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Green synthesis of zinc oxide nanoparticles and potential future applications

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بسِم اللهِ الرحمن الرَحيم

{وَقُلْ رَّبِّ زِدْنِي عِلْمًا}

صدق الله العظيم

سورة طه:114

To gift

I would like to express my thanks and gratitude
For the owner of enlightened thought,
And who returned to the God of virtue?
Reaching that status, and achieving the goal of the desired
(My father is strengthened) may God prolong his life
And to whom
Supported
Success n, and you put on the first ways
(Umm Al-Masda)
To those who had a trace
Adult, and standing next to them was influenced by big (brothers)
To all the professors
The revered
Whoever extended the help to, and they went to the correct path.

This paper and the research behind it would not have been possible without the exceptional support of my supervisors Dr. Salim Naamah Saleh His enthusiasm, knowledge and keen interest in detail would have been an inspiration and kept my work on track from the first true beginning of this research to the list of references.

Contents

Abstract:

Recent years have seen an increase in the acceptance of green chemistry as a viable method for producing nanoparticles. zinc oxide nanoparticles (ZnO NPs) exhibit

distinctive characteristics, making them highly sought-after in many sectors. Nevertheless, conventional techniques for producing ZnO-NPs are linked to environmental and health hazards due to toxic substances. In this review, we study zinc oxide nanoparticles (ZnO NPs) synthesized from plant extracts and their subsequent biomedical uses in detail. Research shows that several different plant extracts are employed in manufacturing ZnO nanoparticles. Leaves, fruits, seeds, roots, and complete plants are all included in these extracts. Phytochemicals such as phenolic compounds, alkaloids, flavonoids, and terpenoids are all a part of these biological matrices. compounds show bioreduction mechanism, act as stabilizing and reducing agent. The attributes of ZnO nanoparticles (NPs), including their size, shape, and crystallinity, may be altered by adjusting the plant extract variety, concentration, and synthesis conditions. Consequently, the formed nanoparticles display notable diversity in their physical and chemical characteristics, subsequently impacting their biological functionality. The biomedical uses of ZnO nanoparticles manufactured using green methods are extensive, including beneficial effects such as antibacterial activity against various pathogens, anti-inflammatory characteristics, and possible anticancer activities. Nanoparticles have been integrated into wound dressings, used as carriers for medication delivery, and utilized in biosensing and imaging applications. The enhanced biocompatibility and reduced toxicity of green-processed

zinc oxide nanoparticles (ZnO NPs) techniques, in comparison to those made using conventional approaches, make them very appealing for use in biomedical contexts. Moreover, the paper examines the synthesis mechanisms, explicitly focusing on the involvement of phytochemicals in the processes of reduction and stabilization. Additionally, this study emphasizes the difficulties and potential future directions in optimizing synthesis processes, increasing manufacturing capacity, and facilitating the therapeutic use of these nanoparticles.

Introduction

Nanotechnology is a recent development in scientific research. This field was founded by American physicist Richard P. Feynman at Caltech when he presented his lecture titled "There is plenty of room at the bottom," in 1959, he had suggested Scaling down to the nanoscale was the way of the future for technology and advancement [1]. The science of nanotechnology deals with understanding and manipulating materials at the nanoscale size, which has dimensions between 1 and 100 nanometers. Nanoparticles are materials having a diameter of less than 100 nm. They have high surface/volume ratios and are smaller than their bulk materials [2]. As the particle size decreases, the number of constituent atoms surrounding the surface of the particles increases. Highly reactive particles with unique chemical, optical, physical , and electronic properties develop as a result. Nanotechnology showed a rapidly expanding branch of technology that holds enormous potential for the chemical, medicinal, engineering, and food-processing industries [3-5]. This rapid development of nanotechnologies suggests that nanoscale production will soon be used in almost every area of science and technology. . Metal oxide nanoparticles such as Fe_3O_4 , AgO, Al_2O_3, MgO, ZrO_2, CeO_2, TiO_2, ZnO, Fe_2O_3, and SnO; are the most adaptable materials because of their wide range of characteristics and uses. Zinc oxide (ZnO), Nanoparticles has received a lot of interest from scientists as a 'future material' *6-10]. ZnO nanoparticles are an important class of metal oxide nanoparticles exhibiting exciting biological and photocatalytic properties due to their small size and enhanced surface chemical reactivity [11], However, the majority of conventional techniques for producing ZnO NPs are based on wet chemical route options, which demand the use of numerous hazardous chemicals during laborious, prolonged multistep processes that result in the production of vast quantities of hazardous by products and dangerous chemical waste [12]. In recent years, the use of more sustainable green techniques for preparation has increased focus on replacing harmful traditional chemicals with more environmentally friendly extracts from various natural materials, such as plants, fungi, bacteria, and algae, in order to prepare ZnO NPs, which demonstrated higher and comparable activities compared to the conventional ones. For instance, *Eucalyptus, Phlomis, pomegranate, Syzygium cumini, Ziziphus,* etc. have all been used as plant part extracts for the green biosynthesis of ZnO NPs. [13-17], whereby plant extracts are utilized as capping agents and stabilizers to both maintain the generated nanoparticles' stability and prevent their aggregation. [18]. besides, ZnONPs produced in green methods is safe for the environment and have also been used for biomedical purposes such as antioxidant, antibacterial, and anticancer properties [19,20]. It is important to note that *C.spinosa L.*is one of the middle east region's most widely-used plant and is distinguished by a variety of medicinal properties and that there are numerous long chains of natural compounds present that could serve as capping and stabilizing agents and avoid the nanoparticles from aggregating [21,22].

nsformative impact on the production of metal oxide nanoparticles, offering notable benefits in comparison to conventional physical and chemical methodologies [1–3]. Plant-based technologies in green synthesis have garnered significant attention due to their extensive array of medicinal and biotechnological applications [4,5]. Zinc oxide nanoparticles (ZnO NPs) have garnered considerable attention in several sectors, including optics, electrics, packaged foods, and medicine, owing to their favorable attributes such as biocompatibility, low cytotoxicity, and cost-effectiveness. A critical element of ZnO nanoparticles (NPs) pertains to their capacity to induce cellular death via the facilitation of reactive oxygen species (ROS) production and the liberation of zinc ions (Zn2+), which exhibit cytotoxic qualities [6,7]. In addition, Zn is a necessary trace element found in the human physiological system. It has biocompatibility owing to its low toxicity and high biodegradability, which is attributed to the solubility of Zn+2 ions [8]. [h1] Nevertheless, the therapeutic use of chemically manufactured ZnO nanoparticles is restricted as a result of the hazardous properties of the chemicals employed in their production [9,10]. Consequently, there is an increasing inclination towards investigating environmentally friendly production techniques for zinc oxide nanoparticles (ZnO NPs). Current advancements have emphasized using various plant components as reducing agents in manufacturing zinc oxide nanoparticles [11–13]. Using plant-based green synthesis technologies has many benefits compared to traditional approaches [14,15]. Firstly, it may be argued that virtual methods are characterized by simplicity, enhanced safety measures, more sustainability, and a more ecologically conscious approach compared to traditional physical and chemical alternatives. In addition, ZnO nanoparticles that are generated by biological processes have significant biological properties, making them appropriate for a wide range of biomedical applications in diverse sectors [16–19]. For example, previous research has shown that the antibacterial activities of ZnO nanoparticles (NPs) generated using plant extracts are superior to those of conventional medications in combating infections [20,21]. Furthermore, it has been shown that these nanoparticles have anticancer properties and display promise as agents that scavenge free radicals while exhibiting antioxidant activity [22,23]. Plant-mediated green synthesis has shown potential in developing innovative therapeutics for illnesses including malaria and urinary tract infections [24–26]. Furthermore, using green-synthesized zinc oxide nanoparticles (ZnOPs) has shown considerable potential for wound healing. The antibacterial characteristics of these substances are primarily responsible for their effectiveness, especially when included in formulations at the nanoscale and microscale levels [27–29]. Additionally, these entities have the potential to function as biosensors for the detection and characterization of biomarkers associated with various clinical states. In contrast to conventionally manufactured ZnO nanoparticles, the ZnO nanoparticles generated using green methods exhibit superior biocompatibility and increased biomedical characteristics, rendering them highly suitable as antibacterial agents and pharmaceuticals for combating cancer. Furthermore, the use of these nanoparticles has been shown in medication distribution and sensing applications [30–32]. In summary, the emergence of nanobiotechnology has brought about a paradigm shift in producing metal oxide nanoparticles. Using plantbased techniques in green synthesis processes has shown to be very advantageous compared to conventional methods. Zinc oxide

Nanoscience

The prefix "nano," which derives from a Greek word meaning "dwarf" or "something very small," represents one billion of a meter (10^{-9}m). It is also a reference to a Greek prefix. There is a clear need to differentiate between nanotechnology and nanoscience. Nanoscience is the study of structures and molecules on the sizes of nanometers ranging from 1 to 100 nm, and the technology that utilises it in practical applications such as electronics, Nanomedicine etc is termed nanotechnology [23]. Nanoscience is an interdisciplinary field of research that focuses on the atomic, molecular, and subatomic levels of matter. Nanotechnology refers to the focused research and development that is done for the purpose of understanding, manipulating, and measuring materials at the atomic, molecular, and supermolecular levels. The term "nanotechnology" refers to materials, systems, and processes that function at a size of one hundred nanometers (nm) or less, according to a tentative definition of the term. One billionth of a metre is equal to one nanometer[24] .As a point of reference, the visible spectrum of light has a wavelength that ranges from 400 to 700 nanometers. The size of a leukocyte is 10000 nm, the size of a bacterium is 1000-10000 nm, the size of a virus is 75-100 nm, the size of a protein is 5-50 nm, the width of deoxyribonucleic acid (DNA) is 2 nm, and the size of an atom is 0.1 nm. On this scale, as seen in Figure (1), the physical, biological, and chemical properties of materials have fundamentally distinct relationships to one another, and as a result, the activities of these materials are often surprising. The size of viruses and other infectious agents is taken into consideration by nanotechnology. Therefore, it has a significant potential to detect and eradicate infections [25].

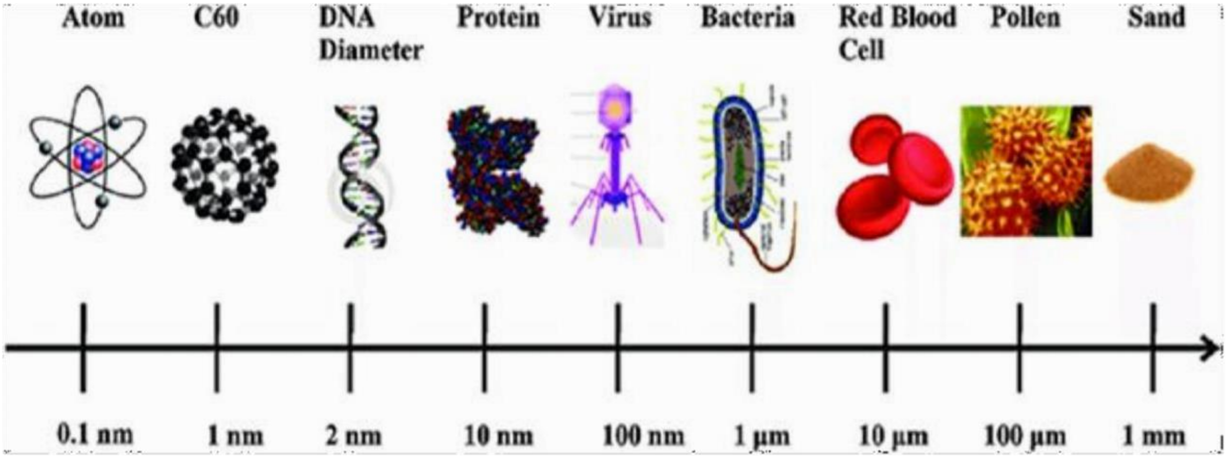


Figure (1) A basic concept on length scale that is showing size of nanomaterial's and their comparison to biological components and the definition of 'micro' and 'Nano' sizes[26].

Synthesis of ZnO Nanoparticle Methods

Prior to the development of nanoscience, it was challenging to synthesise nanomaterials using an easy, affordable, and highly effective process. Three procedures, known as the solid-phase, liquid-phase, and gas-phase processes, are used to create nanoparticles. Solid-phase processes include mechanical ball milling and mechanochemical methods; liquid-phase processes include laser ablation, exploding wire, solution reduction, and decomposition; and gas-phase processes include gas evaporation, exploding wire, laser ablation, and green synthesis. Additionally, chemical, physical, and biological methods may be used to create ZnO NPs[26, 27].

Synthesis of ZnO Nanoparticles by Plants

They are employed for the synthesis of ZnO NPs due to the distinctive phytochemical production of plant parts such stem, leaf, fruit, root , and seed. Utilising natural extracts from plant parts is cost-effective, environmentally beneficial, and sustainable since no intermediary base groups are included. It saves time, doesn't need heavy gear or equipment, and produces a large amount of extremely pure, impurity-free output [28]. NPs plants are a highly preferred source of NPs production due to their extensive production and stable, diversified in form and size [29]. Phytochemicals released by plants, such as polysaccharides, ,amino acids, polyphenolic compounds, vitamins, alkaloids and terpenoids, may convert metal oxides or metal ions to Neutral valence metal nanoparticles in a process known as bioreduction [30, 31].

Important of Green Synthesis

The traditional techniques of making nanoparticles were inefficient in terms of cost and required the use of hazardous chemical compounds or organic solvents as reducing agents, which explain why green nanoparticle synthesis methods have became under scrutiny recently [32]. Green synthesis is also environmentally beneficial and reduces the danger of contamination at the source or begetter scale. It also produces no waste, thus there is no need to scavenge garbage after the synthesis. The use of environmentally and ecologically friendly reagents were given top priority in green synthesis.

Despite the fact that physical and chemical techniques are quick and simple for the synthesis of nanoparticles, as illustrated in Figure(2), the biological approach of synthesis has an advantage over them since it is environmentally safe and non-hazardous [33].

The production of new sources of dynamic materials that are nontoxic, stable, nonhazardous, affordable, eco- and environment-friendly occurs during the synthesis of nanoparticles employing biological organisms in green synthesis. Due to their smaller size, unique structure, and specific biological substrate features utilised in their green production, nanomaterials' properties are heightened[34].

Figure(2) Green Synthesis Advantages[35]

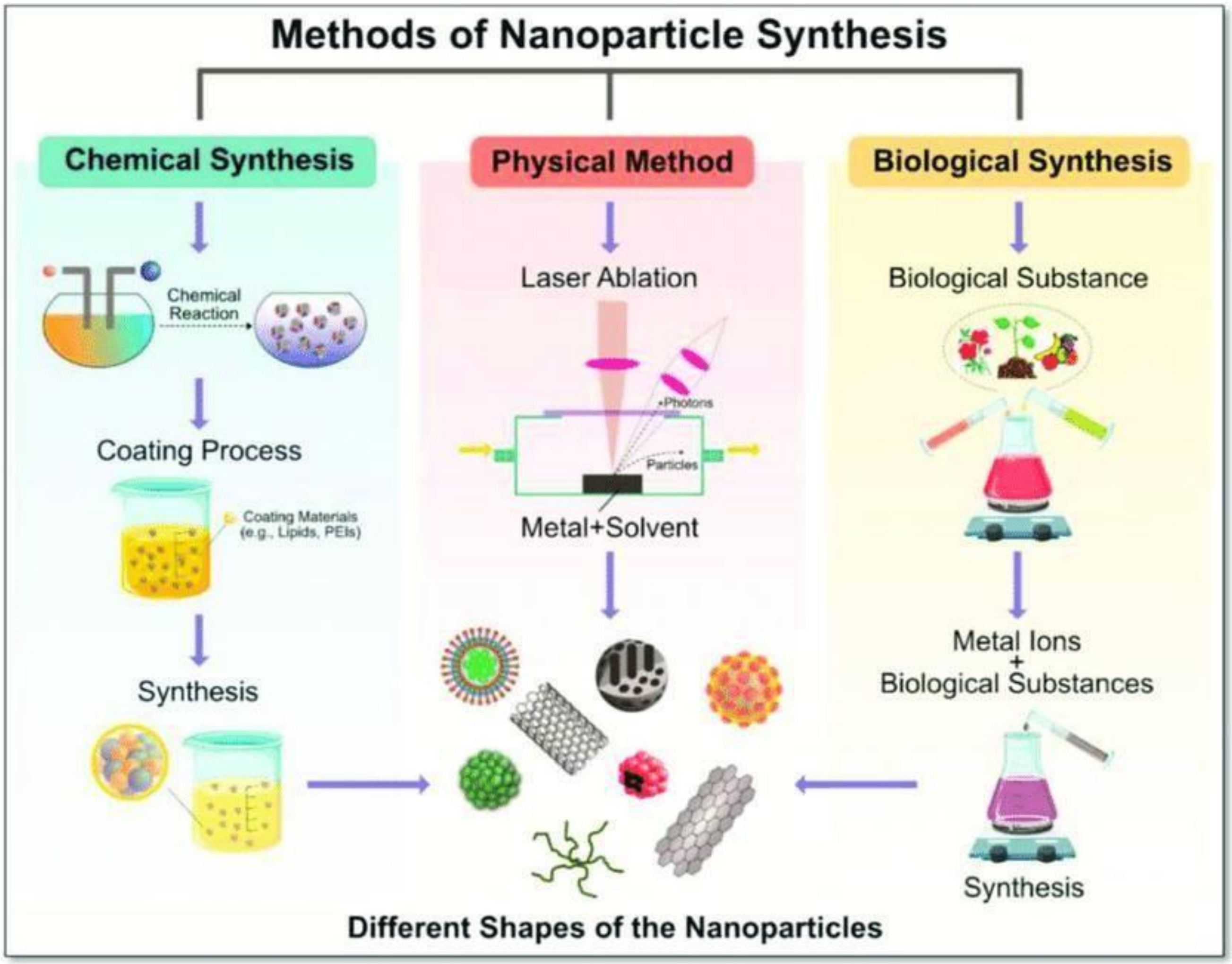
nanoparticles (ZnO NPs) have garnered attention in the scientific community because of their notable biocompatibility, minimal cytotoxicity, and cost-effectiveness, as shown by many studies [33–36]. Using botanical components as reducing agents in the fabrication of zinc oxide nanoparticles (ZnO NPs) has shown significant promise in diverse biomedical domains, encompassing antibacterial, anticancer, antioxidant, wound healing, and biosensing functionalities [37].

Using greensynthesized nanoparticles presents a potentially advantageous pathway for advancing ecologically sustainable and efficacious therapeutic approaches within biomedicine [38]. Many research groups have looked at using this biogenic or green synthesis of metal oxide NPs as an alternative to traditional chemical and physical manufacturing processes. Despite their synthesis technique, Nanoparticles have generated apprehension over their possible ecological ramifications. Their diminutive dimensions and distinctive characteristics may result in varied interactions with creatures and environments [39]. Hence, this review comprehensively discusses the current status of plant-mediated synthesis, its recent achievements, and the challenges and perspectives to provide valuable insights into this innovative research field.

Biological Source	Used Plant Parts	Particle Size (nm)	Morphology of Nanoparticles	Applications	References
Raphanus sativus	Leaf	66.47	spherical hexagonal	breast cancer cells antibacterial;	[6]
Rivina humilis	Leaf	14.4	circular	antioxidant, antibacterial and anticancer	[64]
Pisonia Alba	Leaf	14.08–14.17	hexagonal	antibacterial activity	[65]
Grape	seed	15.86	hexagonal	antibacterial and antioxidant activities	[66]
Boerhavia diffusa	Leaf	23–32	hexagonal	antioxidant, antimicrobial, cytotoxic	[67]
Caesalpinia crista	Seeds	20–44	irregular	Antibacterial, Antioxidant,	[68]
Aloe barbadensis	Leaf	20–40	Spherical	Anticancer and wound healing	[69]
Prosopis farcta	Aerial	40–80	hexagonal	Antifungal and MCF7	[70]
Trifolium pretense	Flower	60–70	Hexagonal	antibacterial activities	[71]
Santalaceae	Leaves	100	nano rods	MCF-7	[72]
Punica granatum	peel	10–45	Spherical	Antimicrobial	[73]
Lepidium sativum	Seeds	36.96——44.50	Spherical	anticancer activity	[74]
Cyathocline purpurea	eaf	80——120	spherical	antimicrobial	[75]

synthesis of zinc oxide nanoparticles

For the synthesis of ZnO-NPs, various techniques, including chemical, physical, and biological methods, are used. Chemical methods include precipitation, coprecipitation, colloidal, sol-gel processing, water-oil microemulsion, hydrothermal synthesis, cellulothermal, and sonochemical and polyol methods [40]. Physical methods include a range of techniques, such as arc plasma, thermal evaporation, physical vapor deposition, ultrasonic irradiation, and laser ablation [41]. The procedures above exhibit many drawbacks, including but not limited to their elevated expenses, presence of contaminants, lack of stability, and limits in terms of repeatability and dependability [42,43]. Furthermore, these processes need hazardous compounds, which pose a significant risk to environmental and medicinal applications [44]. In order to mitigate these drawbacks, researchers have increasingly used alternate environmentally sustainable and economically viable approaches to synthesize ZnO nanoparticles [45–47]. The green technique is a biological approach that utilizes plant extracts to synthesize zinc oxide nanoparticles (ZnO NPs). The present methodology has several benefits compared to conventional approaches, including simplicity, environmental sustainability, cost efficiency, and replicability [48]. Using the green technique mitigates the generation of deleterious byproducts and diminishes the reliance on hazardous solvents or chemical agents often necessary in conventional synthesis methodologies [49]. Manipulating temperature may be used to control and enhance morphological characteristics [50]. Furthermore, ZnO semiconductors possess intrinsic flaws in the form of vacancies of zinc and oxygen, as well as interstitials of zinc and oxygen [51]. Calcination temperatures, also known as annealing temperatures, can potentially remove and repair these defects or impurities, activate the dopant atom, and improve the electrical and optical characteristics of ZnO NPs. The specific changes in these properties may vary depending on the intended uses [52,53]. Recent research has investigated the environmentally friendly production of zinc oxide nanoparticles (ZnO NPs) using several plant extracts. These extracts include royal jelly, Cassia fistula, Melia azadarach, and Limonium bruinosum L. chaz. The dimensions and morphology of the generated zinc oxide nanoparticles (ZnO NPs) exhibit variability contingent upon the specific plant extract used



Methods of Nanoparticle Synthesis
Chemical Synthesis
Physical Method
Biological Synthesis
Chemical Reaction
Coating Process
Coating Materials (e.g., Lipids, PEIs)
Synthesis
Laser Ablation
Photons
Particles
Metal+Solvent
Biological Substance
Metal Ions + Biological Substances
Synthesis
Different Shapes of the Nanoparticles

synthesis of zinc oxide nanoparticles

The use of plant extracts as a means to produce zinc oxide nanoparticles (ZnO NPs) via a sustainable and environmentally friendly process known as green synthesis has garnered considerable interest in the scientific community in recent times. The presence of alkaloids, amino acids, enzymes,

proteins, and polysaccharides in plant extracts contributes to their role as reducing agents and capping agents, simplifying the synthesis process and enhancing its safety, sustainability, and environmental friendliness compared to conventional physical and chemical methods Zinc oxide nanoparticles (ZnO NPs) have garnered considerable attention as viable contenders for a range of biomedical applications owing to their favorable attributes, such as biocompatibility, minimal toxicity, and cost-effectiveness [54–56].

These compounds have robust biological properties and have been used in several sectors for their antibacterial, anticancer, antioxidant, antiinflammatory, and wound-healing properties [57]. Synthesizing zinc oxide nanoparticles (ZnO NPs) by environmentally friendly methods includes utilizing many plant components, including leaves, stems, bark, roots, rhizomes, fruits, flowers, and seeds. The plant extracts mentioned in the statement consist of several phytochemicals such as lupeol, ursolic acid, oleanolic acid, sitosterol, rutin, leucocyanidin, anthocyanins, proanthocyanidins, and glycosides of kaempferol and quercetin. These phytochemicals have reducing properties [58]. Plant-based synthesis techniques have several benefits compared to traditional physicochemical approaches. This method effectively mitigates the utilization of dangerous substances that provide potential health hazards to both the ecosystem and individuals [59].

Green synthesis produces metal and metal oxide NPs, and these phytochemicals are considered vital in their production [60]. The effects of temperatures between 20 and 100 ◦C on the formation and size of ZnO NPs were also studied by Singh et al. [61]. There was an increase in ZnO NPs production at higher temperatures, but the particles grew more slowly and were smaller due to the short reaction response time during synthesis. Several scientific investigations have shown biological substrates to be the only possible raw materials for NP biosynthesis [62]. The chemical process during green synthesis is complicated, making it difficult to measure and quantify. Bacteria that can be reproduced (such as lactic acid-generating bacteria) have become increasingly intriguing in bacterial-mediated NP synthesis because of their ability to produce a wide range of enzymes and non-pathogenic characteristics. Lactic acid bacteria, which are Gram-positive, possess a robust cell wall layer consistingof proteins, polysaccharides.

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