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REVIEW PAPER

Chitosan conjugated silver nanoparticles: the versatile antibacterial agents

Shumaila Mumtaz[1] · Shaukat Ali[1] · Samaira Mumtaz[1] · Tafail Akbar Mughal[2] · Hafiz Muhammad Tahir[1] · Hafiz Abdullah Shakir[3]

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Abstract

Chitosan is one of the most environmental purification functional natural polysaccharides that can successfully prohibit the reproduction and growth of harmful Gram-negative and Gram-positive bacterial pathogens and also control the toxic pollutants. Nowadays, pathogenic microorganisms have multidrug resistance to antimicrobial drugs; therefore, successful identification and management of contagious disorders has become a major impediment. For combating the multidrug resistances in microorganisms' the latest innovations in nanotechnology-based medications have released novel prospects. More attention has been paid to the use of silver nanoparticles (AgNPs) as an effective antibacterial agent. Silver nanoparticles have been used to prevent and cure numerous contagions and disorders due to their strong bactericidal effects. Silver nanoparticles have high bactericidal and antimicrobial actions against methicillin-resistant bacterial strains, e.g., *Pseudomonas aeruginosa, Staphylococcus aureus,* and *Escherichia coli,* etc. The formation of nanoparticles from chitosan sources has been paid pronounced consideration due to hydrophilic characteristics, biodegradability, and biocompatibility. The first part of the literature highlights a general mechanism of antibacterial activity of chitosan, whereas the second part focus on the antibacterial activity of chitosan conjugated silver nanoparticles against broad-spectrum Gram-negative and Gram-positive microbial pathogens. Chitosan is selected as a protective mediator in the formation of silver nanoparticles because chitosan act as a stabilizing agent as well as the capability to sorb silver ions via chelation and ion exchange mechanisms. Chitosan conjugated silver-nanocomposites were suggested as coatings for food packaging, biomedical-engineering as well as wound-dressing applications.

Keywords Chitosan · Antibacterial · Chitosan nanoparticles · Bacterial strains · Antibiotics

✉ Shaukat Ali
dr.shaukatali@gcu.edu.pk

Extended author information available on the last page of the article

Abbreviations

CH	Chitosan
NPs	Nanoparticles
Ag NPs	Silver nanoparticles
ROS	Reactive oxygen species
OH	Hydroxyl group
TEM	Transmission electron microscopic
MDR	Multiple drug resistant

Introduction

Chitosan is the second most natural polysaccharide in the universe after cellulose that can be attained through the deacetylation processes of chitin. Outer shells of mollusks, lobsters, microorganisms, and cuticles of insects are the main sources of chitin or chitosan [1]. Table 1 and Fig. 1 show the various sources of chitosan. Decalcified cuticles of the crustacean members possess approximately 55–85% chitin. Secretion of chitin occurs by a single layer of epidermal cells whereas; the endocuticle contains mineral salts, *e.g.,* phosphates of calcium and carbonates [2]. Chitosan possesses prospective uses in medicine, agriculture, paper, textile, pharmaceutical, and food industries. It has been reported as an antioxidant, anti-tumor antifungal antibacterial, anti-inflammatory anti-thrombogenic, immunoadjuvant, and anti-cholesteric agent due to its non-toxicity, biocompatibility, non-allergenicity, and biodegradability properties [3]. Furthermore, it has also numerous uses in the biomedical field, e.g., tissue engineering, gene delivery, drug delivery, and regenerative rehabilitation [4]. Many applications have been attributed at the industrial level due to its solubility in an acidic aqueous medium. Its solubility depends upon the molecular weight, dispersion of the amino and acetyl groups along the chain, and degree of acetylation [5]. Chitosan possesses broad-spectrum anti bactericidal actions against both Gram-Positive and Gram-negative microbes. Additionally, the anti-bacterial activity of chitosan at low pH has been detected higher due to the occurrence of amino groups in the cationic form [6].

Table 1 Sources of chitosan [1, 7, 8]

Microorganisms	Insects	Marine animals
Green and brown algae	Beetles	Mollusks
Spores	Brachiopods	Annelids
Fungi (cell wall)	Cockroaches	Coelenterates
β-type yeast	Ants	Prawn
Chytridiacea	Scorpions	Shrimps
Blastocladiaceae	Spiders	Lobsters
Mycelia penicillium		Crustaceans

Fig. 1 Sources of Chitosan

Biological and physiochemical characteristics of chitosan

Solubility of Chitosan is found maximum in dilute organic acids, e.g., acetic acid, lactic acid, formic acid, and malic acid insoluble in water due to high viscosity. Chemical features of the chitosan include linear polyamine, reactive –OH groups, the occurrence of reactive amino groups, and a chelating effect with abled transition metal ions. Therefore it could be utilized in numerous high versatility physical forms gels, nanoparticles as filaments and nano-fibers, films, globules, scrubbers, scaffolds, and films [9]. Chitosan contains the following biological features, *e.g.,* DNA binding ability in microbial and mammalian cells, eco-safe, hemostatic, biocompatibility, biodegradability, spermicidal, fungistatic, immunoadjuvant, accelerating effect for bone formation, antitumor, and anti-cholesteremic [10, 11]. Physiochemical features of chitosan (CH) and its determination methods are depicted in Table 2.

Antibacterial effect and mechanism of chitosan

Chitosan in diverse formulas such as solutions, composites, and films has been studied as an antibacterial agent for an extensive range of target entities *for example* microbes, algae, mushrooms, and fungus in various in vitro and in vivo experiments [14]. Abdel-Razek [15], first proposed the broad-spectrum antibacterial activity of CH and its products. The voyage of investigation, assessment, and technical improvement in the antimicrobial properties of chitosan began two decades ago, on

Table 2 Physiochemical characteristics and Determination methods of chitosan [12, 13]

Physicochemical characteristics	Determination methods
Molecular weight	High performance liquid chromatography (HPLC), Viscometer matrix-assisted laser desorption/ionization-mass spectrometer (MLMS), gel permeation chromatography (GPC), light scattering
Crystallinity	X-ray diffraction
	Fourier transform infrared spectroscopy, nuclear magnetic resonance spectroscopy, infrared spectroscopy

soil–borne and foodborne pathogenic fungi in agriculture as well as food production [16]. Many extrinsic and intrinsic aspects, e.g., molecular weight and pH, relied on the antibacterial actions of chitosan and its by-products [17].

The polycationic chitosan interacts to the anionic charged cell wall of the pathogen then alters the permeability of the plasma membrane, inhibiting the replication of DNA,and disrupts the entire cell which results in apoptosis occurs [18]. Due to chelating activity, it inhibits bacterial growth by binding to trace metal elements and production of toxins [19]. Even, high molecular weight solid and water-soluble chitosan containing larger size nanoparticles obstructive the transference of vital solutes into the cell. It has been stated that two positively charged sites asparagine N-conjugated chitosan oligosaccharide offers resilient communication with the cell wall of bacteria that possess carboxyl-negative charges [20]. The polyatomic structure of chitosan predominantly shows a major function against microbes via electrostatic interaction among the negative constituents of the microbes for example cell surface proteins and lipopolysaccharide [14]. It has been described that the antimicrobial effect is enhanced in the incidence of an abundance of carboxyl group[21]. In acidic conditions, the polycationic structure forms superfluously, because the pKa of chitosan at a higher pH value may change due to protonation [22]. Chandrasekaran et al. [21] described that the antibacterial property of chitosan metal complex as well as chitosan will increase when the concentration of chitosan increases. Various states of the cells situated on the surface of the chitosan microsphere (some were leaking intracellular substances, some were intact)that destroy pathogens via interfacial communication [23].

Aspects affecting the antibacterial property

Concentration of chitosan

In a previous study, it is reported that at different concentrations chitosan can prohibit the growth of bacteria depending upon the acetylation degree. Chitosan with (a

7.5% acetylation degree) was more effective than a solution of chitosan with a 15% acetylation degree [24]. Higher concentrations of protonated CH can hide the receptors on the surface of a cell and stop the outflow of internal constituents whereas, CH binds to the negatively charged cell surface at lower concentrations then disrupts the plasma membrane and cause the decease of the microbes via inducing escape of entire constituents and eventually leads to death of bacteria [25]. It has also been found that chitosan bind to Gram-negative bacteria especially only at lower concentrations [26]. It has also been stated that at the lower concentration (20 ppm) chitosan killed almost all bacterial strains when compared to a higher concentration at 50 ppm [27]. The antibacterial experiment results showed that when cotton fabrics were treated with diverse concentrations of chitosan (0.5–0.75%) a significant antibacterial activity has been found and increasing the concentration of CH (1%) leads to a reduction in antibacterial activity [28].

Molecular weight

Various studies reported that low Mw and high Mw of CH have equivocal results for *B. subtilis* and *E. coli* [14]. Xia et al. [14] stated that the molecular weight of chitosan either low or high depends on situations of genetic testing and the bacterial strains. Moreover, HMw (9.3 kDa) and Low molecular weight (4.6 kDa) chitosan and its imitative exhibited enhanced action for mold, fungi, as well as other pathogens. It has also been found that chitosan with high molecular weight (1671, and 1106 kDa) can intermingle with the membrane of the bacteria and stops the transport of nutrients into the plasma membrane of microbes by altering the cell permeability and resulting in cell lysis [29]. However, CH with a low molecular weight (746 kDa) can interact with the nuclei of the microbes and prohibit the synthesis of mRNA [30]. In previous studies, it has also been specified that LMW chitosan revealed stronger bactericidal effects on Gram-negative bacteria, e.g., *E. coli* and *Pseudomonas fluorescens*, whereas, chitosan with high HMW (1671 kDa) is more effective against Gram-positive bacteria such as *Vibrio parahaemolyticus* and *Salmonella typhimurium* [31].

pH

The antibacterial action of CH depends upon the pH of chitosan [25]. Alarfaj [32] reported that chitosan showed the tougher prohibitory effect at lower pH, due to solubility of chitosan in an acid whereas, the antibacterial activity becomes weak when the pH increases. Some researchers reported that under neutral conditions or at pH 7.0 chitosan and its derivatives finally failed to show their antimicrobial activities because it was tough for chitosan to dissolve in water at pH 7.0 and the amino groups of chitosan were no longer significantly charged at neutral pH [33]. Chitosan is polyatomic due to the high density of amino groups present on the polymer and at pH 6.0 it intermingles freely with negatively charged constituents, e.g., anionic polysaccharides, proteins, fatty acids, phospholipids, and bile acids [34]. However,

Yu et al. [23] stated that the chitosan microsphere exhibited antibacterial outcomes. Hosseinnejad and Jafari [22] found that N-alkylated chitosan derivatives indicated the maximum antibacterial activity for *E. coli* when pH enhanced from 5.0 to 6.0 pH. In another study antibacterial activity of chitosan was investigated at pH 7.4 and 6.2 against *Staphylococcus aureus*, and at pH 6.2 chitosan more inhibited the growth of bacteria than pH 7.4 [35]

Temperature and time

Specific characteristics of chitosan and its derivatives such as viscosity/molecular weight might be altered during storage [36]. Therefore, for commercial applications, the stability of prepared chitosan solution should be monitored before storage or further use. After four months of storage, stability of chitosan and antimicrobial action against Gram-negative (*S. enteritidis* and *E. coli*) and Gram-positive (*S. aureus* and *L. monocytogenes*) bacterial strains were inspected at 5 °C and 28 °C [37]. After investigation, it was found that after four months of storage chitosan solutions exhibited less antiseptic action than before storage. In another study, it was also found that Chitosan solutions showed more antibacterial activity at 4 °C as compared to 25 °C. The antibacterial activity of chitosan solutions at different temperatures depends upon the bacterial strains [38]. It was found that *E. coli* showed higher antibacterial activity as temperature increased from 4 to 37 °C. Xia et al. [14] reported that low temperature can decrease the electronegativity for derivatives of CH by changing the cell surface structure.

Chitosan nanoparticles

Nowadays, (NPs) are used as drug-delivery mediators or nanocarriers to develop safer and more effective treatments for diagnosing, monitoring, and preventing syndromes [39]. Alqahtani [40], found that CNPs exhibited greater antimicrobial action against both Gram-positive and Gram-negative bacteria, and an extensive variety of fungus strains as compared to chitosan. Several approaches have been found for the preparation of chitosan NPs, e.g., microemulsion, ionic gelation, spray drying, reverse micellar method, and emulsion droplet coalescence [21, 41]. Among several approaches, ionic gelation was observed to be the better one. According to the ionic gelation scheme, chitosan (w/v) was liquefied in acetic acid (v/v) and the solution was retained under magnetic stirring at room temperature for 24 h. Then 1 mL 0.1% w/v TPPsolution was added dropwise to 5 mL of CH solution at 800 rpm for 1 h under continuous magnetic stirring. Then the nanoparticles were formed and the solution containing nanoparticles was spinned at 10,000 rpm for 15 min. Then NPs were liquefied in double distilled water and then centrifuged for purification [42]. For further characterization and experiments, the CNPs were kept at room temperature. The synergistic effect of chitosan and metals (gold-, silver- or copper) was explored to prepare a novel nanocomposite against human bacterial strains [43].

Chitosan conjugated silver nanoparticles

The production of NPs from chitosan sources has been given prodigious devotion due to their biocompatibility, hydrophilicity, and biodegradable possessions [44]. It intermingles with negatively charged polymers and molecules due to its positive nature. In the formation of metal NPs, CH has been selected as a protecting agent due to the interface of active α-amine groups in CH with metal nanoparticles [45]. Toward some human cells, chitosan displays an antibacterial action for disease resistance due to the occurrence of both active OH functional and amino groups [46]. Suresh et al. [47] described that recently chitosan has been used as both the stabilizing and reducing agents for the production of Ag NPs. Silver nanoparticles (Ag NPs) possess unique physicochemical properties in the field of biomedicine such as antiviral, antibacterial, anti-inflammatory antiplatelet activities, antifungal, and anti-angiogenesis [47, 48]. In various areas of nanotechnology, the syntheses of metal nanoparticles through the improvement of proficient and greener routes have become a major concern. Among several metal nanoparticles, silver nanoparticles are extensively useful in numerous organic and medicinal areas due to their potential as antimicrobial agents, e.g., wound healing, biosensors, curing the burns, and treating the numerous forms of cancers [49, 50].

Chitosan and PVA are well-recognized polymers with tremendous immersion capacities for various metal ions due to the occurrence of (–NH2) and (–OH) groups in their configuration [51]. It has been documented that CH itself possesses antimicrobial action due to its cationic characteristics that cause a membrane-disrupting effect. However, chitosan–silver nanoparticles (CS/AgNP) signifies a bio-nanostructured hybrid material due to their biodegradability and biocompatibility [52].

Antibacterial mechanism of chitosan conjugated silver nanoparticles

Interaction between chitosan and metal nanoparticles takes place due to the positive amino groups chitosan and negatively charged molecules in bacteria [53]. Chitosan has been selected as a therapeutic mediator in the production of metal NPs. Chitosan shows several noteworthy organic functions such as antimicrobial action for diseaseresistant toward several human cell categories due to the incidence of both active NH and OH groups [45]. For many years silver products have been utilized to inhibit and medicate numerous inflammation and disorders due to their resilient prohibitory and bacteriostatic actions. Silver nanoparticles have high bactericidal and antimicrobial actions against methicillin-resistant bacterial strains such as *S. aureus, E. coli*, and *P. aeruginosa* [54]. Apart from stabilization, chitosan also prevents the agglomeration of AgNPs below a critical concentration [55]. Furthermore, the antimicrobial action upsurges with the increased concentration of AgNPs and silver molecules. The greater effective surface area of silver nanoparticles increases the antimicrobial action because

chitosan prevents aggregation of AgNPs. The surface area of both silver ions and nanoparticles decreases in the presence of agglomerates and thus the efficiency of antibacterial is greatly diminished [56]. Shah et al. [52] reported that chitosan can sorb silver ions via chelation and ion exchange mechanisms. Chitosan and silver ions interact with each other through a reduction process as a result of electrospinning among single carboxyl and single amino groups of CH with the molecules of silver. A dual mechanism of action of chitosan-based silver nanoparticles is the effect of cationic chitosan and the bactericidal effect of AgNps [52].

The distraction of plasma membrane and destabilization of entire structures

The mechanism of the antimicrobial act of positively charged chitosan-based silver nanoparticles is interacting with the anionic charged cell membrane of bacteria leading to accretion of NPs on the bacterial cell surface. These NPs cause disruption in the permeability of the plasma membrane, altered configuration,

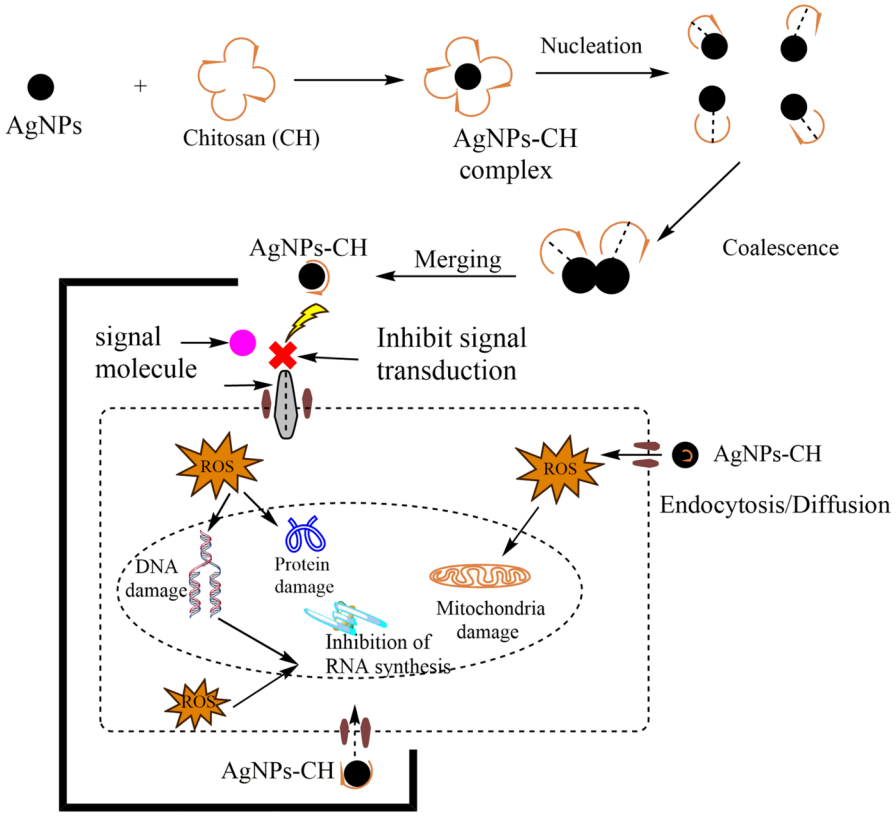

Fig. 2 Antibacterial mechanism of chitosan conjugated silver nanoparticles

transportation action, and destabilization of the cell envelope as shown in Fig. 2 [57]. These nanoparticles release the silver ions from particles and can enter the cell via intermingling with phosphorus- and sulfur-containing compounds, e.g., protein and DNA [58].

Images of Transmission electron microscopy have shown that the antimicrobial activity of the AgNPs can enhance by the usage of anionic detergents such as sodium dodecyl sulfate and Phosphorus-containing heterocyclic surfactants, and non-heterocyclic ammonium and phosphonium surfactants s that are potent stabilizers of AgNPs with significant cytotoxic activity. Silver nanoparticles with phosphonium surfactants were found to be more stable and exhibited substantial antibacterial effects against Gram-negative and Gram-positive pathogens [59, 60]. The outer membrane of the Gram-negative bacteria consists of "porins (water-filled channels) that are responsible for the acceptance of AgNPs into the microbial cells. These NPs also disrupt DNA replication, various enzymes such as DNA-dependent RNA polymerase and DNA gyrase, division, and respiration by binding to mesosomes, thus damage the entire cell [61]. Thiruvengadam Bansod, [62] also stated that the interaction of AgNPs with ribosomes leads to the prohibition of protein synthesis due to the deactivation of SH functional group of the amino acids existing in the cell surface. Ag (+) ions and AgNPs block active binding sites by interacting with disulfide bonds and modifying the 3D structure of proteins which leads to complete functional imperfections in the bacterial strains [63]. It has also been reported that AgNPs inhibit the metabolism of sugar through the deactivation of the phosphoglucose isomerase [64]. Silver ions can affect the transportation and the discharge of potassium (K+) ions, and escape of cellular constituents, e.g., proteins, reducing sugars and ions from the microbial cells, can also alter [65]. It has been found that Ag (+) ions disrupt the double-helical structure of microorganisms by breaking the H-bonds found within nucleotides of the antiparallel strands of DNA [66]. Yun'an et al. [67] stated that AgNPs also inhibited the cell division and reproduction of S. *aureus* in its initial stages.

Formation of ROS

Accumulations of NPs on the plasma membrane of the bacteria produce oxidative stress which results in the release of ROS. These ROS can decline the production of ATP as well as respiration [68]. A higher concentration of Ag (+) ions causes cellular oxidative stress in microbes due to the generation of free radicals, e.g., hydroxyl radical (OH•), H_2O_2, singlet oxygen, superoxide anion, as well as hypochlorous acid [69]. During mitochondrial oxidative phosphorylation ROS are also generated intracellularly. Productions of free radicals in excessive amounts cause necrosis in the mitochondrial membrane. It has also been reported that higher production of ROS causes hyper oxidation of DNA proteins and lipids. Silver nanoparticles disrupt and inactivate the catalytic activity of various enzymes due to the production of carbonyls which are protein-bound in the environment through catalyzing the chemical reaction of the amino groups which result in the destruction of polymers occurs [70].

Genotoxicity and inhibition of signal transduction

For bacterial growth and cellular action, the sequence of dephosphorylation and phosphorylation cascade mechanism of signal impart plays a vital role [64]. Therefore, bacterial growth can be repressed by the reticence of phosphorylation of amino acids that will obstruct their catalytic action [71]. Silver NPs interrelate with the DNA/RNA due to their electrical possessions and inhibit the signal transduction by harmful effect on the reproductive procedure of chromosomal and plasmid DNA [72]. A higher antimicrobial of CH-based AgNPs was found against Gram-negative (*E. coli*) and Gram-positive microbial strains (*S. aureus,* and *B. subtilis*) when matched to ionic silver and chitosan itself for *S. aureus* and *E. coli* [65].

Effects of physicochemical properties on antibacterial action of AgNPs

In biomedical applications production of metallic derivative nanoparticles relies upon various thermal, chemical, physical, electrical, and photosensitive characteristics [59]. Omran et al. [73] stated that microbial possessions of the silver nanoparticles are intensely affected by their concentration, size, shape, and colloidal state as shown in Fig. 3. It has also been found that the stability and biocompatibility of AgNPs can enhance by reducing their size [74]. Interaction between AgNPs and microorganisms (viruses, bacteria, and fungus) takes place according to shape. Therefore, it is essential to develop applicable shaped and sized NPs with desired superficial characteristics [75]. Treatment with different shaped Ag NPs showed modifications in the plasma membrane of the (*E. coli*) via energy-filtering TEM images [76]. Antibacterial action of truncated triangular shaped AgNPs has been found better with respect to rod shaped / sphere-shaped. The size of AgNPs is another important physicochemical characteristic that is accountable for the conformation of nanoparticles. The size of silver nanoparticles should not be larger than 50 nm [77]. Liao et al. [78] stated that AgNPs with smaller sizes (< 30 nm) showed more antibacterial action against *K. pneumoniae* and *S. aureus*. Both bactericidal as well as bacteriostatic effects against *S. aureus* have also been found at 5–10 nm dimensions of AgNPs as shown in Table 3 [79]. Small-sized AgNPs attached with the plasma membranes, increased membrane permeability, and modifications in lipid bilayer lead to impairment and apoptosis. Crystallographic surface structures and surface area to volume ratio are significant aspects that describe the antimicrobial action of AgNPs [80].

Due to the multidrug resistance of the pathogenic microbes to the antibacterial medications, successful treatment and diagnosis of pathogenic infections of fungal and bacterial origin have become a major concern [85]. Table 4 comprises a list of antibiotics to which the most communal drug-resistant, pathogenic strains of microbes have developed resistance. Nowadays, to overcome MDR,

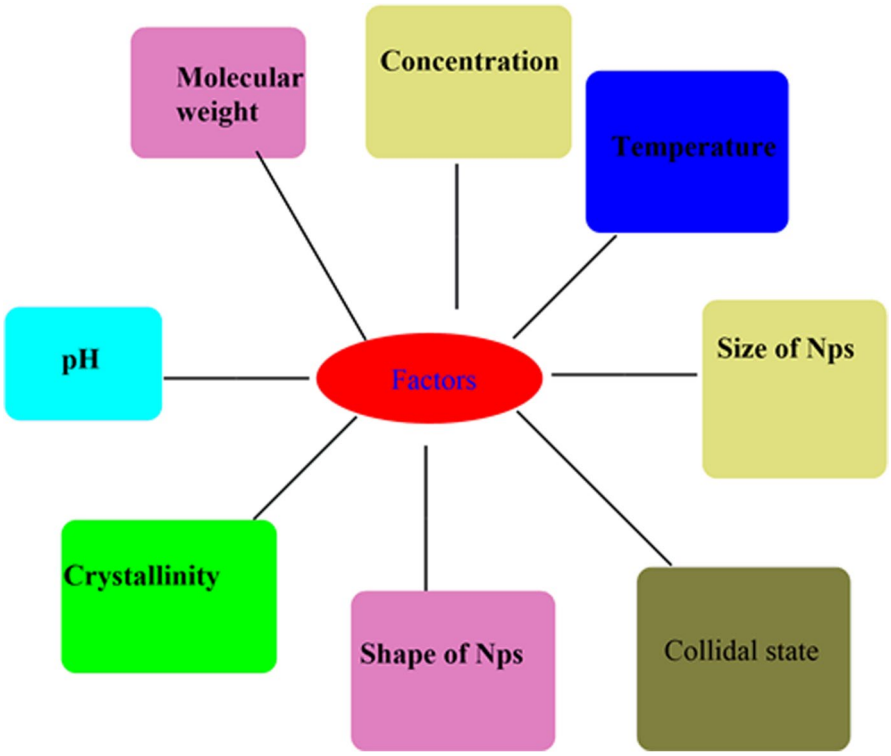

Fig. 3 Factos affecting the antibacterial activity of chitosan

more consideration has been paid to the development of novel, non-traditional antibacterial agents [86]. In clinical and therapeutic applications the benefit of using silver nanoparticles is comparatively less responsive than silver ions [74]. It has been found that both, non-multidrug resistant, as well as multidrug-resistant bacterial strains, showed more antimicrobial activity against AgNPs [87]. Severe clinical and medical problems, *e.g*., disorders in the urinary tract, diarrhea, neonatal meningitis, and pneumonia, etc., are associated with Gram-positive pathogens including *Enterococcus*, *Nocardia*, *Clostridium*, *Actinomyces*, *Mycobacterium Staphylococcus*, *Bacillus*, *Corynebacterium*, *Listeria*, *Streptomyces*, and *Streptococcus* [88]. Among them are antibiotic-resistant microbes; *E. faecium* is vancomycin-resistant, methicillin- and vancomycin-resistant *S. aureus*, penicillin-resistant *Streptococcus pneumonia*, and multidrug-resistant *Listeria Corynebacterium* and macrolides resistant *Streptococcus pyogenes*. The two most dominant and pathogenic Gram-negative bacteria enterotoxin *Escherichia coli* (ETEC) and *Vibrio cholerae* have high morbidity and mortality rate through severe secretory diarrhea [89]. Among Gram-negative bacterial strains *K. pneumoniae, Acinetobacter baumanii*, and *Pseudomonas aeruginosa* some are opportunistic microorganisms that infect mainly immune-compromised patients and are intrinsically

Table 3 Antibacterial mechanism of silver nanoparticles against several Gram-negative and Gram-positive microbes

MICROBES	Mechanism	Size of AgNPs	References
S. aureus	Penetrate to cell wall; detachment of plasma membrane from cell wall; inhibit transcription, inactivation of proteins condensation of DNA plasma membrane damage; communication with P and–S–comprising composites, the reticence of inhalation	5–25 nm	[81]
B. subtilis	Disruption of the plasma membrane, chromosomal DNA, leakage of reducing sugars, increase the production of ROS	5–10 nm	[82]
K. pneumonia	inhibition of cell division, prohibit the replication	< 50 nm	[83]
V. cholera	interaction with P and S–containing compounds, cell wall lysis, prohibition of metabolic pathways	90–100	[84]

Table 4 Resistance in bacterial strains to common antibiotics [86]

Microbes	Antibiotic-resistant
Acinetobacter baumannii	Carbapenems Imipenem
E. coli	Cephalosporins Sulfamethoxazole Rifampin Streptomycin Tetracycline Ampicillin Chloramphenicol
V. cholera	Tetracycline, Fluoroquinolones
P. aeruginosa	Tetracycline, *β*-lactams, Trimethoprim Chloramphenicol, Fluoroquinolones Novobiocin, Sulfonamides
S. flexneri	Nalidixic acid, Ciprofloxacin
Salmonella typii	Ampicillin, Trimethoprim, Amoxycillin Chloroamphenicol, Fluoroquinolones
Gram-positive	
Bacillus subtilis	Erythromycin, Streptomycin, Penicillin Chloramphenicol, Lincomycin, Tetracycline
Streptococcus pneumonia	Penicillin, Erythromycin
Staphylococcus aureus	Vancomycin, Methicillin
Corynebacterium diphtheriae	Tetracycline, *β*-lactam antibiotics, Chloramphenicol, Sulfamethoxazole Trimethoprim

resistant to multiple drugs [90]. Niño-Martínez et al. [91] stated that the antiseptic action of silver nanoparticles has been found in contradiction to drug-resistant pathogenic strains of bacteria, e.g., *E. faecalis*, *Bacillus subtilis*, *E. coli, P. aeruginosa*, *S. aureus,* and *K. pneumonia*. Antimicrobial effect of silver nanoparticles has also been found against *S. typhi, S. pyogenes*, methicillin-resistant *Staphylococcus epidermidis*, and *K. pneumonia* and methicillin-resistant *S. aureus* (MRSA). Antibacterial effect of AgNPs only or amalgamation with antibiotics against drug-resistant bacterial strains has also been found [92].

Conclusion

The current study showed that nowadays pathogenic microorganisms have multidrug resistance to antimicrobial drugs therefore, successful diagnosis and management of infectious disorders has become a foremost barrier. Significant antibacterial action of CH has been found against a broad spectrum of microorganisms. Chitosan-silver nanoparticles (CS/AgNPs) signify bio-nanostructured crossbreed constituents due to their biocompatibility, and biodegradability with improved antimicrobial characteristics. Bactericidal possessions of the AgNPs can be intensely affected through their size, concentration, shape, and colloidal state. Silver nanoparticles of smaller size (< 30 nm) showed more antibacterial action against Gram-positive and Gram-negative bacterial pathogens. Chitosan-conjugated silver-nanocomposites were suggested as coatings for food packaging, biomedical-engineering as well as wound-dressing applications.

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Declarataions

Conflict of interest The authors declare no conflicts of interest.

Ethical approval This article does not contain any studies with human participants or animals accomplished by any of the authors.

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Authors and Affiliations

Shumaila Mumtaz[1] · Shaukat Ali[1] · Samaira Mumtaz[1] · Tafail Akbar Mughal[2] · Hafiz Muhammad Tahir[1] · Hafiz Abdullah Shakir[3]

[1] Applied Entomology and Medical Toxicology and Laboratory, Department of Zoology, Government College University, Lahore, Pakistan

[2] Department of Zoology, Women University of Azad Jammu and Kashmir, Bagh, Pakistan

[3] Institute of Zoology, University of the Punjab, Lahore, Pakistan