

# Plant-Mediated ZnO Nanoparticles for Biomedical Applications: A Review

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## Abstract:

Nanotechnology has revolutionized various scientific fields, with nanomaterials, such as zinc oxide nanoparticles (ZnO NPs), garnering significant attention due to their unique properties, including a high surface area-to-volume ratio, biocompatibility, and low cost. While conventional chemical and physical methods for synthesizing ZnO NPs are effective, they often involve the use of toxic chemicals and high energy consumption, posing significant environmental and health risks. To address these limitations, a shift towards green synthesis methods, particularly those employing plant extracts, has emerged as a sustainable, eco-friendly, and cost-effective alternative. This review provides a comprehensive overview of the plant-mediated synthesis of ZnO NPs, detailing the underlying mechanisms and characterization techniques. Furthermore, it critically examines the diverse biomedical applications of these biosynthesized nanoparticles, including their potent antimicrobial, anticancer, antioxidant, and wound-healing properties. The review concludes by highlighting the current challenges in this field and outlining future perspectives for the clinical translation of plant-mediated ZnO NPs.

**Keywords:** ZnO NPs; Green method; Biomedical applications; Nanomaterials.

## 1. INTRODUCTION

The field of nanotechnology, which involves manipulating matter at the nanoscale (1–100 nm), has opened up unprecedented possibilities in medicine, agriculture, and industry [1]. Among the vast array of nanomaterials, metal oxide nanoparticles have shown immense promise, with zinc oxide nanoparticles (ZnO NPs) standing out due to their exceptional physical and chemical attributes, such as their wide bandgap, photocatalytic activity, and inherent biocompatibility [2, 12]. These properties make them highly suitable for a wide range of applications, including optoelectronics, food packaging, and, importantly, biomedicine [13, 14]. However, traditional synthesis routes, which rely on toxic solvents and energy-intensive processes such as chemical precipitation or hydrothermal methods, have raised concerns regarding environmental safety and the potential for residual toxicity in biomedical applications [15, 16]. Consequently, researchers have turned to **green synthesis**, a sustainable approach that utilizes biological entities such as plants, bacteria, or fungi to produce nanoparticles [17, 18]. This review focuses specifically on the plant-mediated synthesis of ZnO NPs and comprehensively explores their significant and expanding role in various biomedical applications, offering a safer and more viable path for their clinical development [19, 20].

## 2. Green Synthesis of ZnO Nanoparticles

The plant-mediated synthesis of ZnO nanoparticles is a simple, single-step, and environmentally benign process that leverages the rich phytochemical composition of plant extracts [21, 22]. The mechanism involves using plant components, such as flavonoids, polyphenols, terpenoids, and alkaloids, which act as both reducing and capping agents [23, 24]. These biomolecules reduce zinc ions from a metal salt precursor, typically zinc nitrate ( $\text{Zn}(\text{NO}_3)_2$ ) or zinc chloride ( $\text{ZnCl}_2$ ), to form nascent ZnO NPs [25, 26]. Subsequently, the same or other phytochemicals adsorb onto the surface of the nanoparticles, providing a protective layer that prevents agglomeration and confers stability [27, 28]. A wide variety of plant sources have been

successfully employed for this purpose, including leaves from *Azadirachta indica* (neem) [29, 30], flowers from *Moringa oleifera* [31], fruit extracts from *Cocos nucifera* (coconut) [32], and the whole plant extract of *Aloe vera* [33, 34]. The properties of the resulting nanoparticles, including their size and shape, are highly dependent on various synthesis parameters such as the concentration of the plant extract and the metal salt, the reaction temperature, and the pH of the reaction mixture [35, 36]. Optimizing these parameters is crucial for achieving nanoparticles with desired characteristics for specific applications [37, 38].

### 3. Characterization of Plant-Mediated ZnO NPs

Following synthesis, the plant-mediated ZnO NPs must be rigorously characterized to confirm their formation and analyze their physicochemical properties [39, 40]. Ultraviolet-visible (UV-Vis) spectroscopy is a primary tool for preliminary confirmation, as the formation of ZnO NPs is indicated by a characteristic surface plasmon resonance (SPR) peak typically observed in the 350–380 nm range [41, 42]. Fourier-Transform Infrared (FTIR) spectroscopy is employed to identify the functional groups from the plant extract that are responsible for the reduction and capping of the nanoparticles, thus providing insight into the synthesis mechanism [43, 44]. The crystalline structure, average crystallite size, and phase purity of the nanoparticles are determined using X-ray diffraction (XRD), which provides a unique "fingerprint" of the material [45, 46]. Finally, electron microscopy techniques, such as Scanning Electron Microscopy (SEM) and Transmission Electron Microscopy (TEM), are used to visualize the morphology (e.g., spherical, rod-shaped, or hexagonal) and to accurately measure the size of the synthesized nanoparticles [47, 48]. These analytical methods are crucial for ensuring the quality and consistency of biosynthesized nanomaterials for their intended biomedical applications [49, 50].

### 4. Biomedical Applications

The biocompatibility and potent biological activity of plant-mediated ZnO NPs have positioned them as promising candidates for a wide array of biomedical applications [5, 51]. One of their most studied and significant roles is as a potent antimicrobial agent against a broad spectrum of bacteria and fungi [9, 15]. The proposed mechanisms of action include the generation of reactive oxygen species (ROS), such as superoxide radicals and hydroxyl radicals, which cause oxidative stress and subsequent damage to cellular components [18, 20]. Additionally, the gradual release of toxic zinc ions ( $Zn^{2+}$ ) from the nanoparticles can disrupt cellular metabolic processes and inhibit cell division [22, 27]. ZnO NPs have also shown great potential in anticancer therapy, where they can selectively induce programmed cell death (apoptosis) in cancer cells while showing low toxicity to normal cells [16, 21]. This selective toxicity is often attributed to the higher metabolic rate of cancer cells, which makes them more susceptible to the effects of ROS generation and intracellular  $Zn^{2+}$  accumulation [24, 28]. Furthermore, their antioxidant properties, stemming from their ability to scavenge free radicals, are beneficial for reducing oxidative stress-related diseases [29, 31]. The combined antimicrobial and anti-inflammatory effects of these nanoparticles also make them highly effective for wound healing applications, where they can be incorporated into topical formulations and dressings to prevent infection and promote tissue regeneration [32, 35].

### 5. Challenges and Future Perspectives

Despite the significant advancements in the green synthesis of ZnO NPs and their promising biomedical applications, several challenges must be overcome to facilitate their clinical translation [4, 30]. The primary challenges include achieving consistent and reproducible synthesis at a large scale, as the phytochemical composition of plant extracts can vary depending on geographical location, climate, and harvest season [34, 37]. Additionally, while *in vitro* studies have shown great promise, there is a critical need for more extensive *in vivo* and clinical studies to evaluate their long-term efficacy, bioavailability, and potential for systemic toxicity [38, 40]. Future research should focus on optimizing synthesis protocols to produce highly uniform nanoparticles with predictable properties [41, 44]. Furthermore, exploring the use of new plant sources, functionalizing the nanoparticles with specific targeting ligands, or combining them with other therapeutic agents could enhance their specificity and therapeutic effectiveness [46, 49]. Addressing these challenges will be crucial for unlocking the full potential of plant-mediated ZnO NPs and establishing them as a cornerstone of future nanomedicine [1, 2, 5].

## 6. Literature Survey

Table 1 provides a summary of key studies on the green synthesis of ZnO nanoparticles from various plant extracts, highlighting the synthesis methods, characterization techniques, and primary applications.

Table 1. Summary of key studies on the green synthesis of ZnO nanoparticles.

Plant Source	Synthesis Method	Characterization Techniques	Application	Reference
<i>Acalypha indica</i> leaf extract	Green synthesis	UV-Vis, XRD, FTIR, TEM, SEM	Antimicrobial	[3]
<i>Punica granatum</i> peel extract	Green synthesis	UV-Vis, XRD, TEM, SEM	Wound healing	[12]
<i>Azadirachta indica</i> leaf extract	Green synthesis	UV-Vis, XRD, TEM, FTIR	Antimicrobial	[13]
<i>Euphorbia prostrata</i>	Green synthesis	UV-Vis, XRD, FTIR, TEM	Anticancer	[14]
<i>Moringa oleifera</i> leaf extract	Green synthesis	UV-Vis, XRD, FTIR, TEM	Antimicrobial	[15]
<i>Aloe vera</i> leaf extract	Green synthesis	UV-Vis, XRD, FTIR, TEM, SEM	Anticancer	[16]
<i>Mentha spicata</i> leaves	Green synthesis	UV-Vis, XRD, FTIR, TEM	Antioxidant, Anti-inflammatory	[17]
<i>Cinnamomum verum</i> bark extract	Green synthesis	UV-Vis, XRD, TEM, SEM	Wound healing	[18]
<i>Ocimum sanctum</i> leaf extract	Green synthesis	UV-Vis, XRD, TEM, SEM	Antimicrobial	[19]
<i>Centella asiatica</i> leaf extract	Green synthesis	UV-Vis, XRD, TEM, SEM	Antimicrobial, Antioxidant	[20]
<i>Trigonella foenum-graecum</i> seed extract	Green synthesis	UV-Vis, XRD, TEM, SEM	Anticancer	[21]
<i>Citrus paradisi</i> (grapefruit) peel extract	Green synthesis	UV-Vis, XRD, TEM, FTIR	Wound healing, Antimicrobial	[22]
<i>Zingiber officinale</i> (ginger) rhizome extract	Green synthesis	UV-Vis, XRD, TEM, SEM	Antimicrobial	[23]
<i>Cocos nucifera</i> (coconut) leaf extract	Green synthesis	UV-Vis, XRD, FTIR, TEM	Antimicrobial	[24]
<i>Lantana camara</i> leaf extract	Green synthesis	UV-Vis, XRD, TEM, SEM	Antimicrobial, Larvicidal	[25]
<i>Calotropis gigantea</i> flower extract	Green synthesis	UV-Vis, XRD, TEM, FTIR	Antimicrobial	[26]
<i>Curcuma longa</i> (turmeric) rhizome extract	Green synthesis	UV-Vis, XRD, TEM, FTIR	Anticancer, Antimicrobial	[27]
<i>Ficus benghalensis</i> leaf extract	Green synthesis	UV-Vis, XRD, SEM, TEM	Antimicrobial	[28]
<i>Syzygium aromaticum</i> (clove) bud extract	Green synthesis	UV-Vis, XRD, TEM	Antimicrobial, Larvicidal	[29]

<i>Lagerstroemia speciosa</i> flower extract	Green synthesis	UV-Vis, XRD, TEM, FTIR	Anticancer, Anti-inflammatory	[30]
<i>Eucalyptus globulus</i> leaf extract	Green synthesis	UV-Vis, XRD, TEM, SEM	Antibacterial, Wound healing	[31]
<i>Camellia sinensis</i> (green tea) extract	Green synthesis	UV-Vis, XRD, TEM	Antimicrobial, Antioxidant	[32]

## 7. Conclusion:

In conclusion, the plant-mediated synthesis of zinc oxide nanoparticles (ZnO NPs) has emerged as a promising and environmentally friendly alternative to conventional physical and chemical methods. This review highlights the significant progress made in utilizing a diverse range of plant extracts to create ZnO NPs with tunable properties. The phytochemicals present in these extracts, such as flavonoids and alkaloids, serve a dual purpose as effective reducing and stabilizing agents, eliminating the need for hazardous chemicals. The research reviewed here highlights the remarkable versatility of these green-synthesized nanoparticles in various biomedical applications. Their potent antimicrobial activity against a broad spectrum of pathogens is primarily attributed to the generation of reactive oxygen species (ROS). Furthermore, their selective cytotoxicity towards cancer cells, which triggers apoptosis, showcases their promising potential as a targeted therapeutic. The literature also confirms their significant antioxidant and wound-healing capabilities. Despite these successes, the field faces challenges in achieving large-scale, reproducible synthesis for industrial applications and in conducting more comprehensive in vivo and clinical studies to fully realize their therapeutic potential. Future research should focus on optimizing synthesis parameters and exploring new plant sources to enhance the efficacy and safety of these promising nanomaterials.

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