor application in electronics, optical, and biological contexts, ZnO NP has piqued interest in the last two contexts, and ZnO NP has piqued interest in the last two three years [[6,8,12,20,37](#page-5-0)–40]

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Available online 1 November 2022 1387-7003/© 2022 Published by Elsevier B.V. Received 9 August 2022; Received in revised form 20 October 2022; Accepted 27 October 2022 [[23\]](#page-6-0). Several inorganic metal oxides have been found and are recently under investigation, including TiO2, ZnO, and CuO. Among the different metal oxides, ZnO nanoparticles are the most attractive due to their low cost, safety, and ease of fabrication. ZnO nanoparticles have been clas-sified by the US FDA as a GRAS (generally regarded as safe) [\[5\].](#page-5-0)

ZnO nanoparticles exhibit strong exciton binding energy (60 meV) and wide bandwidth (3.37 eV), and also the strong catalytic activity, optic, UV filtering properties, anti-inflammatory, and wound healing such a massive semiconducting feature exhibited by ZnO NPs [\[41](#page-6-0)–47]. Because of its UV-filtering characteristics, it is frequently used in beauty care products like sunscreens [\[48\].](#page-6-0) It has several biomedical applications including medicine delivery, rural properties, disease resistance, Control in diabetics, and antibacterial and antifungal activity (Fig. 1). Although ZnO is employed for particular drug transport, it does have a cytotoxicity restriction that has yet to be rectified [106–[108\].](#page-7-0) Various studies show that the ZnO nanoparticles are seen to be effective against gram-positive as well as gram-negative bacteria. It was found that the ZnO NPs have been used for the assembly of elastomers, and the removal of sulfur and arsenic from water also has. Piezoelectric and pyroelectric properties.

2. Different methods for ZnO NP synthesis

2.1. Physical & chemical method for the synthesis of ZnO NP

Generally, ZnO nanoparticles synthesized by physical and chemical methods show a high synthesizing rate and production of controlled-size nanoparticles. Despite this scenario, it has high capital costs, requires large amounts of energy, and uses hazardous and life-threatening synthetic compounds so it will have a negative impact. These substances thus cause additional environmental pollution. A previous study also revealed that chemically produced NPs are hazardous and less biocompatible [\[29\]](#page-6-0). Consequently, this has restricted their use in clinical and biological settings. Therefore, there is a need to research and create more cost-effective, ecologically friendly, and biocompatible NP synthesis options.

2.2. Green method for synthesis of ZnO NP

By leveraging natural intervention methodologies, a replacement for

conventional physical and chemical processes is the green process of NPs. strategies in recent years. Metal and metal oxide NPs are synthesized biologically by employing unicellular and multicellular microorganisms such as bacteria [\[30\]](#page-6-0), yeast [\[14\]](#page-5-0), fungi [\[31\],](#page-6-0) viruses [\[32\]](#page-6-0), and algae [\[33\].](#page-6-0) These methods are simple, non-harmful, and environmentally friendly. With the addition of proteins, enzymes, and other bimolecular components secreted or given by the organisms, the microorganisms serve as a small Nano-factory, converting metal salts into metal NPs. By the way, a few bacteria have been identified as having the potential to orchestrate ZnO NPs. More plausible microorganisms for the synthesis of ZnO NPs should be investigated in the future. In this vein, the current paper examines the role of microorganisms in the synthesis of ZnO NPs, the process of NP formation, and their potential use as antimicrobials, anticancer agents, antioxidants, and other compounds.

3. Mechanism of nanoparticles synthesis

Biomolecules such as proteins, enzymes, carbohydrates, and other molecules are produced by both plants and microorganisms. The reduction of various metal ions into nanoparticles is carried out by these biomolecules as reported in different studies. Extracellular production of ZnO nanoparticles is claimed to be carried out by a nitrate reductase enzyme, which is responsible for the reduction of zinc precursor into ZnO nanoparticles, according to various research. The enzyme responsible for converting nitrate to nitrite is nitrate reductase (NR) [\[21\].](#page-6-0) In the nitrogen assimilation pathway, this is usually the slowest phase. The extracellular pathway involves the secretion of this enzyme by a plant extract or a microbe, with any zinc precursor metal as a substrate. Because nitrate reductase is an NADH-dependent enzyme, NADH serves as an electron donor in this situation. As a result, nitrate reductase oxidizes NADH while also reducing $Zn + 2$ ions to ZnO nanoparticles. Schematic of extracellular biosynthesis of ZnO nanoparticles illustrated in [fig. 2](#page-2-0).

4. Characterization

Physical, chemical, and biological methods have all been used to synthesize nanoparticles. Fig. 1 depicts the various biological applications of these synthesized nanoparticles. The importance of

Fig. 1. Different applications of green synthesized ZnO Nanoparticles

Fig. 2. Schematic representation of the extracellular mechanism of biosynthesis of ZnO Nanoparticles.

characterizing synthesized nanoparticles for various physical, chemical, and biological properties is critical given the nature of its applications. Nanoparticles can be characterized according to their optical, structural, electrical, and magnetic properties, as shown in Fig. 3

5. Literature study

Biosynthesis of nanoparticles is a methodology of synthesis of nanoparticles by using different biological entities such as microbes and plant material. This gives an eco-friendly, cost-effective, and biocompatible approach [\[25\].](#page-6-0) Green synthesis of nanoparticles involves plant extract, bacteria, fungi, algae, and so on. These microbes are used for the large-scale production of NPs and also they produce NPs which are free from impurities [\[26\]](#page-6-0). Nanoparticles produced by the biomimetic approach seem to have more catalysis and restrict the use of costly and hazardous chemicals. Natural strains and plant extract produces phytochemicals that can act as reducing agent as well as capping or stabilizing agent; for instance, Bacillus licheniformis produces ZnO nanoparticles of uniform size by soluble proteins of cell also it seems that it gives better photocatalytic action and photostability as compared to other sources. ZnO Nano flowers showed 74% degradation of dye which shows photostability [\[27\]](#page-6-0). Fungal strain Aspergillus fumigatus TFR-8 is known to produce oblate spherical and hexagonal-shaped ZnO NPs of the size range of 1.2 to 6.8 nm, and the particle size analyzer confirmed the stability of the above-synthesized nanoparticles and agglomeration is seen after 90 days only [\[28\]](#page-6-0).

The reducing and stabilizing agent is a phytochemical obtained from the extract of different parts of the plant for instance roots, leaves, stems, seeds, and natural products [\[29](#page-6-0)–35]. The flower extract obtained from the Trifolium pretense is used for the synthesis of ZnO nanoparticles; it shows a similar peak in UV–vis spectroscopy after 24, 48, 72, 96, and 120 h and produced stable nanoparticles [\[36\]](#page-6-0). Furthermore, Rosa canina fruit extract contains a variety of phytochemicals that act as a reducing and stabilizing agent for biologically synthesized nanoparticles, as well as a bio-capping agent. This is completed by the use of carboxylic and phenolic acid present in the fruit extract, as confirmed by FTIR analysis. Aloe vera leaf extract was used in the fabrication of nanoparticles, yielding spherical-shaped nanoparticles.

Fig. 3. Different techniques used for characterization of ZnO NPs.

5.1. Green synthesis of ZnO NPs using plant extract

Plant parts generally used in the biogenesis of ZnO nanoparticles such as leaves, fruit, flowers, stem, root, and seeds because they contain different phytochemicals. Using ordinary extracts from parts of the plant could be very environmentally friendly and produce a pure as well as a superior quality product that has zero contamination. It also seems that it is cost-effective, less time-consuming, and does not require highly sophisticated labs [\[55\]](#page-6-0). As plants produce stable nanoparticles of different sizes and shapes on the optimal scale, it is the primary source of the synthesis of nanoparticles [\[56\].](#page-6-0) Plants produce different phytochemicals such as polysaccharides, alkaloids, polyphenol compounds, amino acids, vitamins, and terpenoids in return they are used to turn particles of metals or oxides of metal into null (zero) valence metal nanoparticles [\[55,56\].](#page-6-0) The method for synthesizing various metal nanoparticles is in practice but the synthesis of Zinc oxide from plant parts like leaves and flowers is discussed here. Firstly, mix the plant part with 90% ethanol (or some used Tween 20 for sterilization) for surface sterilization and then put into twofold distilled water thoroughly for removal of excess ethanol so the sterilization of the plant part process is successfully achieved. Then drying of that particular plant at specifically room temperature before the step of pulverization. For achieving a suitable concentration plant extract is mixed with Milli-Q water and boiled onto the hot plate with continuous stirring using a magnetic stirrer [\[55](#page-6-0)–59]. So to obtain clear solution filtration is done by using Whatman filter paper No. 41 and generally stored at 16 0C. Then some part of the prepared extract is mixed with different salts of Zinc such as zinc nitrate, zinc oxide, or zinc sulfate to obtain productive mixing and the mixture is heated at a suitable temperature and time on the hot plate [\[58,59\].](#page-6-0) At this level, some go with the optimization of parameters like temperature, pH, extract concentration, and duration to achieve great results. Then the visible detection of the synthesized Nanoparticles is done by observing color changes to yellow after the incubation period [\[58,59\].](#page-6-0) The next step is final verification which is done by using UV–vis spectrophotometry, next to it is centrifugation of the mixture and production of crystals by placing pellets in a hot air broiler [\[60\].](#page-6-0)

Additionally, synthesized nanoparticles are characterized using Fourier Transform Infrared Spectroscopy (FTIR), Transmission Electron Microscopy (TEM), Scanning Electron Microscopy (SEM), Energy Scattering Examination of X-ray (EDAX), X-ray diffractometer (XRD), Field Emanation Checking Electron Microscopy (FE- SEM), Atomic Force Microscopy (AFM), Thermal-gravimetric Differential Thermal Analysis (TG-DTA), Photoluminescence Investigation (PL), UV–Visible Diffuse Reflectance Spectroscopy (UV- DRS), and Energetic Light Scattering (DLS) [\[59](#page-6-0)–61]. The results of Conventional heating (CH) and microwave irradiation (MI) which are unique techniques for the synthesis of nanoparticles compared by Jafarirad et al. and they observed that MI requires less time for NPs synthesis, owing to the high warming rate that MI provides and therefore faster reaction rate [\[62\]](#page-6-0). Plants belonging to the Lamiaceae family, such as Anisochilus carnosus [\[63\]](#page-7-0), Plectranthus amboinicus [\[64\],](#page-7-0) and Vitex negundo [\[65\]](#page-7-0), have been studied largely and have shown various sizes and shapes, including spherical, quasispherical, hexagonal, and rod-shaped Nanoparticle formation with agglomeration. The results show there is an inverse relationship between plant extract and the size of the nanoparticle synthesized [\[63](#page-7-0)–65]. The size ranges detected using diverse methods such as FE-SEM, TEM, and XRD appeared to have similar extended values [\[64,65\].](#page-7-0) The results of SEM and EDAX appeared to be comparable to those of XRD. XRD examination using the Debye-Scherrer condition revealed that NPs produced from Vitex negundo leaf and flower had a comparable size of 38.17 nm [\[65\].](#page-7-0) For the most part, leaves of the Meliaceae family' s Azadirachta indica have been used to make ZnO NP [\[66,67\]](#page-7-0). All of the studies revealed NPs in the same size range, as determined by XRD and TEM, with spherical and hexagonal disc shapes, as well as Nano-buds. Aloe vera fresh leaf extract contains phenolic compounds, alcohol, terpenoids, alkane, carboxylic group, and carbonate which were validated

by FTIR analysis [\[68,69\]](#page-7-0). Synthesized NP had a difference in size (NP synthesized from peel had a larger size, as validated by SEM and TEM inspection), but similar forms (hexagonal and spherical). Agglomeration was seen in NPs made using extracts of Agathosma betulina, Calotropis Gigantea, Moringa oleifera, Nephelium lappaceum, Plectranthus amboinicus, and Pongamia pinnata. [Table 1](#page-4-0) summarizes the many plants that have been employed to synthesize ZnO NP so far.

5.2. Green synthesis of ZnO NPs using algae

Algae are eukaryotic photosynthetic organisms that can exist as unicellular or multicellular organisms, such as chlorella and spirogyra, respectively. Algae are divided into three groups according to the pigments they contain: Chlorophyceae (Green Algae), Phaeophyceae (Brown Algae), and Rhodophyceae (Red Algae). The green pigments they include are cholorophyll a and b, the brown pigments cholorephyll a and c, and the red pigment phycoerythrin. Although algae are frequently used to create gold and silver nanoparticles, there is limited evidence that algae are also used to produce zinc oxide nanoparticles [\[70\]](#page-7-0). Particular focus has been paid to the ability of microalgae to degrade toxic metals and transform them into less damaging forms [\[77\]](#page-7-0). The Sargassaceae family includes *Sargassum muticum* and *Sargassum myriocystum*, which are employed in the manufacture of ZnO nanoparticles. According to investigations by Azizi et al., *Sargassum muticum* was utilised to create ZnO nanoparticles, and XRD and FE-SEM measurements verified the NPs' sizes [\[78\]](#page-7-0). ZnO NPs are also synthesised using *Sargassum myriocystum*, and DLS and AFM analysis reveals that the generated NPs are spherical in shape and range in size from 46.6 nm and up [\[79\].](#page-7-0) [Table 2](#page-4-0) describes the properties of ZnO NP synthesized using algae.

5.3. Green synthesis of ZnO NPs using bacteria

Although the use of bacteria to synthesize NP is a green approach, it has several disadvantages, including the time required to screen bacteria, the need for continuous monitoring of broth culture and the overall process to avoid contamination, also to control different sizes and shapes and need of costly media to cultivate bacteria.

ZnO nanoflowers produced by Bacillus licheniformis with an ecofriendly method give photocatalytic activity and degradation of Methylene blue dye takes place. The greater oxygen vacancy produced by nanoparticles is responsible for better photocatalytic activity than available photo-catalytic chemicals. The mechanism of photocatalysis involves the production of free radicals by light absorption, which degrades organic waste and is hence utilized as an effective bioremediation method. Nano flowers produced by Bacillus licheniformis showed a three-dimensional appearance of 200 nm in size and petals of nanoflower had a width of 40 nm and a height of 400 nm [\[74\]](#page-7-0). The ability of Rhodococcus to survive in harsh environments and the ability to metabolize hydrophobic chemicals, which can aid in biodegradation [\[49,70,73\].](#page-6-0) By utilizing zinc as a substrate Rhodococcus pyridinivorans produced spherical NPs which are confirmed concerning size and are in the range of 100–130 nm by FE- SEM and XRD analysis. FTIR analysis confirmed the presence of alkane, amide I bowing band, amide II extending band, β-lactone, band of mononuclear benzene, Phosphorus compound, secondary sulfonamide, and monosubstituted alkyne, [\[74\]](#page-7-0). By using ZnO NPs as a substrate *Aeromonas* hydrophila manufactured ZnO NPs of 42–64 nm in size range which is confirmed by AFM and XRD analyses, with various forms such as oval and spherical [\[75\].](#page-7-0) Singh et al. observed that rhamnolipid produced by Pseudomonas aeruginosa has a long carbon chain and is unable to form micelle on the surface of carboxymethyl cellulose (CMC) and also the property of capping so it is responsible for stabilizing bare ZnO nanoparticles [\[21,53,76\]](#page-6-0). This stabilization has spherical morphology with a Nano measurement of 27–81 nm supported by TEM, XRD, and DLS investigations [\[76\]](#page-7-0). A study by A. Krl et al. demonstrates the intracellular synthesis of zinc oxide

Table 1

Plant extract mediated synthesis of ZnO NPs.

Table 2

Algae mediated synthesis of ZnO NPs.

Nanocomposites by lactic corrosive micro-organisms [\[89\]](#page-7-0). [Table 3](#page-5-0) describes the properties of ZnO NP synthesized using bacterial strains.

5.4. Green synthesis of ZnO NPs using fungus

Fungal strains are generally superior to bacterial strains as far as the synthesis of nanoparticles is concerned because the Extracellular synthesis of NPs from fungi is extremely valuable due to large-scale production, easy downstream processing, and economic viability [\[78\]](#page-7-0). Because of their superior resistance and metal bioaccumulation properties [\[80\].](#page-7-0) Aspergillus fumigatus mycelia were used to obtain ZnO nanoparticles and the size range of nanoparticles was analyzed by DLS analysis and found to be 1.2 to 6.8 nm size range, with an average size of 3.8 nm. The height of the nanoparticle was confirmed by AFM which is 8.56 nm. Up to 90 days, the molecule size was greater than 100 nm, but after 90 days, they formed an agglomerate of normal estimated 100 nm, implying that the formed NPs were stable for 90 days [\[81\]](#page-7-0). NPs synthesized from Aspergillus terreus had a size range of 54.8–82 nm confirmed by SEM and an average size of 29 nm calculated using the Debye-Sherrer equation based on XRD analysis results. FTIR study confirmed some groups present with nanoparticles such as essential alcohol, primary or secondary amine, amide, and aromatic compounds [\[82\]](#page-7-0). Shamsuzzaman et al. confirmed the size of nanoparticles by using SEM, TEM, and XRD analysis and NPs synthesized by Candida albicans had comparable size ranges of 15–25 nm [\[22\].](#page-6-0) For the synthesis of nanoparticles, fungi are used as the primary source among the fungi Aspergillus Spp. widely used in the synthesis of ZnO NPs which mostly produced spherical in shape nanoparticles. [Table 4](#page-5-0) provides a brief

Table 3

Bacterial synthesis of ZnO NPs.

Sr. No.	Bacterial Name	Size (nm)	Shape	Application	Ref.
$\mathbf{1}$	Aeromonas	$42 - 64$	Spherical	Antimicrobial	[16]
$\overline{2}$	hydrophila Lactobacillus	$5 - 15$			
	sporogenes		Hexagonal	Antimicrobial, Controlling pollutant	[38, 90]
3	Pseudomonas aeruginosa	$35 - 80$	Spherical	Antioxidant	[76]
4	Lactobacillus paracasei	1179	Spherical	Antimicrobial	[89]
5	Bacillus licheniformis	200	Flower	Photocatalytic activity	[74]
6	Serratia ureilytica	170-250	Spherical	Antimicrobial	[91]
7	Bacillus	$45 - 95$	Rod and	Antimicrobial	[15]
	megaterium		cubic		
8	Halomonas elongata	18	Multiform	Antimicrobial	[92]
9	Lactobacillus johnsonii	$4 - 9$	Spherical		[44]
10	Lactobacillus plantarum	$7 - 19$	Spherical		[93]
11	Rhodococcus pyridinivorans	$100 - 120$	Roughly spherical	UV	[21]
				protection,	
				antibacterial	
12	Sphingobacterium thalpophilum	40	Triangle	Antimicrobial	[94]
13	Staphylococcus aureus	$10 - 50$	Acicular	Antimicrobial	[95]
14	Streptomyces sp.	$20 - 50$	Spherical	Antimicrobial	[96]

Table 4

Biological synthesis of ZnO NPs using different fungi.

overview of commonly used organisms for ZnO NP synthesis.

6. Conclusion

Within the last decade, a significant study has focused on the biogenesis of nanoparticles using an environmentally benign method. In the production of shape and size-controlled nanoparticles, green sources operate as both stabilizing and reducing agents. Because green source produces stable nanoparticles the laboratory-based work is extended to

the production scale and more clarification of phytochemicals involved in nanoparticle synthesis with the help of bioinformatics instruments, and derivation of the exact mechanism involved in pathogenic bacteria inhibition are all possibilities for the future of plant-mediated nanoparticle synthesis. Plant-based nanoparticles offer a wide range of applications in the food, pharmaceutical, and therapeutic industries, and have thus been a focus of research.

Organisms create biologically active chemicals in addition to plantmediated biosynthesis, which acts as both a reducing and stabilizing specialist. The microbiological synthesis process is easier, less timeconsuming, and does not require the use of toxic chemicals. All things considered, getting the desired NPs and producing high-yield NPs remain problems in microbe-mediated synthesis. In addition, ZnO NPs have the potential to be used as therapeutics because of their antimicrobial effects on a broad spectrum of bacteria and fungi. As a result, this might potentially replace traditional antibiotics, which are known to breed multidrug-resistant bacteria.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

Data will be made available on request.

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