

Review

An Overview of Chitosan-Based Composites Containing Silver or Zinc Oxide Nanoparticles: Antimicrobial and Antibacterial Properties, and Biomedical Perspectives

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Highlights

- Chitosan-based composites with AgNPs or ZnONPs exhibit broad-spectrum antimicrobial activity.
- Synergistic interactions between chitosan and metal nanoparticles enhance antibacterial efficacy.
- The properties of the chitosan-based composites depend on the size, concentration, and preparation methods of AgNPs or ZnONPs.
- Biomedical applications include wound dressings and tissue engineering.

Abstract

The increasing prevalence of antimicrobial resistance has stimulated the development of alternative antimicrobial materials capable of preventing microbial growth and biofilm formation. Chitosan, a natural polysaccharide derived from chitin through deacetylation, possesses intrinsic antimicrobial properties, biodegradability, biocompatibility, and low toxicity, making it an attractive matrix for nanocomposite materials. However, the antimicrobial efficacy of pure chitosan is often limited by different factors, such as pH sensitivity, mechanical weakness, and poor solubility at neutral pH. To overcome these limitations, researchers have developed chitosan composites containing nanoparticles to enhance antimicrobial and antibacterial efficacy. This review provides an update on the status of the action mechanisms, synthesis methods, antimicrobial and antibacterial performances, and potential biomedical applications of chitosan-based composites containing silver nanoparticles (AgNPs) or zinc oxide nanoparticles (ZnONPs).



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Keywords: chitosan; silver nanoparticles; zinc oxide nanoparticles; antimicrobial activity; antibacterial performance; biomedical applications

1. Introduction

Antimicrobial resistance has emerged as a critical global health concern, threatening the effective prevention and treatment of infectious diseases [1]. The extensive use and misuse of antibiotics in healthcare, animal husbandry, and agricultural practices have

accelerated the evolution and spread of resistant microorganisms, resulting in a substantial reduction in the efficacy of many conventional antimicrobial agents. As a result, infections caused by multidrug-resistant pathogens are becoming increasingly difficult to manage, leading to higher rates of morbidity and mortality, prolonged hospitalization, and escalating healthcare costs [2]. The increasing limitations of traditional antibiotic therapies have stimulated intensive research into alternative antimicrobial strategies that can effectively inhibit microbial growth while reducing the likelihood of resistance development [3,4]. In this context, natural polymers, such as cellulose, chitosan, and starch, have attracted considerable attention as sustainable and biocompatible materials for biomedical, pharmaceutical, and environmental applications due to their abundance, renewability, non-toxicity, and biodegradability [5,6]. Moreover, their chemical structures contain functional groups that enable facile modification and incorporation of bioactive compounds, allowing the design of advanced materials with enhanced antimicrobial, mechanical, and barrier properties [7–9].

Chitosan is a naturally derived polysaccharide that has attracted considerable scientific interest because of its unique combination of biological and physicochemical properties (e.g., degree of deacetylation, molecular weight, crystallinity, solubility, and pH of the environment). Its cationic nature enables strong interactions with negatively charged molecules and biological surfaces [10]. Furthermore, chitosan exhibits intrinsic antimicrobial activity, film-forming ability, mucoadhesive characteristics, and versatile chemical reactivity, allowing structural modification and functionalization for specific purposes [11]. Unlike widely used synthetic polymers (e.g., polyvinyl alcohol (PVA), polylactic acid (PLA), polycaprolactone (PCL), and polyethylene glycol (PEG)), which are generally biologically inert, chitosan exhibits essential antibacterial, antifungal, and hemostatic properties without the need for additional functional additives [12]. In contrast to collagen and gelatin, which possess excellent cellular recognition properties but are susceptible to rapid enzymatic degradation and relatively poor mechanical stability, chitosan offers greater structural stability and a slower degradation rate [13]. Compared to silk fibroin, a polymer known for its exceptional mechanical strength, chitosan demonstrates lower tensile properties but offers superior antimicrobial activity and greater ease of chemical functionalization [14]. Contrasted with dextran, a highly biocompatible polysaccharide widely used in drug delivery, chitosan exhibits stronger mucoadhesive properties due to its cationic character, promoting prolonged residence time and enhanced interaction with negatively charged biological membranes [15]. Compared to starch, which is inexpensive and readily biodegradable but exhibits limited stability in aqueous media, chitosan forms more stable matrices and hydrogels, suitable for sustained drug delivery and tissue engineering [16–18].

These features have promoted its extensive investigation in areas such as drug delivery, tissue engineering, wound healing, food preservation, water treatment, and agricultural technologies [19].

Chitosan serves not only as a biocompatible and biodegradable matrix but also as an effective stabilizing and dispersing agent that prevents agglomeration of nanoparticles and promotes their uniform distribution throughout the composite structure [20]. The presence of protonated amino groups in chitosan facilitates electrostatic interactions with negatively charged microbial cell surfaces, thereby enhancing the adhesion of nanoparticles to microorganisms and increasing their local antimicrobial concentration. This synergistic effect significantly improves the antimicrobial performance of nanocomposites against a wide range of pathogenic microorganisms [21]. Numerous studies have reported potent antibacterial activity against Gram-positive bacteria, such as *Staphylococcus aureus*, including Methicillin-resistant *Staphylococcus aureus* (*S. aureus*) (MRSA), *Bacillus subtilis* (*B. subtilis*), and *Listeria monocytogenes* (*L. monocytogenes*), as well as Gram-negative bacteria, including *Escherichia coli* (*E. coli*), *Pseudomonas aeruginosa* (*P. aeruginosa*), *Salmonella enterica*

(*S. enterica*), and *Klebsiella pneumoniae* (*K. pneumoniae*). The combined action of chitosan and nanoparticles enhances membrane disruption, generation of oxidative stress, and inhibition of biofilm formation, resulting in superior antimicrobial efficacy compared to either component used individually [22–24].

Despite its favorable characteristics, pure chitosan exhibits several limitations, including low mechanical strength and reduced antimicrobial efficiency under physiological conditions [25]. To overcome these limitations, researchers have developed chitosan-based nanocomposites containing metallic and metal oxide nanoparticles [26,27]. Silver nanoparticles (AgNPs) have gained considerable attention due to their potent broad-spectrum antimicrobial activity and their ability to inhibit biofilm formation. Their multiple mechanisms of action, including membrane disruption, oxidative stress induction, and interference with cellular functions, make them effective against both susceptible and resistant microorganisms [28,29]. Zinc oxide nanoparticles (ZnONPs) have emerged as an attractive alternative because they combine good antimicrobial activity with relatively low cost, good biocompatibility, and ease of large-scale production [30–32]. The integration of AgNPs or ZnONPs into the chitosan matrix creates multifunctional systems in which the intrinsic antimicrobial properties of chitosan are complemented by the unique physicochemical characteristics of the nanoparticles (e.g., size, distribution, shape, and chemical composition) [33,34]. Tayel et al. [35] reported that ZnONPs exhibited higher antibacterial activity than zinc powder, probably due to the higher surface area-to-volume ratio. Their findings showed that *S. aureus* was more susceptible than the Gram-negative bacteria *E. coli* and *P. aeruginosa*, as evidenced by the larger zones of inhibition (21 mm for *E. coli*, 17 mm for *P. aeruginosa*, and 31 mm for *S. aureus*). Although the absolute diameters of the inhibition zone differed from those reported by Tayel et al. [35], the same susceptibility pattern was also observed in the study described by Bagheri et al. [36], with *S. aureus* being the most susceptible strain (21.51 ± 0.20 mm). This difference is commonly attributed to the structural characteristics of Gram-negative bacteria, whose outer membrane acts as an additional barrier limiting the penetration of nanoparticles. Similar observations, including the synergistic antibacterial effects of AgNPs and ZnONPs, have also been reported by Hu et al. [37].

Although numerous studies have investigated the antimicrobial properties of chitosan and metal-based nanoparticles, respectively [38–40], the novelty of this review lies in an updated perspective on chitosan-based nanocomposites containing AgNPs or ZnONPs, with a focus on the design of multifunctional antimicrobial and antibacterial biomaterials. It explores recent advances in environmentally friendly and sustainable synthesis, controlled nanoparticle incorporation, and smart wound dressing technologies. Particular attention is paid to the relationship between nanocomposite architecture and biological performance, including antimicrobial efficacy, biocompatibility, and tissue regeneration. In addition, the review discusses key challenges associated with clinical translation, regulatory approval, scalable manufacturing, and the development of personalized antimicrobial therapies.

2. Structure and Antibacterial Mechanism of Chitosan

Structurally, chitosan consists of β -(1→4)-linked D-glucosamine and N-acetyl-D-glucosamine units. The presence of amino and hydroxyl functional groups enables extensive chemical modification and interaction with other compounds [41]. Chitosan can be obtained by enzymatic or chemical deacetylation of chitin (a linear polymer of N-acetyl-2-amino-2-deoxy-d-glucopyranose units with β -(1→4) bonds), the second most abundant natural polysaccharide after cellulose [42]. Chitin is commonly extracted from crustacean shells, fungal cell walls, and insect exoskeletons. Chemical deacetylation remains the most widely applied method for chitosan production due to its simplicity, high conversion efficiency, and suitability for large-scale industrial processes. Both chemical and biological

deacetylation processes are typically associated with a certain extent of depolymerization, which may affect the molecular weight of the resulting chitosan [43]. The schematic representation of the production of chitosan from shrimp is shown in Figure 1 [44].

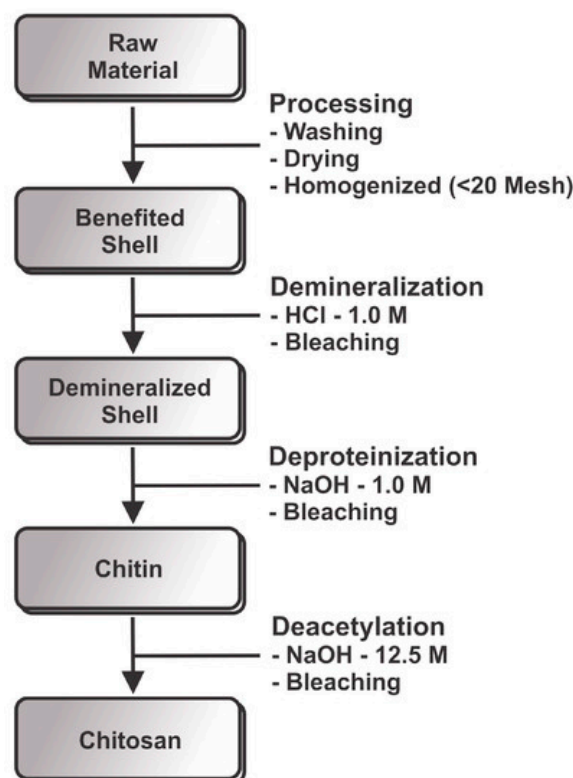


Figure 1. Schematic representation of the production process of chitosan from shrimp (adapted from Ref. [44]).

Although the antimicrobial activity of chitosan has been extensively documented [45], its exact mechanism of action remains multifactorial and has not yet been fully elucidated. Current evidence suggests that chitosan exerts its antimicrobial effects through a combination of physicochemical interactions and intracellular disruption [46,47]. The antimicrobial action of chitosan is mainly attributed to its polycationic nature. In acidic environments, the amino groups ($-\text{NH}_2$) of chitosan become protonated, generating positively charged sites that interact with negatively charged components of microbial cell surfaces, including lipopolysaccharides in Gram-negative bacteria and teichoic acids in Gram-positive bacteria. This interaction can disrupt cell membrane integrity, increase membrane permeability, and cause leakage of intracellular constituents [48].

Beyond membrane disruption, low molecular weight chitosan and its oligomers can penetrate microbial cells and bind to nucleic acids, interfering with DNA transcription, replication, and protein synthesis (Figure 2) [49]. Chitosan also exhibits chelating properties, allowing it to sequester essential metal ions and nutrients required for microbial growth, thereby inhibiting vital metabolic processes. In addition, chitosan-based structures, such as nanoparticles, microspheres, and nanocomposites, can create protective barriers around microorganisms or facilitate sustained antimicrobial activity through increased surface contact [50]. However, further mechanistic studies are needed to clarify the relative contribution of each antimicrobial pathway and to optimize chitosan-based materials for specific therapeutic and industrial applications.

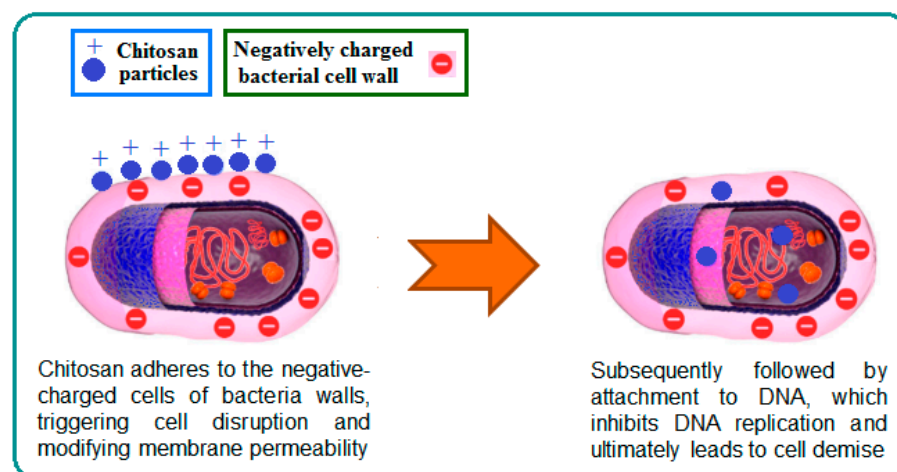


Figure 2. Proposed mechanism of antibacterial activity of chitosan particles, including disruption of bacterial cell wall and membrane, interaction with bacterial DNA that inhibits DNA replication, and ultimately induction of bacterial cell death (adapted from Ref. [49]).

3. Chitosan-Based Antimicrobial Composites

3.1. Chitosan–Silver Nanoparticle Composites

AgNPs are among the most widely studied antimicrobial agents due to their broad-spectrum activity. Incorporation of AgNPs into chitosan matrices significantly enhances antimicrobial performance [51,52].

Madhusudanan et al. [52] synthesized AgNPs using *Crassula ovata* leaf extract and incorporated them into chitosan-based nanocomposite films to enhance antibacterial activity against *E. coli*, *P. aeruginosa*, *S. epidermidis*, and MRSA. Chitosan encapsulation improved nanoparticle stability and interactions with bacterial cells. Chitosan-based films were prepared by mixing 0.05% chitosan nanoparticles, chitosan nanoparticles loaded with AgNPs, or chitosan nanoparticles containing both AgNPs and gentamicin (1 µg/mL) with a PVA solution (1.5%) used as a plasticizer. The obtained mixtures were poured into Petri dishes and dried under ambient conditions to obtain uniform polymer films. Unlike pure chitosan films, which showed negligible antibacterial activity, AgNPs-containing films produced clear inhibition zones, confirming the enhanced antimicrobial performance of the nanocomposite system. Incorporation of gentamicin into the AgNP-loaded chitosan film resulted in a further increase in antibacterial performance. This finding suggests a cooperative interaction between AgNPs and gentamicin within the chitosan matrix, resulting in improved suppression of bacterial growth (Figure 3) [52].

Several parameters affect the biological performance of chitosan–AgNPs composites, such as AgNPs size, silver concentration, degree of deacetylation of chitosan, and environmental pH [53,54]. Smaller nanoparticles possess larger surface area-to-volume ratios and exhibit stronger antimicrobial activity [55]. Increasing silver concentration generally enhances antimicrobial performance but may increase cytotoxicity [56,57]. Higher deacetylation increases amino-group density and improves electrostatic interaction with microbial cells. Under acidic conditions, increased protonation of amino groups increases the positive charge density, strengthening electrostatic interactions with microbial cells and consequently improving chitosan solubility and antimicrobial activity [58].

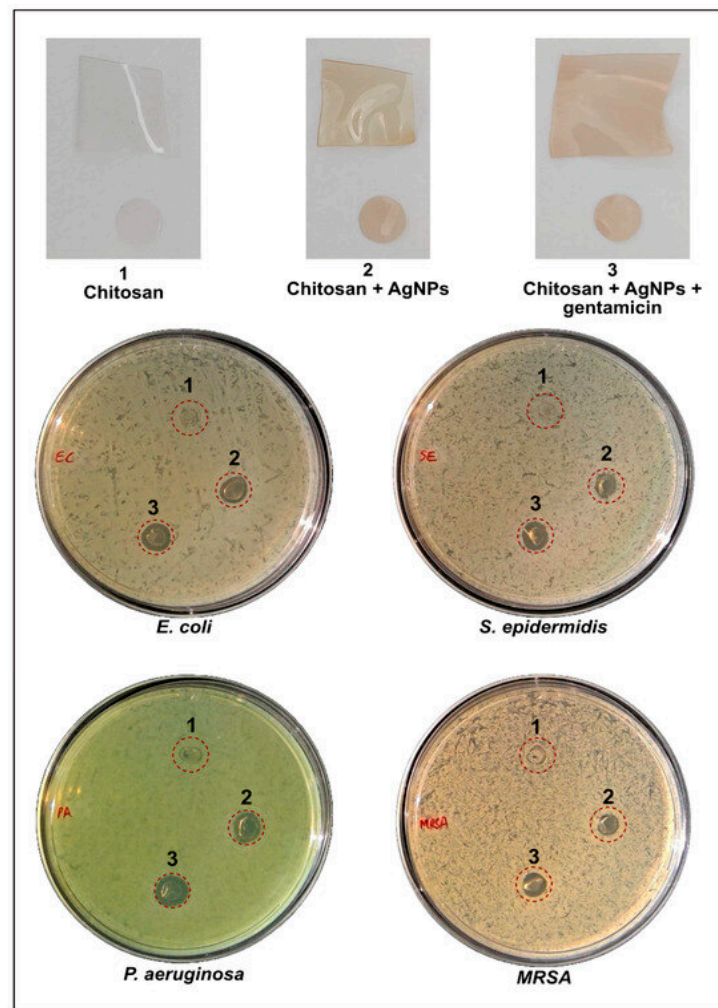


Figure 3. Images of chitosan/PVA-based films: (1) pristine chitosan/PVA, (2) chitosan/PVA containing AgNPs, and (3) chitosan/PVA containing both AgNPs and gentamicin. Antibacterial activity was evaluated by the agar disk diffusion assay against *E. coli*, *P. aeruginosa*, *S. epidermidis*, and MRSA (adapted from Ref. [52]).

Among the various nanoparticle systems investigated, chitosan composites containing AgNPs have consistently demonstrated the highest antimicrobial performance due to the multiple mechanisms by which AgNPs exert their antimicrobial action. These mechanisms include the release of Ag^+ ions, disruption of microbial cell membranes, generation of reactive oxygen species (ROS), inhibition of essential enzymatic pathways, and interference with DNA replication [59]. Consequently, chitosan–AgNPs nanocomposites often achieve rapid and highly effective microbial inactivation even at relatively low nanoparticle concentrations. However, concerns related to the high cost of silver, potential cytotoxicity towards mammalian cells, and environmental risks associated with the release of nanoparticles have motivated the exploration of alternative antimicrobial nanomaterials [59].

Incorporation of AgNPs-loaded chitosan into a β -1,3-glucan/hyaluronic acid composite, using L-ascorbic acid as the reducing agent and chitosan as both a template and stabilizer, resulted in a multifunctional wound dressing with improved biocompatibility, hemocompatibility, blood coagulation, and cell migration, while maintaining effective antibacterial activity. The optimized chitosan concentration promoted the formation of well-dispersed AgNPs with favorable physicochemical properties, while the composite matrix balanced antimicrobial performance with enhanced tissue regeneration functions, supporting its suitability for advanced wound-healing applications (Figure 4) [60].

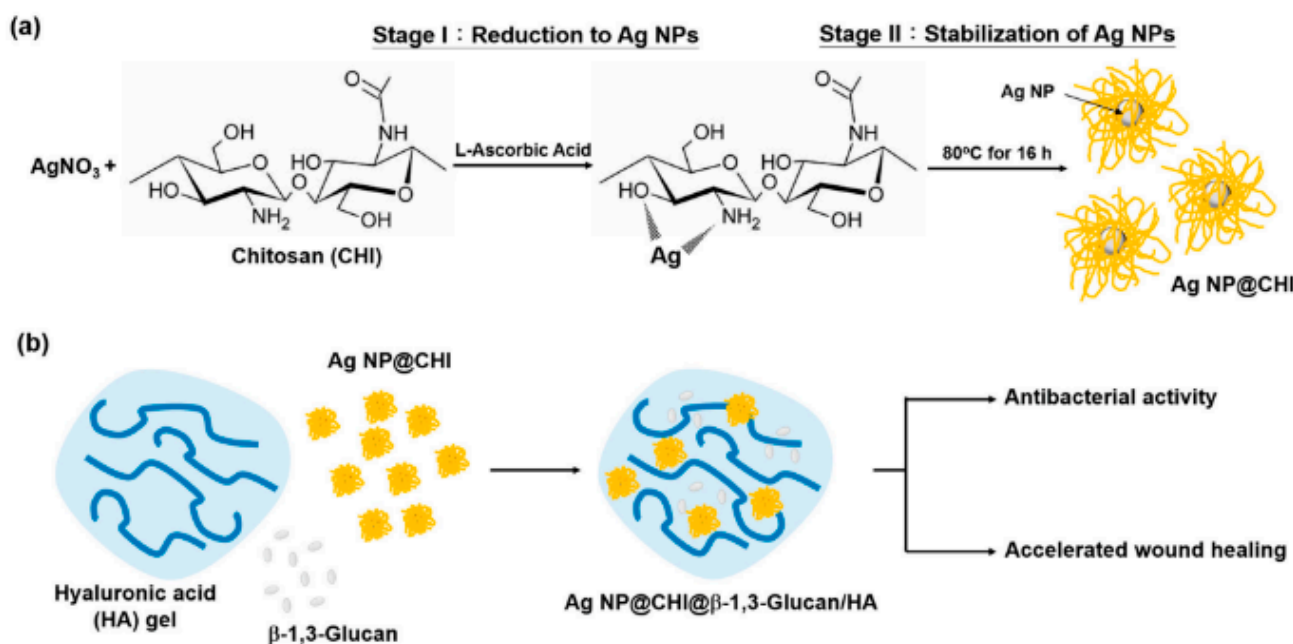


Figure 4. (a) Schematic illustration of the in situ synthesis of chitosan-stabilized AgNPs (Ag NP@CHI), where L-ascorbic acid reduces Ag^+ ions to Ag^0 and chitosan functions as both the stabilizing matrix and supporting template; (b) Preparation of the Ag NP@CHI@ β -1,3-glucan/HA composite and its intended application as an antibacterial wound dressing with enhanced healing properties (adapted from Ref. [60]).

Table 1 summarizes key parameters reported in the literature, including AgNPs size distributions, target microbial strains used in antimicrobial assays, the resulting inhibition zone diameters, and potential applications. Comparative analysis of these data reveals that the physicochemical characteristics of the nanocomposites, such as nanoparticle size, dispersion, and stabilization strategy, strongly influence their antimicrobial and antibacterial effectiveness. Among the reported preparation techniques, chemical reduction remains one of the most widely applied methods due to its simplicity, reproducibility, and ability to generate well-dispersed AgNPs within the chitosan matrix. In these approaches, silver ions are converted into metallic nanoparticles through the action of reducing agents, which may simultaneously affect nanoparticle growth kinetics and final morphology.

AgNPs were successfully synthesized within a montmorillonite/chitosan (MMT/CS) matrix through a wet chemical reduction method using chitosan solution (soluble chitosan dissolved in 1.0 wt.% acetic acid solution), AgNO_3 , and NaBH_4 (reducing agent) [61]. The incorporation of AgNPs into the interlayer and surface regions of the MMT/CS support resulted in nanoparticles with diameters ranging from approximately 6 to 10 nm. The resulting Ag/MMT/CS nanocomposites exhibited strong antibacterial activity against both Gram-positive bacteria (*S. aureus* and MRSA) and Gram-negative bacteria (*E. coli* and *P. aeruginosa*), as demonstrated by disk diffusion assays. These findings suggest that Ag/MMT/CS nanocomposites are promising materials for biomedical applications (e.g., antimicrobial coatings, drug delivery systems, and medical devices). Li et al. [62] reported that the green synthesis of AgNPs mediated by curcumin in the presence of clay minerals, such as palygorskite and montmorillonite, allowed the formation of uniformly dispersed AgNPs (30–40 nm) with enhanced antioxidant and antibacterial properties. When incorporated into chitosan films, these nanocomposites improved the water resistance and antimicrobial activity of the composites. In particular, chitosan films containing curcumin-coated AgNPs supported on mixed-dimensional palygorskite exhibited comprehensive antibacterial activity against *E. coli* and *S. aureus*, demonstrating their potential

as sustainable active packaging materials. Shinde et al. [63] developed an eco-friendly synthesis method for AgNPs and chitosan–silver bioconjugates (CS-AgNPs) using *Prunus cerasus* leaf extract. In this case, a 0.1% (*w/v*) chitosan solution was prepared by dissolving chitosan powder (derived from shrimp shells, $\geq 75\%$ deacetylated) in an aqueous solution of 1% (*v/v*) acetic acid. The cytotoxicity was evaluated on Vero cells using the 3-[4,5-dimethylthiazol-2-yl]-2,5-diphenyltetrazolium bromide (MTT) assay, while antibacterial activity was evaluated against standard ATCC strains and clinical multi-susceptible (MS) and multi-drug resistant (MDR) strains of *E. coli*, *E. faecalis*, *K. pneumoniae*, and *S. aureus* by broth microdilution and minimal inhibitory concentration (MIC) assays. CS-AgNPs demonstrated improved antibacterial activity, especially against MDR strains, lower cytotoxicity than AgNPs, and good colloidal stability, emphasizing the potential of this environmentally friendly and cost-effective synthesis approach for the development of safe antimicrobial agents. Li et al. [64] elaborated a multifunctional natural sponge based on carboxymethyl chitosan (CMC), sericin–silver nanoparticles (Ser-AgNPs), and halloysite (HNT), exhibiting favorable hygroscopicity, porosity, cytocompatibility, and hemocompatibility. The concentration of HNT was varied (0.5 g, 1 g, and 2 g). Sericin-mediated in situ synthesis of AgNPs provided effective antibacterial activity against *E. coli* and *S. aureus*. In a rat full-thickness skin defect model, the CMC/Ser-AgNPs/HNT4 sponge significantly enhanced wound healing by promoting epithelialization, collagen deposition, angiogenesis, and reducing inflammation, underlining its potential as an effective wound dressing for hemorrhagic and infected wounds.

In another study, chitosan-coated AgNPs were shown to exhibit potent antibacterial and antibiofilm activity against MRSA and *P. aeruginosa*, with greater biofilm disruption observed for *P. aeruginosa*. In addition, chitosan–AgNPs demonstrated good biocompatibility and significantly improved the antibacterial performance of wound dressings, supporting their suitability as multifunctional biomaterials for infection-controlled tissue repair [65]. Mathew et al. [66] indicated that AgNPs synthesized from silver acetate through a sol–gel approach and stabilized within functionalized chitosan exhibited notable antibacterial and antifungal activity against both bacterial (*S. aureus* and *E. coli*) and fungal (*Aspergillus flavus* (*A. flavus*) and *Aspergillus terreus* (*A. terreus*)) strains, as evidenced by significant inhibition zones in disk diffusion tests (20, 20, 20.2 and 27 mm, respectively).

Mirda et al. [67] investigated the microbial activity of AgNPs–chitosan composite particle spheres. The formation of AgNPs–chitosan spheres was achieved by combining a chitosan solution with 2% AgNO₃ solution, followed by treatment with different NaOH concentrations. During the synthesis, the appearance of a brown-to-dark brown color confirmed the in situ formation of AgNPs. As illustrated in Figure 5a, the NaOH concentration significantly affected the morphology of the resulting spheres. Samples prepared with 40% and 50% NaOH exhibited a more uniform, compact, and glossy structure (samples C and D), whereas those obtained using 20% and 30% NaOH displayed less homogeneous surfaces and inferior structural integrity (samples A and B). These findings demonstrate that increasing the NaOH concentration enhances the gelation process and contributes to the production of AgNPs–chitosan-spheres with improved morphological characteristics. The results of antimicrobial screening showed that the sample prepared with the highest concentration of NaOH exhibited the strongest inhibitory effect against *S. aureus*, *E. coli*, and *C. albicans*, producing zones of inhibition of 19.5, 18.5, and 12.2 mm, respectively (Figure 5b).

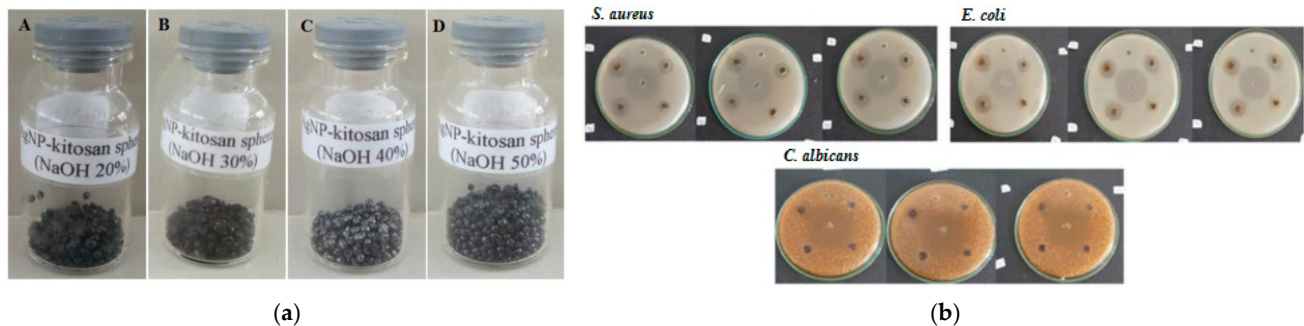


Figure 5. (a) Products of AgNPs–chitosan–spheres synthesized using different NaOH concentrations: (A) 20%; (B) 30%; (C) 40%; (D) 50%; (b) Antimicrobial efficacy of AgNPs–chitosan–spheres against *S. aureus*, *E. coli*, and *C. albicans* following 24 h of incubation time (adapted from Ref. [67]).

Carboxymethyl chitosan hydrogels loaded with AgNPs have demonstrated enhanced antibacterial activity against *E. coli* and *S. aureus* through a “kill-release” stratagem, due to the synergistic effects of the polymer matrix and the sustained release of Ag⁺ ions. Microscopic analyses have confirmed nanoparticle internalization and severe bacterial membrane damage, supporting their strong bactericidal activity. Owing to their improved antimicrobial performance, chitosan–Ag nanocomposites represent promising candidates for biomedical applications, particularly in combating antibiotic-resistant infections [68]. Shehabeldine et al. [69] investigated biological activity (antibacterial, antifungal, antibiofilm, antioxidant, and wound-healing properties) of chitosan-stabilized AgNPs. The nanoparticles, synthesized by chemical reduction in the presence of chitosan (0.2%) (produced by mixing in 0.5% acetic acid), exhibited a spherical morphology and a nanoscale size in the range of 9–65 nm, contributing to their high biological performance. Studies have shown effective inhibition of both *S. aureus* and *P. aeruginosa*, as well as antifungal activity against *Candida albicans* (*C. albicans*), *Aspergillus fumigatus* (*A. fumigatus*), *Aspergillus terreus* (*A. terreus*), and *Aspergillus niger* (*A. niger*). Moreover, the chitosan–AgNPs biofilm promoted fibroblast migration and accelerated wound closure, highlighting their potential as multifunctional nanomaterials for biomedical and wound care applications.

Table 1. Comparative analysis of chitosan–silver nanocomposites based on antimicrobial/antibacterial efficacy.

AgNPs Size (nm)	Microbes Tested	Antimicrobial/Antibacterial Activity Zone Inhibition (mm)	Potential Applications	Ref.
21.9–175.3	<i>S. aureus</i>	20.7	Antibacterial materials	[53]
6.28–9.84	<i>S. aureus</i> , <i>E. coli</i> , <i>P. aeruginosa</i> , and MRSA	8.4, 11.1, 11.3, and 11.9	Antimicrobial coatings, drug delivery systems, and medical devices	[61]
10–50	MRSA and <i>P. aeruginosa</i>	22.8 and 25.5	Wound care	[65]
-	<i>S. aureus</i> , <i>E. coli</i> , <i>A. flavus</i> , and <i>A. terreus</i>	20, 20, 20.2, and 27	Antibacterial and antifungal materials	[66]
33.6–52.3	<i>S. aureus</i> , <i>E. coli</i> , and <i>C. albicans</i>	19.5, 18.5, and 12.2	Skin infections	[67]
-	<i>E. coli</i> and <i>S. aureus</i>	25 and 19	Antibiotic-resistant infections	[68]
9–65	<i>C. albicans</i> , <i>A. fumigatus</i> , <i>A. terreus</i> , and <i>A. niger</i>	22, 29, 20, and 17	Wound-healing	[69]

In another study, chitosan-based coatings reinforced with neem (*Azadirachta indica*)-mediated AgNPs demonstrated enhanced broad-spectrum antimicrobial activity against *E. coli*, *S. aureus*, and *C. albicans*. Compared to pure chitosan, these nanocomposites exhibited significantly improved microbial inhibition due to the synergistic effects of chitosan, AgNPs, and plant-derived bioactive compounds. Their eco-friendly synthesis, prolonged antimicrobial performance, and good stability make them promising materials for biomedical devices, wound dressings, and antimicrobial surface coatings [70]. Rafiullah et al. [71] investigated different chitosan–AgNPs formulations, including chitosan beads, chitosan–AgNPs, and chitosan–Ag microbeads, to evaluate their antibacterial performance. The results demonstrated that increasing the AgNPs content (from 0.01 M to 0.16 M) significantly enhanced the antibacterial activity against *S. aureus* and *P. aeruginosa*, while a higher concentration of chitosan (0.8% *w/v*) produced only a limited effect. Among the tested formulations, chitosan–Ag microbeads exhibited the highest antimicrobial efficacy (50% higher than chitosan–AgNPs), highlighting the importance of both AgNPs loading and nanocomposite architecture in optimizing antibacterial performance.

Chicea et al. [72] determined the antibacterial effect of nanocomposites containing different chitosan concentrations (0.3% *w/v*, 0.6% *w/v*, and 0.9% *w/v*) and based on trisodium citrate dihydrate (TCS) and sodium hydroxide (SH). Antibacterial tests demonstrated that all synthesized nanocomposites were effective against both *E. coli* and *S. aureus*. The antimicrobial activity increased with decreasing AgNPs size, with the AgNP–NaOH–CH0.9 sample (46 nm) exhibiting the strongest inhibitory effect against both bacterial strains. These findings highlight the potential of the developed nanocomposites for antibacterial applications (Figure 6) [72].

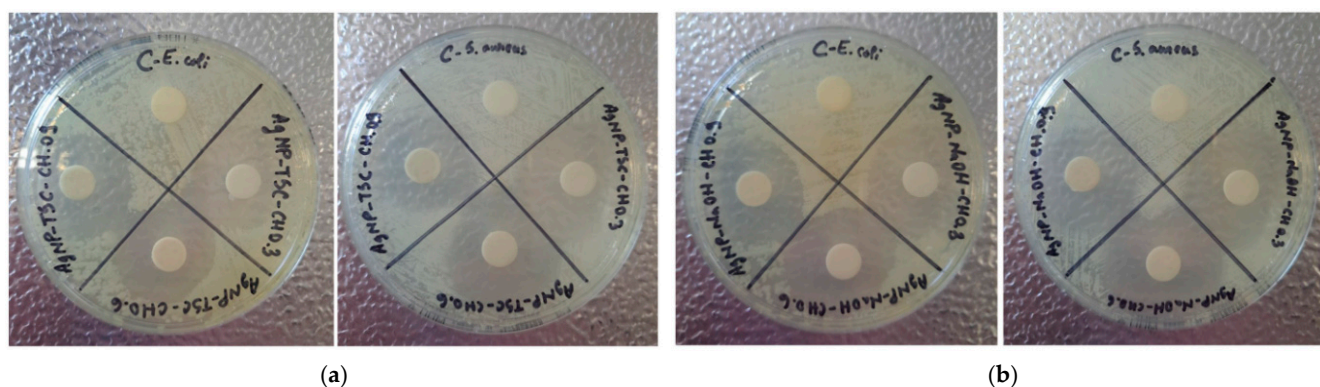


Figure 6. (a) Antibacterial test using *E. coli* and *S. aureus* strains for AgNP–TSC–CH0.3, AgNP–TSC–CH0.6, and AgNP–TSC–CH0.9; (b) antibacterial test using *E. coli* and *S. aureus* strains for AgNP–NaOH–CH0.3, AgNP–NaOH–CH0.6, and AgNP–NaOH–CH0.9 (adapted from Ref. [72]).

Current studies have indicated that AgNPs-loaded chitosan sponges combine favorable cytocompatibility with effective antimicrobial performance, making them attractive candidates for wound management applications [73,74]. In vitro investigations have consistently demonstrated satisfactory viability of skin-associated cell lines, indicating that appropriately optimized concentrations of AgNPs can preserve cellular metabolic activity while minimizing cytotoxic effects. At the same time, these composite materials exhibit broad-spectrum antibacterial activity against clinically relevant pathogens, including *S. aureus* and *E. coli*, thereby reducing the risk of bacterial colonization and biofilm formation. The synergistic interaction between the intrinsic bioactivity of chitosan and the antimicrobial properties of AgNPs contributes to accelerated wound-healing, simultaneously providing a favorable environment for tissue regeneration and preventing microbial infection. Liu et al. [73] developed chitosan/silk fibroin hybrid sponges containing AgNPs

that exhibited sustained nanoparticle release and broad-spectrum antimicrobial activity against *S. aureus*, *E. coli*, *C. albicans*, and *P. aeruginosa*. In vivo wound-healing studies demonstrated significantly improved tissue regeneration, with AgNPs-loaded sponges achieving almost complete wound closure by day 14 (99.38%) compared to the control group without nanoparticles (only 89.22%), confirming their efficacy as multifunctional wound dressings. Huang et al. [74] prepared AgNPs-incorporated chitosan sponges as antibacterial wound dressings, demonstrating potent antibacterial activity against both *S. aureus* and *E. coli*. In vitro cytocompatibility studies further confirmed that the composite sponges supported the viability of MC3T3 cells, indicating their potential suitability for wound-healing applications.

3.2. Chitosan–Zinc Oxide Composites

ZnONPs possess excellent antibacterial and antifungal properties [75–77]. The antimicrobial effect of ZnONPs is primarily attributed to the generation of reactive oxygen species, the release of Zn^{2+} ions, and direct interactions with microbial cell membranes, leading to oxidative stress and cellular damage [78]. Reactive oxygen species, such as hydroxyl radicals ($\bullet\text{OH}$), superoxide radicals ($\text{O}_2\bullet^-$), and hydrogen peroxide (H_2O_2), induce oxidative stress, damaging cellular lipids, proteins, enzymes, and nucleic acids, ultimately leading to microbial cell death. Partial dissolution of ZnONPs releases Zn^{2+} ions, which can penetrate microbial cells and interfere with enzymatic activities, metabolic pathways, and membrane functions (Figure 7) [79,80]. Elevated intracellular zinc concentrations can disrupt cellular homeostasis and inhibit microbial proliferation [81,82].

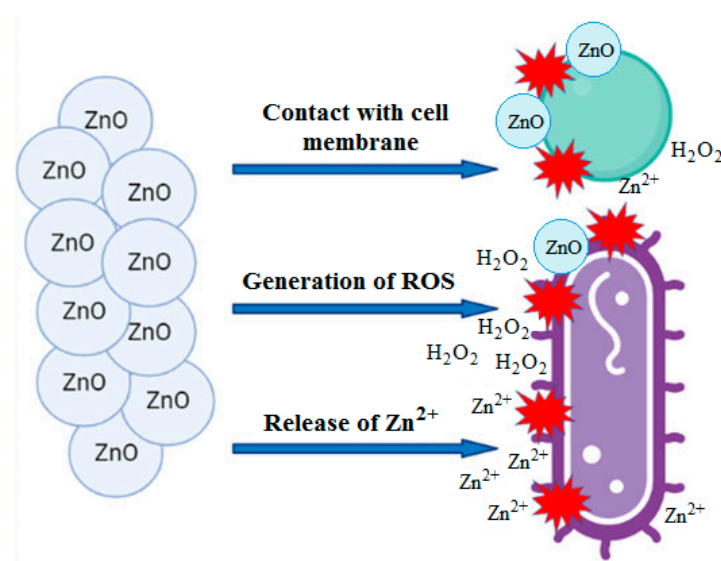


Figure 7. Schematic illustration of the proposed antibacterial mechanisms of ZnONPs, including reactive oxygen species (ROS) generation, Zn^{2+} ion release, nanoparticle internalization into bacterial cells, and electrostatic interactions leading to membrane disruption and bacterial cell death (adapted from Ref. [79]).

It has been reported that Zn^{2+} ions can be formed when chitosan and ZnO are dissolved in a dilute acetic acid solution [83]. At pH = 6–9, the unstable compound $\text{Zn}(\text{OH})_2$ is formed, as described by the following reaction (1):



Since the NH_2 and OH groups in chitosan can form coordination bonds with metal ions [84], by increasing the pH of the solution to $\text{pH} = 10$ by adding NaOH dropwise, the stable chitosan–ZnONPs complex is formed.

Chitosan–ZnO composites effectively prevent microbial adhesion and biofilm development [85]. Chitosan hinders initial surface colonization, while ZnONPs suppress the growth of attached microorganisms and disrupt established biofilms. Homogeneous dispersion of ZnONPs in the chitosan matrix improves the stability of the nanoparticles and their accessibility to the surface. As a result, the generation of reactive oxygen species occurs more efficiently, leading to more serious oxidative damage to microbial cells [86–89]. Banerjee et al. [89] synthesized ZnONPs by a solvothermal approach and prepared ZnO–chitosan biofilm using the precipitation method. The resulting material exhibited an effective bactericidal impact (~96% for *E. faecalis* and 98% for *E. coli* killing after 20 min), demonstrating its potential as a hydrophilic material for wound and burn dressings.

ZnONPs incorporated into chitosan matrices have been shown to contribute not only to antimicrobial activity but also to enhanced mechanical strength, thermal stability, and UV protection properties, making these composites particularly suitable for food packaging and biomedical applications [90–93].

Several studies have shown that sol–gel synthesized chitosan/ZnO nanocomposites exhibit synergistic properties resulting from the combination of the biocompatibility and film-forming ability of chitosan with the antimicrobial activity of ZnO nanoparticles. The homogeneous dispersion of ZnO in the chitosan matrix enhances the structural stability and antibacterial performance of the nanocomposite, making it a promising material for applications in biomedical devices, antimicrobial coatings, food packaging, and environmental remediation [94].

Rahman et al. [95] synthesized chitosan–ZnONPs composite films by solution casting technique. They reported that the obtained chitosan–ZnONPs composite films, compared to the pure chitosan film, exhibited the highest antimicrobial activity against both *S. aureus* and *E. coli*, due to the presence of ZnONPs in the matrix. It was also observed that the chitosan–ZnONPs composite films had the highest inhibition efficiency and could be applied as antimicrobial packaging materials.

Gamboa-Solana et al. [96] modified chitosan with ZnONPs and analyzed the antimicrobial activity against *S. aureus* and *S. typhimurium*. Antibacterial evaluation showed no inhibitory effect against *S. aureus* for pristine chitosan, cross-linked chitosan, or films containing 5 wt.% ZnO and 1 wt.% Cu nanoparticles. In contrast, all films exhibited antimicrobial activity against *S. typhimurium*, indicating that chitosan contributed to bacterial inhibition. These findings support the potential use of chitosan-based nanocomposites for medical and dental applications.

Ali et al. [97] developed chitosan–ZnO nanocomposites using physical and chemical synthesis methods and evaluated their antibacterial activity. Chitosan–ZnO nanocomposites were physically prepared by dissolving 1 g of chitosan in 100 mL of 1% acetic acid, followed by the addition of ZnONPs at concentrations of 5, 10, 15, and 20 wt% (CS-Z5, CS-Z10, CS-Z15, and CS-Z20) (Figure 8b). Chitosan–ZnO nanocomposites were chemically synthesized by dissolving chitosan (1 g) in 100 mL of acetic acid (1%), followed by dissolving ZnO (1 g) in 100 mL of distilled water by sonication. The two solutions were mixed and subjected to microwave irradiation at different power levels (80, 240, 560, and 800 W) for 3–10 min, resulting in samples CZ10, CZ30, CZ70, and CZ100 (Figure 8c). Figure 8a shows the morphology of pure ZnONPs and chitosan–ZnO nanocomposites. ZnONPs exhibited approximately hexagonal and spherical shapes (sample a), while both chemically and physically prepared chitosan–ZnO nanocomposites (samples b and c) exhibited uniformly dispersed crystalline ZnONPs embedded in an amorphous chitosan matrix, confirming the

successful formation of the nanocomposites. The chemically synthesized nanocomposites showed superior antibacterial performance against *S. aureus*, producing larger inhibition zones (16.4–18.7 mm) than the physically synthesized counterparts (12.2–13.8 mm). The results highlight the potential of these materials for biomedical and pharmaceutical applications, supporting the development of effective antimicrobial systems [97].

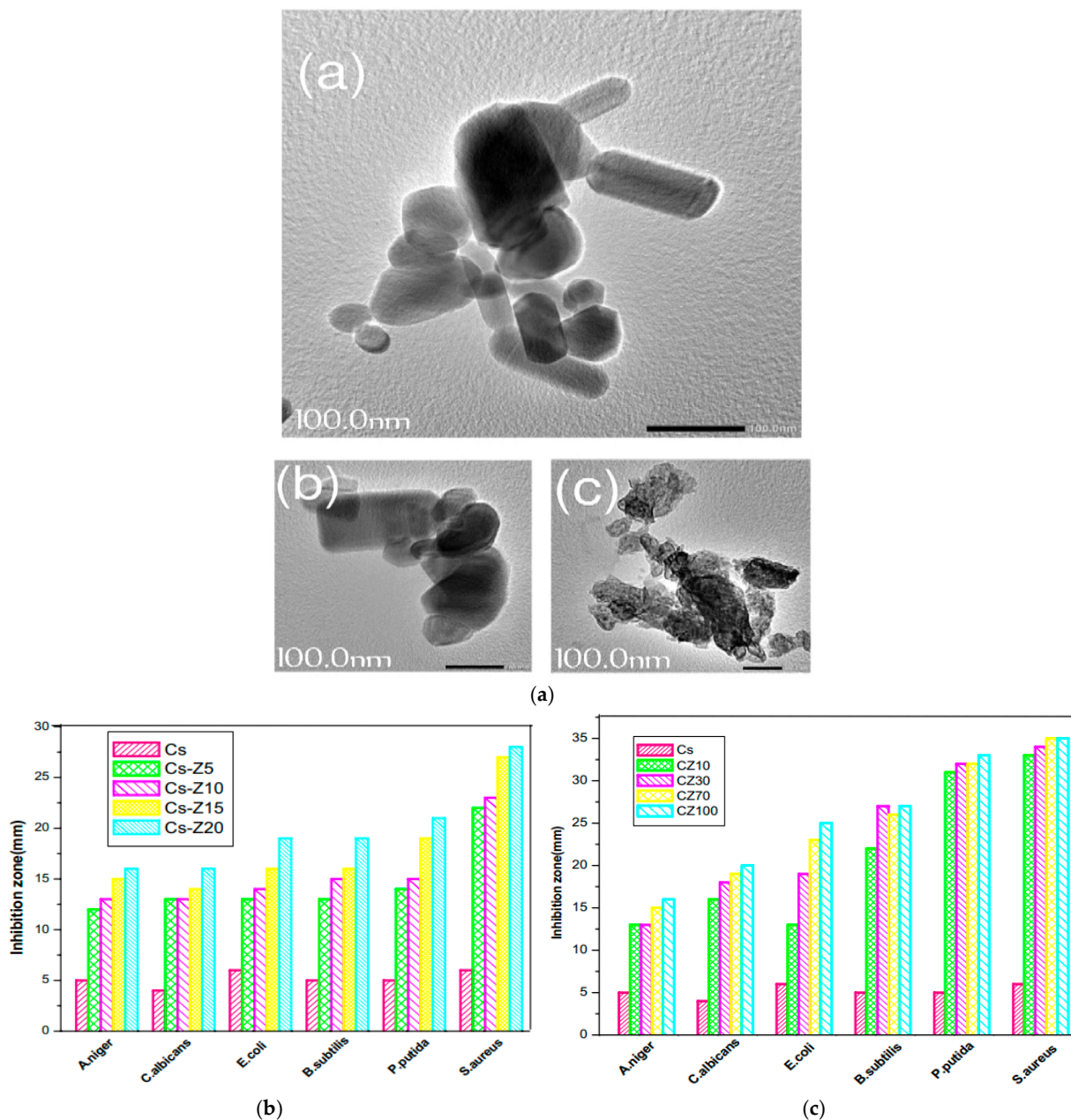


Figure 8. (a) TEM images of ZnONPs (sample a), chitosan–ZnO nanocomposites prepared chemically (sample b), chitosan–ZnO nanocomposites prepared physically (sample c); antimicrobial activity of chitosan–ZnO nanocomposites prepared: (b) physically; (c) chemically (adapted from Ref. [97]).

Umar et al. [98] reported an eco-friendly synthesis for obtaining chitosan-functionalized ZnO nanocomposites using *Moringa stenopetala* extract as a natural reducing and stabilizing agent. The proposed method is simple, cost-effective, and environmentally sustainable, avoiding toxic reagents and harsh reaction conditions. The synthesized chitosan–ZnO nanocomposites demonstrated promising antimicrobial activity against *S. typhi* and *E. coli*, and cytotoxic properties, supporting their potential use in antimicrobial applications. In

another study [99], a chitosan–ZnO nanocomposite was shown to exhibit significantly higher antibacterial activity (37 mm for *E. coli* and 34 mm for *S. aureus*) than ZnONPs alone (22 mm for *E. coli* and 27 mm for *S. aureus*), as assessed using the disk diffusion method. The enhanced inhibition, especially against *E. coli*, was attributed to the interaction of the positively charged nanocomposite with the bacterial cell surface and its enhanced penetration through the cell wall. Li et al. [100] demonstrated that the chitosan–Ag–ZnO blend films, obtained by a sol-cast transformation method, have excellent antimicrobial activities against *B. subtilis*, *E. coli*, *S. aureus*, *Penicillium*, *Aspergillus*, *Rhizopus*, and yeast colonies. They reported that the chitosan–Ag–ZnO blend films have higher antimicrobial activities than chitosan–Ag and chitosan–ZnO blend films, due to strong interaction between chitosan, Ag, and ZnO. The obtained chitosan–Ag–ZnO blend films with 0.1 wt.% Ag and 10 wt.% ZnO can be applied in the medical field. Zhang et al. [101] showed that the obtained chitosan–ZnONPs composite film had a better inhibitory effect on *S. aureus* than on *E. coli*, because *S. aureus* appertains to Gram-positive bacteria, and its cell wall included a large amount of teichoic acid. Majeed et al. [102] reported that chitosan can be chemically modified by forming a Schiff base with aromatic aldehydes and subsequently combined with ZnONPs to obtain well-dispersed nanocomposites with improved functional properties (e.g., chelation ability and high H-bonding ability). The resulting materials exhibited antimicrobial activity against *S. aureus*, *S. epidermidis*, *E. coli*, *Klebsiella* sp., and *C. albicans*, producing zones of inhibition greater than 40 mm. Their high antimicrobial efficacy is attributed to the synergistic effects of chitosan, Schiff base functional groups, and ZnONPs, which collectively promote membrane disruption, oxidative stress through the generation of reactive oxygen species, and the release of Zn^{2+} ions. These results show the potential of chitosan-Schiff base/ZnO nanocomposites as promising antimicrobial materials for biomedical applications.

Alamdari et al. [103] evaluated the antibacterial activity of the extract and green-synthesized ZnO prepared with two different amounts of plant extract (10 and 15 mL) (ZnO-G' and ZnO-G''), synthesized pure chitosan, and ZnO–chitosan (ZnO-CS) composite films against *S. aureus* and *E. coli*. Green-synthesized ZnONPs exhibited significantly higher antibacterial activity than the extract alone, with greater efficacy observed at higher extract concentrations and longer exposure times. After 6 h, bacterial reductions reached 99.9% for *S. aureus* and 97.9% for *E. coli*. Furthermore, ZnO-CS films containing green-synthesized ZnO showed clear zones of inhibition, while pure CS and films filled with chemically synthesized ZnO showed limited antibacterial effects. These findings demonstrate the superior antimicrobial performance of green-synthesized ZnO and its potential for applications in antibacterial films.

Kumar et al. [104] investigated the surface morphology and antimicrobial activity of the chitosan and gelatin nanocomposite hybrid films containing green-synthesized ZnONPs (2% and 4%) using both Gram-negative (*E. coli*) and Gram-positive bacteria (*S. aureus*). Figure 9a indicates that the nanocomposite films retained their translucent character, suggesting a homogeneous distribution of ZnONPs within the polymer matrix. Antimicrobial analysis showed that all films exhibited inhibitory effects against *E. coli*, with inhibition zone diameters ranging from 10.5 mm to 10.7 mm for ZnO concentrations of 2% and 4%, respectively. In contrast, the inhibitory effect against *S. aureus* was less pronounced, indicating a lower susceptibility of this strain to the developed films (Figure 9b). The antimicrobial performance of chitosan–gelatin–ZnONPs films emphasizes their value as active packaging materials capable of improving food preservation and extending product shelf life.

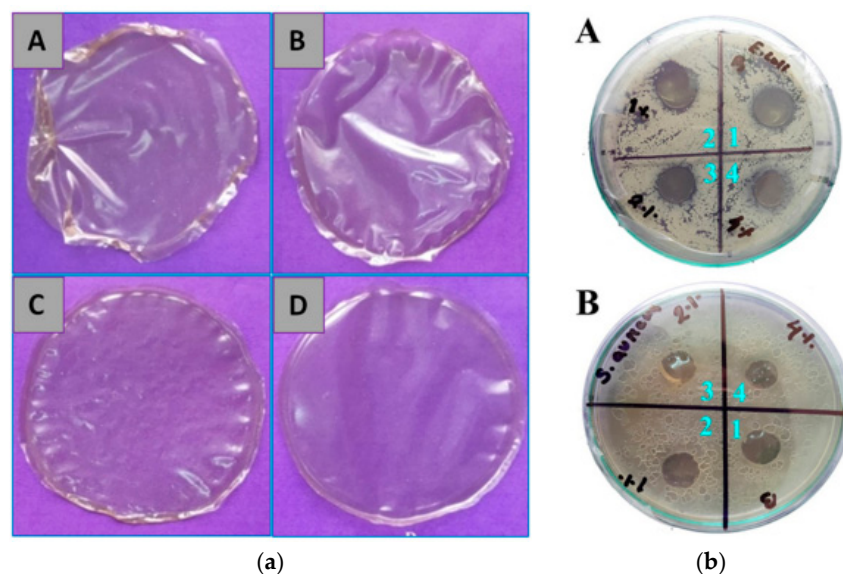


Figure 9. (a) Photographs of the hybrid films; (A) chitosan (CS)/gelatin (GL) only, (B) CS/GL/ZnO (1%), (C) CS/GL/ZnO (2%), and (D) CS/GL/ZnO (4%); (b) antimicrobial activity of the films (1) CS/GL only, (2) CS/GL/ZnO (1%), (3) CS/GL/ZnO (2%), and (4) CS/GL/ZnO (4%) against (A) *E. coli*, and (B) *S. aureus*, after 24 h incubation (adapted from Ref. [104]).

Mariyam et al. [105] incorporated 10 wt.% ZnO and 4 wt.% chitosan solution into the mineral trioxide aggregate (MTA), used as one of the essential materials in dentistry, to obtain a composite with a more compact structure and enhanced antibacterial activity against *E. faecalis* and *P. aeruginosa*. These findings suggest that ZnO–chitosan-modified MTA represents a promising approach for enhancing the performance of dental restorative materials. In another study, it was reported that ZnONPs can be successfully immobilized in a chitosan matrix by a one-step in situ sol–gel synthesis, resulting in nanocomposites with particle sizes ranging from 10 to 18 nm. The composites demonstrated improved antimicrobial activity against both *E. coli* (zone of inhibition diameter 13–15 mm) and *S. aureus* (zone of inhibition diameter 10–12 mm) compared to pure chitosan (7 mm for *E. coli* and 5 mm for *S. aureus*). Due to their biocompatibility, eco-friendly nature, and cost-effective synthesis, these nanocomposites represent a promising antimicrobial agent [106]. Dhillon et al. [107] synthesized ZnO–chitosan nanoparticles by spray drying and precipitation using natural stabilizers (citric acid, glycerol, starch, and whey powder), producing biocompatible nanocomposites. The obtained materials exhibited significant antimicrobial and antibiofilm activity against *Micrococcus luteus* and *S. aureus* ($p < 0.05$), while also showing activity against *C. albicans*. The results indicated the potential of ZnO–chitosan nanocomposites as effective antimicrobial and antibiofilm agents. Lu et al. [108] developed a microporous chitosan–Ag/ZnO composite dressing with interconnected pores (50–150 μm) that exhibited superior antibacterial activity and wound-healing performance compared with chitosan- or ZnO-based dressings alone. The incorporation of both Ag and ZnO nanoparticles promoted faster tissue regeneration, resulting in smoother skin formation and reduced scab development, emphasizing the potential of these multifunctional composites for advanced wound care. Karthikeyan et al. [109] prepared curcumin–chitosan–ZnO nanocomposites by a one-step method, exhibiting remarkable antibacterial activity against MRSA and *E. coli*, compared to commercial amoxicillin. These results showed the potent synergistic antimicrobial effect of curcumin, chitosan, and ZnONPs, supporting their potential for advanced biomedical and clinical applications. A study on chitosan–ZnO nanocomposite membrane, synthesized using a chitosan matrix and green-synthesized ZnONPs, showed that the nanocomposite exhibited enhanced antibacterial activity against

both Gram-negative *Klebsiella planticola* (*K. planticola*) and Gram-positive *B. subtilis*, with stronger inhibition observed for the Gram-negative strain. The simple room-temperature synthesis, which avoids hydrothermal treatment and calcination, provides an efficient route for the production of bioactive chitosan-based nanocomposites, with promising prospects for antimicrobial and antifouling applications in biotechnology [110]. Chitosan–alginate–gelatin and chitosan–bentonite–gelatin composite films containing ZnONPs synthesized from green plants were developed and evaluated for wound-healing applications [111]. The bentonite-based films exhibited greater flexibility, higher water absorption, and effective antibacterial activity against *S. aureus* and *P. aeruginosa*. In vivo studies on burn wounds demonstrated improved re-epithelialization, hair follicle regeneration, and overall tissue repair, indicating the superior wound-healing performance of bentonite-containing composites.

Table 2 summarizes key parameters reported in the literature, including ZnO concentration, target microbial strains used in antimicrobial/antibacterial assays, and potential applications [96,100,103–107].

Table 2. Comparative analysis of chitosan–ZnO nanocomposites based on antimicrobial/antibacterial efficacy.

ZnONPs Concentration (wt.%)	Microbes Tested	Potential Applications	Ref.
5	<i>S. aureus</i> and <i>S. typhimurium</i>	Films for medical and dental applications	[96]
10	<i>B. subtilis</i> , <i>E. coli</i> , <i>S. aureus</i> , <i>Penicillium</i> , <i>Aspergillus</i> , <i>Rhizopus</i> , and yeast colonies	Antimicrobial films for medical applications	[100]
-	<i>S. aureus</i> and <i>E. coli</i>	Antibacterial films	[103]
2 and 4	<i>E. coli</i> and <i>S. aureus</i>	Active packaging materials	[104]
10	<i>E. faecalis</i> and <i>P. aeruginosa</i>	Dental restorative material	[105]
-	<i>E. coli</i> and <i>S. aureus</i>	Antimicrobial agent	[106]
1.5	<i>Micrococcus luteus</i> , <i>S. aureus</i> , and <i>C. albicans</i>	Antimicrobial and antibiofilm agents	[107]

The results presented demonstrate that chitosan combined with ZnONPs, either alone or additionally functionalized with various bioactive compounds, represents a highly versatile platform for the development of advanced biomaterials with improved structural, physicochemical and biological properties. The incorporation of ZnONPs significantly improves the antimicrobial performance of chitosan-based systems through multiple complementary mechanisms, including the generation of reactive oxygen species (ROS), the release of Zn²⁺ ions and the disruption of microbial cell membranes, while the addition of functional molecules (e.g., amino acids, natural extracts, or Schiff base derivatives) further enhances their biological activity and functional versatility. These synergistic interactions allow the design of multifunctional wound dressings capable of preventing microbial colonization and biofilm formation, maintaining a moist wound environment, modulating inflammation, reducing oxidative stress, and promoting cell adhesion, proliferation, angiogenesis, and tissue regeneration. Beyond conventional wound care, chitosan/ZnONPs-based materials have considerable potential for a wide range of biomedical applications, including scaffolds for tissue engineering, antimicrobial coatings for medical devices and implants, and regenerative medicine. Furthermore, the tunable composition and architecture of these biomaterials make it possible to tailor their mechanical properties, degradation rate, and biological performance to specific medical requirements. Overall, the evidence summarized in this subsection highlights the growing potential of chitosan/ZnONPs-based

composites as next-generation multifunctional biomaterials, offering promising strategies for improving infection control, accelerating tissue repair, and advancing the development of innovative medical devices and regenerative therapies.

4. The Status of Approved Applications of Chitosan-Based Composites with AgNPs or ZnONPs in Biomedicine

Chitosan-based nanocomposites containing AgNPs or ZnONPs have attracted considerable interest as multifunctional biomaterials owing to their ability to combine antimicrobial protection with the intrinsic biocompatibility of chitosan. Among these systems, silver-containing formulations have progressed furthest toward clinical use because silver has long been employed as an antimicrobial agent in wound management and infection control. Incorporation of AgNPs into chitosan matrices improves nanoparticle retention, moderates silver ion release, and enhances the overall biological performance of the material [112].

Commercial medical products currently available on the market include silver-containing wound dressings, hydrogels, and antimicrobial coatings designed for burns and post-surgical wounds. In these devices, chitosan contributes hemostatic activity and supports tissue repair, whereas silver provides broad-spectrum antimicrobial protection, reducing the risk of wound infection and accelerating healing [113,114]. Nevertheless, only a limited number of approved products specifically employ engineered AgNPs dispersed within a chitosan matrix, as regulatory approval is generally granted to the finished medical device rather than to the nanocomposite itself [115,116].

ZnONPs-based chitosan composites have shown encouraging performance in experimental studies involving tissue engineering, antimicrobial dressings, drug delivery, and regenerative medicine. Besides their antimicrobial activity, ZnONPs improve the mechanical stability, thermal resistance, and ultraviolet shielding capacity of chitosan-based materials [117,118]. However, their transition to clinical practice has progressed more slowly because comprehensive evidence regarding long-term biosafety, biodistribution, and degradation remains limited. Consequently, most currently marketed zinc-containing biomaterials rely on conventional zinc compounds instead of engineered ZnONPs [119].

Because nanoparticle-containing biomaterials present additional safety considerations compared with conventional polymers, regulatory agencies require extensive characterization before clinical approval. Critical evaluation includes nanoparticle physicochemical properties, stability, release behavior, biocompatibility, toxicological profile, degradation characteristics, manufacturing reproducibility, and environmental safety throughout the product life cycle [120–122].

5. Current Challenges

Although laboratory investigations consistently demonstrate excellent antimicrobial performance [123–125], several factors continue to hinder the large-scale clinical and commercial implementation of chitosan-based nanocomposites. A major challenge is maintaining the stability of nanoparticles during fabrication and storage. Aggregation or non-uniform dispersion of metal nanoparticles can alter antimicrobial activity, mechanical properties, degradation behavior, and release kinetics, resulting in batch-to-batch variability and reduced product reliability [126].

Another critical challenge for the biomedical application of chitosan-based nanocomposites is the comprehensive assessment of their biological safety. The biological behavior of AgNPs and ZnONPs is governed by complex interactions at the nano-bio interface, where physicochemical characteristics strongly influence cellular uptake, protein corona formation, and biodistribution [127–129]. Although increasing nanoparticle loading gen-

erally enhances antimicrobial efficacy, excessive concentrations or uncontrolled release of metal ions can disrupt cellular redox homeostasis, induce oxidative stress, mitochondrial dysfunction, inflammatory signaling, and genotoxic effects, thereby compromising tissue compatibility. Consequently, optimization of nanoparticle dosage, release kinetics, and spatial distribution within the chitosan matrix is essential to achieve a favorable balance between potent antimicrobial activity and long-term biocompatibility, while ensuring the safe clinical performance of these advanced biomaterials.

Further advancement of chitosan-based antimicrobial nanocomposites is also constrained by the limited understanding of the complex molecular and physicochemical interactions responsible for microbial inactivation. Although several mechanisms have been proposed, including electrostatic disruption of microbial membranes, generation of reactive oxygen species (ROS), intracellular oxidative damage, metal ion-mediated toxicity, interference with essential metabolic pathways, and suppression of biofilm maturation [130,131], the contribution of each pathway remains highly dependent on nanoparticle properties, polymer–nanoparticle interactions, microbial physiology, and the surrounding microenvironment. Moreover, the dynamic adaptation of microbial communities following prolonged or sublethal exposure to nanoparticle-based antimicrobials represents an emerging area of concern, as microorganisms may activate stress-response pathways, modify membrane composition, enhance antioxidant defenses, or alter biofilm architecture. A deeper mechanistic understanding of these nano-microbial interactions is therefore essential for the rational optimization of next-generation chitosan nanocomposites with predictable, durable, and clinically relevant antimicrobial performance.

The economic feasibility of these materials is influenced by multiple factors, including the production of medical-grade chitosan, optimization of nanoparticle synthesis routes, energy consumption, specialized equipment, sterilization procedures, batch validation, and regulatory documentation. While ZnONPs offer advantages in terms of cost-effectiveness and availability, AgNPs-containing systems remain associated with higher manufacturing expenses due to silver-related raw material costs and more demanding safety assessments. In addition, the regulatory pathway for nanocomposite-based medical devices requires extensive preclinical evaluation, including cytotoxicity, immunological response, biodistribution studies, and long-term biosafety assessment. The limited availability of standardized evaluation protocols and the requirement for well-controlled clinical investigations further contribute to prolonged development timelines and increased investment risks. Therefore, successful commercialization will depend on the integration of scalable manufacturing strategies, regulatory harmonization, economic optimization, and comprehensive validation of clinical performance [132,133].

Environmental sustainability has become an essential consideration in the development of chitosan-based composites containing AgNPs or ZnONPs. Although chitosan represents an environmentally favorable polymer due to its biodegradability, renewable origin, and potential for utilization of marine-derived waste resources, the incorporation of AgNPs and ZnONPs introduces additional concerns regarding the environmental fate and persistence of engineered nanomaterials. During nanoparticle synthesis, composite fabrication, sterilization, clinical application, degradation, and disposal, released nanoparticles or metal ions may enter surrounding ecosystems and interact with biological components in complex ways. These interactions may influence nanoparticle transformation, mobility, dissolution behavior, and bioavailability, thereby affecting their potential impact on microorganisms, aquatic organisms, and terrestrial environments. Furthermore, the degradation of chitosan-based nanocomposites may involve simultaneous polymer decomposition and nanoparticle release, creating complex exposure scenarios that are difficult to predict using conventional toxicity models. Therefore, understanding the long-term environmental fate

of these materials requires integrated studies combining nanoparticle characterization, degradation assessment, ecotoxicological evaluation, and environmental modeling.

6. Future Perspectives

The next stage in the evolution of chitosan-based antimicrobial nanocomposites will likely be driven by improvements in material design, manufacturing technologies, and translational research. Future formulations are expected to utilize precisely engineered nanoparticles with optimized size, morphology, and surface functionality to enhance antimicrobial selectivity while minimizing unwanted biological effects.

Particular attention is being paid to multifunctional biomaterials capable of dynamically responding to pathological conditions. Stimulus-responsive systems activated by infection-associated signals, including pH changes, oxidative stress, enzymatic activity, or inflammatory mediators, can provide localized therapeutic action, improve treatment efficacy, and minimize unnecessary exposure to nanoparticles.

Future development strategies for chitosan–AgNPs and chitosan–ZnONPs composites should incorporate sustainability principles from the early stages of material design. Life cycle assessment (LCA) approaches should be employed to evaluate environmental impacts associated with raw material extraction, nanoparticle production, processing, clinical use, and end-of-life management. In parallel, the implementation of green synthesis routes, resource-efficient manufacturing processes, controlled nanoparticle immobilization within the chitosan matrix, and environmentally responsible disposal strategies may reduce potential ecological risks. Integrating environmental safety with biomedical performance will be critical for achieving sustainable commercialization of antimicrobial chitosan-based nanocomposites and ensuring their long-term compatibility with both human health requirements and ecological protection objectives.

Successful clinical implementation will depend not only on technological advances but also on stronger collaboration between researchers, clinicians, manufacturers, and regulatory agencies. International harmonization of testing methodologies, standardized biological evaluation protocols, and robust multicenter clinical trials will be essential to accelerate regulatory approval and increase confidence in nanoparticle-based biomaterials.

Ultimately, chitosan-based composites containing AgNPs and ZnONPs are expected to evolve into multifunctional therapeutic platforms that combine antimicrobial protection, tissue regeneration, immunomodulation, controlled drug delivery, and smart implant technologies. Their future impact will depend on successfully integrating scientific innovation with scalable manufacturing, regulatory compliance, economic feasibility, and environmental responsibility, thereby enabling broader implementation in regenerative medicine, wound care, implantology, and advanced biomedical engineering.

Table 3 highlights the main antimicrobial mechanism, practical advantages, limitations, technological readiness levels, and application prospects of AgNPs- versus ZnONPs-based chitosan systems.

Analyzing Table 3, it can be concluded that AgNPs-based chitosan systems remain the most technologically mature and clinically established antimicrobial biomaterials, making them suitable for commercial medical applications requiring maximum antimicrobial performance. In contrast, ZnONPs-based chitosan systems offer a more economical, biocompatible, and sustainable alternative with additional regenerative and multifunctional properties, positioning them as promising candidates for next-generation biomedical materials.

Table 3. The main antimicrobial mechanism, advantages, limitations, technological readiness levels, and application prospects of AgNPs versus ZnONPs-based chitosan systems.

Parameter	AgNPs-Based Chitosan Systems	ZnONPs-Based Chitosan Systems
Main antimicrobial mechanism	Release of Ag ⁺ ions, disruption of bacterial membranes, protein inactivation, DNA damage, ROS generation.	Release of Zn ²⁺ ions, ROS generation, membrane disruption.
Antimicrobial effectiveness	Very high; broad-spectrum activity against Gram-positive, Gram-negative bacteria and fungi, including multidrug-resistant strains.	High; broad-spectrum antibacterial and antifungal activity, generally lower potency than Ag systems.
Biocompatibility	Good at optimized AgNPs concentrations; cytotoxicity increases with excessive Ag release.	Generally good biocompatibility; zinc is an essential trace element, although high concentrations may also induce cytotoxicity.
Advantages	Exceptional antimicrobial efficacy; rapid bactericidal action; effective at low concentrations; suitable for infection-prone applications.	Lower cost; lower toxicity; good chemical stability; potential to promote wound healing and tissue regeneration.
Limitations	Higher material cost; potential cytotoxicity; risk of silver accumulation; possible environmental concerns; discoloration in some formulations.	Lower antimicrobial potency; ZnONPs aggregation can reduce effectiveness.
Technology Readiness Level	Mature technology with numerous commercial wound dressings, coatings, and medical devices.	Pilot-scale and early commercial biomedical applications; ongoing optimization for clinical translation.
Environmental Considerations	Greater environmental concern due to silver persistence and toxicity.	Generally considered more environmentally benign than silver-based systems.
Representative Applications	Antimicrobial wound dressings, implant coatings, catheters, tissue engineering scaffolds, medical textiles.	Wound dressings, tissue engineering scaffolds, antimicrobial coatings, food packaging.
Future Application Prospects	Smart wound dressings with controlled Ag ⁺ release, multifunctional antimicrobial implants, precision antimicrobial biomaterials.	Regenerative medicine, multifunctional biomaterials, hybrid nanocomposites, sustainable antimicrobial materials, responsive drug delivery systems.

7. Conclusions

Chitosan-based composites containing AgNPs or ZnONPs represent a promising class of multifunctional antimicrobial materials. Their major advantages include enhanced antimicrobial efficacy, synergistic activity, biodegradability, and multifunctionality. The synergistic interactions between chitosan and nanoparticles significantly enhance antimicrobial performance against a broad spectrum of bacteria and fungi. Silver-containing composites generally provide the highest antimicrobial activity, while ZnO systems offer attractive alternatives due to their lower toxicity and cost-effectiveness. In films and coatings, AgNPs and ZnONPs are generally well dispersed within the chitosan matrix, providing uniform antimicrobial activity and improved mechanical stability. AgNPs typically offer stronger and more rapid antibacterial effects due to the sustained release of Ag⁺ ions, whereas ZnONPs additionally impart UV-shielding, making them particularly attractive for food packaging and surface coatings. Studies have shown that hydrogels containing AgNPs are particularly suitable for infected wounds requiring rapid bacterial eradication, while hydrogels loaded with ZnONPs have the additional benefit of promoting cell proliferation

and tissue regeneration. In microspheres and nanoparticles, the biological performance depends largely on nanoparticle encapsulation efficiency and controlled release behavior. Well-designed chitosan carriers can provide sustained delivery of Ag⁺ or Zn²⁺ ions, reducing cytotoxicity while maintaining prolonged antimicrobial activity. However, challenges related to cytotoxicity, nanoparticle aggregation, environmental impact, regulatory approval, and production costs continue to limit widespread commercialization. Future developments should aim to optimize the balance between antimicrobial effectiveness, safety, sustainability, and economic feasibility, enabling broader implementation of these advanced nanocomposite materials.

Continued research aimed at optimizing composition, understanding antimicrobial mechanisms, and evaluating long-term safety will facilitate the broader implementation of these materials in biomedical, environmental, and industrial applications.

Future research should focus on the development of safer, more sustainable, and highly efficient nanocomposite systems through advanced nanoparticle engineering, green synthesis methods, smart-responsive technologies, and comprehensive in vivo evaluations. Addressing these challenges will facilitate the translation of chitosan-based antimicrobial and antibacterial nanocomposites from laboratory research to practical applications, contributing to improved infection control and public health outcomes.

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References

1. Salam, M.A.; Al-Amin, M.Y.; Salam, M.T.; Pawar, J.S.; Akhter, N.; Rabaan, A.A.; Alqumber, M.A.A. Antimicrobial Resistance: A Growing Serious Threat for Global Public Health. *Healthcare* **2023**, *11*, 1946. [[CrossRef](#)] [[PubMed](#)]
2. Caneschi, A.; Bardhi, A.; Barbarossa, A.; Zaghini, A. The Use of Antibiotics and Antimicrobial Resistance in Veterinary Medicine, a Complex Phenomenon: A Narrative Review. *Antibiotics* **2023**, *12*, 487. [[CrossRef](#)] [[PubMed](#)]
3. Gupta, R.; Sharma, S. Role of alternatives to antibiotics in mitigating the antimicrobial resistance crisis. *Indian J. Med. Res.* **2022**, *156*, 464–477. [[CrossRef](#)] [[PubMed](#)]
4. Alaoui Mdarhri, H.; Benmessaoud, R.; Yacoubi, H.; Seffar, L.; Guennouni Assimi, H.; Hamam, M.; Boussettine, R.; Filali-Ansari, N.; Lahlou, F.A.; Diawara, I.; et al. Alternatives Therapeutic Approaches to Conventional Antibiotics: Advantages, Limitations and Potential Application in Medicine. *Antibiotics* **2022**, *11*, 1826. [[CrossRef](#)] [[PubMed](#)]
5. Pires, P.C.; Mascarenhas-Melo, F.; Pedrosa, K.; Lopes, D.; Lopes, J.; Macário-Soares, A.; Peixoto, D.; Giram, P.S.; Veiga, F.; Paiva-Santos, A.C. Polymer-based biomaterials for pharmaceutical and biomedical applications: A focus on topical drug administration. *Eur. Polym. J.* **2023**, *187*, 111868. [[CrossRef](#)]
6. Abdulsalam, L.; Abubakar, S.; Permatasari, I.; Lawal, A.A.; Uddin, S.; Ullah, S.; Ahmad, I. Advanced Biocompatible and Biodegradable Polymers: A Review of Functionalization, Smart Systems, and Sustainable Applications. *Polymers* **2025**, *17*, 2901. [[CrossRef](#)] [[PubMed](#)]
7. Xie, H.; Li, S.; Tian, H.; Lou, Y.; Ouyang, Y.; Wu, M.; Song, X. Modifying polysaccharides to realized advanced function of novel food packaging materials. *Trends Food Sci. Technol.* **2025**, *163*, 105195. [[CrossRef](#)]

8. Amponsah, O.; Nopuo, P.S.A.; Manga, F.A.; Catli, N.B.; Labus, K. Future-Oriented Biomaterials Based on Natural Polymer Resources: Characteristics, Application Innovations, and Development Trends. *Int. J. Mol. Sci.* **2025**, *26*, 5518. [[CrossRef](#)] [[PubMed](#)]
9. Madhusudanan, M.; Zhang, J.; Pandit, S.; Singh, P.; Jeong, G.-J.; Khan, F.; Mijakovic, I. Green Synthesis of Silver Nanoparticles: A Review of Polymer and Antimicrobial Drug Combinations for Enhanced Antimicrobial Applications. *Adv. NanoBiomed Res.* **2025**, *5*, 2400194. [[CrossRef](#)]
10. Zhang, L.; Zhang, Y.; Li, W.; Zhou, Y.; Guo, R.; Pei, X.; Xie, J. Chitosan and its functional derivatives for nutraceutical delivery: Focus on quaternized, hydrochloride, and carboxymethyl forms. *Trends Food Sci. Technol.* **2025**, *164*, 105237. [[CrossRef](#)]
11. Morin-Crini, N.; Lichtfouse, E.; Torri, G.; Crini, G. Applications of chitosan in food, pharmaceuticals, medicine, cosmetics, agriculture, textiles, pulp and paper, biotechnology, and environmental chemistry. *Environ. Chem. Lett.* **2019**, *17*, 1667–1692. [[CrossRef](#)]
12. Yu, B.H.; van de Pas, R.; Zahidi, I. Polylactic Acid (PLA), Polycaprolactone (PCL), and Chitosan: The Biodegradable Transition in Medical Waste Management. *Adv. Sustain. Syst.* **2025**, *9*, e00636. [[CrossRef](#)]
13. Calderon Moreno, J.M.; Chelu, M.; Popa, M. Biocompatible Stimuli-Sensitive Natural Hydrogels: Recent Advances in Biomedical Applications. *Gels* **2025**, *11*, 993. [[CrossRef](#)] [[PubMed](#)]
14. De Giorgio, G.; Matera, B.; Vurro, D.; Manfredi, E.; Galstyan, V.; Tarabella, G.; Ghezzi, B.; D'Angelo, P. Silk Fibroin Materials: Biomedical Applications and Perspectives. *Bioengineering* **2024**, *11*, 167. [[CrossRef](#)] [[PubMed](#)]
15. Mura, P.; Maestrelli, F.; Cirri, M.; Mennini, N. Multiple Roles of Chitosan in Mucosal Drug Delivery: An Updated Review. *Mar. Drugs* **2022**, *20*, 335. [[CrossRef](#)] [[PubMed](#)]
16. Davodabadi, F.; Sargazi, S.; Bairo, F. Recent advances in hydrogel-based drug delivery systems for enhanced cancer therapy: A review. *Mater. Today Commun.* **2025**, *48*, 113615. [[CrossRef](#)]
17. Tiwari, G.; Shirsat, V.; Gupta, M.; Tiwari, R.; Tewari, V.; Ramachandran, V. Chitosan in Drug Delivery Systems and Tissue Engineering: Versatile Prospects. *Pharmacogn. Res.* **2025**, *18*, 17–35. [[CrossRef](#)]
18. Rajinikanth, B.S.; Rajkumar, D.K.K. Chitosan-Based Biomaterial in Wound Healing: A Review. *Cureus* **2024**, *16*, e55193. [[CrossRef](#)] [[PubMed](#)]
19. Khubiev, O.; Egorov, A.; Anatoly, K.; Khrustalev, V.; Tskhovrebov, A.; Kritchenkov, A. Chitosan-Based Antibacterial Films for Biomedical and Food Applications. *Int. J. Mol. Sci.* **2023**, *24*, 10738. [[CrossRef](#)] [[PubMed](#)]
20. Biswas, R.; Mondal, S.; Ansari, M.A.; Sarkar, T.; Condiuc, I.P.; Trifas, G.; Atanase, L.I. Chitosan and Its Derivatives as Nanocarriers for Drug Delivery. *Molecules* **2025**, *30*, 1297. [[CrossRef](#)] [[PubMed](#)]
21. Dumitru, C.D.; Ilie, C.-I.; Neacșu, I.A.; Moteliță, L.; Oprea, O.; Totan, A.; Pițuru, S.; Bălașea, B.V.; Marinescu, F.; Andronescu, E. Antimicrobial Composite Films Based on Alginate–Chitosan with Honey, Propolis, Royal Jelly and Green-Synthesized Silver Nanoparticles. *Int. J. Mol. Sci.* **2025**, *26*, 6809. [[CrossRef](#)] [[PubMed](#)]
22. Tamer, T.M.; Hassan, M.A.; Omer, A.M.; Valachová, K.; Eldin, M.S.M.; Collins, M.N.; Šoltés, L. Antibacterial and antioxidative activity of O-amine functionalized chitosan. *Carbohydr. Polym.* **2017**, *169*, 441–450. [[CrossRef](#)] [[PubMed](#)]
23. Confederat, L.G.; Tuchilus, C.G.; Dragan, M.; Sha'at, M.; Dragostin, O.M. Preparation and antimicrobial activity of chitosan and its derivatives: A concise review. *Molecules* **2021**, *26*, 3694. [[CrossRef](#)] [[PubMed](#)]
24. Hipalaswini, W.M.B.; Jagadeeswari, S. Synthesis, characterization and antibacterial activity of chitosan nanoparticles and its impact on seed germination. *J. Acad. Ind. Res.* **2016**, *5*, 65.
25. Pellis, A.; Guebitz, G.M.; Nyanhongo, G.S. Chitosan: Sources, Processing and Modification Techniques. *Gels* **2022**, *8*, 393. [[CrossRef](#)] [[PubMed](#)]
26. Bui, V.K.H.; Park, D.; Lee, Y.C. Chitosan Combined with ZnO, TiO₂ and Ag Nanoparticles for Antimicrobial Wound Healing Applications: A Mini Review of the Research Trends. *Polymers* **2017**, *9*, 21. [[CrossRef](#)] [[PubMed](#)]
27. Franco, D.; Calabrese, G.; Guglielmino, S.P.P.; Conoci, S. Metal-Based Nanoparticles: Antibacterial Mechanisms and Biomedical Application. *Microorganisms* **2022**, *10*, 1778. [[CrossRef](#)] [[PubMed](#)]
28. Huq, M.A.; Ashrafudoulla, M.; Rahman, M.M.; Balusamy, S.R.; Akter, S. Green Synthesis and Potential Antibacterial Applications of Bioactive Silver Nanoparticles: A Review. *Polymers* **2022**, *14*, 742. [[CrossRef](#)] [[PubMed](#)]
29. Alshameri, A.W.; Owais, M. Antibacterial and cytotoxic potency of the plant-mediated synthesis of metallic nanoparticles Ag NPs and ZnO NPs: A review. *OpenNano* **2022**, *8*, 100077. [[CrossRef](#)]
30. Kavitha, A.; Doss, A.; Praveen Pole, R.P.; Kumari Pushpa Rani, T.P.; Prasad, R.; Sathesh, S. A mini review on plant-mediated zinc oxide nanoparticles and their antibacterial potency. *Biocatal. Agric. Biotechnol.* **2023**, *48*, 102654. [[CrossRef](#)]
31. Lebaka, V.R.; Ravi, P.; Reddy, M.C.; Thummala, C.; Mandal, T.K. Zinc Oxide Nanoparticles in Modern Science and Technology: Multifunctional Roles in Healthcare, Environmental Remediation, and Industry. *Nanomaterials* **2025**, *15*, 754. [[CrossRef](#)] [[PubMed](#)]
32. Lakshmi Priya, T.; Gopinath, S.C.B.; Rajasingam, M.; Arun, S.I.; Fakhri, M.A.; Salim, E.T. Advancements with Zinc Oxide Nanomaterials: From Green Chemistry to Biomedical Applications. *BioNanoScience* **2026**, *16*, 310. [[CrossRef](#)]

33. Kulka, K.; Szmejkowska, A.; Sionkowska, A.; Wypij, M.; Golińska, P. Materials based on chitosan enriched with zinc nanoparticles for potential applications on the skin. *Eng. Biomater.* **2022**, *167*, 24–31. [\[CrossRef\]](#)
34. Krishnan, S.; Prokhorov, Y.; Hernández-Iturriaga, M.; Mota-Morales, J.; Vazquez-Lepe, M.; Kovalenko, Y.; Sanchez, I.; Luna-Barcenas, G. Chitosan/silver nanocomposites: Synergistic antibacterial action of silver nanoparticles and silver ions. *Eur. Polym. J.* **2015**, *67*, 242–251. [\[CrossRef\]](#)
35. Tayel, A.A.; El-Tras, W.F.; Moussa, S.; El-Baz, A.F.; Mahrous, H.; Salem, M.F.; Brimer, L. Antibacterial action of zinc oxide nanoparticles against foodborne pathogens. *J. Food Saf.* **2011**, *31*, 211–218. [\[CrossRef\]](#)
36. Bagheri, M.; Validi, M.; Gholipour, A.; Makvandi, P.; Sharifi, E. Chitosan nanofiber biocomposites for potential wound healing applications: Antioxidant activity with synergic antibacterial effect. *Bioeng. Transl. Med.* **2021**, *7*, e10254. [\[CrossRef\]](#) [\[PubMed\]](#)
37. Hu, M.; Li, C.; Li, X.; Zhou, M.; Sun, J.; Sheng, F.; Shi, S.; Lu, L. Zinc oxide/silver bimetallic nanoencapsulated in PVP/PCL nanofibres for improved antibacterial activity. *Artif. Cells Nanomed. Biotechnol.* **2018**, *46*, 1248–1257. [\[CrossRef\]](#) [\[PubMed\]](#)
38. Perinelli, D.R.; Fagioli, L.; Campana, R.; Lam, J.K.W.; Baffone, W.; Palmieri, G.F.; Casettari, L.; Bonacucina, G. Chitosan-based nanosystems and their exploited antimicrobial activity. *Eur. J. Pharm. Sci.* **2018**, *117*, 8–20. [\[CrossRef\]](#) [\[PubMed\]](#)
39. Xing, Y.; Wang, X.; Guo, X.; Yang, P.; Yu, J.; Shui, Y.; Chen, C.; Xuanlin, L.; Xu, Q.; Xu, L.; et al. Comparison of Antimicrobial Activity of Chitosan Nanoparticles against Bacteria and Fungi. *Coatings* **2021**, *11*, 769. [\[CrossRef\]](#)
40. Reshad, R.A.I.; Jishan, T.A.; Chowdhury, N.N. Chitosan and its Broad Applications: A Brief Review. *J. Clin. Exp. Investig.* **2021**, *12*, em00779. [\[CrossRef\]](#)
41. Cheung, R.C.F.; Ng, T.B.; Wong, J.H.; Chan, W.Y. Chitosan: An Update on Potential Biomedical and Pharmaceutical Applications. *Mar. Drugs* **2015**, *13*, 5156–5186. [\[CrossRef\]](#) [\[PubMed\]](#)
42. Shukla, R.; Vasdev, N.; Ruwali, M.; Hasnain, M.S.; Beg, S. Chapter 17—Chitosan for Delivery of Biomolecules. In *Chitosan in Drug Delivery*; Hasnain, M.S., Beg, S., Nayak, A.K., Eds.; Academic Press: Cambridge, MA, USA, 2022; pp. 433–460.
43. Rege, P.R.; Block, L.H. Chitosan processing: Influence of process parameters during acidic and alkaline hydrolysis and effect of the processing sequence on the resultant chitosan's properties. *Carbohydr. Res.* **1999**, *321*, 235–245. [\[CrossRef\]](#)
44. De Queiroz Antonino, R.S.C.M.; Lia Fook, B.R.P.; De Oliveira Lima, V.A.; De Farias Rached, R.Í.; Lima, E.P.N.; Da Silva Lima, R.J.; Peniche Covas, C.A.; Lia Fook, M.V. Preparation and Characterization of Chitosan Obtained from Shells of Shrimp (*Litopenaeus vannamei* Boone). *Mar. Drugs* **2017**, *15*, 141. [\[CrossRef\]](#) [\[PubMed\]](#)
45. Ke, C.-L.; Deng, F.-S.; Chuang, C.-Y.; Lin, C.-H. Antimicrobial Actions and Applications of Chitosan. *Polymers* **2021**, *13*, 904. [\[CrossRef\]](#) [\[PubMed\]](#)
46. Yan, D.; Li, Y.; Liu, Y.; Li, N.; Zhang, X.; Yan, C. Antimicrobial Properties of Chitosan and Chitosan Derivatives in the Treatment of Enteric Infections. *Molecules* **2021**, *26*, 7136. [\[CrossRef\]](#) [\[PubMed\]](#)
47. Sahariah, P.; Hjálmarsson, M.; Másson, M. Chapter: 25—Antimicrobial properties of chitosan and chitosan derivatives. In *Marine Glycobiology: Principles and Applications*; Kim, S.-K., Ed.; CRC Press: Boca Raton, FL, USA; Taylor & Francis Group: Abingdon, UK, 2016.
48. Tiwary, A.K.; Sapra, B.; Kaur, G.; Rana, V. Chitosan: Manufacture, Properties and Usage. In *Chitosan: Modifications and Applications in Dosage Form Design*; Nova Science Publishers: New York, NY, USA, 2011; pp. 71–132.
49. Mawazi, S.M.; Kumar, M.; Ahmad, N.; Ge, Y.; Mahmood, S. Recent Applications of Chitosan and Its Derivatives in Antibacterial, Anticancer, Wound Healing, and Tissue Engineering Fields. *Polymers* **2024**, *16*, 1351. [\[CrossRef\]](#) [\[PubMed\]](#)
50. Pokhrel, S.; Yadav, P.N. Functionalization of Chitosan Polymer and Their Applications. *J. Macromol. Sci. Part A* **2019**, *56*, 450–475. [\[CrossRef\]](#)
51. Khalifa, H.O.; Oreiby, A.; Mohammed, T.; Abdelhamid, M.A.A.; Sholkamy, E.N.; Hashem, H.; Fereig, R.M. Silver nanoparticles as next-generation antimicrobial agents: Mechanisms, challenges, and innovations against multidrug-resistant bacteria. *Front. Cell. Infect. Microbiol.* **2025**, *15*, 1599113. [\[CrossRef\]](#) [\[PubMed\]](#)
52. Madhusudan, M.; Singh, P.; Ghai, V.; Pandit, S.; Kádár, R.; Mijakovic, I. A Novel Approach to Combating Antibiotic Resistance: A Chitosan-Based Nanocomposite with Green AgNPs and Gentamicin. *Int. J. Mol. Sci.* **2026**, *27*, 1036. [\[CrossRef\]](#) [\[PubMed\]](#)
53. Honary, S.; Ghajar, K.; Khazaeli, P.; Shalchian, P. Preparation, characterization and antibacterial properties of silver-chitosan nanocomposites using different molecular weight grades of chitosan. *Trop. J. Pharm. Res.* **2011**, *10*, 69–74. [\[CrossRef\]](#)
54. Zienkiewicz-Strzałka, M.; Deryło-Marczewska, A.; Skorik, Y.A.; Petrova, V.A.; Choma, A.; Komaniecka, I. Silver Nanoparticles on Chitosan/Silica Nanofibers: Characterization and Antibacterial Activity. *Int. J. Mol. Sci.* **2020**, *21*, 166. [\[CrossRef\]](#) [\[PubMed\]](#)
55. Fahim, M.; Shahzaib, A.; Nishat, N.; Jahan, A.; Bhat, T.A.; Inam, A. Green Synthesis of Silver Nanoparticles: A Comprehensive Review of Methods, Influencing Factors, and Applications. *JCIS Open* **2024**, *16*, 100125. [\[CrossRef\]](#)
56. Yin, I.X.; Zhang, J.; Zhao, I.S.; Mei, M.L.; Li, Q.; Chu, C.H. The Antibacterial Mechanism of Silver Nanoparticles and Its Application in Dentistry. *Int. J. Nanomed.* **2020**, *15*, 2555–2562. [\[CrossRef\]](#) [\[PubMed\]](#)
57. Ma, Z.; Garrido-Maestu, A.; Jeong, K.C. Application, Mode of Action, and in Vivo Activity of Chitosan and Its Micro- and Nanoparticles as Antimicrobial Agents: A Review. *Carbohydr. Polym.* **2017**, *176*, 257–265. [\[CrossRef\]](#) [\[PubMed\]](#)

58. Nasaj, M.; Chehelgerdi, M.; Asghari, B.; Ahmadih-Yazdi, A.; Asgari, M.; Kabiri-Samani, S.; Sharifi, E.; Arabestani, M. Factors influencing the antimicrobial mechanism of chitosan action and its derivatives: A review. *Int. J. Biol. Macromol.* **2024**, *277*, 134321. [[CrossRef](#)] [[PubMed](#)]
59. Shumaila, M.; Shaukat, A.; Samaira, M.; Tafail, A.M.; Hafz, M.T.; Hafz, A.S. Chitosan conjugated silver nanoparticles: The versatile antibacterial agents. *Polym. Bull.* **2023**, *80*, 4719–4736. [[CrossRef](#)]
60. Yao, C.-J.; Yang, S.-J.; Shieh, M.-J.; Young, T.-H. Development of a Chitosan-Silver Nanocomposite/ β -1,3-Glucan/Hyaluronic Acid Composite as an Antimicrobial System for Wound Healing. *Polymers* **2025**, *17*, 350. [[CrossRef](#)] [[PubMed](#)]
61. Shameli, K.; Bin Ahmad, M.; Zargar, M.; Yunus, W.M.; Ibrahim, N.A.; Shabanzadeh, P.; Moghaddam, M.G. Synthesis and characterization of silver/montmorillonite/chitosan bionanocomposites by chemical reduction method and their antibacterial activity. *Int. J. Nanomed.* **2011**, *6*, 271–284. [[CrossRef](#)] [[PubMed](#)]
62. Li, S.; Mu, B.; Zhang, H.; Kang, Y.; Wang, A. Incorporation of silver nanoparticles/curcumin/clay minerals into chitosan film for enhancing mechanical properties, antioxidant and antibacterial activity. *Int. J. Biol. Macromol.* **2022**, *223*, 779–789. [[CrossRef](#)] [[PubMed](#)]
63. Shinde, S.; Folliero, V.; Chianese, A.; Zannella, C.; De Filippis, A.; Rosati, L.; Prisco, M.; Falanga, A.; Mali, A.; Galdiero, M.; et al. Synthesis of Chitosan-Coated Silver Nanoparticle Bioconjugates and Their Antimicrobial Activity against Multidrug-Resistant Bacteria. *Appl. Sci.* **2021**, *11*, 9340. [[CrossRef](#)]
64. Li, S.; Jiang, M.; Zhang, Y.; Xie, X.; Li, W.; Ming, P.; Jiang, X.; Yang, B.; He, Y.; Chen, J.; et al. Multi-functional carboxymethyl chitosan/sericin protein/halloysite composite sponge with efficient antibacterial and hemostatic properties for accelerating wound healing. *Int. J. Biol. Macromol.* **2023**, *234*, 123357. [[CrossRef](#)] [[PubMed](#)]
65. Vijayakumar, S.; Malaikozhundan, B.; Parthasarathy, A.; Saravanakumar, K.; Wang, M.-H.; Vaseeharan, B. Nano Biomedical Potential of Biopolymer Chitosan-Capped Silver Nanoparticles with Special Reference to Antibacterial, Antibiofilm, Anticoagulant and Wound Dressing Material. *J. Clust. Sci.* **2020**, *31*, 355–366. [[CrossRef](#)]
66. Mathew, T.V.; Kuriakose, S. Photochemical and antimicrobial properties of silver nanoparticle-encapsulated chitosan functionalized with photoactive groups. *Mater. Sci. Eng. C* **2013**, *33*, 4409–4415. [[CrossRef](#)] [[PubMed](#)]
67. Mirda, E.; Idroes, R.; Khairan, K.; Tallei, T.E.; Ramli, M.; Earlia, N.; Maulana, A.; Idroes, G.M.; Muslem, M.; Jalil, Z. Synthesis of Chitosan-Silver Nanoparticle Composite Spheres and Their Antimicrobial Activities. *Polymers* **2021**, *13*, 3990. [[CrossRef](#)] [[PubMed](#)]
68. Devi, N.; Pandey, S.K.; Wangoo, N. Cationic carboxymethyl chitosan nanofibers embedded with silver nanoparticles for enhanced antibacterial applications. *Biophys. Chem.* **2026**, *328*, 107537. [[CrossRef](#)] [[PubMed](#)]
69. Shehabeldine, A.M.; Salem, S.S.; Ali, O.M.; Abd-Elsalam, K.A.; Elkady, F.M.; Hashem, A.H. Multifunctional Silver Nanoparticles Based on Chitosan: Antibacterial, Antibiofilm, Antifungal, Antioxidant, and Wound-Healing Activities. *J. Fungi* **2022**, *8*, 612. [[CrossRef](#)] [[PubMed](#)]
70. Manan, K.; Inzimam, U.H.; Basit, S.; Nisar, A.; Sabia, R.; Ansaal, K.R.; Faran, D.; Zainab, S.; Zubair, S. Chitosan-based antimicrobial coating with plant-mediated nanoparticles for biomedical and surface protection applications. *J. Med. Health Sci. Rev.* **2025**, *2*, 1249–1266. [[CrossRef](#)]
71. Rafiullah, M.; Akbardeen, M.; Jayavanth, S.; Al-Rubeaan, K. Chitosan Silver Nanocomposites and Their Antimicrobial Activity. *J. Diabetes Treat.* **2018**, *2018*, 1–5. [[CrossRef](#)]
72. Chicea, D.; Nicolae-Maranciuc, A.; Chicea, L.-M. Silver Nanoparticles-Chitosan Nanocomposites: A Comparative Study Regarding Different Chemical Syntheses Procedures and Their Antibacterial Effect. *Materials* **2024**, *17*, 1113. [[CrossRef](#)] [[PubMed](#)]
73. Liu, J.; Qian, Z.; Shi, Q.; Yang, S.; Wang, Q.; Liu, B.; Xu, J.; Guo, X.; Liu, H. An asymmetric wetttable chitosan–silk fibroin composite dressing with fixed silver nanoparticles for infected wound repair: In vitro and in vivo evaluation. *RSC Adv.* **2017**, *7*, 43909. [[CrossRef](#)]
74. Huang, X.; Bao, X.; Wang, Z. A novel silver-loaded chitosan composite sponge with sustained silver release as a long-lasting antimicrobial dressing. *RSC Adv.* **2017**, *7*, 34655. [[CrossRef](#)]
75. Ouzakar, S.; Senhaji, N.S.; Saidi, M.Z.; Hadri, M.E.; Baaboua, A.E.; Harsal, A.E.; Abrini, J. Antibacterial and antifungal activity of zinc oxide nanoparticles produced by *Phaeodactylum tricornutum* culture supernatants and their potential application to extend the shelf life of sweet cherry (*Prunus avium* L.). *Biocatal. Agric. Biotechnol.* **2023**, *49*, 102666. [[CrossRef](#)]
76. Majeed, S.; Rozali, B.A.B.; Muthukumarasamy, R.; Zakariya, N.A. Green synthesized zinc oxid nanoparticles: Antibacterial, antifungal, and antioxidant activities against multidrug-resistant pathogens. *Next Res.* **2026**, *11*, 102039. [[CrossRef](#)]
77. Jiang, J.; Pi, J.; Cai, J. The advancing of zinc oxide nanoparticles for biomedical applications. *Bioinorg. Chem. Appl.* **2018**, *2018*, 1062562. [[CrossRef](#)] [[PubMed](#)]
78. Perumal, M.K.K.; Rajasekaran, M.B.S.; Renuka, R.R.; Samrot, A.V.; Nagarajan, M. Zinc oxide nanoparticles and their nanocomposites as an imperative coating for smart food packaging. *Appl. Food Res.* **2025**, *5*, 100849. [[CrossRef](#)]

79. Ahamad Khan, M.; Lone, S.A.; Shahid, M.; Zeyad, M.T.; Syed, A.; Ehtram, A.; Elgorban, A.M.; Verma, M.; Danish, M. Phyto-genically Synthesized Zinc Oxide Nanoparticles (ZnO-NPs) Potentially Inhibit the Bacterial Pathogens: In Vitro Studies. *Toxics* **2023**, *11*, 452. [\[CrossRef\]](#) [\[PubMed\]](#)
80. Jafari Sales, A.; Ghahremani, Z.; Golestani, A.; Pashazadeh, M. A review of the antibacterial properties of zinc oxide nanoparticles: Synthesis, mechanism of action, and medical applications. *Int. J. Biophoton. Biomed. Eng.* **2025**, *5*, 29–44. [\[CrossRef\]](#)
81. Sirelkhatim, A.; Mahmud, S.; Seeni, A.; Kaus, N.H.M.; Ann, L.C.; Bakhori, S.K.M.; Hasan, H.; Mohamad, D. Review on Zinc Oxide Nanoparticles: Antibacterial Activity and Toxicity Mechanism. *Nanomicro. Lett.* **2015**, *7*, 219–242. [\[CrossRef\]](#) [\[PubMed\]](#)
82. Jefri, O.A.; Majeed, S.; Danish, M.; Alam, M.G.; Latif, S.; Alanazi, A.M. Multifunctional role of ZnO nanoparticles: Antibacterial, antifungal, synergistic, antioxidant, and dye degradation properties. *J. Taibah Univ. Sci.* **2026**, *20*, 2627090. [\[CrossRef\]](#)
83. AbdElhady, M.M. Preparation and Characterization of Chitosan/Zinc Oxide Nanoparticles for Imparting Antimicrobial and UV Protection to Cotton Fabric. *Int. J. Carbohydr. Chem.* **2012**, *2012*, 840591. [\[CrossRef\]](#)
84. Higazy, A.; Hashem, M.; ElShafei, A.; Shaker, N.; Abdel Hady, M.M. Development of antimicrobial jute packaging using chitosan and chitosan-metal complex. *Carbohydr. Polym.* **2010**, *79*, 867–874. [\[CrossRef\]](#)
85. Hemmati, F.; Salehi, R.; Ghotaslou, R.; Kafil, H.S.; Hasani, A.; Gholizadeh, P.; Rezaee, M.A. The assessment of antibiofilm activity of chitosanzinc oxide-gentamicin nanocomposite on *Pseudomonas aeruginosa* and *Staphylococcus aureus*. *Int. J. Biol. Macromol.* **2020**, *163*, 2248–2258. [\[CrossRef\]](#) [\[PubMed\]](#)
86. Li, Y.; Zhou, Y.; Wang, Z.; Cai, R.; Yue, T.; Cui, L. Preparation and Characterization of Chitosan–Nano-ZnO Composite Films for Preservation of Cherry Tomatoes. *Foods* **2021**, *10*, 3135. [\[CrossRef\]](#) [\[PubMed\]](#)
87. Sathiyaseelan, A.; Vishven, N.; Zhang, X.; Han, K.; Wang, M. Research progress on chitosan-zinc oxide nanocomposites fabrication, characterization, biomedical and environmental applications. *Coord. Chem. Rev.* **2023**, *496*, 215398. [\[CrossRef\]](#)
88. Rashki, S.; Dawi, E.A.; Zilaei, M.R.; Safardoust-Hojaghan, H.; Ghanbari, M.; Ryadh, A.; Lafta, H.A.; Khaledi, A.; Salavati-Niasari, M. ZnO/chitosan nanocomposites as a new approach for delivery LL37 and evaluation of the inhibitory effects against biofilm-producing *Methicillin-resistant Staphylococcus aureus* isolated from clinical samples. *Int. J. Biol. Macromol.* **2023**, *253*, 127583. [\[CrossRef\]](#) [\[PubMed\]](#)
89. Banerjee, A.; Mukherjee, A.; Bag, N.; Halder, P.; Mondal, I.; Roy, J.; Mondal, D.; Bardhan, S.; Majumdar, A.; Das, S. Ultrasonic vibration-assisted enhanced antibacterial activity of ZnO/Chitosan bio-nanocomposite. *J. Mol. Struct.* **2024**, *1298*, 136996. [\[CrossRef\]](#)
90. Dejene, B.K.; Abteu, M.A. Chitosan/zinc oxide (ZnO) nanocomposites: A critical review of emerging multifunctional applications in food preservation and biomedical systems. *Int. J. Biol. Macromol.* **2025**, *316*, 144773. [\[CrossRef\]](#) [\[PubMed\]](#)
91. Dadashi, P.; Bonsale, R.; Babaei, A. Chitosan/ZnO nanohybrid as an efficacious compatibilizer for PLA/PBS blend suitable candidate for biodegradable packaging applications. *Sci. Rep.* **2025**, *15*, 41661. [\[CrossRef\]](#) [\[PubMed\]](#)
92. Rodrigues, C.; de Mello, J.M.M.; Dalcanton, F.; Macuvele, D.L.P.; Padoin, N.; Fiori, M.A.; Soares, C.; Riella, H.G. Mechanical, Thermal and Antimicrobial Properties of Chitosan-Based-Nanocomposite with Potential Applications for Food Packaging. *J. Polym. Environ.* **2020**, *28*, 1216–1236. [\[CrossRef\]](#)
93. Patehkhori, H.A.; Fattahi, M.; Nikou, M.K. Synthesis and characterization of ternary chitosan–TiO₂–ZnO over graphene for photocatalytic degradation of tetracycline from pharmaceutical wastewater. *Sci. Rep.* **2021**, *11*, 24177. [\[CrossRef\]](#) [\[PubMed\]](#)
94. Shafiee, P.; Reisi Nafchi, M.; Eskandarinezhad, S.; Mahmoudi, S.; Ahmadi, E. Sol-gel zinc oxide nanoparticles: Advances in synthesis and applications. *Synth. Sinter.* **2021**, *1*, 242–254. [\[CrossRef\]](#)
95. Mujeeb Rahman, P.; Abdul Mujeeb, V.M.; Muraleedharan, K.; Thomas, S.K. Chitosan/nano ZnO composite films: Enhanced mechanical, antimicrobial and dielectric properties. *Arab. J. Chem.* **2018**, *11*, 120–127. [\[CrossRef\]](#)
96. Gamboa-Solana, C.d.C.; Chuc-Gamboa, M.G.; Aguilar-Pérez, F.J.; Cauch-Rodríguez, J.V.; Vargas-Coronado, R.F.; Aguilar-Pérez, D.A.; Herrera-Atoche, J.R.; Pacheco, N. Zinc Oxide and Copper Chitosan Composite Films with Antimicrobial Activity. *Polymers* **2021**, *13*, 3861. [\[CrossRef\]](#) [\[PubMed\]](#)
97. Ali, S.A.; Ali, E.S.; Hamdy, G.; Badawy, M.S.E.M.; Ismail, A.R.; El-Sabbagh, I.A.; El-Fass, M.M.; Elsayy, M.A. Enhancing physical characteristics and antibacterial efficacy of chitosan through investigation of microwave-assisted chemically formulated chitosan-coated ZnO and chitosan/ZnO physical composite. *Sci. Rep.* **2024**, *14*, 9348. [\[CrossRef\]](#) [\[PubMed\]](#)
98. Umar, H.; Aliyu, M.R.; Usanase, N.; Duwa, B.B.; Uzun Ozsahin, D. Synthesis of chitosan functionalized zinc oxide nanocomposite using *Moringa stenopetala* extract and assessment of its antibacterial and cytotoxic potentials. *Cyprus J. Med. Sci.* **2025**, *10*, 96–100. [\[CrossRef\]](#)
99. Kachare, K.S.; Shendage, S.S.; Vhanbatte, S.B.; Mai, F.D.; Ghule, A.V. Synthesis, characterization, and antibacterial study of chitosan–zinc oxide nano-composite-coated superhydrophobic cotton fabric. *RSC Adv.* **2024**, *14*, 33774. [\[CrossRef\]](#) [\[PubMed\]](#)
100. Li, L.-H.; Deng, J.-C.; Deng, H.-R.; Liu, Z.-L.; Li, X.-L. Preparation, characterization and antimicrobial activities of chitosan/Ag/ZnO blend films. *Chem. Eng. J.* **2010**, *160*, 378–382. [\[CrossRef\]](#)
101. Zhang, X.; Zhang, Z.; Wenyi, W.; Jun, Y.; Qing, Y. Preparation and characterization of chitosan/Nano-ZnO composite film with antimicrobial activity. *Bioprocess Biosyst. Eng.* **2021**, *44*, 1193–1199. [\[CrossRef\]](#) [\[PubMed\]](#)

102. Majeed, A.H.; Mohammed, L.A.; Mohammed, I.K.; Hammoodi, O.G.; Khan, A.S.A.; Ibrahim, M.A.; Alheety, M.A.; Singh, T.; Destegül, A.; Sehgal, S. Computational Investigation of Antimicrobial Properties of Chitosan Based Zinc Oxide Nanocomposites. *Proc. Int. Conf. Appl. Innov. IT* **2026**, *14*, 297–309. [\[CrossRef\]](#) [\[PubMed\]](#)
103. Alamdari, S.; Mirzaee, O.; Nasiri Jahroodi, F.; Tafreshi, M.J.; Ghamsari, M.S.; Shik, S.S.; Ara, M.H.M.; Lee, K.Y.; Park, H.H. Green synthesis of multifunctional ZnO/chitosan nanocomposite film using wild *Mentha pulegium* extract for packaging applications. *Surf. Interfaces* **2022**, *34*, 102349. [\[CrossRef\]](#) [\[PubMed\]](#)
104. Kumar, S.; Mudai, A.; Roy, B.; Basumatary, I.B.; Mukherjee, A.; Dutta, J. Biodegradable Hybrid Nanocomposite of Chitosan/Gelatin and Green Synthesized Zinc Oxide Nanoparticles for Food Packaging. *Foods* **2020**, *9*, 1143. [\[CrossRef\]](#) [\[PubMed\]](#)
105. Mariyam, M.; Sunarintyas, S.; Yuliatun, L.; Irnawati, D.; Hatmanto, A.D.; Nuryono, N. Physicochemical and antibacterial properties of ZnO/chitosan-modified mineral trioxide aggregate composites. *Case Stud. Chem. Environ. Eng.* **2024**, *9*, 100749. [\[CrossRef\]](#)
106. Rahman, M.; Muraleedaran, K.; Abdul Mujeeb, V.M. Applications of Chitosan Powder with In Situ Synthesized Nano ZnO particles as an Antimicrobial Agent. *Int. J. Biol. Macromol.* **2015**, *77*, 266–272. [\[CrossRef\]](#) [\[PubMed\]](#)
107. Dhillon, G.S.; Kaur, S.; Brar, S.K. Facile fabrication and characterization of chitosan-based zinc oxide nanoparticles and evaluation of their antimicrobial and antibiofilm activity. *Int. Nano Lett.* **2014**, *4*, 107. [\[CrossRef\]](#)
108. Lu, Z.; Gao, J.; He, Q.; Wu, J.; Liang, D.; Yang, H.; Chen, R. Enhanced antibacterial and wound healing activities of microporous chitosan-Ag/ZnO composite dressing. *Carbohydr. Polym.* **2017**, *156*, 460–469. [\[CrossRef\]](#) [\[PubMed\]](#)
109. Karthikeyan, C.; Varaprasad, K.; Akbari-Fakhrabadi, A.; Hameed, A.S.H.; Sadiku, R. Biomolecule chitosan, curcumin and ZnO-based antibacterial nanomaterial, via a one-pot process. *Carbohydr. Polym.* **2020**, *249*, 116825. [\[CrossRef\]](#) [\[PubMed\]](#)
110. Malini, M.; Thirumavalavan, M.; Yang, W.-Y.; Lee, J.-F.; Annadurai, G. A versatile chitosan/ZnO nanocomposite with enhanced antimicrobial properties. *Int. J. Biol. Macromol.* **2015**, *80*, 121–129. [\[CrossRef\]](#) [\[PubMed\]](#)
111. Nozari, M.; Gholizadeh, M.; Oghani, F.Z.; Tahvildari, K. Studies on novel chitosan/alginate and chitosan/bentonite flexible films incorporated with ZnO nano particles for accelerating dermal burn healing: In vivo and in vitro evaluation. *Int. J. Biol. Macromol.* **2021**, *184*, 235–249. [\[CrossRef\]](#) [\[PubMed\]](#)
112. Hosney, A.; Kundrotaitė, A.; Drapanauskaitė, D.; Urbonavičius, M.; Varnagiris, Š.; Ullah, S.; Barčauskaitė, K. Green Synthesis of Chitosan Silver Nanoparticle Composite Materials: A Comparative Study of Microwave and One-Pot Reduction Methods. *Polymers* **2025**, *17*, 2960. [\[CrossRef\]](#) [\[PubMed\]](#)
113. Ferraz, M.P. Wound Dressing Materials: Bridging Material Science and Clinical Practice. *Appl. Sci.* **2025**, *15*, 1725. [\[CrossRef\]](#)
114. Vanti, G.; Poondla, N.; Manogaran, P.; Teradal, N.; S, V.; Kaulgud, R.; Kurjogi, M. Synthesis and Characterization of Multifunctional Chitosan–Silver Nanoparticles: An In-Vitro Approach for Biomedical Applications. *Pharmaceuticals* **2024**, *17*, 1229. [\[CrossRef\]](#) [\[PubMed\]](#)
115. Jin, S.G. Recent Applications of Chitosan-Based Biomaterials as Wound Dressings. *Int. J. Mol. Sci.* **2026**, *27*, 1637. [\[CrossRef\]](#) [\[PubMed\]](#)
116. Lu, P.; Ruan, D.; Huang, M.; Tian, M.; Zhu, K.; Gan, Z.; Xiao, Z. Harnessing the potential of hydrogels for advanced therapeutic applications: Current achievements and future directions. *Signal Transduct. Target. Ther.* **2024**, *9*, 166. [\[CrossRef\]](#) [\[PubMed\]](#)
117. Halarnekar, D.; Ayyanar, M.; Gangapriya, P.; Kalaskar, M.; Redasani, V.; Gurav, N.; Nadaf, S.; Saoji, S.; Rarokar, N.; Gurav, S. Eco synthesized chitosan/zinc oxide nanocomposites as the next generation of nano-delivery for antibacterial, antioxidant, antidiabetic potential, and chronic wound repair. *Int. J. Biol. Macromol.* **2023**, *242*, 124764. [\[CrossRef\]](#) [\[PubMed\]](#)
118. Ali, A.M.; Hamed, A.M.; Taher, M.A.; Abdallah, M.H.; Abdel-Motaleb, M.; Ziora, Z.M.; Omer, A.M. Fabrication of Antibacterial and Antioxidant ZnO-Impregnated Amine-Functionalized Chitosan Bio-Nanocomposite Membrane for Advanced Biomedical Applications. *Molecules* **2023**, *28*, 7034. [\[CrossRef\]](#) [\[PubMed\]](#)
119. Vagena, I.-A.; Gatou, M.-A.; Theocharous, G.; Pantelis, P.; Gazouli, M.; Pippa, N.; Gorgoulis, V.G.; Pavlatou, E.A.; Lagopati, N. Functionalized ZnO-Based Nanocomposites for Diverse Biological Applications: Current Trends and Future Perspectives. *Nanomaterials* **2024**, *14*, 397. [\[CrossRef\]](#) [\[PubMed\]](#)
120. Mohamed, T.E.-S.; Ahmed, M.S.; Mahmoud, S.; Samar, S.A.; Mthokozisi, D.; Soumya, G.; Dina, M.M.; Tarek, N.S.; Essam, H.I.; Mohamed, A.F.; et al. Chitosan nanoparticles: Green synthesis, biological activities, and sustainable frontiers in targeted drug delivery and cancer nanomedicine—A comprehensive review. *Mater. Today Bio* **2025**, *35*, 102358. [\[CrossRef\]](#) [\[PubMed\]](#)
121. Yanyun, G.; Wu, Y. Recent advances of chitosan-based nanoparticles for biomedical and biotechnological applications. *Int. J. Biol. Macromol.* **2022**, *203*, 379–388. [\[CrossRef\]](#) [\[PubMed\]](#)
122. Gonciarz, W.; Balcerzak, E.; Brzeziński, M.; Jeleń, A.; Pietrzyk-Brzezińska, A.J.; Narayanan, V.H.B.; Chmiela, M. Chitosan-based formulations for therapeutic applications. A recent overview. *J. Biomed. Sci.* **2025**, *32*, 62. [\[CrossRef\]](#) [\[PubMed\]](#)
123. Luong, J.H.T. Chitosan nanocrystals as next-generation antimicrobials: Mechanistic insights, antibiotic synergy, and biomedical potential. *Biotechnol. Adv.* **2026**, *90*, 108879. [\[CrossRef\]](#) [\[PubMed\]](#)
124. Murugesan, S.; Scheibel, T. Chitosan-based nanocomposites for medical applications. *J. Polym. Sci.* **2021**, *59*, 1610–1642. [\[CrossRef\]](#)

125. Frances, I.; Enejioye, S.O.; Chimbekujwo, K.I.; Oyewole, O.A.; Adetunji, C.O.; Adeyomoye, O.I.; Adetunji, J.B.; Ogundolie, F.A.; Mathew, J.T.; Inobeme, A.; et al. Chapter 9—Application of chitosan-based nanoparticles as an effective antibacterial agent. In *Chitosan-Based Nanoparticles for Biomedical Applications*; Adetunji, C.O., Danquah, M.K., Jeevanandam, J., Hefft, D.I., Pan, S., Khan, T.A., Eds.; Woodhead Publishing Series in Biomaterials; Woodhead Publishing: Cambridge, UK, 2025; pp. 195–216.
126. Zehra, S.H.; Ramzan, K.; Viskelis, J.; Viskelis, P.; Balciunaitiene, A. Advancements in Green Synthesis of Silver-Based Nanoparticles: Antimicrobial and Antifungal Properties in Various Films. *Nanomaterials* **2025**, *15*, 252. [[CrossRef](#)] [[PubMed](#)]
127. Zhang, T.; Wang, L.; Chen, Q.; Chen, C. Cytotoxic potential of silver nanoparticles. *Yonsei Med. J.* **2014**, *55*, 283–291. [[CrossRef](#)] [[PubMed](#)]
128. Mumtaz, M.; Khalid, S.; Naz, A.; Shahzadi, S.; Ahmad, S.; Khan, A.; Rahman, M.; Arif, A.; Shahid, A. Possible Solutions to the Associated Cytotoxicity of Silver Nanoparticles. *J. Surv. Fish. Sci.* **2024**, *11*, 135–151. [[CrossRef](#)]
129. Noga, M.; Milan, J.; Frydrych, A.; Jurowski, K. Toxicological Aspects, Safety Assessment, and Green Toxicology of Silver Nanoparticles (AgNPs)—Critical Review: State of the Art. *Int. J. Mol. Sci.* **2023**, *24*, 5133. [[CrossRef](#)] [[PubMed](#)]
130. Wu, K.; Yan, Z.; Wu, Z.; Li, J.; Zhong, W.; Ding, L.; Zhong, T.; Jiang, T. Recent Advances in the Preparation, Antibacterial Mechanisms, and Applications of Chitosan. *J. Funct. Biomater.* **2024**, *15*, 318. [[CrossRef](#)] [[PubMed](#)]
131. Liu, M.; Lü, R.; Chen, J.; Jiao, R.; Mi, C.; Li, X.; Ren, D.; Wu, L.; Wang, Q.; Zhou, H. A Review of the Antibacterial Activity of Chitosan and Its Application in Antibacterial Packaging. *Food Sci.* **2024**, *45*, 261–271. [[CrossRef](#)]
132. Yadav, H.; Malviya, R.; Kaushik, N. Chitosan in biomedicine: A comprehensive review of recent developments. *Carbohydr. Polym. Technol. Appl.* **2024**, *8*, 100551. [[CrossRef](#)]
133. Ezzaki, C.; Chaari, A.; Al-Othman, A. Recent Advances on Chitosan-Based Nanoparticles for Brain Drug Delivery. *Polymers* **2025**, *17*, 3055. [[CrossRef](#)] [[PubMed](#)]

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