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Research Progress of Nano ZnO and Its Composites in the Field of Antibacterial Technology

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Abstract

The misuse of antibiotics has led to a global increase in antimicrobial resistance, necessitating the development of novel antibacterial strategies. Inorganic nanomaterials, with their unique physicochemical properties and multifaceted antimicrobial mechanisms, offer a promising alternative. This review comprehensively discusses recent advances in zinc oxide (ZnO) nanoparticles and their composites within the field of antibacterial technology. Pure ZnO nanoparticles exhibit intrinsic antibacterial activity through the generation of reactive oxygen species (ROS) and the release of zinc ions (Zn^{2+}), with efficacy highly dependent on particle size, morphology, and crystallinity. Strategies such as morphological control (e.g., nanosheets, nanorods), noble metal modification (e.g., Ag, Pt, Pd), metal ion doping (e.g., Co, Nd), and compositing with other metal oxides or carbon-based materials (e.g., GO, rGO) have been shown to significantly enhance antibacterial performance. The antimicrobial mechanisms of ZnO-based nanomaterials are explored in depth, emphasizing the synergistic effects of ROS-induced oxidative stress, Zn^{2+}-mediated membrane disruption and enzyme inactivation, and physical damage. Despite the considerable potential of ZnO composites in combating multidrug-resistant bacteria and biofilms, challenges remain regarding biocompatibility, environmental toxicity, and scalable synthesis. Future research should focus on green synthesis routes, targeted delivery systems, combination therapies, and long-term safety assessments to facilitate clinical and industrial translation.

Keywords

Zinc Oxide Nanoparticles, Antibacterial Materials, Composites, Reactive Oxygen Species, Antibiotic Resistance, Biofilm

1. Introduction

Antibiotics revolutionized modern medicine, profoundly impacting public health by effectively combating bacterial infections and significantly reducing morbidity and mortality rates [1]. Their discovery and widespread use enabled advanced medical procedures like organ transplantation and chemotherapy, which rely on effective infection control. However, overuse and misuse of antibiotics have led to a global crisis: the rapid emergence and spread of antibiotic-resistant bacteria [2]. This resistance renders conventional treatments less effective or ineffective, posing a severe threat to global health and economic stability. The rise of multidrug-resistant (MDR) pathogens, including Methicillin-resistant *Staphylococcus aureus* (MRSA) and Extended-spectrum β-lactamase (ESBL)-producing *Escherichia coli* and *Klebsiella pneumoniae*, demands urgent exploration of novel antibacterial strategies [3].

Biofilms pose a major risk by dispersing planktonic cells, potentially causing new infections. Bio-contamination is a primary cause of biofilm-associated infections, occurring on medical devices (catheters, implants), industrial surfaces, and human tissues, leading to persistent and recurrent infections such as chronic wounds and cystic fibrosis lung infections. The mechanism of formation and risk of dissemination involves initial attachment, microcolony development, maturation, and dispersion. This complex process utilizes quorum sensing and genetic regulation, allowing bacteria to resist environmental stresses. Traditional antibacterial strategies rely heavily on chemical agents and antibiotics, including disinfectants (e.g., alcohol, chlorine compounds), antiseptics (e.g., iodine, chlorhexidine), and broad-spectrum antibiotics targeting processes like cell wall synthesis, protein synthesis, and DNA replication [4]. While effective, many face limitations such as toxicity, environmental concerns, and the critical challenge of increasing bacterial resistance. An ideal antibiofilm material should have broad-spectrum activity, low host cell toxicity, high stability, EPS penetration capability, and minimal propensity to induce resistance. Current approaches to control biofilm involve physical removal, chemical disinfection, and combination therapies, but they often show limited efficacy against established biofilms.

In this context, inorganic nanomaterials offer promising alternatives. Their unique physical and chemical properties confer potent antibacterial activity through mechanisms distinct from traditional antibiotics, potentially mitigating resistance development. This review comprehensively discusses research progress on zinc oxide (ZnO) nanoparticles and their composites in antibacterial technology, focusing on intrinsic properties, the influence of morphology and composition, and underlying antibacterial mechanisms. (e.g., reactive oxygen species (ROS) generation, metal ion release, membrane disruption) make them potent antimicrobials [5]. Inorganic nanoparticles typically exhibit higher thermal and chemical stability than many organic compounds. Among these, zinc oxide (ZnO) has garnered significant attention due to its excellent antibacterial efficacy, low cost, low toxicity to human cells at relevant concentrations, and Generally Recognized as Safe (GRAS) status by the FDA [6]. This review comprehensively discusses research progress on ZnO nanoparticles

and their composites in antibacterial technology, focusing on intrinsic properties, the influence of morphology and composition, and underlying antibacterial mechanisms.

2. Antibacterial Materials Based on ZnO

Zinc oxide is a versatile semiconductor material with a wide bandgap (3.37 eV) and large exciton binding energy (60 meV), suitable for applications including catalysis, sensors, UV protection, and, prominently, antimicrobial agents [7]. Its antibacterial properties are multifaceted and can be tuned by controlling morphology, size, and composition.

2.1. Pure ZnO's Antibacterial Properties

Pure ZnO nanoparticles exhibit intrinsic antibacterial activity against a broad spectrum of bacteria, including Gram-positive and Gram-negative strains. This activity primarily stems from their ability to generate reactive oxygen species (ROS) and release zinc ions (Zn^{2+}) [8]. Research indicates that the effectiveness of pure ZnO nanoparticles is often size-dependent; smaller nanoparticles typically show enhanced activity due to their larger surface area and increased number of active sites [6]. For example, facilely synthesized ZnO nanosheets demonstrate potent antibacterial activity against common pathogenic bacteria, suggesting their potential as effective antimicrobial agents [9]. Furthermore, ZnO nanoparticles show significant antibacterial potential against highly resistant strains like ESBL-producing *Escherichia coli* and *Klebsiella pneumoniae* [10]. Sonochemically grown ZnO nanorods also exhibit considerable antibacterial properties, highlighting ZnO's intrinsic toxicity of ZnO to bacterial cells [8].

The differential susceptibility between Gram-positive and Gram-negative bacteria to ZnO nanoparticles is influenced by their distinct cell wall structures. Gram-negative bacteria possess an outer membrane composed of lipopolysaccharides (LPS) that can hinder the penetration of nanoparticles and ions, whereas Gram-positive bacteria have a thick peptidoglycan layer that may offer different resistance mechanisms. These structural differences affect the efficacy of ROS penetration, Zn^{2+} influx, and physical disruption by ZnO nanostructures.

2.2. Influence of ZnO Morphology and Crystallinity on Antibacterial Properties

The shape and crystallographic facets of ZnO nanostructures critically modulate their antibacterial efficacy. Different morphologies—such as nanorods, nanosheets, nanospheres, nanowires, and quantum dots—possess varying surface energies, surface areas, and exposed reactive sites. These factors directly influence interactions with bacterial cells and the ability to generate ROS. Nanosheet structures, with their high surface area and exposed basal planes, consistently show excellent antibacterial performance. For instance, green-synthesized ZnO nanosheets from banana peel extract exhibit notable antibacterial activity, emphasizing morphology's role

in enhancing bioactivity [11]. Similarly, ZnO nanosheets synthesized by other methods demonstrate superior antibacterial efficacy, often attributed to their large surface-to-volume ratio and numerous active sites for ROS generation and direct physical interaction with bacterial membranes [9]. Comparative studies between nanosheet and nanosphere morphologies reveal that shape significantly governs both photocatalytic and antibacterial properties. Nanosheet-dominated structures typically offer more active sites, leading to enhanced ROS generation and consequently superior antibacterial performance compared to nanospheres [12]. This highlights that engineering ZnO morphology at the nanoscale is a crucial strategy for optimizing antimicrobial potential. The high aspect ratio of nanorods can also facilitate mechanical damage to bacterial membranes, contributing to their antibacterial action [8]. Additionally, exposed crystal facets (e.g., polar vs. non-polar surfaces) possess different surface energies and charge distributions, influencing the adsorption of bacterial components and catalytic reactions for ROS production.

2.3. Enhanced Antibacterial Effect of Metal/Noble Metal Modified ZnO

Modifying ZnO with noble metals represents a key strategy to enhance its antibacterial efficacy. Noble metals like silver (Ag), platinum (Pt), and palladium (Pd) possess intrinsic antimicrobial properties and can act as cocatalysts, improving charge separation and photocatalytic activity in semiconductors [13]. Silver (Ag) modification involves Ag nanoparticles, which are powerful antimicrobials. Integrating them with ZnO typically yields a synergistic effect. Ag/ZnO composites often exhibit enhanced antibacterial activity due to combined Ag^+ ion release and improved ROS generation from ZnO. Silver acts as an electron sink, facilitating electron-hole pair separation in ZnO, increasing charge carrier lifespan and promoting ROS production [14]. Platinum (Pt) and Palladium (Pd) modification similarly enhance ZnO's photocatalytic activity by acting as electron traps, reducing electron-hole recombination and boosting ROS generation efficiency. These noble metals also catalyze reduction reactions. Pt and Pd coatings or doping can improve ZnO nanoparticle stability for long-term applications [15]. Their presence can also alter the surface charge of composite and hydrophobicity, promoting stronger interactions with bacterial cell membranes.

2.4. Enhanced Antibacterial Effect of Doping or Surface Modification

Beyond noble metals, doping ZnO with metal ions or forming composites with other metal oxides and carbon-based materials offers another powerful approach to tailor and enhance antibacterial properties. These modifications can alter electronic band structure, increase defect sites, enhance surface area, or provide additional antimicrobial mechanisms. Metal doping, such as with transition metals like cobalt (Co) or neodymium (Nd), shows significant promise. For example, Co-doped ZnO quantum dots exhibit high-performance antibacterial activity primar-

ily driven by enhanced superoxide anion ($O_2 \cdot^-$) generation [8]. Similarly, Nd-doped ZnO nanoparticles demonstrate improved antibacterial effects against ESBL-producing strains, indicating rare-earth element doping can boost intrinsic antimicrobial of ZnO potential against resistant bacteria [10]. Doping introduces lattice defects and alters the local electronic environment, creating active sites for ROS generation or enhancing metal ion release. Metal oxide composites, such as Cu_2O/ZnO and TiO_2/ZnO, combine ZnO with other metal oxides to create heterojunctions that improve charge separation and expand light absorption range, enhancing photocatalytic and antibacterial efficiency. CuO/ZnO composites leverage copper oxide's inherent antimicrobial properties, creating synergistic effects through the p-n heterojunction between CuO and ZnO, which facilitates charge transfer and enhances ROS generation and the release of both Zn^{2+} and Cu^{2+} ions [16]. TiO_2/ZnO composites utilize titanium dioxide's photocatalytic properties, showing improved photoefficiency and broader-spectrum antibacterial activity compared to individual components [17]. Integrating ZnO nanoparticles with graphene oxide (GO) or reduced graphene oxide (rGO) is highly effective, as GO and rGO offer excellent conductivity, high surface area, and inherent antibacterial activity. ZnO/GO or ZnO/rGO composites benefit from enhanced charge separation, where GO/rGO acts as an electron acceptor, promoting efficient electron-hole pair separation in ZnO and increasing ROS production [18]. They also provide increased surface area for more active sites and bacterial cell interaction, along with direct antibacterial activity from sharp GO nanosheet edges that physically damage bacterial membranes and induce oxidative stress. The composite leverages these multiple mechanisms for superior antibacterial efficacy, making it a candidate for advanced biomedical and environmental applications.

2.5. Antibacterial Mechanisms of Nano ZnO

The antibacterial activity of nano ZnO is multifaceted, primarily involving two main pathways: reactive oxygen species (ROS) generation and zinc ion (Zn^{2+}) release, often complemented by direct physical damage.

Under light irradiation (especially UV, but also visible light due to defects), ZnO acts as a photocatalyst. Photon absorption excites electrons from the valence band to the conduction band, creating electron-hole pairs (e^-/h^+). These charge carriers react with adsorbed oxygen and water to form ROS such as superoxide radicals ($O_2 \cdot^-$), hydroxyl radicals (·OH), and hydrogen peroxide (H_2O_2) [8]. In dark conditions, surface defects and oxygen vacancies in ZnO can also mediate ROS generation, though typically at a lower rate.

Zn^{2+} release occurs gradually, especially in slightly acidic environments or upon contact with bacterial exudates. Released Zn^{2+} ions disrupt cell membrane integrity by interacting with thiol groups in proteins, leading to enzyme inactivation, and cause leakage of intracellular components. Additionally, direct physical interaction, particularly with high-aspect-ratio morphologies like nanosheets or nanorods, can mechanically damage bacterial cell walls [8] [9].

The relative contribution of each mechanism depends on factors such as nanoparticle size, morphology, concentration, surface properties, environmental conditions, and bacterial type.

2.6. Biocompatibility and Toxicity Considerations

While ZnO nanoparticles exhibit strong antibacterial properties, their potential cytotoxicity to mammalian cells remains a critical concern for clinical and environmental applications. Studies have shown that ZnO nanoparticles can induce oxidative stress, inflammatory responses, and cell death in human cells, depending on concentration, exposure time, particle size, and surface functionalization [19]. Factors such as high Zn^{2+} release and ROS generation—which contribute to antibacterial activity—may also cause damage to host tissues. Therefore, balancing antibacterial efficacy with biocompatibility is essential [20]. Surface modification, doping, and composite formation can modulate toxicity profiles by controlling ion release kinetics and reducing nonspecific interactions with mammalian cells [21]. Further research into safe-by-design approaches and long-term toxicological assessments is necessary to ensure the safe application of ZnO-based nanomaterials [22].

3. Conclusion and Outlook

The complex challenges of antibiotic resistance and recalcitrant bacterial biofilms demand innovative antibacterial strategies. Nano ZnO and its composites represent a highly promising frontier. This review highlights significant research progress, demonstrating that ZnO nanoparticles possess intrinsic, potent antibacterial capabilities against a wide range of pathogens, including multi-drug resistant strains. Crucially, antibacterial efficacy of ZnO can be precisely tuned and substantially enhanced by controlling morphology (e.g., nanosheets, nanorods) and through strategic modifications like doping with metal ions (e.g., Co, Nd) or forming composites with noble metals (e.g., Ag, Pt, Pd), other metal oxides (e.g., CuO, TiO_2), or carbon-based materials (e.g., GO). These modifications augment the primary antibacterial mechanisms—destructive reactive oxygen species generation and bactericidal zinc ion release—often synergized with direct physical disruption of bacterial membranes.

Despite remarkable progress, several challenges and opportunities remain. A deeper understanding of the long-term environmental impact and potential *in vivo* toxicity of nano ZnO composites to mammalian cells is paramount for safe, widespread application. Standardized synthesis and characterization protocols are needed to ensure reproducibility and comparability. Future research should focus on optimizing synthesis methods to develop green, cost-effective, and scalable routes for diverse ZnO nanostructures and composites. It should also prioritize biofilm eradication by designing advanced ZnO-based materials specifically tailored to penetrate, disrupt, and eradicate mature bacterial biofilms. Targeted delivery strategies should be explored to maximize therapeutic efficacy and minimize off-target effects. Combination therapies involving ZnO nanoparticles and conventional an-

tibiotics or other antimicrobials should be investigated to overcome resistance and enhance outcomes. Long-term stability and biocompatibility in various biological and environmental contexts must be ensured.

In conclusion, nano ZnO and its composites hold immense potential to revolutionize antibacterial technology, offering a robust platform against the escalating threats of antibiotic-resistant infections and biofilm-related diseases. Continued interdisciplinary research, bridging materials science, microbiology, and toxicology, will be vital for translating these promising materials from the laboratory into effective clinical and industrial applications.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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