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Review Article

Bacterial Cellulose–Silver Nanoparticle Composites for Antimicrobial Wound Dressing: A Review of Recent Advances from 2020 to 2025

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Abstract

Chronic wounds, notably diabetic foot ulcers, venous leg ulcers, and pressure injuries, impose significant clinical and financial challenges worldwide due to persistent microbial colonization and poor healing. Bacterial cellulose (BC), produced by *Komagataeibacter xylinus*, is recognized for its purity, mechanical strength, and water retention, but lacks antimicrobial properties. To enhance its effectiveness, functionalization with silver nanoparticles (AgNPs) is suggested, as they provide antimicrobial and antibiofilm benefits. However, their use is restricted by issues of cytotoxicity and stability. This review comprehensively draws together progress from 2020 to 2025 on BC–AgNP composites as futuristic antimicrobial wound dressings. Major segments are dedicated to the discussion of synthesis methods (*in situ*, *ex situ*, electrochemical, and green methods), structure–property relationships and characterization techniques, juxtaposed with studies, *in vitro*, *in vivo*, and an emerging clinical scope of antimicrobial activity, cytocompatibility, and wound-healing efficacy. Recent advancements in hybrid composites with bioactive molecules, graphene oxide, or plant-derived reductants have been noted for their potential to reduce toxicity and enhance healing. Key challenges for clinical translation include issues with reproducibility, scalability, regulatory approval, and long-term safety. Future directions to address these obstacles involve eco-friendly synthesis methods, controlled silver release, multifunctional design, smart sensor integration, and large-scale trials. As a complete unit, BC–AgNP composites can be regarded as one group of composites which display a large potential in being developed as safe, efficient, and sustainable wound dressings for the treatment of chronic wounds.

Keywords: Antimicrobial wound dressings, bacterial cellulose, chronic wounds, cytocompatibility, green synthesis, nanocomposites, silver nanoparticles.

INTRODUCTION

Some of the prominent chronic wounds existing as diabetic foot ulcers, pressure injuries, and venous leg ulcers constitute a major and increasing global healthcare concern from time immemorial. In most developed countries, it has been widely estimated that 1-2% of human population suffer from chronic wounds, as the prevalence of these wounds have also been noted to increase in the elderly and those with comorbidities such as diabetes and vascular disease (Sen, 2021). These wounds not only cause a heavy financial burden for both patients and health systems, but also bring significant pain, reduced quality of life, and the potential of infection to the patients. Their complex pathology with features of extended inflammation, impaired angiogenesis, and persistent microbial biofilms has, however, limited the effectiveness of conventional dressings, thus propelling the need for advanced antimicrobial and bioactive dressings (Falanga *et al*., 2022; Sen, 2023). Traditional dressings such as gauze and bandages by and large only cover wounds and soak up the exudate but do not actively modulate the wound, and generally lead to the phenomenon of sticking to the delicate tissue and causing injury at the time of removal (Kus and Ruiz, 2020; Farahani and Shafiee, 2021; Olutoye *et al*., 2024). Modern passive/semi passive dressings (foams, hydrocolloids, alginates, films) are able to improve the balance of moisture and the protection from the wound but are still faced with the problems of poor microbial and biofilm control, limited therapeutic delivery, adaptability which is variable depending on the nature of the wound, and challenges of exudate management and monitoring. The antimicrobial resistance which is on the rise is turning these shortcomings into a requirement for the scaffolds that can maintain antimicrobial activity while at the same

time be helpful in supporting tissue regeneration (Britto *et al*., 2025).

Bacterial cellulose (BC) that is created by a strain such as *Komagataeibacter xylinus*, is a nanofibrillar, highly pure cellulose without hemicellulose and lignin and thus more crystalline and stable than plant cellulose. BC has a high-water capacity (Lin *et al*., 2023; Meng *et al*., 2023), possesses a porous nanoscale network similar to the extracellular matrix and maintains great mechanical stability when hydrated, making it biocompatible and supporting cell migration. These characteristics allow BC to act as a barrier against pressure, retain moisture, and be gentle to wound beds. Also, it's modifiable surface allows for the inclusion of antimicrobials, such as silver nanoparticles (AgNPs) (Horue *et al*., 2023). Silver nanoparticles (AgNPs) are known to be effective against bacteria, fungi, and a few viruses. In addition to antibacterial potential, they also have strong antibiofilm effects.

This review assembles and summarizes the core developments in the field of bacterial cellulose–silver nanoparticle (BC–AgNP) composites for antimicrobial wound dressings from 2020 to 2025, concerning the design, synthesis, characterization, structure–property relationships, preclinical evaluation, safety assessment and future perspectives.

METHODOLOGY

This assessment was completed via an orderly and methodical literature investigation aimed at locating and scrutinizing pertinent studies on BC–AgNP composites for antimicrobial wound dressings, with reference to the research progress made between 2020 and 2025, as depicted in Figure 1.

Literature search strategy

Five major electronic databases were examined for articles that are peer-reviewed and published between January 2020 and August 2025. The five databases selected for the search include *PubMed, Scopus, Web of Science, ScienceDirect,* and *Google Scholar.* For effective search towards getting better results, some specific keywords and phrases were employed. They include *"bacterial cellulose," "silver nanoparticles," "nanocomposites," "wound healing," "antimicrobial wound dressings," "green synthesis," "in situ synthesis," and "ex situ incorporation."* The Boolean operators (AND/OR) were used to make searches more exact and widen the coverage.

Inclusion and exclusion criteria

The studies that dealt with the synthesis, characterization, or applications of BC–AgNP composites reported were included for the present review. Works that also demonstrated antimicrobial-related activity, cytocompatibility, or wound healing were along with the performance evaluation of experiments *in vitro*, *in vivo*, or in clinical settings were considered eligible. Moreover, these studies were even taken into account if they gave information about the fabrication processes, such as *in situ*, *ex situ*, or green synthesis, or if they had the composites as the research topic of the structure-property relationship. Articles, which have been peer-reviewed scholarly and published in the English language only in the period from 2020 to 2025, have been the center of attention for this research. On the other hand, those publications have been excluded from the analysis if they were not direct works on BC-AgNP composites, like reviews on unrelated nanomaterials, or if they were such non-peer-reviewed sources as conference abstracts, theses, patents, or opinion papers. Any research that does not give detailed methodology and performance data have also been removed from the analysis.

Screening and selection

The initial search was about 135 records. Duplicates were removed, and then titles and abstracts were screened for relevance. At the next stage, full texts were evaluated against the inclusion criteria. Reference lists of selected papers were hand searched in order to locate further eligible studies.

Data extraction and analysis

For each article belonging to the eligible ones, the type of bacterial cellulose and the method of silver nanoparticle synthesis, including *in situ* reduction, *ex situ* loading, and green synthesis, were identified. The publication also contributed to reporting the features of nanoparticles in the aspects of size, distribution, surface capping agents, and release profiles. Furthermore, the compositional data of their physicochemical properties such as mechanical strength, crystallinity, water-holding capacity, and permeability were registered. The biological performances of the composites were reviewed, focusing strongly on the areas of antibacterial activity, antibiofilm effects, cytocompatibility, and wound healing outcomes. Moreover, the studies were examined to find the difficulties they recognized, as well as safety issues and the possibility of clinical translation. The data extracted were then thematically arranged to reflect trends in fabrication strategies, structure-property relationships, biomedical performance, and translational challenges. The results were finally combined into a narrative that acknowledged the methodological rigor, comparative reflections and directions for future research.

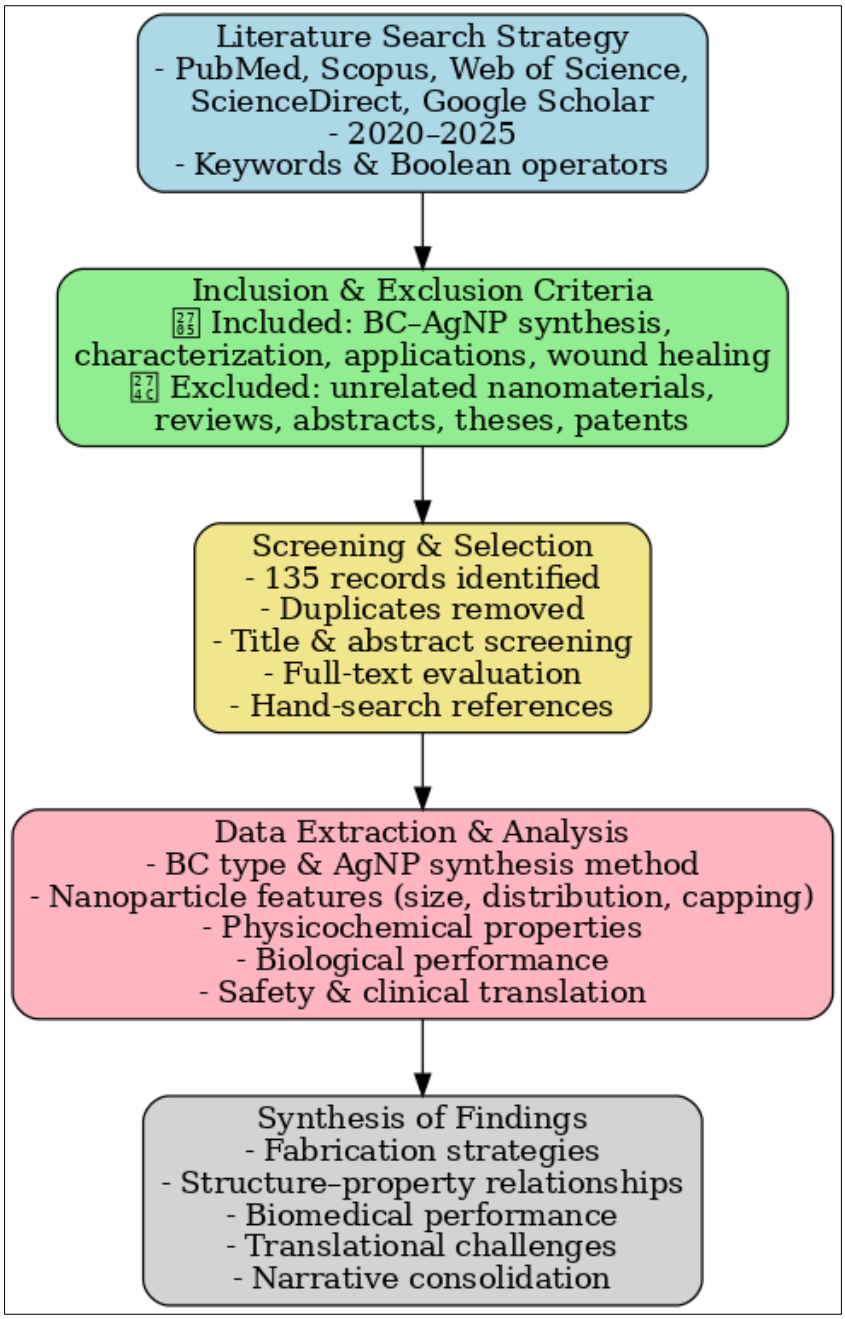

Figure 1: Flow diagram illustrating the methodology adopted for this review

The process involved a systematic literature search across major databases, application of inclusion and exclusion criteria, screening and selection of eligible studies, extraction of data on synthesis methods, nanoparticle features, physicochemical and biological properties, and integration of findings into thematic categories for comparative evaluation.

FINDINGS AND DISCUSSION

Properties of Bacterial Cellulose Relevant to Wound Healing

Essentially, one of the prominent members of the family of biomaterials known as bacterial cellulose (BC) has been implicated to have a number of advantageous properties. These properties that are necessary for the creation of wound dressing include, mechanical strength, water retention, biocompatibility, purity and an architecture resembling extracellular matrix (ECM). The studies (2020–2025) conducted on BC-AgNP composites verify these characteristics while suggesting ways as AgNP introduction and preparation could tune them further to antimicrobial and functional performance (Wasim *et al*., 2022).

a) Biocompatibility, high purity, and non-toxicity

Pure BC, for example, from genetically modified *Komagataeibacter,* is devoid of lignin and hemicellulose, thus it is less likely to cause an immune reaction and it shows strong biocompatibility *in vitro* and *in vivo*. Hybrid BC–AgNP materials may still achieve

this feature if the size of the nanoparticles, their distribution, and release are well managed and optimized. Ciftci *et al*. (2024) demonstrated that BC/AgNP films with fibrils loaded were antimicrobial and biocompatible because of no significant cytotoxicity. In the same way, Mutiara *et al*. (2023) showed that green-fabricated BC-AgNP hybrids effectively stopped the growth of *Staphylococcus aureus* and *Escherichia* coli as well as keeping the cells viable. In other words, BC is a good environment for bio-purity and safe usage, yet at the same time, a silver release without control might lead to cytotoxicity.

b) Mechanical strength and flexibility

The native BC is a material with excellent intrinsic mechanical properties, such as high tensile strength, good Young's modulus, and remarkable flexibility in a hydrated state. Studies have shown that AgNPs usage can vary these values to a large extent subject to the methods of preparation. Jenkhongkarn and Phisalaphong (2023) tried several *in-situ* reductions (sodium hydroxide, ascorbic acid, chitosan, UV irradiation) and found that the ascorbic acid-reduced composites reached the highest Young's modulus (~8960 MPa), whereas the UV-reduced composites had the highest tensile strength and elongation. Typically, the crystallinity is compromised when silver nanoparticles are introduced, however, it was found that it increased with the ascorbic reduction. Superiority may be achieved in mechanical performance, as well as in antimicrobial functionality if reduction methods are chosen carefully. Similarly, Ciftci *et al*. (2024) reported the development of flexible and bendable BC-AgNP films that can adapt to the shape of irregular wound beds.

c) High water-holding capacity and permeability

Hydration and moisture regulation are extremely important in the process of wound healing and in that case native BC performs excellently in water absorption, retention, and vapor transmission. A AgNP incorporation may affect these features, in general, depending on the methods of synthesis. Jenkhongkarn and Phisalaphong (2023) have demonstrated that most of the BC–Ag composites lead to a decrease in water absorption, however, the chitosan-reduced composites appeared to raise it (~344%) substantially. Moreso, Shaaban *et al*. (2023) verified that just as the green-synthesized BC–AgNP utilizing *Moringa oleifera* extract was able to maintain the water-holding capacity at the high level, it exhibited effective antibacterial activity also. Despite the limited permeability data, those composites with nanoparticles being well-dispersed generally assure the retention of flexibility and continuity which imply that the gas or vapor exchange is less likely to be interrupted.

d) Structural similarity to the extracellular matrix

The ECM-like composition of BC, a nanofibrillar network with porous structure, provides the conditions for cell attachment, movement, and eventually tissue integration. These traits are mainly kept in BC–AgNP composites when silver is infiltrated in the fibrils, and not the one that breaks the structure (Abdellatif *et al*., 2023). Through the scanning electron microscopy (SEM), Jenkhongkarn and Phisalaphong (2023) captured the image of the most successful AgNP distribution, i.e., in the chitosan-reduced composite without the network being fallen apart. They had the same observations as well. Shaaban *et al*. (2023) revealed that the film of the green-synthesized BC-AgNP retained the three-dimensional network while the AgNPs resided in the pores and attached to the fibrils. These results point out the synthetic approaches that allow the continued existence of the BC-mimetic scaffold as well as the compatibility of the composites by not causing the coalescence of the metal particles.

Synthesis Methods of AgNPs on Bacterial Cellulose

Recent studies show BC generally retains its beneficial properties when combined with silver nanoparticles, provided synthesis methods ensure proper particle size and dispersion. While AgNPs may reduce crystallinity, water uptake, or mechanical strength, approaches like chitosan reduction or green synthesis can mitigate drawbacks, preserve BC's ECM-like architecture, and enhance wound-healing performance (Jenkhongkarn and Phisalaphong, 2023).

a) ***Thermal and in-situ chemical reduction*****:** A common method, which lowers the amount of silver nitrate in BC hydrogels *in situ*. Adding green reductants, such plant extracts, or hydroxyl groups to cellulose makes it easier for silver nanoparticles to form. The particles that come out are evenly spread out through the cellulose fibrils and are usually round, measuring 20 to 50 nm (Du *et al*., 2022; Siengchin *et al*., 2022). This easy and cheap procedure makes it possible to directly add AgNPs to the cellulose matrix.

b) ***Electrochemical synthesis*****:** Electrochemical reduction, due to ability to precisely regulate the size and distribution of nanoparticles, it has attracted attention in recent years. The synthesis of nearly contamination-free AgNPs is possible by adjusting the electrolyte conditions, current density, and potential (Moghaddam *et al*., 2025). Compared to thermal methods, electrochemical BC-Ag composites have improved crystallinity and narrower size distributions (Perevezentseva *et al*., 2025).

c) ***Eco-friendly and photochemical methods*****:** In new developments, the focus on an environmentally friendly synthesis have focused on the use of polysaccharides, photochemical activation, and reductants derived from plants. Composites of cellulose nanofibrils aided by ultraviolet light are more stable and less harmful to cells (Zeng *et al*., 2023). Enhanced antibacterial activity were observed in AgNPs inserted inside cellulose,

which was produced using microwave-assisted eco-friendly synthesis of biomass extracts.

Structure-Property Relationships

Particle size, dispersion, and surface interactions are strongly related to the characteristics of BC-AgNP composites. Nanoparticle production can be measured from the characteristic surface plasmon band ranging roughly from 400 to 450 nm as it has been illustrated by UV-Vis spectroscopy (Kumar *et al*., 2024). Based on Fourier transform infrared spectroscopy (FT-IR) analysis the binding between cellulose hydroxyl groups and silver is indicated while X-ray diffraction pattern reveals the existence of face-centered cubic [FCC] crystalline silver peaks at around 38°, 44° and 64° (Zulkifli *et al*., 2024). In addition to that, the behaviour of atomic force microscopy (AFM) and scanning electron microscopy (SEM) is supported by the images of nanoparticles being integrated inside BC fibrils which leads to changed surface roughness and higher surface area available for antimicrobial action (Cristescu *et al*., 2016). The sizes of particles that are smaller and more uniform dispersion are correlated with higher antibacterial efficacy due to greater ion release and enhanced interaction with bacterial membranes (Ershov *et al*., 2024).

Silver Nanoparticles in Antimicrobial Applications

The AgNP group is one of the best nanoparticles widely used in the medical field because of their powerful antimicrobial effect (Table 1). Recently, the fast development of new bacterial strains resistant to antibiotics has severely limited the use of antibiotics. This notion has led to an increased interest in AgNPs as an alternative to antibiotics (Sharma *et al*., 2023). Basically, one of the most viable solutions that is necessary to fight the new strains of resistant bacteria and fungi is AgNPs. This is because they have a wide range of activities, both against Gram-positive and Gram-negative bacteria (e.g., *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Escherichia coli*) as well as against fungi of clinical importance. Besides that, AgNPs are activated by biofilms, which are one of the reasons for chronic wound healing being difficult and tough to antibiotics. Thus, the effectiveness AgNPs have against biofilms makes them a very valuable tool in the treatment of chronic wounds.

Studies focused on *in vitro* and recent reviews report that AgNPs inhibit planktonic growth, prevent biofilm establishment, and that mature biofilms interfere with their penetration of the ECM, and, as a result, the embedded cells are killed. The antimicrobial activity varies with the nanoparticle's size, coating, and ionic environment, with smaller particles being more potent in general. Recent studies show a strong confirmation of the effectiveness of AgNPs against multidrug-resistant (MDR) strains; however, they also point out the differences in methodologies (Rodrigues *et al*., 2024). Toxicity is still cored despite the silver's efficacies. The toxic nature of silver is such that it has a narrow therapeutic window and may cause damage to mammalian cells or get accumulated in tissues. The newest toxicology research is very clear about the need for dose optimization and surface functionalization as safety measures (Jaswal and Gupta, 2023). Stability is yet one more problem; over the period, there has been a significant improvement in the stability of the advanced capping, *in situ* synthesis, or encapsulation methods that allow for a more precise release of silver (Li and Xu, 2024). It is true that AgNPs are capable of multiple mechanisms; however, resistance might still be developed under selective pressure. One of the experimental studies on evolution shows that *E. coli* and *S. aureus* may increase resistance to silver by releasing silver-binding proteins, bringing more pumps into play, changing the membranes, and causing nanoparticle aggregation along with that area (Hochvaldová *et al*., 2024). Therefore, the responsible use of the right dose, combination therapy, and taking continuous care constitute the main safety measures. The regulatory translation is also hampered by several factors including lack of universal nanoparticle characterization, variable kinetics of release, and nonexistence of standardized assays. On top of that, the reviews call for standardized industry protocols and prolonged safety in the body data (More *et al*., 2023; Hochvaldová *et al*., 2024).

Table 1: Silver nanoparticles and antimicrobial applications.

AgNPs *of L. acapulcensis*	Green synthesis of chemically reduced AgNPs by *Lysiloma acapulcensis*	Spheric	1.2–62 nm	*C. albicans, E. coli, S. aureus*, and *P. aeruginosa*	Inactivation 0.06–0.25 µg/mL	Disk diffusion
AgNPs *of Citrus limon* (L.)	Green synthesis of chemically reduced AgNPs by aqueous extract of *Citrus limon* (L.) zest	Spheric and cubic	7–28 nm	*S. aureus, E. coli*, and *C. albicans*	Inactivation	Disk diffusion
AgNPs of *Cynodon dactylon*	Green synthesis of AgNPs reduced by *Cynodon dactylon* leaf extract	Spheric	15 nm	*P. fluorescens*	Inactivation	Disk diffusion
MOF-AgNPs	Green synthesis of	Spheric	22 nm	*K. pneumoniae*	Inactivation	Disk

	AgNPs reduced by *Moringa oleifera* flower extract			and *S. aureus*		diffusion
Sb-AgNP	Green synthesis of reduced AgNPs with aqueous extract of *Scutellaria barbata*	Spheric	20–40 nm	*E. coli, P. aeruginosa, S. aureus* and *K. pneumoniae*	Inactivation 2.8, 3.1, 3.4, and 2.2 µL	Disk diffusion
AgNPs of *Phyllanthus emblica*	Biological synthesis of AgNPs with *Phyllanthus emblica* fruit extract	Spheric	19–45 nm	*K. pneumoniae* and *S. aureus*	Inactivation 10 µg both	Disk diffusion
AgNPs of *Gardenia thailandica* (GTLE)	Green synthesis of AgNPs reduced by *Gardenia thailandica* leaf extract (GTLE)	Spheric	11.02–17.92 nm	*S. aureus*	Reduction of CFU, regeneration of the epidermis and reduction of inflammatory cell infiltration 4-64 µg/mL	Disk diffusion and *in vivo* antibacterial activity in rats
AgNPs of *Penicillium oxalicum*	Biogenic synthesis of AgNPs from fungal metabolites of *Penicillium oxalicum*	Spheric	60–80 nm	*S. aureus, S. dysenteriae* and *S. typhi*	Inactivation	Disk diffusion and broth dilution
AgNPs of *Berberis vulgaris*	Green synthesis of reduced AgNPs with aqueous extract of *Berberis vulgaris* leaves and roots	Spheric	30–70 nm	*E. coli* and *S. aureus*	Inactivation or reduction 0.20 and 400 µg/mL	Disk diffusion and broth dilution
AgNPs of *Padina* sp.	Green synthesis of AgNPs reduced by aqueous extract of marine macroalgae *Padina* sp.	Spheric	25–60 nm	*S. aureus, B. subtilis, P. aeruginosa, S. typhi* and *E. coli*	Inactivation 0.25 mg/mL for all strains	Disk diffusion
AgNPs of *Carissa carandas L.*	Green biosynthesis of silver nanoparticles using *Carissa carandas* L leaf extract.	Not specified	Not specified	*S. flexneri, Citrobacter* spp., *S. typhimurium, E. faecalis,* and *Gonococos* spp.	Inactivation 60, 80, and 100 µL for other strains	Disk diffusion

Source: Rodrigues *et al*. (2024)

Fabrication Approaches of Bacterial Cellulose–Silver Nanoparticle Composites

BC-AgNP composites can be fabricated through diverse methods, each balancing silver dispersion, particle size, release, mechanics, cost, and biocompatibility, with recent refinements highlighted in recent studies (Recent literature, 2023–2025).

a) In situ synthesis of AgNPs within BC matrix

The *in-situ* method reduces silver ions directly within the BC matrix, enabling uniform AgNP dispersion, stronger fiber adhesion, moderated release, and improved stability. Jenkhongkarn and Phisalaphong (2023) compared multiple reduction routes (NaOH, ascorbic acid, chitosan, UV) and reported variations in AgNP size, crystallinity, and mechanical performance. Ascorbic acid-reduced composites showed the highest Young's modulus, while UV-, NaOH-, and chitosan-reduced composites displayed distinct tensile and elongation properties. Another study demonstrated antibacterial efficacy of BC membranes impregnated *in situ* with *Moringa oleifera*-mediated AgNPs (24–40 nm) against *S. aureus* ATCC 6538 and *P. aeruginosa* ATCC 9027 (Jenkhongkarn and Phisalaphong, 2023). In related work, the antimicrobial potency of BC–AgNP composites varied with BC microstructure when produced from different carbon sources and reduced *in situ* (Yang, 2012). Fahrurrozi *et al*. (2023) also reported green *in situ* incorporation of AgNPs, with SEM, X-ray diffraction (XRD), FTIR, and energy dispersive X-ray spectroscopy (EDX) characterization confirming activity against *E. coli* and *S. aureus* (Dias *et al*., 2024).

b) Ex situ incorporation of pre-formed AgNPs

In an *ex-situ* process, AgNPs are produced separately and thereafter incorporated in BC matrices. The nanoparticle properties being controlled independently, but at the same time there are problems with dispersion, adhesion, and aggregation. Homwan *et al.* (2023) carried out the preparation of BC-AgNP composites by the impregnation of AgNPs in the permeable BC network, which was identified by field emission scanning electron microscope (FESEM) and XRD, and that showed a very good antibacterial property against both Gram-negative and Gram-positive bacteria in comparison to pure BC. In the same way, it was reported that the membranes of BC-graphene oxide (GO)-Ag produced by the *ex-situ* method improved antimicrobial properties against *Escherichia coli*, *Staphylococcus aureus*, and *Pseudomonas aeruginosa* as well as maintained fibroblast cytocompatibility (Han *et al*., 2022; Luz *et al*. (2024).

c) Green synthesis approaches (plant extracts, microbial methods)

Biosynthetic or green methods produce AgNPs by using plant extracts, microbes, or reductants derived from bio-sources so that the final nanoparticles have reduced toxicity and increased biocompatibility. Among all test metallic nanoparticles, AgNPs have the highest percentage (42%) in a five-year trend of publications on green synthesis of nanoparticles (Figure 2). AgNPs (24–40 nm) were developed by the use of the *Moringa oleifera* extract and then embedded in BC, during which the structure of BC was kept and the antimicrobial property was exhibited (Shaaban *et al*., 2023). Mutiara *et al*. (2023) revealed that green BC–AgNP composites not only have good thermal stability but also show antimicrobial activity against *S. aureus* and *E. coli* (Dias *et al.*, 2024). Charti *et al*. (2025) took advantage of a microwave-assisted *in situ* reduction that made AgNPs well-dispersed and allowed anaerobic bacteria to be efficiently killed.

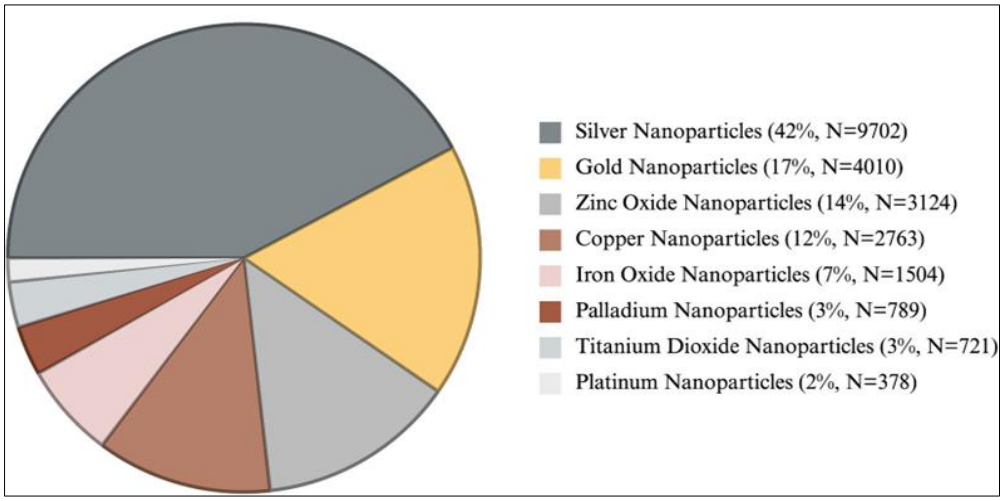

Figure 2: Five-year trend in publications on green synthesis of nanoparticles.
Source: Eker *et al*. (2025)

d) Surface modifications and functionalization strategies

Not only AgNPs are incorporated into the nanocomposites, but their properties can be also improved by advanced methods that use surface modification, functional nanomaterials, or multifunctional scaffolds for the composites. For instance, the GO–Ag functionalization has brought improvements in the antibacterial efficacy, exudate absorption, mechanics, and cytocompatibility of bacterial cellulose membranes (Phan *et al*., 2022). The authors Dias, Nagar *et al*. (2024) fabricated BC–Cur-AgSeNP composites in which curcumin was the source of antioxidant/anti-inflammatory properties, the nanoparticles were the surface adsorbed and embedded, resulting in antimicrobial, antioxidative, and biocompatible characteristics (Dao *et al*. 2023). Indrianingsih *et al*. (2025) exploited the phenolic compounds in the *Clitoria ternatea*extract to improve the antioxidant activity, surface roughness, and antibacterial property of BC–Ag films by making them rougher with the phenolic compounds.

Comparative Remarks and Synthesis of Approaches

Recently published works illuminate significant components of biocompatible cellulose-silver nanoparticle (BC–AgNP) manufacturing. Tools fabricated directly or '*in situ*' achieve, among other things, better cohesion between the host material and the metal, more even 'silver' particle distribution, and stronger atomic bonding. At the same time, the dimension and the degree of particle crystallinity depend largely on the type of reduction agent and reaction conditions used. Nanoparticles prepared *ex situ* can be controlled precisely in terms of their size and morphologies, yet they usually have issues related to dispersion and bonding with the host matrix. The green method of synthesis (plant-based or microbial extracts, microwave-assisted reactions) opens the way for biocompatibility-boosting while, arguably, it might

reduce the morphological control of materials. Surface modifications with graphene oxide (GO), curcumin, or flower extracts enable the regulated release of silver and the multifunctional (antioxidant, anti-inflammatory, and wound-healing benefits) effects to mix with BC. They are not flawless, though, and there are still some compromises that alter the composites' mechanics or swelling capabilities, produce fluctuating AgNP distributions, or adversely influence BC crystallinity.

Recent Advances

a) Novel synthesis techniques for enhanced antimicrobial activity and reduced cytotoxicity

The synthesis of BC–AgNP composites was fine-tuned with the aim of increasing the antimicrobial power of the materials and, at the same time, lowering their cytotoxicity, which was carried out between 2023 and 2025. The main strategies could be summarized as follows: (1) the *in-situ* reduction process was optimized to allow the researchers to better control particle sizes, crystallinities, and the like, as well as dispersion, and (2) the addition of capping or co-agents (e.g., chitosan, ascorbic acid, biopolymers) was used to moderate Ag^+ release. Jenkhongkarn and Phisalaphong (2023) reveal that the reduction chemistry is a very influential factor in silver nanoparticle size, BC crystallinity, and mechanics, with chitosan giving smaller, well-dispersed particles as a result. The combination of polymeric capping and bioactive co-loading, such as GM-CSF, not only extended the silver release but also enhanced the wound healing effect. These findings are a great example of increased therapeutic windows (Du *et al*., 2022; Siengchin *et al*., 2022).

b) Hybrid composites (BC-AgNPs combined with nanomaterials, bioactive compounds, or other polymers)

Hybrid BC–Ag composites, which combine silver with graphene oxide, curcumin, selenium, or polyphenols to provide antibacterial, antioxidant, and anti-inflammatory qualities, respectively, were popular between 2023 and 2025. BC/GO-Ag membranes contributed to the improvement of the flexibility, antibacterial activity, and fibroblast compatibility (Luz *et al*., 2024), whereas Ag–curcumin/selenium ensembles were capable of attracting living matter (Ciftci, 2024). These multifunctional castellations not only lowered the amount of silver used, but also increased the healing efficiency as well as familiarized with the physiology of wounds beyond infection control (Luz *et al*., 2024).

c) Smart wound dressings

BC–Ag dressings with stimuli responsiveness, which have been conceptualized to release silver selectively, are moving next to the stage for practical uses. Experiments connecting pH-sensitive polymers or nanozyme composites to break down EPS for easier microbial access or trigger silver release in infection-related alkaline pH have been published recently (2024–2025). These intelligent systems can lower the background toxicity, supply the targeted silver, and facilitate the degradation of biofilm EPS, thus improving microbial access. Although mainly *in vitro* or animal model research, they display the concepts of safety and efficacy of on-demand wound dressings (Alberts *et al*., 2025).

d) Clinical and pre-clinical studies

Preclinical *in vivo* experiments (2023–2025) indicate that BC–Ag composites are capable of hastening wound closure, lowering bacterial load, and upgrading histology as compared to controls. The 2024 Wistar rat study, according to the report, witnessed the healing process becoming effective without systemic toxicity, whereas the silver–bioactive hybrids (e.g., GM-CSF) potentiated re-epithelialization and angiogenesis. However, there are still very few human trials done; the regulatory step requires coordinated safety data and standardized protocols for antimicrobial assays, cytotoxicity, and release kinetics (Punjataewakupt *et al*., 2019; Zhou *et al*., 2002; Ozelin *et al*., 2024).

e) Comparative analyses with other antimicrobial wound dressings

Recently, scientific papers have been comparing BC–Ag composites to next-generation antimicrobial dressings such as silver-impregnated foams, iodine, PHMB, peptides, and hydrogels (Blackburn *et al*., 2023; Ousey *et al*., 2023; Ma *et al*., 2024). Reviews (2023–2024) indicate that Ag-based dressings are effective in reducing the microbial load and promoting wound healing, however, the effectiveness is still dependent on the dose, release and cytocompatibility. In terms of moisture and conformance, BC matrices perform better than gauze, and with controlled AgNP loading, they can provide antibacterial outcomes comparable to those of commercial silver products with a lower amount of silver. The different forms of Ag and methods of assay have made it difficult to compare, hence the importance of standardized trials (Xu *et al*., 2018). In general, 2023–2025 studies show the progress in development of multifunctional, environmentally-friendly, and stimulus-responsive BC–Ag composites; however, clinical validation remains critical (Jenkhongkarn and Phisalaphong, 2023).

Biomedical Performance of BC–AgNP Composites

a) antimicrobial efficacy against multidrug-resistant pathogens

BC–AgNP composites, when designed optimally, are effective antimicrobial agents against wound pathogens and also kill MDR strains. A series of tests (2023–2025) have pointed out that the composites are effective against *S. aureus* (MRSA), *P. aeruginosa*, and *E. coli*. Silver nanoparticles made by using a green method (24–40 nm) that were incorporated in BC not only kept their original lattice but also showed a bactericidal effect. The rat model of wound demonstrated the decrease in microbial load with the application of

Ag–BC. The experimental data are consistent with the findings in the literature which broadly acknowledge the anti-MDR potential of silver nanomaterials upon the thorough mastering of release kinetics and particle features (Shaaban *et al*., 2023).

b) Cytocompatibility and effects on fibroblast/keratinocyte proliferation

BC–AgNP composites represent a good model of antimicrobial activity of interest from the point of view of the cytocompatibility paradigm. Although the presence of BC has a positive impact on cell growth, excessive release of Ag^+ or poor control of the nanoparticles leads to cell viability impairment. The production of these materials using the strategies of capping agents, *in situ* formation, and reduced loading has had a very positive effect on the performance of fibroblast and keratinocyte cells. Evidence (2023–2024) shows that the dispersed, small AgNPs, which are frequently stabilized by chitosan or other green reductants, do not hinder the viability of fibroblasts and encourage keratinocyte migration vis-à-vis the high-dose control group. Still, however, they are not absolutely safe, and the cytotoxicity is dose-dependent, which is the reason why controlled release and standard test methods for the evaluation of cytocompatibility are necessary (Munhoz *et al*., 2023).

c) Wound healing acceleration (angiogenesis, collagen deposition, re-epithelialization)

The preclinical explorations suggest that BC–AgNP composites may have dual-functionality, i.e., along with controlling infection, the wound healing can be promoted much better than the case of BC or untreated wounds. There is the evidence of faster wound healing, which is the basis for various parameters, such as the development of granulation tissue being assessed for both collagenization and re-epithelialization/angiogenesis. Histological and immunochemical results demonstrated rat dermal wounds treated with Ag-BC showed quicker wound closure, formation of well-organized collagen, and neovascularization. These composites with Ag combined with growth factors or antioxidants gave even more significant results of regeneration. Still a lot of work needs to be done related to long-term histopathology and systemic safety (Ozelin *et al*., 2024).

d) Anti-inflammatory and antioxidant effects

One of the recent works describes the preparation of BC–AgNP composites to get not only an antimicrobial but also an anti-inflammatory/antioxidant function. The primary strategy was chitosan capping or co-loading with antioxidants (such as curcumin and plant extracts), which control inflammation, reduce cytokines, and also act as ROS scavengers. *In vivo*, these impregnated materials have been found to reduce the local inflammatory infiltration and the oxidative stress load, thus prolonging the wound healing process. One of the most important properties of the nanoparticles is their modifiable nature, through which a silver agent can be employed to balance infection control and inflammation management. According to the research, silver nanoparticle functionalization might be precisely engineered using co-agents for this purpose (Munhoz *et al*., 2023).

The Silver Nano-Particles (AgNPs) Antimicrobial Action Mechanisms

AgNPs gradually kill microbes through several, sometimes simultaneous, ways (Figure 3 and Table 2). A few of such mechanisms are revealed below.

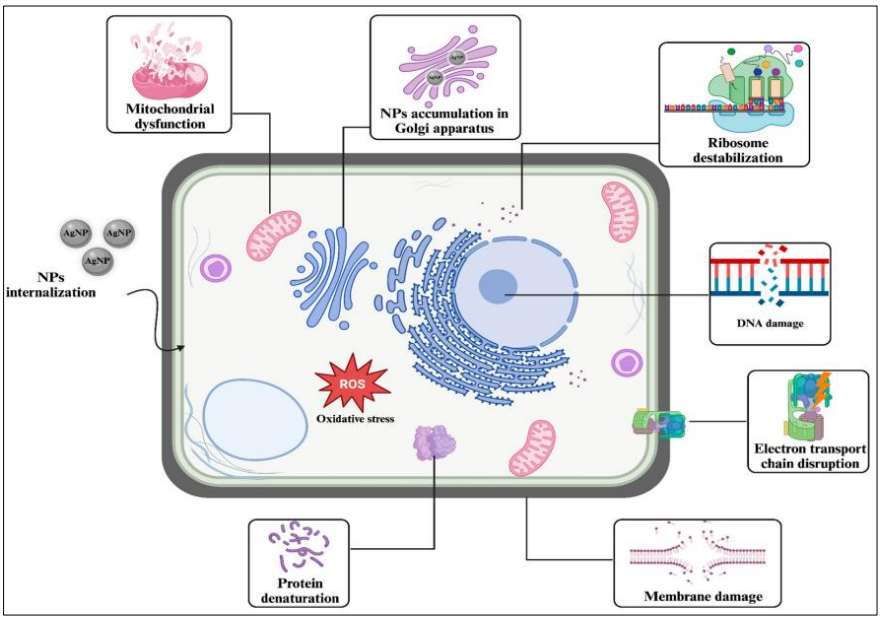

Figure 3: Antibacterial mechanisms of silver nanoparticles
Source: Anees *et al*. (2020)

a) Destruction of bacterial cell walls

Bacterial cell walls are targets of nano-clarified particles (either by electrostatic attraction or through interaction with membrane proteins). These particles then are introduced into the lipid bilayer and disturb the membrane's function. This raises permeability, causes membrane depolarization, and results in the leakage of both ions and cytoplasmic contents. Along with membrane integrity breakdown, respiration and nutrition transport are deprived as well. In research using electron microscopy, the presence of AgNPs has been observed to accompany deformations of cell surfaces and membranes. Also, the nanoparticles can adhere to the bacterial cell wall, enter the bacterial cell, and change the various metabolic pathways as part of the mechanical strategy for using NPs against the bacteria and the biofilm. It has an impact on protein synthesis and DNA replication; oxidative stress causes ROS to be generated. Moreover, it eventually results in cell death, as shown in Figure 4 (More *et al*., 2023). The suitability of BC–AgNP dressings, therefore, is because bacterial cellulose although a porous and hydrophilic matrix, allows it to display AgNPs at the wound interface where direct contact with planktonic cells and surface-attached cells can be maximized, facilitating membrane-targeted killing (More *et al*., 2023).

Table 2: Mechanism of action detected by proteomics: proteins expressed in bacteria after treatment with AgNPs

Material	**Size**	**AgNPs effect**	**Bacteria**	**Marker**			**Method**	**References**
				Upregulation	Downregulation	Inhibition		
AgNPs reduced by branched cyclodextrin solution	5–20 nm	Inhibition of adhesion and motility, ROS, alteration of iron homeostasis, blockade of aerobic and anaerobic respiration, changes in quorum sensing (QS) and inhibition of the expression of virulent factors	*P. aeruginosa*	AntA, AntB and NarL	Dnr and NarX	ArcA, ArcD, NADH dehydrogenases (NuoE, NuoL and PA0949) and SdhC	TMT-labeled quantitative proteomic	Zhang et al. (2020)
AgNP stock solution	5–7 nm	Damage to bacteria, inhibition of peptidoglycan synthesis, damage to biofilm structure and bacterial adhesion, disturbances in QS, decreased bacterial proliferation and induction of ROS	*S. suis* (MDR)	S-ribosylhomocysteine lyase and cps2J	Chromosomal replication initiation protein DnaA, cell division initiation proteins FtsZ and DivIB and proteolytic subunit of the ATP-dependent Clp protease	Penicillin-binding proteins (PBPs)	iTRAQ-based proteomic analysis	Liu et al. (2023)

AgNPs reduced by DAMP (AgDAMP)	21.87 ± 0.06 nm	Alteration in the expression of regulators of protein synthesis, DNA replication, membrane transport, ROS and cell motility	*Salmonella*	ROS (A0A0K0HA36) and toxicity (A0A0K0HBQ0)	DEPs of protein biosynthesis (A0A724WMT2 and G5LUI4), effiux pump (A0A1S0Z705), phosphorylation transduction (A0A740TKQ2) and transcriptional modulation (A0A724WUQ6)	-	High-throughput sequencing	Wang et al. (2023)
AgNPs reduced by sodium borohydride	10 nm	Inhibition of protein synthesis, disruption of antioxidant enzymes, induction of ROS and dysregulation of homeostasis of pentose phosphate oxidative pathway	*S. aureus*	-	-	Enzymes of the oxidative pentose phosphate pathway (oxPPP): 6-phosphogluconolactonase (Pgl) and 6-phosphogluconate dehydrogenase (6PGDH)	LC-GE-ICP-MS	Wang et al. (2021)

Enterococcus faecalis, Escherichia coli, Pseudomonas aeruginosa, Staphylococcus aureus, and *Streptococcus suis*.
Source: Rodrigues *et al*. (2024)

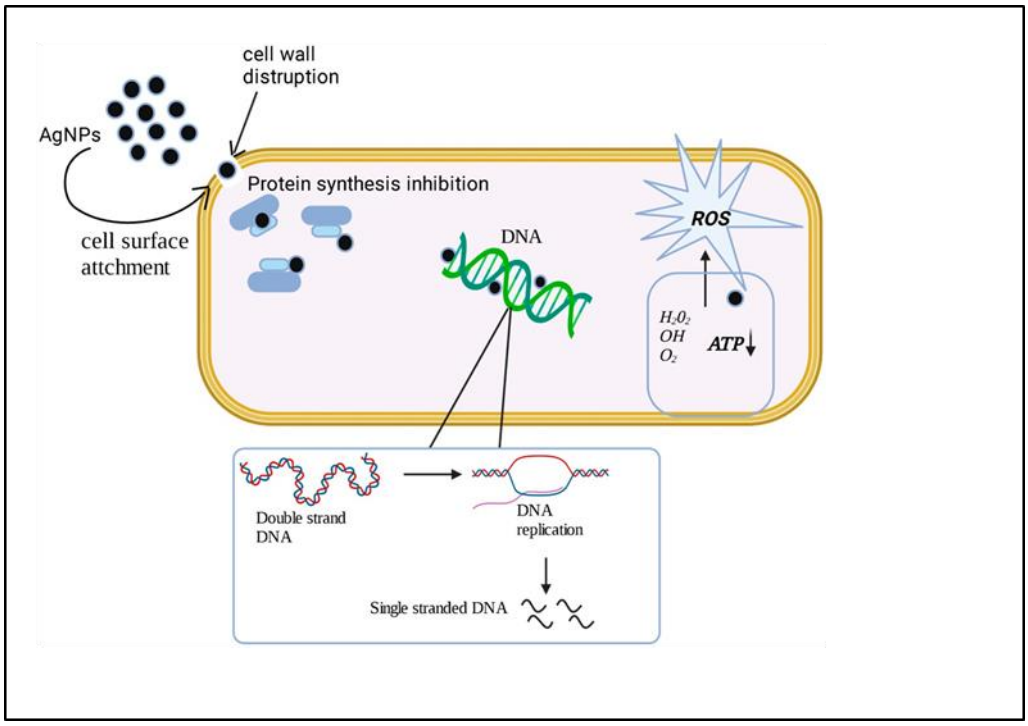

Figure 4: Mechanism action of the antibacterial activity of nanoparticles

The nanoparticles attach to the bacterial cell wall, penetrate the bacterial cell, and alter the different metabolic pathways. It affects DNA replication and protein synthesis; due to oxidative stress, ROS generation takes place. Furthermore, ultimately, it leads to cell death. **Source:** More *et al*. (2023)

b) The production of reactive oxygen species/ oxidative damage

AgNPs (or Ag^+ coming from them) greatly immerse the environment to generate reactive oxygen species (ROS) like superoxide ($O_2 \cdot^-$), hydrogen peroxide (H_2O_2), and hydroxyl radicals ($\cdot OH$). Consequently, the ROS symbiotically oxidize membrane lipids (lipid peroxidation), proteins (side-chain oxidation, carbonylation), and nucleic acids (strand breaks, base oxidation). One of the ways that AgNPs kill cells is through lipid peroxidation, which leads to extensive cell damage and implies similar mechanisms in microbial cells (Rohde *et al*., 2021). In bacteria, Rodrigues *et al*. (2024) explain the role of ROS generation as the main mechanism for the antimicrobial activity of AgNPs along with membrane disruption and enzyme inactivation. Composite dressings are highly beneficial in maximizing antibacterial reactive-oxygen species ROS generation at a wound through controlling AgNP size, surface coating, and release kinetics, while at the same time minimizing oxidative damage to the host tissue (Kwiatkowska *et al*., 2022; Sadeghi-avalshahr, 2025; Michalicha *et al*., 2024).

c) Release of silver ions

One of the ways by which AgNPs are effective is that they serve as a slow-release reservoir, in which Ag^+ is gradually released through oxidative dissolution under aerobic conditions. The released ions attach themselves to the thiol (–SH) groups in proteins, thus, only a few of the enzymes such as dehydrogenases and respiratory chain proteins, which are the sources of cellular energy in a cell, can be active at a time. Besides that, they bind to only a few of the bases and phosphate backbones of DNA/RNA, hence, replication and transcription are disrupted (Figure 5). To sum up, Yin *et al*. (2020) conclude that the essential matter in bacterial death is that Ag^+ interacts with membrane and intracellular proteins. According to Reidy *et al*. (2013), the particle dissolution, ageing, and surface chemistry are variables which regulate whether the metal will be in the ionic form or as particles. The BC structures can be modified in such a way that they guarantee the safety and efficacy of the product (e.g., by using porosity control, crosslinking, or AgNP capping agents) to precisely adjust Ag^+ release while sustaining antimicrobial activity and cytocompatibility (Duman *et al*., 2024; Eker *et al*., 2024; Eker *et al*., 2025).

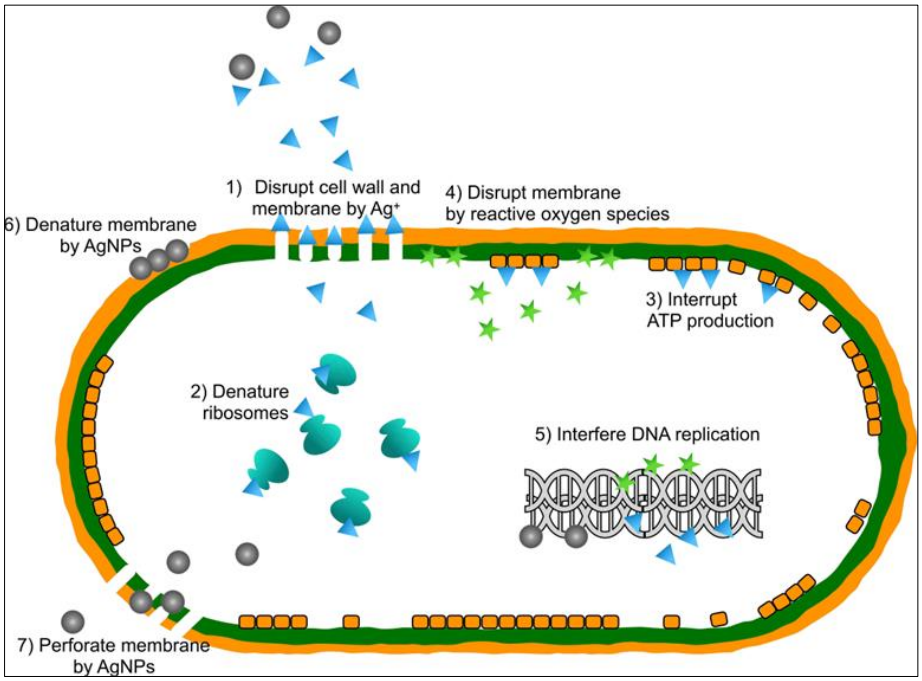

Figure 5: The antibacterial actions of silver nanoparticles (AgNPs).
Source: Yin et al. (2020)

(1) Disruption of cell wall and cytoplasmic membrane: silver ions (Ag+) released by silver nanoparticles adhere to or pass through cell wall and cytoplasmic membrane. (2) Denaturation of ribosomes: silver ions denature ribosomes and inhibit protein synthesis. (3) Interruption of adenosine triphosphate (ATP) production: ATP production is terminated because silver ions deactivate respiratory enzyme on cytoplasmic membrane. (4) Membrane disruption by reactive oxygen species: reactive oxygen species produced by the broken electron transport chain can cause membrane disruption. (5) Interference of

deoxyribonucleic acid (DNA) replication: silver and reactive oxygen species bind to deoxyribonucleic acid and prevent its replication and cell multiplication. (6) Denaturation of membrane: silver nanoparticles accumulate in the pits of cell wall and cause membrane denaturation. (7) Perforation of membrane: silver nanoparticles directly move across cytoplasmic membrane, which can release organelles from cell.

d) Biofilm inhibition and disruption

Wounds that have been present for a long time are usually home to biofilm-forming bacteria such as *Pseudomonas aeruginosa* and *Staphylococcus aureus*, and hence the miniaturized AgNPs that have lost their configuration are now the most potent antibiofilm agents. AgNPs interrupt the formation of biofilms at different stages: obstructing bacterial attachment, inhibiting quorum sensing, lessening the production of extracellular polymeric substance (EPS), the most recent discovered and the fastest discovered is penetration of biofilm matrices to discharge ROS and Ag^+ which results in killing the cells which are embedded. They also destabilize biofilm structures, exposing pathogens to antimicrobials and host defenses. Reviews emphasize silver's diverse antibiofilm mechanisms, including interference with DNA replication and gene expression (Sedighi *et al*., 2024; Iaconis *et al*., 2024; More *et al*., 2023). Surveys highlight AgNPs' promise in chronic wound biofilm control, especially when embedded in BC dressings that provide sustained release, reduce biofilm burden, and promote healing progression (Jing *et al*., 2024).

e) Synergistic and overlapping action; reduced likelihood of classical resistance

Because multiple mechanisms (membrane attack, ROS, ionic interactions, biofilm targeting) operate simultaneously, bacteria must adapt along several fronts to survive. This multivalent attack raises the barrier for classical (single-gene) resistance. In addition, in many systems AgNPs show synergy with conventional antibiotics, enabling lower antibiotic doses and reducing selective pressure for antibiotic resistance. For instance, Rodrigues *et al*. (2024) mention the enhancement of antibiotic efficacy when combined with AgNPs. However, adaptive responses (e.g. efflux pump upregulation, increased production of extracellular matrix, silver ion sequestration) have been reported and warrant attention. The Reidy *et al*.'s review argues for rigorous risk–benefit assessment given the possibility of resistance evolution and ecological impacts.

***In Vitro* and *In Vivo* Performance**

In vitro studies consistently show BC–AgNP composites provide markedly enhanced antibacterial activity over BC alone. Green-synthesized AgNPs (24–40 nm) in BC using *Moringa oleifera* extract inhibited *Staphylococcus aureus* and *Pseudomonas aeruginosa* (Shaaban *et al*., 2023). Similarly, an Ag-pDA/BC(rGO) film achieved >84% bactericidal activity against *Escherichia coli* for 72 h with good NIH3T3 biocompatibility (Bal-Öztürk *et al*., 2024). These findings highlight BC–AgNP composites' broad-spectrum efficacy and cytocompatibility advantages. *In vivo* studies confirm AgNP–BC composites enhance wound healing. In a rat second-degree wound model, AgNP–BC gel membranes accelerated closure, reduced microbial flora, lowered inflammation, and supported fibroblast growth with low cytotoxicity (Wu *et al*., 2014). Similarly, biosynthesized AgNPs from *Nepeta cataria* achieved ~94% closure by day 10 with organized collagen and epithelialization (Sari *et al*., 2025). Clinically, the evidence is quite limited but growing. A recent randomized trial that compared nanocellulose, silver-foam, and ibuprofen-foam dressings showed that infection control, healing, and tolerance were comparable, and no major silver-related adverse events were reported (Hecker *et al*., 2022). These results indicate that silver-based dressings, e.g., BC–AgNPs, may be the next generation of wound care products that combine safety with efficacy.

Safety and Cytocompatibility

Even with the demonstrated health benefits of BC–AgNP composites, the issue of silver-induced toxicity to the cellular environment of the human body keeps being raised. For instance, Tripathi and Goshisht in their paper of 2022 experimented with human keratinocytes and fibroblasts that had been exposed to high concentrations of AgNPs and found out that the cells' viability was greatly reduced due to oxidative stress. Along these lines, the control of Ag^+ release from nanomaterials is very instrumental. The surface-modified bacterial cellulose carriers using biopolymer materials such as chitosan and polyphenols have been proven in research to both lower the toxicity level and retain antimicrobial activity (Abdellatif *et al*., 2024). These factors determine the importance of concentration dosage as excessive silver can delay the healing process in low-term studies. What can now be observed from recent BC–AgNP scaffold designs is that there are concepts of a dual-function where AgNPs provide antibacterial properties whereas biocompatible molecules like GM-CSF improve cell regeneration and consequently healing progress (Zhang *et al*., 2025).

Challenges and Limitations

The chief obstacles and drawbacks that have been recently discussed in the scientific works with respect to BC-AgNP composites as antimicrobial wound dressings are outlined herein. The different problem themes are indicated along with references to some of the recent experimental studies and review articles that report the issues.

a) Cytotoxicity of AgNPs at higher concentrations

The antimicrobial activity of AgNPs is still linked to the release of silver ions (Ag^+) and the production of ROS, even though BC provides a biocompatible matrix. These processes, while

responsible for the antimicrobial efficacy, can also harm mammalian cells at higher concentrations. A number of both *in vitro* and *in vivo* research studies have been published which indicate the occurrence of concentration-dependent cytotoxicity (reduced fibroblast/keratinocyte viability, oxidative stress markers) and point out the narrow therapeutic window between the antimicrobial activity that is efficient and host-cell toxicity. In this way, a basic design trade-off emerges: increasing AgNP loading boosts the antimicrobial potency but at the same time raises the risk of delayed wound healing or local tissue toxicity, especially with prolonged exposure (Jangid *et al*., 2024).

b) Stability and release kinetics of silver ions

The release of bioactive Ag^+ should ideally be done in a controlled and sustained manner. A sudden release can lead to toxicity thus a rapid depletion of the effective agent, whereas, if the release is too slow, the infection will not be prevented. The release of silver is dependent on many factors such as particle size, the use of a capping agent, the aggregation of AgNPs, porosity, and crosslinking of BC, and the local wound's chemistry. The results of these factors show a wide range of variability across the studies. A number of works provide the controlled-release systems of various types (hydrogels, crosslinked BC matrices, polymer coatings) as substantially promising, but the comparative and quantitative release data under physiologically relevant conditions are few and inconsistent, which complicates the clinic translation. Stability for a long time (AgNP oxidation, aggregation, or dissolution during storage) is also a problem that is not fully resolved in many reports (Jiang *et al*., 2020).

c) Standardization and reproducibility of synthesis methods

There are several methods for the production of AgNPs such as chemical reduction, physical methods, and a large number of "green"/biogenic syntheses that are based on plant extracts or microbes. Although the green synthesis line is more sustainable and can easily produce biocompatible surface coatings, it has the disadvantage of having batch-to-batch variability because biological extracts are not always of the same composition (Shaheen *et al*., 2022). Additionally, there is inconsistency in the methods used to report data: details about the particle size distribution, surface charge, surface chemistry, endotoxin testing, and detailed processing of the base carbon are either not provided or measured using disparate techniques, which makes it challenging to replicate and compare study findings. In the literature, there is a growing demand for standardised protocol and at least minimum checklists for characterisation of AgNP-composites (Fahim *et al*., 2024).

d) Scale-up and cost-effectiveness

Laboratory methods for producing BC and loading AgNPs (static fermentation, small-scale green syntheses, manual impregnation) rarely translate directly to cost-competitive, GMP-compliant manufacturing. Challenges include achieving consistent BC quality at scale (strain selection, reactor design), controlling AgNP size/distribution in large batches, solvent/reagent costs, and downstream sterilization without altering composite properties. A complete set of economic analyses will be difficult to obtain. Some recent reviews just only point to the role of process intensification and integration (*in situ* AgNP synthesis during BC fermentation, continuous production lines) as a means to reduce costs. Nevertheless, these methods are still in need of engineering validation and financial support (Sorourian *et al*., 2024).

e) Regulatory and safety concerns

The safety regulations system for antimicrobial wound dressings, which implement nanomaterials, is still under development. The regulatory bodies (for instance, the Food and Drug Administration [FDA]) have taken the step of clarifying the category of some solid wound dressings and giving the signal for a very close examination of the new composite dressings. Recent proposals and notices indicate regulators' re-evaluation of device codes and evidentiary needs for safety and efficacy. The main difficulties in the regulatory area are proving long-term safety (local and systemic silver exposure), providing clinically significant advantage over existing dressings, and presenting manufacturing controls and release/sterility data of a standardised nature. The lack of a harmonised set of international guidelines for nanomaterial-containing dressings makes it harder for such products to enter the market (Trucillo and Di Maio, 2021).

f) Unresolved clinical and workflow challenges

There are many limitations for BC–AgNP wound dressings that lead to the problem of clinical translation. Among the issues is the lack of strong clinical evidence. Most research is limited to *in vitro* experiments or small animal models. There are nearly no comprehensive, rigorously controlled human clinical trials. As a result, clinical efficacy, dosing, application duration, and patient selection, among other factors, are still ambiguous (Munhoz *et al*., 2023; Jangid, 2024). Furthermore, the integration of a dressing for wound care processes remains largely unconsidered. Problems relating to the manner in which the product is handled, how it sticks to a wound, the period of its use, if the product causes any discomfort and if the dressing interacts with standard wound care products are hardly discussed, which in turn hampers their applicability in the field.

Practical Implications and Short Recommendations

Practical recommendations to advance BC–AgNP composites for antimicrobial wound dressings focus on standardization, safety, scalability, and regulatory alignment. Researchers are encouraged to set up and document a minimum characterization standard

that should include the measurement of particle size, surface chemistry, endotoxin levels, silver ion release in simulated wound fluid, and cytotoxicity on relevant cells for better reproducibility and allowing cross-study comparisons (Fahim, 2024; Akhter *et al*., 2024). The research should mainly focus on the dose–response range that will link the antimicrobial efficacy with the host-cell toxicity under the condition of realistic exposure times which will be of help in clarifying the narrow therapeutic window of AgNPs (Jangid, 2024). It is vital for clinical translation to demonstrate the scalable synthesis with pilot reactor data, production/storage stability, sterilization impact, and cost modelling (Sorourian, 2024; Munhoz *et al*., 2023). Along with this, early addressing the regulatory bodies' requirements for preclinical safety packages as well as safe clinical trial designing is their way to easing the process of approval plus the use of the product (Chen *et al*., 2023; Nusgart, 2024; Padula *et al*., 2025).

Future Perspectives

a) Designing multifunctional BC–AgNP wound dressings

The next-generation BC–AgNP dressings are being developed with the goal of incorporating the controlled release of silver alongside agents that are capable of promoting regeneration such as growth factors (VEGF, PDGF, GM-CSF), small molecules, or bioactive peptides. In this way, these agents when used together with AgNPs can provide both infection management and the stimulation of angiogenesis and re-epithelialization simultaneously. Preclinical BC/Ag/GM-CSF composites have been shown to improve wound closure and histology more quickly. This is because the release kinetics were successfully adjusted, maintaining the bioactivity of the regenerative agents while also keeping the silver within a safe antimicrobial range through the use of techniques like affinity-based BC binding and micro/nano-carriers (Zhang *et al*., 2025).

b) Integration with digital health (smart sensors for real-time wound monitoring)

The use of sensors for BC-AgNP dressings is the real-time monitoring of wound parameters; pH, temperature, moisture, and protease levels, which enables the alert of the clinician or the automatic response. Smart bandages with flexible, colorimetric, or electronic indicators are possible interfaces with smartphones or dashboards. Embedding sensors of this kind in conformable, permeable BC matrices allows for Ag^+ release on demand or timely dressing changes, which in turn reduces unnecessary silver exposure and enables precision dosing. Recently, some proof-of-concept studies have shown the possibilities, thus defining the next stage as the actual implementation of these methods to multi-functional BC-AgNP platforms (Wang *et al*., 2024; Zarepour *et al*., 2024).

c) Personalized wound care applications

The main feature of personalized wound care is that it gives the possibility to adapt BC-AgNP dressing in relation to the wound type, microbial profile, and patient biology (such as age, comorbidities, renal function). Wound management principles contain adjustable silver loadings directed by rapid diagnostics, sensor-actuated Ag^+ release, and co-therapies specific to patients (such as growth factors or peptides). The application of digital twins and predictive models is the combination of sensor and health data for dressing changes that will be carried out in an optimized way or the silver dosing will be adjusted. For successful implementation, there is the need for compatible standards of data, secure connections, and clinical trials for the new modalities with adaptive and individualized regimens in comparison with the standard of care (Sarp *et al*., 2023).

d) Prospects for commercial translation and clinical adoption

The commercial uptake and translation of BC–AgNP dressings into clinical use will depend to a large extent on the stability of manufacturing, the extent of clinical benefit that can be demonstrated, as well as safety that meets regulatory standards. In the reviews, the importance of thorough physicochemical characterization of the material (primary particle size, particle surface chemistry, loading, release kinetics), standardized preclinical testing, and safety data from the first human trial is emphasized as a prerequisite for any approval. About silver, the sustainable production of BC, the ECM-like structure, and the superior moisture removal ability of BC can be factors that lead to lower dosing of silver by improving local retention. However, production at GMP scale, consistency of batches, and long-term safety and resistance monitoring are still issues to be addressed. Pricing and reimbursement, along with early collaboration of the academic community, manufacturers, clinical networks, and regulators will be the driver of uptake in the coming years. Recent literature indicates the availability of clinical products from prototypes is contingent on the addressing of standardized characterization, safety assessment and clinical value addition (Dias *et al*., 2025).

e) Hybrid AgNP composites with antibiotics or natural antimicrobials for synergy

One of the most promising strategies for the development of novel antimicrobial agents is the combination of AgNPs with traditional antibiotics or natural substances. These combinations result in synergistic antimicrobial effects, allowing the use of lower doses and thus reducing cytotoxicity and the risk of resistance development. As an illustration, plant-derived AgNPs combined with clarithromycin and clove extract significantly elevated the antimicrobial activity against *Bacillus subtilis* and *Staphylococcus aureus* in comparison to the corresponding components (Edis *et al*., 2025). We can also mention that biogenic AgNPs together with antibiotics present a powerful effect on the

multidrug-resistant strains (Maniah *et al*., 2024). Future work should focus on embedding such hybrids inside BC matrices, releasing both Ag^+ and co-antimicrobials in a controlled manner, predicting release, and evaluating the extent of safety in mammalian models.

f) Clinical translation and large-scale trials for long-term safety and efficacy

The human data on BC–AgNP wound dressings are extremely scarce, with most of the evidence coming from preclinical studies. It is necessary to conduct large randomized controlled trials to compare the performance of BC–AgNP composites and the standard care in the treatment of different types of wounds (burns, diabetic foot ulcers, venous leg ulcers). Moreover, these trials should not only focus on the early stages of healing but also evaluate the long-term outcomes, such as scar formation, re-infection, and systemic silver absorption. In general, the currently published RCTs on nanocellulose or silver foams can be used as a reference, but there are very few BC–AgNP trials (Hecker *et al*., 2022). Safe assessments should include local cytotoxicity and systemic effects, alongside consistent manufacturing, storage stability, and regulatory compliance.

g) green synthesis for scalable production

One of the main aims of the researchers is to find an eco-friendly way to synthesize BC–AgNP composites without compromising the antimicrobial effectiveness of the resulting material. This is a trend that is reflected in the research papers cited by Garcia *et al* (2025). The latest research papers are focusing on an environmentally friendly and scalable method as an example, a post fermentation sugar solution is used as a reductant of silver ions to synthesize silver nanoparticles of about 100 nm in size which have a strong bacterial growth inhibition ability of *E. coli* (Marangoni *et al*., 2024). Photocatalytic and *in situ* BC modification via *Acetobacter* were among the preparation methods of the composites with stable antibacterial and antifungal activities and acceptable hemocompatibility (Mansoor *et al*., 2024). Moreover, cellulose nanofibers from spent mushroom substrate along with biomass extracts made silver nanocomposite coated cellulose nanofiber composites which showed a strong antimicrobial property as well as a lower cytotoxicity when compared to free silver nanoparticles (Hossain *et al*., 2025). Such environmentally friendly methods can be a viable way to make a stable and effective BC-AgNP wound dressing.

CONCLUSION

Bacterial cellulose–silver nanoparticle composites are one of the most advantageous materials in the construction of antimicrobial wound dressings, as they combine the structural and biocompatible properties of BC, along with the potent antimicrobial and antibiofilm effects of AgNPs. Progress from 2020 to 2025 shows to the great extent implementation of the different methods of synthesis, the use of hybrid functionalizations, and the creation of a smart delivery system, all these changes in the developments of the tune that become effective against the target as well as the reduction in their cytotoxicity. Preclinical studies show good results in the acceleration of wound healing, improved tissue regeneration, and infection control in all the cases consistently. Yet, these materials are still facing such challenges as cytotoxicity at higher silver concentrations, variations in synthesis, scalability issues, and regulatory ambiguities. The implementation of standardized protocols, the use of sustainable green synthesis, and the designing of clinical trials to be well thought out are necessary steps that will definitely help in overcoming those challenges. With continued innovation, BC-AgNP composites can be very close to becoming the next-generation wound dressings for chronic wound management.

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