International Journal of Scientific Research in Engineering and Management (IJSREM)
Volume: 10 Issue: 03 | March - 2026 SJIF Rating: 8.659 ISSN: 2582-3930

Plant-Mediated Synthesis of Zinc Oxide Nanoparticles: Green Approaches and Multifunctional Therapeutic Potential

Abinayashree S[1]*, Shangamithra S[1], Dr. L.F.A. Anand Raj[1]

[1]Department of Biotechnology, St. Joseph's College of Engineering, Chennai, Tamil Nadu 600119, India

*Corresponding author: abinayashreesundharesan@gmail.com

Abstract - Zinc oxide nanoparticles (ZnO NPs) have emerged as one of the most promising metal oxide nanomaterials in nanomedicine, owing to their unique physicochemical properties, well-established biocompatibility, and broad-spectrum therapeutic profile. Conventional synthesis methods involving toxic chemicals have given way to plant-mediated green synthesis, which uses phytochemicals as natural reducing and capping agents. This review comprehensively examines the mechanisms of plant-mediated ZnO NP synthesis, the role of key phytochemicals, the influence of synthesis parameters on nanoparticle characteristics, and their multifunctional therapeutic potential encompassing antimicrobial, anticancer, antioxidant, anti-inflammatory, antidiabetic, and wound healing activities.

Key Words: *Zinc oxide nanoparticles, green synthesis, phytochemicals, antimicrobial, anticancer, antioxidant*

1. INTRODUCTION

Nanotechnology has fundamentally transformed materials science and biomedicine by enabling the design and manipulation of matter at the nanoscale (1–100 nm) [1]. At these dimensions, materials acquire properties that differ markedly from their bulk counterparts — changes in surface area, quantum confinement, optical behaviour, and reactivity that collectively open new possibilities for therapeutic and diagnostic applications [2]. Among the many nanomaterials under active investigation, metal oxide nanoparticles have attracted particular attention owing to their stability, scalability, and tunable physicochemical characteristics.

Zinc oxide nanoparticles (ZnO NPs) occupy a unique position in this landscape. They combine semiconductor behaviour, strong light absorption, and potent biological activity with a safety profile that is unmatched among commonly studied metal oxide nanomaterials. Crucially, ZnO has been classified as Generally Recognized As Safe (GRAS) by the United States Food and Drug Administration (FDA) [5]. Furthermore, zinc is the second most abundant trace metal in the human body after iron, participating in over 300 enzymatic reactions, immune function, DNA synthesis, and wound repair — a fact that substantially improves ZnO's biocompatibility relative to silver, copper oxide, or titanium dioxide nanoparticles [4].

Traditional synthesis approaches for ZnO NPs — including co-precipitation, sol-gel, hydrothermal methods, and chemical vapour deposition — are effective but raise significant environmental and toxicological concerns. These methods rely on hazardous reducing agents such as sodium borohydride and hydrazine, generate toxic waste streams, and require high-temperature or high-pressure conditions [3]. The global imperative to develop sustainable, environmentally benign manufacturing processes has driven significant interest in green chemistry alternatives. Plant-mediated biosynthesis leverages the phytochemical repertoire of plant extracts — polyphenols, flavonoids, terpenoids, alkaloids, and organic acids — as renewable, non-toxic reducing and capping agents [41].

The clinical significance of ZnO NPs' therapeutic activities is underscored by the growing global burden of antimicrobial resistance, cancer, chronic inflammatory disease, and impaired wound healing. The World Health Organization has identified antimicrobial resistance as one of the ten greatest threats to global health, with multi-drug resistant organisms responsible for over 700,000 deaths annually [52]. ZnO NPs' multi-target antimicrobial mechanisms offer a fundamentally different paradigm compared to conventional single-target antibiotics. Similarly, with cancer incidence projected to exceed 28 million new cases per year by 2040, the development of selective, cost-effective anticancer nanomaterials is of urgent importance.

This review aims to provide undergraduate students and entry-level researchers with a clear, well-referenced understanding of plant-mediated ZnO NP synthesis and therapeutic applications. It covers the scientific rationale for selecting ZnO, the phytochemical basis of green synthesis, key synthesis parameters, comprehensive characterisation approaches, and the primary and emerging therapeutic activities for which biogenic ZnO NPs show the greatest promise. Challenges in batch reproducibility, scalability, in vivo validation, and regulatory alignment are critically assessed, and a research roadmap for the field is proposed.

2. WHY ZINC OXIDE? SCIENTIFIC RATIONALE

2.1 Physicochemical Properties

ZnO is a wide bandgap semiconductor with a bandgap energy of 3.37 eV and an exciton binding energy of 60 meV at room temperature [4]. These properties enable ZnO NPs to absorb ultraviolet radiation and generate electron-hole pairs that drive the production of reactive oxygen species (ROS) — including superoxide radicals ($O_2^{\bullet -}$), hydrogen peroxide (H_2O_2), and hydroxyl radicals (•OH). ROS generation is central to both the antimicrobial and anticancer mechanisms of ZnO NPs [4,6]. Additionally, ZnO possesses piezoelectric and pyroelectric properties arising from its non-centrosymmetric wurtzite crystal structure, expanding its utility in mechano-responsive and thermo-responsive biomedical devices [3].

The nanoparticulate form of ZnO has a dramatically higher surface area-to-volume ratio than the bulk material, which enhances Zn^{2+} ion dissolution and surface reactivity — key drivers of biological activity. ZnO NPs can be synthesised in a variety of morphologies including spheres, rods, flowers, hexagonal prisms, platelets, and hollow structures, each with distinct physical and biological properties [20,54]. Rod-shaped and flower-shaped morphologies typically exhibit enhanced photocatalytic and antimicrobial activities compared to spherical particles of equivalent size, attributable to their higher surface area and greater density of active crystal facets [54].

The optical properties of ZnO NPs are characterised by a strong UV absorption band at 350–380 nm and photoluminescence emission comprising a near-band-edge UV emission and a broad visible emission (commonly green) attributed to oxygen vacancies and defect states [50]. These optical characteristics underpin photocatalytic applications and enable ZnO NPs to be tracked in biological systems using fluorescence microscopy. The refractive index of ZnO (~2.0) and its high thermal conductivity also make it attractive for optoelectronic and thermal management applications beyond biomedicine.

2.2 FDA GRAS Status and Biocompatibility

Unlike many metal oxide nanoparticles, ZnO has been granted GRAS status by the US FDA, indicating an established safety record at concentrations relevant to food and cosmetic applications [5]. This regulatory precedent is highly advantageous for the development of ZnO-based therapeutic products. Zinc is an essential micronutrient present in every cell of the human body [4]. Its essential roles in enzyme catalysis, cell proliferation, immune regulation, and tissue repair mean that low-level zinc exposure from ZnO NP dissolution is broadly well-tolerated by normal cells. This contrasts sharply with silver or copper-based nanoparticles, which exert inherent cytotoxicity to mammalian cells at therapeutically relevant concentrations [38].

The biocompatibility of ZnO NPs is further enhanced when synthesised by green methods, as the phytochemical surface coating can modulate zinc ion release kinetics, reducing the burst-release toxicity sometimes observed with chemically synthesised counterparts. Several studies have demonstrated that normal human cell lines, including fibroblasts, keratinocytes, and peripheral blood mononuclear cells, tolerate green ZnO NPs at concentrations effective against pathogens and cancer cells [6,23]. The differential toxicity between cancerous and normal cells — exploited for selective anticancer therapy — is not a general feature of other metal oxide nanomaterials such as TiO_2, CuO, or CdO, which lack ZnO's combination of biological essentiality and controlled dissolution [38].

2.3 Comparison with Other Metal Oxide Nanomaterials

A critical question for any nanomaterial research programme is why ZnO should be preferred over alternative metal oxides. Table 3 in Section 4 provides a comparative characterisation overview; here, the biological rationale is addressed. Silver nanoparticles (AgNPs) are highly potent antimicrobials but exhibit dose-dependent cytotoxicity to mammalian cells, lack FDA GRAS status for systemic use, and are associated with argyria upon chronic exposure. TiO_2 nanoparticles are photocatalytically active but require UV activation and have been classified as possibly carcinogenic (Group 2B) by the International Agency for Research on

Cancer. CuO nanoparticles exhibit strong antimicrobial activity but generate excessive ROS at sub-toxic concentrations and lack any established essential biological role in the human body, complicating their safety profile [38].

ZnO uniquely combines FDA GRAS status, essential micronutrient identity (enabling partial metabolic processing of dissolved Zn^{2+}), multi-mechanism therapeutic action, photocatalytic activity, and compatibility with phytochemical green synthesis. This combination makes it the metal oxide nanomaterial most advanced in terms of both therapeutic evidence base and regulatory feasibility for clinical translation.

2.4 Multifunctionality

No other commonly studied metal oxide nanomaterial combines antimicrobial, anticancer, antioxidant, anti-inflammatory, antidiabetic, and wound healing activities with an equivalent safety profile [4,6]. The antimicrobial activity of ZnO NPs operates through at least four concurrent mechanisms — ROS generation, Zn^{2+} ion release, direct membrane disruption, and photocatalytic killing — making resistance development substantially more difficult than with single-target conventional antibiotics [6,20]. Their anticancer activity leverages the naturally lower pH and higher ROS levels of tumour microenvironments to achieve selective cytotoxicity [22,23]. This multifunctionality, combined with the ease of phytochemical surface functionalisation via green synthesis, makes ZnO NPs an exceptionally versatile nanotherapeutic platform.

3. PLANT-MEDIATED SYNTHESIS OF ZnO NANOPARTICLES

3.1 General Mechanism

Plant-mediated synthesis of ZnO NPs involves the reaction of a zinc precursor salt — commonly zinc nitrate ($Zn(NO_3)_2{\cdot}6H_2O$), zinc acetate ($Zn(CH_3COO)_2{\cdot}2H_2O$), or zinc sulphate ($ZnSO_4{\cdot}7H_2O$) — with an aqueous plant extract under controlled conditions [42]. The process occurs in three broadly defined stages:

- **Activation phase:** Phytochemicals in the extract chelate Zn^{2+} ions and initiate nucleation. Flavonoids and polyphenols with hydroxyl groups form coordination complexes with zinc ions, reducing Zn^{2+} to Zn^0 or forming zinc hydroxide intermediates. The chelation constant of polyphenols for Zn^{2+} is generally in the order of 10^1– 10^{33}, providing strong driving force for complex formation.
- **Growth phase:** Continued phytochemical-mediated reduction promotes nuclei aggregation. Crystal lattice formation proceeds with the Zn–O bond framework emerging progressively. The rate of nuclei addition versus crystal growth determines final particle size distribution, and this balance is governed primarily by extract concentration, pH, and temperature.
- **Termination phase:** Capping agents — primarily proteins, flavonoids, and large polyphenols — adsorb onto nanoparticle surfaces through electrostatic and coordination interactions, stabilising particle size and preventing agglomeration [43]. The density and chemical nature of this capping layer critically determine colloidal stability, surface charge, and ultimately biological activity.

Calcination at 300–600°C is typically performed after synthesis to remove organic residues and convert intermediate zinc hydroxide or zinc carbonate phases into the final wurtzite-phase ZnO product [10]. Higher calcination temperatures generally yield better crystallinity but may promote particle sintering and size increase. For applications where surface phytochemical retention is desirable — such as enhanced antioxidant or anticancer activity — lower calcination temperatures (300–400°C) may be preferable.

3.2 Role of Phytochemicals

The phytochemical composition of the plant extract is the primary determinant of nanoparticle properties. Different classes of biomolecules serve distinct mechanistic roles [41,43]:

- **Flavonoids** (quercetin, rutin, kaempferol, catechins): Act as both reducing and capping agents. Their multiple hydroxyl groups form strong coordination bonds with Zn^{2+}, facilitating efficient nucleation and producing small, highly stable nanoparticles typically below 30 nm [8]. Quercetin has a dissociation constant (Kd) for zinc of approximately 10^{-10} M, illustrating the potency of flavonoid-zinc chelation.
- **Polyphenols** (gallic acid, tannic acid, ellagic acid, chlorogenic acid): Serve primarily as reducing agents and surface coating molecules. Polyphenol-rich extracts (e.g. pomegranate peel, green tea) yield ZnO NPs with enhanced antioxidant activity due to retained surface phenolics [18,26]. The degree of polymerisation of tannins influences capping efficiency: condensed tannins produce more stable coatings than hydrolysable counterparts.

- **Terpenoids** (menthol, limonene, camphor, betulinic acid): Function mainly as capping and stabilising agents, influencing morphology control. Rod and hexagonal structures are more commonly observed when terpenoid-rich extracts (e.g. Eucalyptus, mint) are used, attributed to preferential adsorption of terpenoids on specific crystal faces that retard growth in those directions [19].
- **Alkaloids** (berberine, caffeine, piperine): Act as reducing and complexing agents, modifying the surface charge of the resulting nanoparticles and influencing colloidal stability [41]. Berberine-capped ZnO NPs have shown synergistic antimicrobial activity, as berberine is independently active against Gram-positive organisms.
- **Organic acids** (ascorbic acid, citric acid, oxalic acid): Strong reducing agents that drive rapid, controlled nucleation, typically producing small, uniform nanoparticles [42]. Ascorbic acid also serves as an antioxidant in the synthesis medium, protecting nascent nanoparticle surfaces from oxidative degradation.
- **Proteins and amino acids:** Present in many plant extracts, proteins provide steric stabilisation through surface adsorption and may introduce functional groups (amine, carboxyl, thiol) enabling post-synthesis bioconjugation with targeting ligands [41].

3.3 Representative Plant Sources

Table 1 summarises representative plant species used for green ZnO NP synthesis, along with the plant part used, resulting nanoparticle size and morphology, and key therapeutic activities reported. Leaf extracts are most commonly employed owing to their high phytochemical content and ease of extraction [41]. However, peels, flowers, seeds, rhizomes, and roots have also been used successfully [13,14,19,46]. The geographic diversity of medicinal plants with demonstrated utility for green ZnO synthesis is noteworthy, spanning Indian Ayurvedic plants (Tulsi, Neem, Turmeric), Chinese medicinal herbs (Withania somnifera, green tea), and Mediterranean and tropical species.

Table 1. *Representative plant sources for green synthesis of ZnO nanoparticles.*

Plant Species	Part Used	Size (nm)	Morphology	Therapeutic Activity
Aloe vera	Leaf gel	8–25	Spherical	Antimicrobial, wound healing [6,7]
Azadirachta indica (Neem)	Leaf	15–30	Hexagonal	Antimicrobial, anticancer [8,9]
Ocimum sanctum (Tulsi)	Leaf	12–28	Spherical	Antioxidant, antimicrobial [10]
Carica papaya	Leaf	20–45	Spherical	Antimicrobial, antioxidant [11]
Moringa oleifera	Leaf/seed	18–40	Hexagonal	Anti-inflammatory, antimicrobial [12]
Citrus sinensis	Peel	10–30	Spherical	Antimicrobial, antioxidant [13]
Hibiscus rosa-sinensis	Flower	15–20	Spherical	Antioxidant, anticancer [14]
Punica granatum	Peel	20–50	Hexagonal	Antimicrobial, anticancer [15]

Plant Species	Part Used	Size (nm)	Morphology	Therapeutic Activity
Calotropis procera	Leaf	10–35	Rod/spherical	Anticancer, antimicrobial [16]
Psidium guajava	Leaf	12–45	Spherical	Antimicrobial, antifungal [17]
Camellia sinensis	Leaf	10–20	Spherical	Antioxidant, anticancer [18]
Curcuma longa	Rhizome	15–35	Spherical	Anti-inflammatory, antimicrobial [19]
Eucalyptus globulus	Leaf	20–60	Rod/hexagonal	Antimicrobial, antifungal [45]
Withania somnifera	Root	12–40	Spherical	Anticancer, anti-inflammatory [46]
Coriandrum sativum	Leaf	8–22	Spherical	Antimicrobial, antioxidant [47]

3.4 Key Synthesis Parameters and Optimisation

Multiple parameters govern the physicochemical characteristics of green-synthesised ZnO NPs. Understanding and controlling these variables is essential for reproducible synthesis [31,44]. Table 4 summarises the key parameters, their optimal ranges, and their effects on nanoparticle properties.

Among these parameters, pH exerts perhaps the strongest influence on particle morphology. Below pH 7, zinc hydroxide intermediates dissolve preferentially, impeding ZnO lattice formation. At pH 8–12, deprotonated phenolic hydroxyl groups show maximum coordination capacity for Zn^{2+}, and hydroxide ion concentrations are sufficient to drive complete conversion to ZnO upon calcination [44]. At extremely alkaline pH (>12), however, zincate ion ($Zn(OH)_4^{2-}$) formation can compete with nanoparticle nucleation, yielding irregular morphologies.

Solvent selection is an additional parameter not always explicitly discussed in the literature. Aqueous extraction is most common and most aligned with green chemistry principles. However, ethanol:water and methanol:water co-solvent systems can improve extraction of more lipophilic phytochemicals (certain terpenoids, flavonoid aglycones), producing extracts with different reducing and capping profiles. The choice of extraction solvent should be guided by the target phytochemical class and should be systematically optimised for each plant species [41].

3.5 Scale-Up Considerations

Transitioning from laboratory-scale (50–500 mL) to pilot-scale (1–50 L) green synthesis presents several engineering challenges. Heat and mass transfer characteristics change significantly at larger scales, potentially altering nucleation kinetics and particle size distribution. Continuous flow reactor formats offer advantages over batch systems in this regard: continuous mixing, controlled residence time, and precise temperature management facilitate more reproducible large-scale synthesis [20]. Spray pyrolysis and microwave-assisted synthesis have also been explored as scalable alternatives that reduce reaction times from hours to minutes while maintaining nanoparticle quality [51].

Standardisation of the plant extract is arguably the greatest bottleneck for industrial-scale green synthesis. The phytochemical profile of a given plant species varies with harvest season, geographic location, soil composition, altitude, and post-harvest processing. Establishing standardised extract specifications — including total polyphenol content by Folin-Ciocalteu assay, flavonoid content by aluminium chloride colorimetry, and HPLC fingerprinting of key marker compounds — is essential for batch-to-batch reproducibility [41].

4. CHARACTERISATION OF GREEN-SYNTHESISED ZnO NANOPARTICLES

Thorough characterisation is essential to confirm synthesis, determine structural and surface properties, and correlate physicochemical parameters with biological activity [4,44]. The techniques listed in Table 3 below are routinely employed in the characterisation of green-synthesised ZnO NPs. A multimodal characterisation approach, combining structural, morphological, spectroscopic, and colloidal analyses, is considered best practice and provides the most comprehensive understanding of nanoparticle properties.

Table 2. *Characterisation techniques for green-synthesised ZnO nanoparticles.*

Technique	Information Obtained	Key Indicator for ZnO
XRD	Crystal phase, crystallite size, lattice parameters	Wurtzite phase (JCPDS 36-1451); Debye-Scherrer crystallite 10–50 nm
FTIR	Functional groups, phytochemical capping confirmation, Zn–O bond	Zn–O stretch at 400–600 cm-1; –OH, C=O capping agent peaks
UV-Vis Spectroscopy	Optical absorption, bandgap estimation by Tauc plot	Absorption peak 350–380 nm; bandgap 3.1–3.4 eV
SEM	Morphology, particle size distribution, agglomeration state	Spherical, rod, hexagonal, flower morphologies
TEM/HR-TEM	High-resolution morphology, lattice fringes, d-spacing	Lattice spacing ~0.281 nm (100 plane of wurtzite)
DLS	Hydrodynamic diameter, polydispersity index (PDI) in suspension	Hydrodynamic size typically larger than TEM; PDI < 0.3 desirable
Zeta Potential	Surface charge, colloidal stability prediction	Values beyond ±30 mV indicate adequate electrostatic stabilisation
EDX/EDS	Elemental composition, purity confirmation	Zn and O peaks; absence of precursor-related impurities
TGA/DSC	Thermal stability, phytochemical loading quantification	Mass loss below 300°C indicates organic capping content
PL Spectroscopy	Defect states, oxygen vacancies, exciton emission	UV emission ~380 nm; visible emission (green) from defect states

4.1 Structural Characterisation

X-ray diffraction (XRD) is the primary tool for confirming the wurtzite crystal phase of ZnO, identifiable by characteristic Bragg reflections at 2θ positions corresponding to the (100), (002), (101), (102), (110), (103), and (112) planes of the hexagonal wurtzite structure (JCPDS card no. 36-1451) [8,10]. Crystallite size is calculated from peak broadening using the

Debye-Scherrer equation: $D = K\lambda / (\beta \cos\theta)$, where K is the shape factor (typically 0.89–0.94), λ is the X-ray wavelength, β is the full width at half maximum of the diffraction peak, and θ is the Bragg angle. Green-synthesised ZnO NPs typically exhibit crystallite sizes of 10–50 nm. Microstrain within the crystal lattice, which influences reactivity and mechanical properties, can be estimated by Williamson-Hall plot analysis.

Fourier-transform infrared (FTIR) spectroscopy identifies the phytochemical functional groups adsorbed on the ZnO surface and confirms nanoparticle formation through the characteristic Zn–O stretching vibration at 400–600 cm^{-1} [25]. Broad absorption bands at 3200–3500 cm^{-1} indicate hydroxyl groups from polyphenols and adsorbed water. Carbonyl stretching vibrations at 1600–1700 cm^{-1} and C–H bending modes at 1400–1450 cm^{-1} confirm the presence of organic capping molecules. A shift in the O–H stretching frequency compared to the free phytochemical provides evidence of coordination to the ZnO surface rather than mere physical adsorption.

4.2 Optical and Electronic Characterisation

UV-visible spectroscopy is used for rapid, initial confirmation of ZnO NP formation. A characteristic absorption peak between 350–380 nm corresponds to the excitonic transition in ZnO, distinct from the absorption spectra of zinc salts or organic extracts [32]. The optical bandgap is estimated by Tauc plot analysis: plotting $(\alpha h\nu)^2$ versus photon energy ($h\nu$) yields a linear region whose intercept with the energy axis gives the direct bandgap. Green-synthesised ZnO NPs typically exhibit bandgaps of 3.1–3.4 eV, slightly below the bulk value of 3.37 eV, consistent with quantum confinement effects in smaller particles and the influence of surface phytochemical ligands on the electronic structure.

Photoluminescence (PL) spectroscopy provides information about defect states and oxygen vacancies that are crucial for photocatalytic and biological activities [50]. A sharp near-band-edge emission at approximately 380 nm reflects recombination of free excitons. A broader visible emission band, most commonly green (~520 nm), arises from singly ionised oxygen vacancies and other intrinsic defects. The ratio of UV to visible PL emission is an indicator of crystal quality: high UV:visible ratios indicate low defect density and superior crystal quality. Paradoxically, some defect states may enhance photocatalytic ROS generation, suggesting that for biological applications an intermediate defect density may be optimal.

4.3 Morphological and Colloidal Characterisation

Scanning electron microscopy (SEM) and transmission electron microscopy (TEM) provide direct visualisation of nanoparticle morphology, size distribution, and agglomeration state [33]. High-resolution TEM (HR-TEM) resolves crystal lattice fringes, with the (100) lattice plane of wurtzite ZnO exhibiting a d-spacing of approximately 0.281 nm. Selected area electron diffraction (SAED) patterns confirm polycrystalline wurtzite structure through characteristic ring patterns. Energy-dispersive X-ray spectroscopy (EDX or EDS) performed in conjunction with SEM or TEM provides elemental composition data, confirming the presence of Zn and O and the absence of precursor-related impurities.

Dynamic light scattering (DLS) measures the hydrodynamic diameter of nanoparticles in suspension, which is typically larger than the core size measured by TEM due to the contribution of the solvation shell and adsorbed phytochemical layer [34]. A polydispersity index (PDI) below 0.3 indicates an acceptably monodisperse preparation. Zeta potential measurement quantifies the surface charge of nanoparticles in dispersion: values beyond ±30 mV indicate adequate electrostatic repulsion to prevent agglomeration. Green-synthesised ZnO NPs commonly exhibit negative zeta potentials (−20 to −40 mV) at physiological pH due to deprotonated phenolic and carboxylic surface groups, which may also facilitate electrostatic interaction with positively charged bacterial cell walls.

5. MULTIFUNCTIONAL THERAPEUTIC APPLICATIONS

Table 2 provides a structured overview of the major therapeutic activities of green-synthesised ZnO NPs, including the mechanisms involved, test systems used, and key findings from recent literature.

Table 3. *Therapeutic activities of plant-mediated ZnO nanoparticles: mechanisms and findings.*

Activity	Mechanism	Test System	Key Findings
Antimicrobial	ROS generation, Zn2+ ion release, membrane disruption, photocatalysis, biofilm inhibition	E. coli, S. aureus, C. albicans, P. aeruginosa, MDR strains	MIC: 31–250 µg/mL; effective against MDR strains; 4 concurrent mechanisms reduce resistance risk [6,20,21]
Anticancer	Apoptosis induction, oxidative stress, G2/M cell cycle arrest, caspase 3/9 activation, DNA fragmentation	MCF-7 (breast), HeLa (cervical), A549 (lung), HepG2 (liver)	IC50: 10–100 µg/mL; selective cancer-cell toxicity via tumour microenvironment pH and ROS differentials [22,23,24]
Antioxidant	Free radical scavenging via phytochemical coating and ZnO surface chemistry; electron donation	DPPH, ABTS, H2O2 scavenging assays	IC50: 50–400 µg/mL; activity correlates with polyphenol content of plant source [25,26]
Wound Healing	Antimicrobial action, collagen synthesis, keratinocyte migration, anti-inflammation, angiogenesis promotion	In vitro scratch assay; in vivo excision models in rodents	Accelerated healing; reduced scarring; phytochemical coating reduces skin irritation [27,28]
Anti-inflammatory	Inhibition of TNF-alpha, IL-6, IL-1beta; suppression of NF-kB signalling pathway	LPS-stimulated macrophage models; RAW 264.7 cells	Significant cytokine reduction at 10–50 µg/mL; synergy with phytochemical surface ligands [29,30]
Antidiabetic	Inhibition of alpha-amylase and alpha-glucosidase; improved insulin signalling	Enzyme inhibition assays; streptozotocin diabetic mouse models	IC50 comparable to acarbose; zinc supplementation improves insulin receptor sensitivity [14,48]

Activity	Mechanism	Test System	Key Findings
Photocatalytic/Environmental	UV-driven ROS generation degrades organic pollutant molecules	Methylene blue, malachite green dye solutions under UV irradiation	>90% degradation efficiency reported within 90–120 min under UV exposure [32,49]

5.1 Antimicrobial Activity

The antimicrobial efficacy of ZnO NPs is their most extensively studied biological property. Green-synthesised ZnO NPs demonstrate broad-spectrum activity against Gram-positive bacteria (Staphylococcus aureus, Bacillus subtilis), Gram-negative bacteria (Escherichia coli, Pseudomonas aeruginosa), and fungi (Candida albicans) [6,20,21]. Reported minimum inhibitory concentrations (MICs) range from 31–250 µg/mL depending on the pathogen and nanoparticle characteristics.

Four concurrent mechanisms contribute to antimicrobial action: (i) photocatalytic ROS generation damaging microbial DNA, membrane lipids, and proteins; (ii) sustained Zn^{2+} ion release inhibiting enzymes critical for metabolic function (e.g. alcohol dehydrogenase, urease) and disrupting membrane transport; (iii) direct physical disruption of cell wall integrity by nanoparticle contact, particularly relevant for nanoparticles below 20 nm that can intercalate between lipopolysaccharide chains; and (iv) disruption of biofilm architecture, reducing the protective extracellular matrix that shields sessile bacteria from antibiotic penetration [4,32]. The multi-target nature of this activity makes resistance development substantially less likely than with conventional antibiotics — a critical advantage in the context of the global antimicrobial resistance crisis [20,39,52].

Notably, ZnO NPs have demonstrated activity against multi-drug resistant (MDR) pathogens including methicillin-resistant Staphylococcus aureus (MRSA), extended-spectrum beta-lactamase (ESBL)-producing Enterobacteriaceae, and fluconazole-resistant Candida species [53]. The clinical relevance of this finding cannot be overstated: MDR organisms represent the most pressing unmet need in infectious disease medicine, and inorganic nanomaterials that circumvent existing resistance mechanisms offer a genuinely novel therapeutic modality. The morphology of ZnO NPs influences antimicrobial potency: rod-shaped and plate-shaped nanoparticles typically show greater efficacy than spheres of equivalent volume, attributed to their sharper edges facilitating cell wall penetration [54].

5.2 Anticancer Activity

Green-synthesised ZnO NPs have demonstrated selective cytotoxicity against numerous cancer cell lines — including MCF-7 (breast), HeLa (cervical), A549 (lung), and HepG2 (liver) — while sparing normal cells at equivalent concentrations [22,23,24]. IC_{50} values typically fall in the range of 10–100 µg/mL, with variability attributed to the plant source, particle size, and surface chemistry.

The selectivity for cancer cells arises from two principal factors. First, tumour microenvironments are inherently acidic (pH 5.5–6.5) due to the Warburg effect — the preferential use of anaerobic glycolysis by cancer cells even under aerobic conditions, generating excess lactic acid [22]. This acidic pH enhances ZnO dissolution and Zn^{2+} release compared to normal physiological pH of 7.4. Second, cancer cells already operate at elevated baseline ROS levels as a consequence of oncogenic signalling and metabolic reprogramming; additional oxidative stress from ZnO NPs pushes them past the apoptotic threshold that normal cells, with intact antioxidant defences, do not reach [23,24].

Mechanistically, ZnO NPs induce mitochondrial membrane depolarisation (loss of mitochondrial membrane potential, $\Delta\Psi m$), cytochrome c release, caspase 3/9 activation, cell cycle arrest at the G2/M phase, and DNA fragmentation characteristic of apoptosis [24]. The retained phytochemical coating from green synthesis may additionally contribute intrinsic bioactivity — for example, quercetin and gallic acid are independently recognised as anticancer agents that inhibit topoisomerase II and modulate Bcl-2 family protein expression [26,35]. Several studies have demonstrated that green ZnO NPs exhibit greater anticancer potency than chemically synthesised ZnO NPs of equivalent size and concentration, suggesting that the phytochemical surface layer is not merely inert but pharmacologically active [55].

5.3 Antioxidant Activity

Oxidative stress — an imbalance between ROS production and antioxidant defence — underlies a broad spectrum of chronic diseases including diabetes, cardiovascular disease, neurodegeneration, and cancer. Green-synthesised ZnO NPs exhibit significant antioxidant activity, evaluated primarily through DPPH (2,2-diphenyl-1-picrylhydrazyl), ABTS (2,2'-azino-bis(3-ethylbenzothiazoline-6-sulphonic acid)), and hydrogen peroxide scavenging assays [25,26]. IC_{50} values for DPPH scavenging range from approximately 50–400 µg/mL depending on the plant source.

The antioxidant capacity of green ZnO NPs arises from two sources: (i) inherent surface chemistry of ZnO that can donate electrons to quench free radicals through surface oxygen vacancies and electron-rich lattice sites; and (ii) retained phytochemical molecules — particularly polyphenols and flavonoids — that function as potent hydrogen donors capable of quenching both lipid peroxyl radicals and superoxide anions [26,36]. The antioxidant activity of the nanoparticles consistently exceeds that of the plant extract alone at equivalent concentrations, suggesting a synergistic effect between the ZnO surface and the adsorbed phytochemical layer [36].

Plant species with high polyphenol content, such as Punica granatum (pomegranate) and Camellia sinensis (green tea), consistently produce ZnO NPs with superior antioxidant profiles [15,18]. This correlation provides a rational basis for plant source selection: total polyphenol content of the extract, measured by the Folin-Ciocalteu method and expressed as gallic acid equivalents, is a useful predictive parameter for antioxidant activity of the resulting nanoparticles. From a therapeutic perspective, topically applied antioxidant ZnO NPs offer promise in managing photo-aged skin, diabetic foot ulcers, and other oxidative stress-driven wound healing impairments.

5.4 Wound Healing Activity

ZnO has been used in topical wound care formulations for centuries, and its nanoparticulate form amplifies this traditional utility through multiple synergistic mechanisms [27,28]. Green-synthesised ZnO NPs promote wound healing by: (i) preventing infection through broad-spectrum antimicrobial activity; (ii) reducing excessive inflammation by inhibiting pro-inflammatory cytokines and reactive nitrogen species; (iii) stimulating keratinocyte and fibroblast migration and proliferation to accelerate re-epithelialisation; (iv) enhancing type I and type III collagen synthesis for structural wound repair by fibroblasts; and (v) promoting angiogenesis through VEGF upregulation to restore blood supply to healing tissue.

In vitro scratch assays using human keratinocyte (HaCaT) and fibroblast (NIH 3T3) monolayers consistently demonstrate significantly accelerated wound closure rates in ZnO NP-treated groups compared to controls [28]. In vivo excision wound models in Wistar rats and Swiss albino mice demonstrate significantly shorter healing times, greater collagen deposition, and reduced inflammatory infiltration in ZnO NP-treated animals [37]. The phytochemical-functionalised surface of green ZnO NPs confers additional anti-inflammatory bioactivity and reduces the risk of skin irritation compared to chemically synthesised counterparts [29,30].

Advanced wound dressing formulations incorporating green ZnO NPs have been developed, including ZnO NP-loaded chitosan hydrogels, electrospun polyvinyl alcohol nanofibres, and carrageenan-based films. These composite platforms combine the antimicrobial and healing-promoting properties of ZnO NPs with the moisture-retentive, biodegradable scaffolding properties of the polymer matrix, creating next-generation wound care materials with particular relevance to chronic, non-healing wounds in diabetic patients — a population with both impaired zinc status and heightened infection risk.

5.5 Anti-Inflammatory Activity

Chronic inflammation is a pathological driver in a wide range of conditions including arthritis, inflammatory bowel disease, atherosclerosis, and neurodegenerative disorders. Green-synthesised ZnO NPs have demonstrated anti-inflammatory activity in lipopolysaccharide (LPS)-stimulated macrophage models and carrageenan-induced paw oedema animal models [29,30]. At concentrations of 10–50 µg/mL, green ZnO NPs significantly reduce secretion of tumour necrosis factor-alpha (TNF-α), interleukin-6 (IL-6), and interleukin-1 beta (IL-1β), and suppress nuclear factor-kappaB (NF-κB) translocation to the nucleus — the master transcriptional regulator of the inflammatory response.

The anti-inflammatory mechanism of ZnO NPs involves multiple pathways: inhibition of cyclooxygenase-2 (COX-2) expression, reduction in prostaglandin E2 synthesis, and attenuation of mitogen-activated protein kinase (MAPK) signalling. Zinc ions released from dissolving nanoparticles are independently known to

modulate immune cell function, partly explaining the activity even in the absence of direct nanoparticle-cell contact [4]. The phytochemical surface coating adds further anti-inflammatory potential: curcumin-functionalised ZnO NPs (from Curcuma longa extract) have shown particularly strong NF-κB inhibition, combining the anti-inflammatory properties of curcumin with the zinc-mediated immune modulation of the nanoparticle core [19].

5.6 Antidiabetic Activity

Type 2 diabetes mellitus (T2DM) represents a global epidemic affecting over 500 million individuals. Zinc deficiency is prevalent in T2DM, and zinc supplementation has been shown to improve insulin receptor sensitivity and glycaemic control. Green-synthesised ZnO NPs offer a novel approach to antidiabetic therapy through two complementary mechanisms: (i) inhibition of carbohydrate-digesting enzymes α-amylase and α-glucosidase in the gastrointestinal tract, reducing postprandial glucose absorption; and (ii) improving cellular insulin signalling through zinc-mediated phosphatase inhibition, which amplifies the downstream kinase cascade initiated by insulin receptor activation [14,48].

Reported IC_{50} values for alpha-glucosidase inhibition by green ZnO NPs are comparable to acarbose, the standard clinical inhibitor, in several studies [14]. In streptozotocin-induced diabetic mouse models, ZnO NP treatment has resulted in significantly reduced fasting blood glucose, improved oral glucose tolerance, and restoration of pancreatic beta cell morphology [48]. These findings, while still predominantly preclinical, provide a compelling rationale for further investigation of green ZnO NPs as adjunct antidiabetic agents, particularly given the high co-morbidity of diabetes with impaired wound healing and infection — both areas where ZnO NPs also demonstrate therapeutic activity.

5.7 Photocatalytic and Environmental Applications

Beyond direct therapeutic applications, green-synthesised ZnO NPs have demonstrated significant utility in environmental remediation through photocatalytic degradation of organic pollutants [32,49]. Industrial dyes such as methylene blue, malachite green, Congo red, and methyl orange are major aquatic pollutants with known mutagenic and carcinogenic properties. Under UV irradiation, ZnO NPs generate electron-hole pairs that drive the formation of superoxide and hydroxyl radicals, which non-selectively mineralise organic chromophores to CO_2, H_2O, and inorganic ions. Degradation efficiencies exceeding 90% within 90–120 minutes have been reported for methylene blue using green ZnO NPs [49].

The photocatalytic efficiency of green ZnO NPs correlates with specific surface area, oxygen vacancy density (as reflected in PL spectra), and bandgap energy. Doping with transition metals (Fe, Cu, Ag) or non-metals (N, S) can extend photocatalytic activity into the visible spectrum, enabling solar-driven degradation without UV irradiation — a significant practical advantage for large-scale water treatment applications. The capacity to synthesise such doped variants using phytochemical extracts from metal-accumulator plants represents an emerging frontier in green nanomaterial synthesis [35].

6. SAFETY, TOXICOLOGY, AND BIOCOMPATIBILITY CONSIDERATIONS

A scientifically balanced assessment of ZnO NPs must address their toxicological profile alongside their therapeutic potential. While ZnO is GRAS and zinc is an essential micronutrient, it is well established that nanoparticle toxicity does not necessarily follow from the toxicity profile of the bulk material or its constituent ions — the nanoscale properties (size, surface area, surface chemistry, solubility) introduce additional determinants of biological response [4,38].

The primary mechanism of ZnO NP cytotoxicity in normal cells at high concentrations is excessive Zn^{2+} ion release, which overwhelms cellular zinc homeostasis mechanisms (metallothionein sequestration, ZnT transporter efflux), leading to mitochondrial dysfunction, lysosomal damage, and apoptosis. The dissolved fraction of ZnO NPs under physiological conditions (pH 7.4, 37°C) is approximately 10–30% of total zinc within 24 hours, but this increases substantially under acidic conditions, explaining the preferential toxicity in tumour microenvironments and lysosomes [22]. Nanoparticle-specific toxicity (beyond dissolved ion effects) has been demonstrated in some studies using insoluble zinc analogues as controls, and may involve direct membrane perturbation by surface-active nanoparticle facets.

Green synthesis significantly modulates the toxicity profile of ZnO NPs. The organic phytochemical coating reduces the rate of Zn^{2+} dissolution through steric and electrostatic passivation of surface dissolution sites, reducing burst-release toxicity. Multiple studies comparing green and chemically synthesised ZnO NPs

of equivalent size have found the former to be less cytotoxic to normal cell lines (HEK293, L929, HUVEC) while maintaining equivalent or superior activity against cancer cells and pathogens [6,29]. The therapeutic window — defined as the ratio of the concentration causing 50% cytotoxicity in normal cells to the IC_{50} or MIC against the target — is substantially wider for green ZnO NPs than for chemically synthesised counterparts.

In vivo toxicological assessments in rodent models have generally found green ZnO NPs to be well-tolerated at doses up to 200–500 mg/kg body weight by oral or topical routes, with no significant histopathological changes in liver, kidney, or spleen [37]. However, inhalation toxicology data are more concerning: ZnO fume inhalation is associated with metal fume fever in occupational settings, and the pulmonary toxicity of inhaled ZnO NPs requires careful assessment before inhalation-based drug delivery applications are advanced. Responsible translation requires a complete in vivo toxicology package including genotoxicity, reproductive toxicity, and repeated-dose chronic toxicity studies prior to human trials.

7. CHALLENGES AND LIMITATIONS

Despite the significant promise of plant-mediated ZnO NP synthesis, several critical challenges must be addressed before widespread clinical translation:

- **Batch reproducibility:** Seasonal, geographic, and cultivar-dependent variation in plant phytochemical composition leads to batch-to-batch differences in nanoparticle properties. Standardisation of extract preparation — including fixed harvest season, drying conditions, extraction solvent, and phytochemical profiling by HPLC — is essential [41]. Without these controls, synthesis protocols published in the literature cannot be reliably reproduced in different laboratories or geographic locations.
- **Scalability:** Laboratory-scale protocols must be optimised for industrial production while maintaining nanoparticle quality, size uniformity, and biological activity [20]. Changes in heat and mass transfer at scale, and the practicalities of large-volume plant extract preparation, represent significant engineering challenges that have not been systematically addressed in the green synthesis literature.
- **In vivo validation:** The vast majority of therapeutic studies remain at the in vitro level. In vitro results, while necessary, are insufficient to predict clinical efficacy. Rigorous in vivo pharmacokinetic (absorption, distribution, metabolism, excretion — ADME), biodistribution, and toxicology studies in appropriate animal models are critically needed before human application [22,23].
- **Cytotoxicity at high doses:** While ZnO is GRAS, high concentrations of ZnO NPs can induce cytotoxicity in normal cells through excessive Zn^{2+} ion release. Safe therapeutic windows must be rigorously established for each application and route of administration [4,38]. The relationship between particle size, surface chemistry, dissolution rate, and therapeutic index requires systematic investigation.
- **Regulatory pathway:** No established regulatory framework specifically addresses biogenic nanoparticles. Regulatory agencies in the US (FDA), Europe (EMA), and India (CDSCO) have issued guidance on nanotechnology-derived drug products, but the unique characteristics of phytochemical-coated biogenic nanoparticles — their complex, variable surface chemistry; their potential for seasonal variation; and the dual contribution of the nanoparticle core and phytochemical coating to biological activity — create regulatory complexity that has not been fully resolved [5].
- **Mechanistic understanding:** Many studies in the field report biological activities without rigorous mechanistic investigation, particularly at the molecular level. The specific phytochemical molecules responsible for capping and reducing activity are often not identified; their surface binding modes and orientations are rarely characterised by advanced spectroscopic techniques (NMR, XPS, Raman); and the relative contributions of dissolved Zn^{2+} and intact nanoparticles to biological effects are not always distinguished. This gap in mechanistic understanding hinders rational optimisation of nanoparticle design.

8. FUTURE RESEARCH DIRECTIONS

Several research avenues hold particular promise for advancing the field of plant-mediated ZnO NP therapeutics:

- **Phytochemical profiling and structure-activity relationships:** Systematic correlation of phytochemical profiles (via HPLC, LC-MS, and NMR analysis) with resulting nanoparticle characteristics and biological activities will identify which individual molecules drive synthesis efficiency, morphology control, and therapeutic potency. This knowledge will

enable rational plant source selection and guided optimisation of extract composition.

- **Hybrid nanocomposites:** Development of ZnO/TiO_2, ZnO/Ag, ZnO/Fe_3O_4, and other bimetallic or metal-metal oxide nanocomposites using green synthesis methods for synergistically enhanced antimicrobial, anticancer, and photocatalytic activity [35]. Magnetic ZnO/Fe_3O_4 composites offer the additional advantage of magnetic separability for environmental remediation applications.
- **Targeted drug delivery:** Surface functionalisation of green ZnO NPs with tumour-targeting ligands (folic acid, hyaluronic acid, monoclonal antibodies) for cancer-specific drug delivery applications. ZnO NPs can serve simultaneously as the drug carrier (through surface adsorption or pore loading in structured morphologies) and the therapeutic agent itself, enabling synergistic chemo-nanoparticle combination therapy.
- **Advanced wound formulations:** Incorporation of green ZnO NPs into hydrogels, electrospun nanofibres, 3D-printed scaffolds, and microneedle patches for next-generation wound dressing applications [28,37]. Integration with growth factors (VEGF, EGF, PDGF) and probiotics represents a further frontier in smart wound biomaterials.
- **Computational modelling:** Molecular docking and molecular dynamics simulations to predict phytochemical–Zn^{2+} binding affinities and guide rational plant source selection. Density functional theory (DFT) calculations can illuminate the electronic structure of phytochemical-ZnO interfaces and their influence on optical and biological properties, reducing empirical screening effort.
- **Clinical translation pathway:** Collaborative engagement between academic researchers, regulatory authorities, and industry partners is needed to establish clear development and approval pathways for biogenic nanoparticle therapeutics. Pilot clinical studies in defined indications — topical antimicrobial treatment of chronic wounds, for example — represent realistic near-term clinical translation targets.

9. CONCLUSION

Plant-mediated synthesis of zinc oxide nanoparticles represents a compelling convergence of green chemistry, phytochemistry, and nanobiotechnology. The unique combination of ZnO's FDA GRAS status, the essential biological role of zinc, the wide bandgap semiconductor properties enabling ROS generation, the piezoelectric and morphological tunability of ZnO, and the exceptional affinity of phytochemicals for Zn^{2+} ions makes this an ideal system for sustainable nanoparticle synthesis [4,5,42].

Green-synthesised ZnO NPs exhibit broad-spectrum antimicrobial activity through multi-target mechanisms that mitigate resistance risk — of outstanding relevance to the global antimicrobial resistance crisis; selective anticancer cytotoxicity exploiting tumour microenvironment chemistry; potent antioxidant capacity from both ZnO surface chemistry and phytochemical functionalisation; accelerated wound healing through coordinated antimicrobial, anti-inflammatory, and regenerative mechanisms; and emerging antidiabetic and photocatalytic activities that expand the therapeutic and environmental utility of these versatile nanomaterials [6,22,25,27,32].

Challenges in batch reproducibility, scalability, in vivo validation, complete mechanistic characterisation, and regulatory alignment must be systematically addressed through rigorous, multidisciplinary research. The foundation provided by this review — spanning the scientific rationale for ZnO selection, synthesis mechanisms, phytochemical roles, parameter optimisation, comprehensive characterisation approaches, and a critical evaluation of therapeutic evidence — provides a clear and accessible roadmap for undergraduate and early-career researchers entering this rapidly evolving field. Future integration of green ZnO NPs with targeted delivery systems, advanced wound biomaterials, hybrid nanocomposites, and clinical development frameworks holds considerable promise for translating these remarkable materials from laboratory to clinic and realising their full therapeutic potential [35,37,40].

REFERENCES

1. Sajjad A, Asad S, Bhatt DL. Green nanotechnology: sustainable approaches to metal oxide nanoparticle synthesis. Nano Today. 2020;35:100943.

2. Nasrollahzadeh M, Sajadi SM, Sajjadi M, Issaabadi Z. An introduction to green nanotechnology. Interface Sci Technol. 2019;28:1–27.

3. Mirhosseini M, Firouzabadi FB. Antibacterial activity of zinc oxide nanoparticle suspensions on food-borne pathogens. Food Control. 2013;34:539–46.

4. Sirelkhatim A, Mahmud S, Seeni A, et al. Review on zinc oxide nanoparticles: antibacterial activity and

toxicity mechanism. Nano-Micro Lett. 2015;7(3):219–42.

5. FDA. Agency Response Letter GRAS Notice No. GRN 000294: Zinc Oxide. Washington DC: US Food and Drug Administration; 2009.

6. Umar H, Kavaz D, Rizaner N. Biosynthesis of zinc oxide nanoparticles using Aloe barbadensis miller leaf extract and evaluation of their cytotoxic, antibacterial, and antifungal activities. Int J Nanomedicine. 2019;14:2325–41.

7. Datta A, Bhattacharyya D, Singh SK, et al. Role of alkaloids and phenolics from Aloe vera in stabilisation of zinc oxide nanoparticles. Mater Chem Phys. 2020;246:122840.

8. Elumalai K, Velmurugan S. Green synthesis, characterization and antimicrobial activities of zinc oxide nanoparticles from the leaf extract of Azadirachta indica (L.). Appl Surf Sci. 2015;345:329–36.

9. Sharma D, Rajput J, Kaith BS, Kaur M, Sharma S. Synthesis of ZnO nanoparticles and study of their antibacterial and antifungal properties. Thin Solid Films. 2010;519(3):1224–9.

10. Ramesh M, Anbuvannan M, Viruthagiri G. Green synthesis of ZnO nanoparticles using Solanum nigrum leaf extract and their antibacterial activity. Spectrochim Acta A. 2015;136:864–70.

11. Jayaseelan C, Rahuman AA, Kirthi AV, et al. Novel microbial route to synthesize ZnO nanoparticles using Aeromonas hydrophila and their activity against pathogenic bacteria and fungi. Spectrochim Acta A. 2012;90:78–84.

12. Okafor F, Janen A, Kukhtareva T, Edwards V, Curley M. Green synthesis of silver nanoparticles, their characterization, application and antibacterial activity. Int J Environ Res Public Health. 2013;10(10):5221–38.

13. Nava OJ, Soto-Robles CA, Gomez-Gutierrez CM, et al. Fruit peel extract mediated green synthesis of zinc oxide nanoparticles. J Mol Struct. 2017;1147:1–6.

14. Bala N, Saha S, Chakraborana M, et al. Green synthesis of zinc oxide nanoparticles using Hibiscus subdariffa leaf extract: effect of temperature on synthesis, anti-bacterial activity and anti-diabetic activity. RSC Adv. 2015;5(7):4993–5003.

15. Karimi J, Mohsenzadeh S. Effects of zinc oxide nanoparticles on Raphanus sativus growth. Bull Environ Contam Toxicol. 2016;96(5):601–6.

16. Ali ZA, Yahya R, Sekaran SD, Puteh R. Green synthesis of silver nanoparticles using apple extract and its antibacterial properties. Adv Mater Sci Eng. 2016;2016:4102196.

17. Iqbal J, Abbasi BA, Ahmad R, et al. Biogenic synthesis of green and cost-effective iron nanoparticles and evaluation of their potential biomedical properties. J Mol Struct. 2020;1199:126979.

18. Dhanemozhi AC, Rajeswari V, Sathyajothi S. Green synthesis of zinc oxide nanoparticle using green tea leaf extract for supercapacitor application. Mater Today Proc. 2017;4(2):660–7.

19. Vijayakumar S, Vaseeharan B, Malaikozhundan B, Shobiya M. Laurus nobilis leaf extract mediated green synthesis of ZnO nanoparticles: characterization and biomedical applications. Biomed Pharmacother. 2016;84:1213–22.

20. Naveed Ul Haq A, Nadhman A, Ullah I, et al. Synthesis approaches of zinc oxide nanoparticles: the dilemma of ecotoxicity. J Nanomater. 2017;2017:8510342.

21. Dobrucka R, Dlugaszewska J. Biosynthesis and antibacterial activity of ZnO nanoparticles using Trifolium pratense flower extract. Saudi J Biol Sci. 2016;23(4):517–23.

22. Rasmussen JW, Martinez E, Louka P, Wingett DG. Zinc oxide nanoparticles for selective destruction of tumor cells and potential for drug delivery applications. Expert Opin Drug Deliv. 2010;7(9):1063–77.

23. Hanley C, Layne J, Punnoose A, et al. Preferential killing of cancer cells and activated human T cells using zinc oxide nanoparticles. Nanotechnology. 2008;19(29):295103.

24. Akhtar MJ, Ahamed M, Kumar S, et al. Zinc oxide nanoparticles selectively induce apoptosis in human cancer cells through reactive oxygen species. Int J Nanomedicine. 2012;7:845–57.

25. Rajiv P, Rajeshwari S, Venckatesh R. Bio-Fabrication of zinc oxide nanoparticles using leaf extract of Parthenium hysterophorus L. and its size-dependent antifungal activity. Spectrochim Acta A. 2013;112:384–7.

26. Gnanasangeetha D, Thambavani SD. Biogenic production of zinc oxide nanoparticles using Acalypha indica. J Chem Pharm Res. 2014;6(2):745–51.

27. Khatami M, Alijani HQ, Heli H, Sharifi I. Rectangular shaped zinc oxide nanoparticles: green synthesis by Stevia and its biomedical efficiency. Ceram Int. 2018;44(13):15596–602.

28. Yahya R, Ali ZA, Sekaran SD. Green synthesis of silver and zinc oxide nanoparticles using leaf extracts: characteristics and wound healing properties. J Nanomater. 2019;2019:3195378.

29. Nagajyothi PC, Cha SJ, Yang IJ, et al. Antioxidant and anti-inflammatory activities of zinc oxide nanoparticles synthesised using Polygala tenuifolia root extract. J Photochem Photobiol B. 2015;146:10–7.

30. Thovhogi N, Diallo A, Gurib-Fakim A, Maaza M. Nanoparticles green synthesis by Hibiscus sabdariffa flower extract: main physical properties. J Alloys Compd. 2015;647:392–6.

31. Yuvakkumar R, Suresh J, Nathanael AJ, Sundrarajan M, Hong SI. Novel green synthetic strategy to prepare ZnO nanocrystals using rambutan peel extract and its antibacterial applications. Mater Sci Eng C. 2014;41:17–27.

32. Ishwarya R, Vaseeharan B, Kalyani S, et al. Facile green synthesis of zinc oxide nanoparticles using Ulva lactuca seaweed extract and evaluation of their photocatalytic, antibiofilm and insecticidal activity. J Photochem Photobiol B. 2018;178:249–58.

33. Ahmad W, Kalra D. Green synthesis, characterization and anti-microbial activities of ZnO nanoparticles using Euphorbia hirta leaf extract. J King Saud Univ Sci. 2020;32(4):2358–64.

34. Bindhu MR, Umadevi M, Esmail GA, Al-Dhabi NA, Arasu MV. Green synthesis and characterization of zinc oxide nanoparticles using Ruta graveolens L. plant extract. J Photochem Photobiol B. 2020;209:111906.

35. Prasad AR, Garvasis J, Oruvil SK, Joseph A. Bio-inspired green synthesis of zinc oxide nanoparticles using Abelmoschus esculentus mucilage and selective degradation of cationic dye pollutants. J Phys Chem Solids. 2019;127:265–74.

36. Sharmila G, Muthukumaran C, Saraswathi H, et al. Green synthesis, characterization and biological activities of ZnO nanoparticles from leaf extract of Bauhinia tomentosa. Chem Data Collect. 2019;21:100211.

37. Vijayakumar S, Malaikozhundan B, Saravanakumar K, et al. Nano zinc oxide from leaf extract of Pongamia pinnata: synthesis, characterization and their biomedical application. J Cluster Sci. 2019;30(4):995–1006.

38. Rezaei-Zarchi S, Javed A, Ghani MJ, et al. Comparative study of antimicrobial activities of TiO2 and CdO nanoparticles against the pathogenic strains. Iran J Pathol. 2010;5(2):83–9.

39. Bhuyan T, Mishra K, Khanuja M, Prasad R, Varma A. Biosynthesis of zinc oxide nanoparticles from Azadirachta indica for antibacterial and photocatalytic applications. Mater Sci Semicond Process. 2015;32:55–61.

40. Patil BN, Taranath TC. Limonia acidissima L. leaf mediated synthesis of zinc oxide nanoparticles: a potent tool against Mycobacterium tuberculosis. Int J Mycobacteriol. 2016;5(2):197–204.

41. Salam HA, Rajiv P, Kamaraj M, et al. Plants: green route for nanoparticle synthesis. Int Res J Biol Sci. 2012;1(5):85–90.

42. Kumar B, Smita K, Cumbal L, Debut A. Green approach for fabrication and applications of zinc oxide nanoparticles. Bioinorg Chem Appl. 2014;2014:523869.

43. Sangeetha G, Rajeshwari S, Venckatesh R. Green synthesis of zinc oxide nanoparticles by aloe barbadensis miller leaf extract: structure and optical properties. Mater Res Bull. 2011;46(12):2560–6.

44. Pillai AM, Sivasankarapillai VS, Rahdar A, et al. Green synthesis and characterization of zinc oxide nanoparticles with antibacterial and antifungal activity. J Mol Struct. 2020;1211:128107.

45. Sutradhar P, Saha M, Maiti D. Microwave synthesis of copper oxide nanoparticles using tea leaf and coffee powder extracts and its antibacterial activity. J Nanostruct Chem. 2014;4:86.

46. Moharram AH, Mansour SA, Hussein MA, Rashad M. Direct precipitation and hydrothermal synthesis of ZnO nanostructures. J Nanomater. 2014;2014:716210.

47. Geetha MS, Nagabhushana H, Shivananjaiah HN. Green mediated synthesis and characterization of ZnO nanoparticles using Euphorbia Jatropa latex as reducing agent. J Sci Adv Mater Devices. 2016;1(3):301–10.

48. Umashankari J, Inbakandan D, Ajithkumar TT, Balasubramanian T. Mangrove plant, Rhizophora mucronata (Lamk, 1804) mediated one pot green synthesis of silver nanoparticles and its antibacterial activity against aquaculture pathogens. Aquat Biosyst. 2012;8:11.

49. Sampath M, Vijayan R, Tamilarasu E, Tamilselvan A, Sengottuvelan B. Novel synthesis of algae-mediated silver nanoparticles and its efficiency as a photocatalytic degradation. J Nanostruct Chem. 2014;4:89.

50. Kavitha T, Harinidevi B, Iswarya M, Karthikeyan P. Photoluminescence studies of ZnO nanoparticles synthesized by co-precipitation method. J Appl Phys. 2015;8(3):49–52.

51. Dhanalakshmi T, Rajendran S. Synthesis of ZnO nanoparticles by co-precipitation method. Nanosci Nanotechnol. 2012;2(3):17–19.

52. WHO. Global Antimicrobial Resistance and Use Surveillance System (GLASS) Report 2022. Geneva: World Health Organization; 2022.

53. Miller KP, Wang L, Benicewicz BC, Decho AW. Inorganic nanoparticles engineered to attack bacteria. Chem Soc Rev. 2015;44(21):7787–807.

54. Talebian N, Amininezhad SM, Doudi M. Controllable synthesis of ZnO nanoparticles and their morphology-dependent antibacterial and optical properties. J Photochem Photobiol B. 2013;120:66–73.

55. Bisht G, Rayamajhi S. ZnO nanoparticles: a promising anticancer agent. Nanobiomedicine. 2016;3:9.