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Green Synthesis of Zno and Cuo Nanostructures Using Plant Extracts: A Sustainable Route from Natural Resources to Biomedical Innovation

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ABSTRACT: Zinc oxide (ZnO) and copper oxide (CuO) nanostructures are among the most widely investigated metal oxide nanomaterials in biomedicine, owing to their broad-spectrum antimicrobial, anticancer, and wound-healing activity combined with comparatively low cost and favorable biocompatibility. While these nanomaterials are conventionally produced by physical and chemical routes such as magnetron sputtering, ion-plasma deposition, and chemical precipitation, a rapidly growing body of literature has established plant-extract-mediated green synthesis as a sustainable, low-toxicity alternative that directly converts natural botanical resources into functional biomedical nanomaterials. This review synthesizes recent evidence on the mechanisms of plant-mediated green synthesis of ZnO and CuO nanostructures, their demonstrated antimicrobial, anticancer, antioxidant, and wound-healing efficacy, and the methodological relationship between green and physical synthesis routes for these same oxide systems. The reviewed literature demonstrates that green-synthesized ZnO-CuO bimetallic and trimetallic nanostructures achieve potent, dose-dependent anticancer cytotoxicity against breast cancer cell lines, near-complete biofilm reduction against multidrug-resistant bacterial pathogens, and accelerated diabetic wound closure exceeding

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90 percent within one week in preclinical models, positioning plant-mediated synthesis as a scientifically and environmentally compelling complement to physically deposited ZnO/CuO thin-film systems. Given the convergence of sustainability imperatives, antimicrobial resistance concerns, and the demonstrated multifunctionality of these nanostructures, this area represents one of the most active and rapidly citing fronts in contemporary nanomedicine research.

1. INTRODUCTION

The convergence of two urgent global priorities, environmental sustainability and the escalating crisis of antimicrobial resistance, has positioned green nanotechnology at the forefront of contemporary materials and biomedical research. Among the metal oxide nanomaterials under investigation, zinc oxide (ZnO) and copper oxide (CuO) occupy a particularly prominent position because both oxides combine a favorable safety profile, well-characterized semiconductor and catalytic properties, and a wide spectrum of demonstrated biological activity, including antibacterial, antifungal, antioxidant, and anticancer effects. These same oxide systems have long been produced by physical vapor deposition techniques, including magnetron sputtering and ion-plasma deposition, which yield thin films and nanostructures with precisely controlled stoichiometry and crystallinity but require energy-intensive vacuum processing and hazardous precursor handling.

Over the past several years, an increasingly large and rapidly citing body of literature has instead turned to plant-extract-mediated green synthesis as a route to the same ZnO and CuO nanostructures, exploiting the natural reducing, capping, and stabilizing phytochemicals present in leaves, flowers, and other plant tissues to convert simple metal salt precursors into functional nanomaterials without toxic solvents or high-energy input. Because this approach directly transforms botanical natural resources into biomedically active nanomaterials, it sits precisely at the intersection that defines the scope of natural-resource-oriented human health research, and its rapid growth reflects both genuine scientific promise and the broader sustainability imperative reshaping materials science. This review synthesizes current evidence on the mechanisms, biomedical efficacy, and comparative standing of plant-mediated green synthesis of ZnO and CuO nanostructures relative to physically deposited analogues of the same oxide systems.

2. MECHANISMS OF PLANT-MEDIATED GREEN SYNTHESIS

Green synthesis of metal oxide nanoparticles relies on biomolecules naturally present in plant extracts, including polyphenols, flavonoids, terpenoids, and other reducing sugars and proteins, which serve a dual function: reducing dissolved metal ions to their oxide or elemental nanoparticle form, and subsequently capping and stabilizing the resulting nanostructures to control their size and prevent uncontrolled aggregation. A comprehensive review of green synthesis principles identifies plant-mediated synthesis as one of several biomass-based routes, alongside bacteria-, algae-, and fungi-mediated approaches, and notes that plant extracts are particularly favored because the same phytochemicals that reduce metal ions simultaneously stabilize the resulting nanoparticles, simplifying the overall synthesis workflow relative to routes requiring separate capping agents [1]. The same review emphasizes that reaction parameters, including solution pH, temperature, precursor concentration, and reaction time, critically determine final nanoparticle size and morphology, with alkaline conditions generally favoring smaller, more narrowly distributed particles through enhanced electrostatic repulsion during nucleation [1].

This chemistry-driven, ambient-condition synthesis stands in direct methodological contrast to the physical vapor deposition routes used to produce ZnO, CuO, and Cu2O thin films and nanostructures for sensing and optoelectronic applications, in which layer growth is controlled through vacuum-based magnetron sputtering and ion-plasma parameters such as substrate temperature, working gas pressure, and deposition time rather than through phytochemical concentration and pH; recent work on ion-plasma-deposited ZnO/CuO/Cu2O heterostructures for piezoelectric and radiation-sensitive sensing applications illustrates this physical route and the degree of structural and band-gap control it affords, which complements rather than competes with the chemical control achievable through green synthesis [2]. The two routes accordingly serve differing application niches: physical deposition where precise crystallinity, layer thickness, and interface quality are paramount, and green synthesis where biocompatibility, low cost, and environmentally benign production of dispersed, surface-functionalized nanoparticles for direct biological application are the priority.

2.1. Comparison of Green and Physical Synthesis Routes

Figure 1 schematically contrasts the two synthesis philosophies discussed above. Panel (a) illustrates the plant-mediated green synthesis route, in which phytochemicals from a plant extract reduce a dissolved metal salt precursor at ambient or mildly elevated temperature, and Panel (b) illustrates the ion-plasma and magnetron sputtering route used to physically deposit ZnO/CuO thin films and heterostructures under vacuum. The two routes converge on chemically related ZnO and CuO end products but diverge sharply in energy requirements, achievable form factor (dispersed nanoparticles versus continuous thin films), and the resulting application niche, as summarized in Table 2 below.

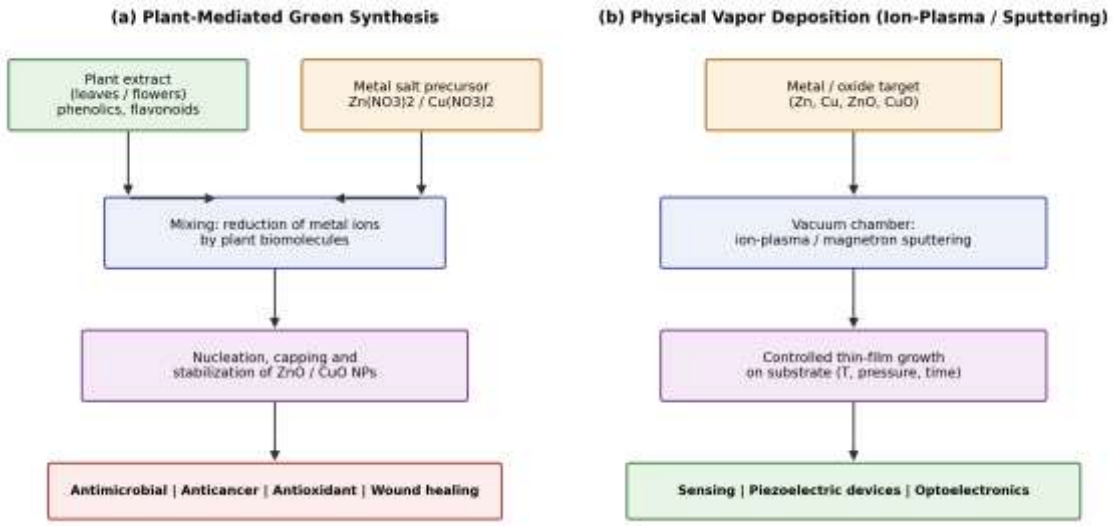


Figure 1. Schematic comparison of (a) plant-mediated green synthesis and (b) physical vapor deposition (ion-plasma / magnetron sputtering) routes to ZnO/CuO nanostructures.

Table 1. Summary of representative green-synthesized ZnO/CuO nanostructures and their reported biomedical activity.

Plant Source	Nanostructure	Particle Size	Key Bioactivity	Reference
Eryngium foetidum (leaf)	CuO-ZnO bimetallic NPs	~16.49 nm	89.20% cytotoxicity vs MCF-7 (IC50 239.99 μg/mL); MIC vs E. coli 7.81 μg/mL	Daimari & Deka, 2024 [3]
Ziziphus spina-christi (leaf)	CuO/Ag/ZnO trimetallic nanocomposite	~7.11 nm	Biofilm reduction 98.06% (E. coli) and 97.47% (S. aureus), multidrug-resistant isolates	El-Sawaf et al., 2024 [4]
Althaea officinalis (flower)	Chitosan-coated ZnO NPs	~76 nm	93.3% diabetic wound closure at 7 days; ↓TNF-α, IL-6, IL-1β; ↑IL-10	Elhabal et al., 2024 [5]

3. ANTIMICROBIAL AND ANTICANCER EFFICACY OF GREEN-SYNTHESIZED ZNO/CUO NANOSTRUCTURES

Recent experimental studies of plant-extract-synthesized ZnO-CuO bimetallic and multi-metallic nanostructures have reported potent and multifunctional biological activity that substantially exceeds what either oxide typically achieves alone. Bimetallic CuO-ZnO nanoparticles synthesized using Eryngium foetidum leaf extract, with an average particle size of 16.49 nm, demonstrated a cytotoxic inhibition rate of 89.20 percent against MCF-7 breast cancer cells at 500 micrograms per milliliter,

with a half-maximal inhibitory concentration of 239.99 micrograms per milliliter, alongside strong antioxidant activity and differential antibacterial potency, with a minimum inhibitory concentration against Escherichia coli of just 7.81 micrograms per milliliter, markedly lower than the concentrations required against Staphylococcus aureus and Bacillus subtilis [3].

Extending this bimetallic approach to a three-component system, a trimetallic CuO/Ag/ZnO nanocomposite synthesized using Ziziphus spina-christi plant extract and optimized through Taguchi statistical design achieved spherical, dot-like nanostructures averaging 7.11 nanometers in diameter, and at a concentration of 200 micrograms per milliliter produced biofilm reduction of 98.06 percent against Escherichia coli and 97.47 percent against Staphylococcus aureus among multidrug-resistant clinical isolates over 36 hours of exposure, findings the authors describe as the first industrial-scale demonstration of this specific trimetallic formulation as an antimicrobial agent [4]. Together, these studies indicate that combining zinc and copper oxide phases, and in some formulations a third metallic component, within a single plant-synthesized nanostructure produces synergistic antimicrobial and anticancer effects that directly address the growing clinical problem of multidrug-resistant bacterial biofilms alongside conventional oncological targets.

4. WOUND-HEALING APPLICATIONS: A DIRECT ROUTE TO CLINICAL TRANSLATION

Beyond antimicrobial and anticancer effects in isolation, green-synthesized ZnO nanoparticles have shown particular promise in composite wound-healing formulations relevant to diabetic wound management, a condition for which conventional treatment options remain limited. Zinc oxide nanoparticles synthesized from Althaea officinalis flower extract and subsequently coated with chitosan produced spherical particles of approximately 76 nanometers in diameter with a stabilizing zeta potential of positive 30 millivolts, and when applied to diabetic wounds in an in vivo model achieved 93.3 percent wound closure within seven days, substantially outperforming untreated controls and standard treatment comparators [5]. Mechanistic analysis in the same study linked this accelerated healing to modulation of the inflammatory cascade, with the treated group showing reduced levels of the pro-inflammatory mediators interleukin-6, interleukin-1 beta, and tumor necrosis factor-alpha alongside increased levels of the anti-inflammatory cytokine interleukin-10, indicating that the therapeutic benefit of the green-synthesized nanoparticle formulation operates through active immunomodulation rather than antimicrobial action alone [5].

Histopathological confirmation of organized tissue regeneration and reduced inflammatory cell infiltration in the same wound-healing model further supports the translational relevance of this approach, and taken together with the antimicrobial and anticancer findings discussed above, illustrates how a single plant-derived synthesis platform can be tuned, through choice of plant source, coating polymer, and metal oxide composition, toward distinct but complementary biomedical endpoints spanning infection control, oncology, and regenerative wound care.

Table 2. Comparison of plant-mediated green synthesis and physical vapor deposition routes to ZnO/CuO nanostructures.

Parameter	Green Synthesis (Plant Extract)	Physical Vapor Deposition (Ion-Plasma / Sputtering)
Typical product form	Dispersed nanoparticles, colloidal suspensions	Continuous thin films, layered heterostructures
Processing conditions	Ambient to mild temperature, aqueous, atmospheric pressure	High vacuum, controlled substrate temperature and gas pressure
Size/morphology control	Governed by extract chemistry, pH, precursor concentration [1]	Governed by deposition time, power, and substrate parameters [2]
Reproducibility	Sensitive to plant batch, season, extraction protocol	High, process-controlled and instrument-defined
Primary application niche	Antimicrobial, anticancer, wound-healing nanomedicine [3-5]	Piezoelectric, radiation-sensitive, and optoelectronic sensing [2]
Sustainability profile	Low energy input, non-toxic reagents, valorizes plant biomass [1]	Energy-intensive vacuum processing, precise but resource-demanding

5. SUSTAINABILITY, TRANSLATIONAL OUTLOOK, AND LIMITATIONS

The rapid expansion of this literature reflects a genuine convergence of scientific and practical incentives: green synthesis directly valorizes botanical natural resources, many of them regionally available medicinal or wild plant species, into nanomaterials with measurable biomedical activity, while avoiding the toxic reducing agents, high energy consumption, and hazardous waste streams associated with conventional chemical and physical nanoparticle production routes [1]. This sustainability rationale, combined with the multifunctional antimicrobial, anticancer, and wound-healing activity documented above, explains why plant-mediated synthesis of ZnO and CuO nanostructures has become one of the most actively growing and highly cited fronts within nanomedicine and materials-for-health research over the past several years.

Nonetheless, important limitations temper immediate clinical translation. Batch-to-batch variability in plant extract composition, driven by plant growing conditions, harvest season, and extraction protocol, poses a substantial reproducibility challenge that is largely absent from physically deposited nanostructures produced under tightly controlled vacuum conditions [1, 2]. Most of the antimicrobial, anticancer, and wound-healing findings reviewed here derive from in vitro assays or small-animal in vivo models rather than human clinical trials, and long-term biodistribution, systemic toxicity, and regulatory pathway data for green-synthesized ZnO/CuO nanostructures remain considerably less developed than for their physically manufactured counterparts. Establishing standardized extract preparation protocols, and pairing green synthesis screening with the structural and compositional characterization rigor already routine in physically deposited oxide systems, represents a necessary next step before these promising nanomaterials can progress toward clinical application.

6. CONCLUSION

Plant-extract-mediated green synthesis has established itself as a scientifically robust and environmentally sustainable route to biomedically active ZnO and CuO nanostructures, directly converting botanical natural resources into nanomaterials with demonstrated anticancer, antimicrobial, and wound-healing efficacy that in several recent studies rivals or exceeds that of single-phase oxide nanoparticles. This green chemistry route complements, rather than replaces, the physical vapor deposition methods used to produce structurally precise ZnO/CuO/Cu2O thin films and heterostructures for sensing and optoelectronic applications, with each route suited to distinct application requirements. Given the dual momentum of sustainability-driven materials science and the urgent clinical need for new antimicrobial and wound-healing strategies in the face of rising antimicrobial resistance, plant-mediated green synthesis of metal oxide nanostructures constitutes one of the most active and rapidly advancing research fronts at the interface of natural resources and human health, warranting continued rigorous, standardized, and ultimately clinical investigation.

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