
















Harnessing nanomaterials to overcome antimicrobial resistance in Gram-positive bacteria: a systematic review

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Abstract

Background: Antimicrobial resistance (AMR) among Gram-positive bacteria has emerged as a significant global health threat, with pathogens such as methicillin-resistant *Staphylococcus aureus* (MRSA) and vancomycin-resistant *Enterococcus faecium* (VRE) exhibiting increasing resistance to conventional antibiotics. This systematic review evaluates new advances in nanomaterial-based antimicrobial agents as innovative solutions to combat AMR in Gram-positive bacteria.

Methods: Following Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, studies published between 2014 and 2024 were systematically screened and analysed from databases including PubMed, Scopus, Google Scholar, and HINARI. From an initial 1,405 articles, 131 experimental studies that met the inclusion criteria were systematically analysed to harness the advances in nanomaterial-based antimicrobial agents in combating AMR in Gram-positive bacteria.



Results: The included studies demonstrated that various nanomaterials, including silver nanoparticles (AgNPs), gold nanoparticles (AuNPs), zinc oxide nanoparticles (ZnO NPs), copper and copper oxide nanoparticles (Cu/CuO NPs), as well as polymeric and hybrid systems, exhibited potent antibacterial and antibiofilm activities. Key mechanisms of action included bacterial membrane disruption, reactive oxygen species (ROS) generation, intracellular interference, and targeted drug delivery. Many nanomaterials showed enhanced efficacy and synergistic effects when combined with conventional antibiotics, effectively reducing bacterial load and inhibiting biofilm formation in resistant strains like MRSA.

Discussion: Nanomaterials offer a multifaceted approach to overcome the evolving resistance mechanisms in Gram-positive pathogens, showing significant preclinical and clinical success. Despite these substantial preclinical results, challenges such as cytotoxicity, environmental impact, scalability, and the potential for resistance adaptation remain unaddressed. Furthermore, important translational barriers persist, most notably insufficient pharmacokinetic data and unclear regulatory pathways. Future efforts must focus on standardized manufacturing, comprehensive toxicity studies, and robust clinical trials to bridge the gap between laboratory innovation and practical therapeutic application.

Keywords

nanotechnology, nanoparticle, antimicrobial resistance, Gram-positive bacteria, drug delivery systems, antimicrobial peptides, multidrug resistance

Introduction

Antimicrobial resistance (AMR) is a major global health challenge, responsible for approximately 1.27 million deaths in 2019 and contributing to 4.95 million more globally [1, 2]. Overuse of antibiotics in humans, animals, and agriculture drives the emergence of multidrug-resistant (MDR) pathogens, including methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant *Enterococcus faecium* (VRE), and β -lactam-resistant *Streptococcus pneumoniae* [3–5]. Gram-positive bacteria readily acquire resistance via altered penicillin-binding proteins (e.g., PBP2a), thickened cell walls, efflux pumps, and biofilm formation, which hinder antibiotic efficacy [6–9]. Compounding the crisis, new antibiotic development is constrained by high research and development costs, regulatory hurdles, and limited profitability [10].

Nanomaterials offer a promising strategy to combat Gram-positive AMR pathogens due to their multimodal antimicrobial mechanisms, including membrane disruption, reactive oxygen species (ROS) generation, biofilm penetration, and intracellular delivery [11]. Among these, antimicrobial peptides (AMPs) disrupt microbial membranes, while nanomaterials enhance solubility, stability, and controlled drug release [12]. Their activity is influenced by physicochemical properties such as size, shape, charge, and composition. For instance, CuO NPs disrupt membranes and generate ROS, and chitosan nanoparticles interact electrostatically with bacterial surfaces to inhibit biofilms [13, 14]. Broadly, antimicrobial nanoparticles can be metallic (e.g., silver, copper, zinc), polymeric [e.g., chitosan, poly(lactic-co-glycolic acid) (PLGA)], lipid-based (e.g., liposomes), or carbon-based (e.g., graphene oxide), each employing distinct mechanisms to overcome bacterial resistance [11, 15].

Despite promising preclinical results, most studies remain *in vitro* or in animal models, with limited data on long-term safety, biodistribution, or chronic toxicity [15, 16]. Translational challenges include standardization, manufacturing, and the potential impact on beneficial microbiota and ecosystems. Gram-positive pathogens are a critical focus due to their thick peptidoglycan walls and escalating resistance, which necessitate targeted nanomaterial strategies [17]. Emerging diagnostic and therapeutic technologies, including dual-function nanomaterials, hold potential but require careful evaluation to prevent resistance and mitigate ecological risks [18, 19]. This review aims to consolidate current preclinical nanomaterial-based strategies against Gram-positive AMR pathogens, emphasizing translational barriers and future research priorities.

Materials and methods

Study design

This systematic review followed PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines, covering article items including title, abstract, introduction, methods, results, and discussion. The study protocol included research questions, aims, inclusion/exclusion criteria, and a methodological approach. A PRISMA 2020 Checklist (S1) was used to ascertain that this systematic review followed PRISMA guidelines.

Review questions

- What is the efficacy of nanotechnology-based antimicrobial agents against AMR Gram-positive bacteria?
- What types of nanomaterials have been used to target Gram-positive bacteria?
- What are the mechanisms of action of these nanotechnology-based antimicrobials?
- What are the limitations, toxicity concerns, and future potentials of these technologies?

Search strategy

A comprehensive literature search was conducted using PubMed, Scopus, Google Scholar, and HINARI to identify studies published between 2014 and 2024. This timeframe was chosen to capture a decade of significant advances in nanomaterial-driven antimicrobial research and its application against AMR pathogens. The search strategy employed precise Boolean strings, including combinations of keywords and MeSH terms such as “nanotechnology” OR “nanoparticle” OR “nanomaterial” AND “antimicrobial resistance” OR “AMR” OR “antibiotic resistance” AND “Gram-positive bacteria”. Boolean operators (AND, OR) and truncations were systematically applied to maximize the retrieval of relevant records, specifically evaluating the effectiveness of nanomaterial-based antimicrobials in combating AMR, specifically in Gram-positive bacteria, while filtering duplicates. Google Scholar results were filtered for quality by prioritizing peer-reviewed journal articles published in reputable and indexed journals. Studies from non-indexed or low-impact sources were excluded after assessing methodological rigor and citation relevance. In addition to database searching, manual screening and backward citation tracking were performed to identify additional studies referenced in the bibliographies of eligible articles. Two researchers (UOA and OJ Okesanya) independently conducted database searches and preliminary analyses to ensure consistency and completeness of retrieved data.

Eligibility criteria

Included studies comprised experimental preclinical designs (in vitro, in vivo, or combined) and clinical observational or interventional studies that evaluated the antibacterial effects of nanomaterials against Gram-positive bacteria.

The following inclusion criteria were established using the population, intervention, comparison, and outcome (PICO) framework:

Population (P): Gram-positive bacteria exhibiting resistance to conventional antibiotics.

Intervention (I): Nanomaterial-based antimicrobial agents.

Comparison (C): Conventional antibiotics or untreated controls.

Outcome (O): Antimicrobial efficacy, bacterial load reduction, biofilm disruption, toxicity, and resistance modulation.

Harnessing nanomaterials to overcome AMR in Gram-positive bacteria

This review included studies that focused on utilizing nanomaterial-based antimicrobial agents to combat Gram-positive AMR bacteria. Eligible studies were published between 2014 and 2024 and in English.

Studies that did not provide relevant data or focused solely on other microorganisms were excluded. Qualitative studies, preprints, narrative and systematic review articles, editorials, commentaries, conference abstracts, and data from grey and unpublished sources were excluded due to inconsistency in reporting. Data on nanomaterial-based agents, mechanisms of action, and key findings were extracted.

Study selection process

Study selection was conducted in a two-stage process by two independent reviewers (KBO and OBA) who screened titles and abstracts for relevance based on predefined inclusion and exclusion criteria. Full-text screening was conducted for potentially eligible articles. Any disagreements were resolved through discussion or consultation with a third reviewer (CNC). Manual backward citation screening was also applied to ensure comprehensiveness. To minimize bias, no restrictions were placed on author affiliation, journal of publication, or study outcomes. Only studies that met the inclusion criteria were considered. Paper titles reported in tables were preserved or paraphrased for clarity and neutrality.

Data extraction, synthesis, and statistical analysis

Data from eligible studies were independently extracted by two reviewers (AKY and KOT) using a standardized form that included nanomaterials used, pathogen targeted, antimicrobial mechanism of action, study type, key findings, advantages of nanomaterials over conventional agents, and limitations. Nanomaterials were categorized based on their chemical composition and synthesis origin into one of seven classes: metal-based, metal oxide-based, polymeric, lipid-based, carbon-based, biologically derived, or inorganic-based. This classification enabled clearer interpretation of mechanisms of action and antibacterial effectiveness across material types. All extracted data were verified for consistency against the original publication. Inconsistencies were resolved through consensus. Descriptive analysis was performed to summarize trends in nanomaterial types, pathogen types, and in vitro/in vivo outcomes. As this is a descriptive systematic review, no inferential statistical tests were applied.

Quality assessment

The Joanna Briggs Institute's Critical Appraisal Checklist was used to evaluate the methodological quality of the included studies, with an 8-point rating system and a minimum score of 50% required.

Results

Overview of included studies

A total of 1,530 articles were identified through database searches. After removing 125 duplicates, 1,405 records were screened by title and abstract, excluding 1,052 that did not meet the inclusion criteria. An additional 18 studies were excluded due to non-material interventions, focus on Gram-negative bacteria, review articles, or incomplete data. Of 335 full-text articles assessed for eligibility, a total of 204 were excluded, of which ($n = 108$) were for inappropriate methodology, article type (reviews/commentaries, $n = 62$), or mixed bacterial outcomes without separable Gram-positive data ($n = 34$). Ultimately, 131 studies were included in the final synthesis (Figure 1, Table 1 [20–150]). Included studies were primarily in vitro, with China and India accounting for the highest representation (16% each). Many studies utilized green-synthesized nanoparticles from plant extracts. Some employed composite or hybrid nanoparticles, including polymer-coated, drug-loaded, or biologically stabilized forms. Targeted Gram-positive pathogens included *Staphylococcus aureus* (MRSA and MSSA) [20, 22, 24], other *Staphylococcus* spp. [29, 45], *Streptococcus* spp. [61, 64], *Listeria* spp. [82], *Clostridium perfringens* [109], *Bacillus* spp. [39, 44], and *Enterococcus* spp. [93, 94], highlighting the broad-spectrum activity of nanomaterials against resistant strains.

Nanomaterials used, class, and their antimicrobial efficacy

Nanomaterials were classified as metallic (AgNPs, AuNPs, CuO NPs, ZnO NPs), polymeric (chitosan, PLGA), lipid-based (liposomes, solid lipid NPs), and carbon-based (graphene oxide, CNTs) [11, 15]. AgNPs, often

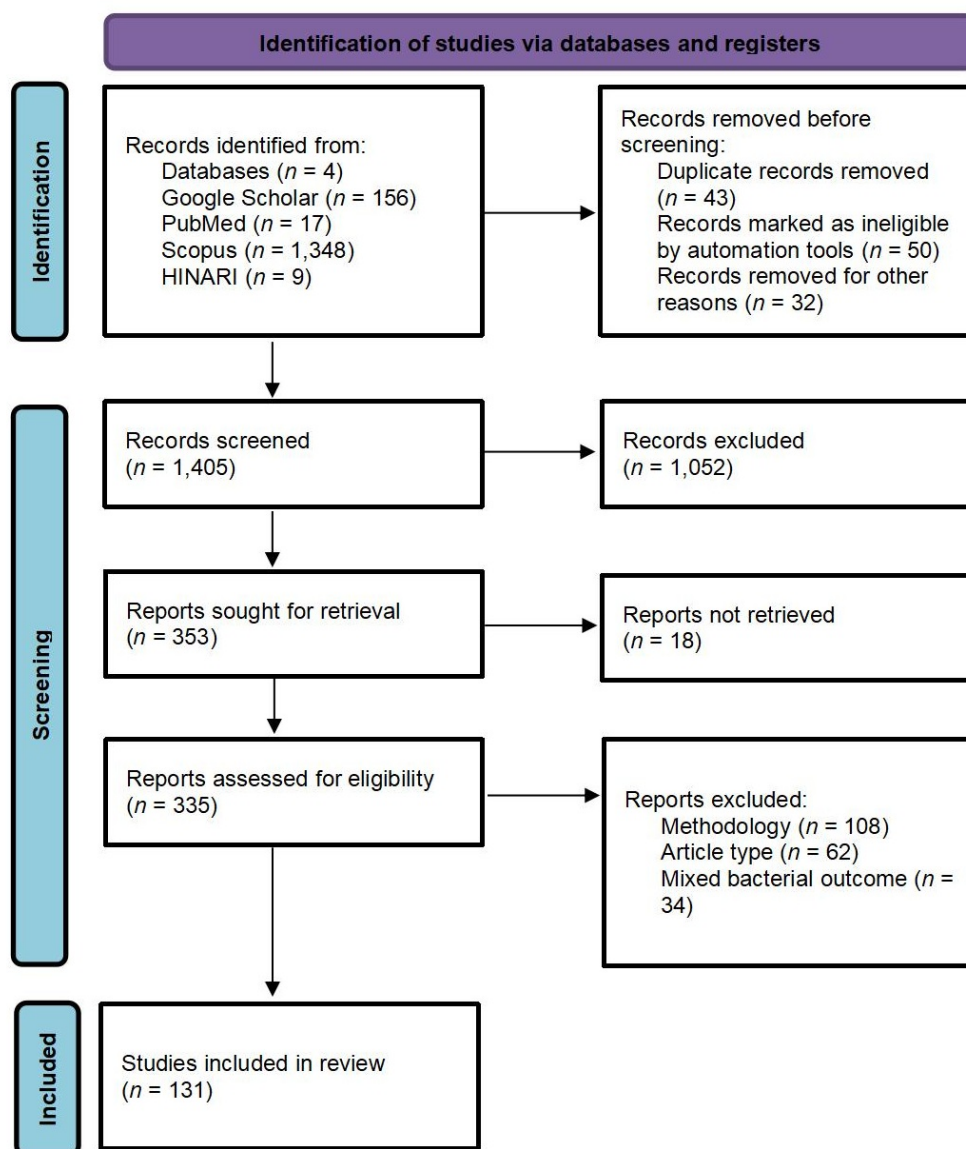


Figure 1. PRISMA flowchart of included studies. Adapted from [151]. © 2024-2025 the PRISMA Executive. Licensed under a CC BY 4.0. PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

metal-based and being the most frequently reported in over 50 studies, exhibited strong bactericidal and antibiofilm activity via ROS production, membrane disruption, and interference with bacterial metabolism [26, 29, 31–34, 39, 57, 68, 114, 146]. AuNPs, frequently functionalized or combined with drugs, enhanced antimicrobial and wound-healing potential [21, 34, 40, 63, 67, 72, 101]. ZnO NPs and Cu/CuO NPs demonstrated ROS-mediated antibacterial and antibiofilm effects, often synergistic with antibiotics [73, 78, 94, 119, 121]. Some studies explored hybrid or functionalized nanomaterials with advanced properties. For example, MXF@UiOUBIPEGTK, a biologically derived ROS-responsive system, enabled targeted drug release in oxidative infection environments [52]. Polymeric nanoparticles, including chitosan and PLGA-based formulations, offered controlled antibiotic release and improved biofilm inhibition, supporting long-term antimicrobial therapy [108]. Collectively, these nanomaterials enhanced antibacterial effectiveness, often achieving substantial bacterial suppression at low antibiotic doses, thus mitigating resistance development, demonstrating broad-spectrum activity, and reducing high-dose side effects. Notably, biogenic CuNPs and ZnO NPs exhibited strong synergistic activity against MRSA, producing significantly larger inhibitory zones against Gram-positive pathogens such as *Staphylococcus aureus*, *S. saprophyticus*, *S. sciuri*, and *S. epidermidis* [28, 42, 46, 123, 127, 132, 142, 146, 149]. Biologically derived AgNPs, including CAgNPs, disrupted biofilms in both *S. aureus* and MRSA strains, highlighting their potential in treating chronic Gram-positive infections [30, 138].

Table 1. Summary of nanomaterial-based antimicrobials targeting Gram-positive bacteria.

S/N	Citation	Country	Nanomaterial type used	Nanomaterials class	Pathogen (s) targeted	Study type	Key findings	Mechanism of action	Advantages over conventional agents	Limitations	Translational stage/clinical phase
1	[20]	China	Quercetin (Qu) and acetylcholine (Ach) to the surface of Se nanoparticles (Qu–Ach@SeNPs)	Metal-based	<i>Staphylococcus (S.) aureus</i>	Experimental	Efficient antibacterial and bactericidal activities against superbugs without resistance	Combined with the acetylcholine receptor on the bacterial cell membrane and increase the permeability of the cell membrane	Efficient antibacterial activity against MDR superbugs	-	Preclinical (unspecified)
2	[21]	Pakistan	Ciprofloxacin-loaded gold nanoparticles (CIP-AuNPs)	Metal-based	<i>Enterococcus (E.) faecalis</i> JH2-2	Experimental	Promising, biocompatible therapy for drug-resistant <i>E. faecalis</i> infections warrants further study	Disrupts membrane potential, inhibits ATPase, and blocks ribosome–tRNA binding, impairing bacterial metabolism	Exerted enhanced antibacterial activity compared with free CIP	Required further studies on its effects in animal models, which may aggregate and unload due to high salt concentrations	In vivo (animal model)
3	[22]	India	Copper oxide nanoparticles (CuO NPs)	Metal oxide-based	<i>S. aureus</i>	Experimental	Strong antifungal and antibacterial activity	Effective against Gram-positive bacteria	Low-cost and possesses a high surface area	-	Preclinical (unspecified)
4	[23]	India	Platinum nanoparticles (Pt NPs)	Metal-based	<i>Bacillus (B.) cereus</i>	Experimental	Shows dose-dependent antibacterial activity	Denature critical bacterial enzyme thiol groups	Synthesized using eco-friendly biological methods	In vitro only; in vivo efficacy and toxicity not assessed	In vivo (animal model)
5	[24]	Australia	Selenium nanoparticles (SeNPs)	Metal-based	MRSA, <i>E. faecalis</i>	Experimental	Strong antibacterial effect against eight species, including drug-resistant strains	ATP depletion, reactive oxygen species (ROS) generation, membrane depolarization, and membrane disruption	Unlike the conventional antibiotic, kanamycin's NP-ε-PL did not readily induce resistance	Further work is required to investigate use in a real clinical setting	Clinical
6	[25]	South Korea	Magnetic core-shell nanoparticles (MCSNPs)	Metal-oxide-based	MRSA	Experimental	Radiofrequency (RF) current kills trapped bacteria in 30 minutes by disrupting the membrane potential and complexes	RF stimulation of MCSNP-bound bacteria disrupts the membrane potential and complexes	-	Study performed in vitro; further in vivo validation is necessary	In vivo (animal model)
7	[26]	India	Silver nanoparticles (AgNPs)	Metal-based	<i>S. aureus</i>	Experimental	< 50 nm AgNPs act against drug-resistant bacteria	-	-	-	Preclinical (unspecified)
8	[27]	China	Nanoparticles functionalized with oligo(thiophene ethynylene (OTE) and hyaluronic acid (HA) (OTE-HA nanoparticles)	Polymeric	MRSA	Experimental	Bacterial hyaluronidase hydrolyzes OTE-HA NPs, releasing OTE fragments to kill bacteria	OTE fragments disrupt bacterial membranes by hydrophobic interactions and van der Waals forces	OTE-HA NPs prevent premature drug leakage and show superior biocompatibility	Potential cytotoxicity of OTE-based agents is a major concern.	Preclinical (unspecified)
9	[28]	India	Biogenic copper nanoparticles (CuNPs) and zinc oxide nanoparticles (ZnONPs)	Metal-and metal-oxide-based	<i>S. aureus</i> , including MRSA	Experimental	Exhibit strong low-dose antibiofilm activity and boost antibiotic efficacy	Nanoparticles interact closely with microbial membranes due to their small size	Synergistic enhancement with antibiotics	-	Preclinical (unspecified)
10	[29]	India	AgNPs	Metal-based	<i>B. subtilis</i> , <i>S. haemolyticus</i> , and <i>S. epidermidis</i>	Experimental	AgNPs block bacterial growth and biofilms below the antibiotic minimum inhibitory concentration (MIC), with minimal cytotoxicity to mammalian cells	Mislocalizes FtsZ/FtsA, damages membranes, and blocks cell division	Reduced cytotoxicity towards mammalian cells	Limited Ag ⁺ release and hydrogel shielding reduce AgNP effectiveness	Preclinical (unspecified)

Table 1. Summary of nanomaterial-based antimicrobials targeting Gram-positive bacteria. (continued)

S/N	Citation	Country	Nanomaterial type used	Nanomaterials class	Pathogen (s) targeted	Study type	Key findings	Mechanism of action	Advantages over conventional agents	Limitations	Translational stage/clinical phase
11	[30]	Spain	Mesoporous silica nanoparticles (MSNs)	Inorganic-based	<i>S. aureus</i>	Experimental	MSN _{EPL-Cin} demonstrated excellent antimicrobial activity at very low doses	Microbial proteases trigger cinnamaldehyde release from MSNs for localized antimicrobial action	Enhanced antimicrobial efficacy via biocontrolled uncapping for targeted delivery	Raw data cannot be shared due to technical limitations	In vivo (animal model)
12	[31]	China	Curcumin-stabilized silver nanoparticles (C-Ag NPs)	Metal-based/biologically derived	<i>S. aureus</i> and MRSA	Experimental	Polyvinyl alcohol (PVA)/citric acids (CA)/C-Ag nanofibers show sustained broad-spectrum activity, remove biofilms, and suppress MRSA resistance genes	Antimicrobial action via ROS and membrane damage; disrupts MRSA carbohydrate and energy metabolism	-	-	Preclinical (unspecified)
13	[32]	India	AgNPs	Metal-based	<i>S. aureus</i> (tetracycline-resistant)	Experimental	Strong antibacterial at 100 µg/mL, plus antioxidant and anti-HeLa/MCF-7 activity	Interrupt genes involved in the cell cycle	Enhanced antibacterial properties compared to conventional agents	-	Preclinical (unspecified)
14	[33]	China	Single-walled carbon nanotubes (SWCNTs) decorated with AgNPs coated with mesoporous silica via TSD mediation (SWCNTs@mSiO ₂ -TSD@Ag)	Carbon/Metal-based	<i>S. aureus</i>	Experimental	Significantly enhanced antibacterial activity against <i>S. aureus</i> , with MICs below commercial AgNPs	Damages bacterial cell membranes and accelerates Ag ⁺ release, boosting antibacterial activity	Outperformed commercial AgNPs and SWCNTs@mSiO ₂ -TSD, enhancing bacterial clearance and wound healing in vivo	Grafting Ag NPs onto CNTs requires complicated procedures, risking structural damage	Preclinical (unspecified)
15	[34]	China	AuNPs modified with 5-methyl-2-mercaptobenzimidazole (mMB-AuNPs)	Metal-based/organic-functionalized	MRSA	Experimental	Neutral MMB-AuNPs destroyed MRSA, unlike charged AMB- and CMB-AuNPs	Induce bacterial cell membrane damage, disrupt membrane potential, and downregulate ATP levels, leading to bacterial death	-	-	Preclinical (unspecified)
16	[35]	Jordan	Silver, magnetite nanoparticles (Fe ₃ O ₄ /AgNPs), and magnetite/silver core-shell (Fe ₃ O ₄ /Ag) nanoparticles	Metal/Metal oxide-based	<i>S. aureus</i>	Experimental	Fe ₃ O ₄ /Ag NPs exhibited superior antibacterial activity compared to Fe ₃ O ₄ or Ag NPs, strongly inhibiting pathogens	-	-	-	Preclinical (unspecified)
17	[36]	USA	Polydopamine nanoparticles (PD-NPs)	Polymer-based	MRSA	Experimental	Composite nanoparticles fully eradicated MRSA and removed toxic heavy metals from water	Membrane captures pathogens; ε-poly-L-lysine kills bacteria. Metal is removed by active binding sites	Surface area for enhanced reactivity and effective capture of heavy metals and superbugs	-	Preclinical (unspecified)
18	[37]	China	Mixed-charge hyperbranched polymer nanoparticles (MCHPNs)	Polymer-based	<i>S. aureus</i> (ATCC 6538), MRSA	Experimental	Highly selective (SI > 564), eradicates resistant bacteria, delays resistance, and blocks biofilms	Charge-targeted membrane disruption alters permeability, causing bacterial death	Offers greater bacterial selectivity and lower mammalian toxicity than other cationic materials	-	Preclinical (unspecified)

Table 1. Summary of nanomaterial-based antimicrobials targeting Gram-positive bacteria. (continued)

S/N	Citation	Country	Nanomaterial type used	Nanomaterials class	Pathogen (s) targeted	Study type	Key findings	Mechanism of action	Advantages over conventional agents	Limitations	Translational stage/clinical phase
19	[38]	-	Silver, copper oxide, and titanium dioxide nanoparticles (AgNPs, CuO NPs, and TiO ₂ NPs)	Metal/Metal oxide-based	<i>S. aureus</i> , MRSA	Experimental	Silver nanoparticle coatings achieved > 99% bacterial growth inhibition within 24 h	Nanoparticles disrupt bacterial cell membranes and produce ROS	The nanoparticles overcome biofilm barriers that conventional antibiotics struggle with	Needs further studies on long-term safety, biocompatibility, and large-scale trials; clinical data are lacking	Clinical
20	[39]	India	AgNPs	Metal-based	<i>Bacillus licheniformis</i>	Experimental	AgNP-treated cotton fabrics showed wash-durable antimicrobial activity with 93.3% inhibition	Induces higher ROS production inside bacterial cells	Offer improved wash durability compared to conventional agents	Limited exploration of AgNPs resistance in various bacterial strains	In vivo (animal model)
21	[40]	China	AuNPs	Metal-based	MRSA	Experimental	Showed strong antibacterial effects and enhanced wound healing against MDR bacteria	Disrupts bacterial membrane structure and cytoplasmic leakage	-	-	Preclinical (unspecified)
22	[41]	China	AgNPs	Metal-based	<i>S. aureus</i>	Experimental	Showed strong bactericidal effects on MDR bacteria; biofilm formation was inhibited in a dose-dependent manner	Effectively hinders biofilm formation, with inhibition rising at higher AgNP concentrations	Significant bactericidal effect on a variety of drug-resistant bacteria	No regulation on AgNP morphology, size, surface, or antibacterial properties	Preclinical (unspecified)
23	[42]	India	AgNPs stabilized with poloxamer (AgNPs@Pol)	Biologically derived	MRSA and methicillin-susceptible <i>S. aureus</i> (MSSA)	Experimental	Synergistic effect with methicillin was observed. ROS increased, and antimicrobial resistance (AMR)-related genes were downregulated	Induction of ROS and downregulation of AMR and adhesion genes	Significant 100% efficacy against MRSA and MSSA, reduction in colony-forming units (CFU)	Further primary cells and in vivo models are required for validation	In vivo (animal model)
24	[43]	India	Palladium nanoparticles (PdNPs)	Metal-based	<i>S. aureus</i>	Experimental	Showed MICs of 52–68 µg/mL against MDR <i>S. aureus</i>	-	PdNPs can be effective in the clinical management of MDR pathogens	-	Preclinical (unspecified)
25	[44]	UAE	Cinnamic acid-coated magnetic iron oxide and mesoporous silica nanoparticles	Metal-based/biologically derived	MRSA, <i>B. cereus</i>	Experimental	Greatly enhanced destruction of MDR bacteria over drugs alone, with minimal cytotoxicity	-	Completely eradicated MRSA at much lower doses than antibiotics alone	Further in vivo and clinical studies are needed for validation	Clinical
26	[45]	Saudi Arabia	AgNPs	Metal-based	<i>S. aureus</i> and <i>S. epidermidis</i>	Experimental	Exhibited strong antibacterial activity with an MIC of 9.375 µg/mL against MDR strains	Ag ⁺ ions bind thiols, disrupt membranes, cause oxidative damage, and kill bacterial cells	Metal nanoparticles (m-NPs) bypass resistance mechanisms in bacteria	-	Preclinical (unspecified)
27	[46]	Nigeria	AgNPs	Metal-based	<i>S. aureus</i>	Experimental	Exhibited antibacterial at 25 µg/mL; MIC 25–50 µg/mL, minimum bactericidal concentration (MBC) 75–100 µg/mL	-	-	Need more studies on environmental effects, antibacterial mechanisms, and AgNP–antibiotic synergy	In vivo (animal model)

Table 1. Summary of nanomaterial-based antimicrobials targeting Gram-positive bacteria. (continued)

S/N	Citation	Country	Nanomaterial type used	Nanomaterials class	Pathogen (s) targeted	Study type	Key findings	Mechanism of action	Advantages over conventional agents	Limitations	Translational stage/clinical phase
28	[47]	Mexico	AgNPs	Metal-based	<i>S. aureus</i> ATCC 25923	Experimental	Seasonal sample from winter (SPw)-AgNPs showed potent antibacterial/antibiofilm activity (MBC 25–100 µg/mL), driven by quercetin/galangin, and were non-cytotoxic to HeLa and ARPE-19 cells	-	Reduced cytotoxicity due to biosynthesis; effective at low concentrations compared to previous reports using chemically synthesized AgNPs	Future work should test strains with defined virulence and resistance to evaluate clinical relevance	Clinical
29	[48]	China	LL-37@MIL-101-Van (MIL-101 nanoparticles loaded with LL-37 peptide and Vancomycin)	Biologically derived	MRSA	Experimental	Showed strong antibacterial effects, enhanced wound healing, enabled near infrared (NIR) imaging, and synergistically killed MRSA via •OH, LL-37, and vancomycin	MIL-101 (Fe ³⁺) drives Fenton-like •OH production from H ₂ O ₂ in acidic sites; LL-37 disrupts membranes, vancomycin blocks cell wall synthesis	-	-	Preclinical (unspecified)
30	[49]	India	Ag–Cu NPs	Metal-based	<i>S. aureus</i> and MRSA	Experimental	Effective at MIC 156.3–312.5 µg/mL. Inhibited growth rapidly, reusable, and eco-friendly synthesis	Membrane damage and ROS overproduction leading to lipid oxidation	Reusability, rapid action (30 min), green synthesis from agro-waste, stability for repeated use	-	Preclinical (unspecified)
31	[50]	Iran	Silver chloride nanoparticles (AgCl NPs)	Metal-based	<i>S. aureus</i> and <i>B. subtilis</i>	Experimental	Showed strong antibacterial activity against drug-resistant strains and cytotoxicity to MCF-7 and HepG2; MIC 12.5–50 µg/mL	Disrupts bacterial membranes and binds to proteins and DNA; Ag ⁺ inhibits replication and inactivates proteins; ROS contributes to cytotoxicity	The nanoparticles exhibit higher antioxidant activity than conventional agents	-	Preclinical (unspecified)
32	[51]	Nigeria	Chitosan nanoparticles	Polymeric	<i>S. aureus</i> (haemolytic and clinical strains) and <i>S. saprophyticus</i>	Experimental	39 mm inhibition zone against <i>S. saprophyticus</i> ; MIC: 0.0781–0.3125 mg/mL	Increases bacterial membrane permeability and binds DNA, blocking mRNA synthesis	More effective than levofloxacin against <i>S. saprophyticus</i> ; comparable efficacy for other tested strains	-	Preclinical (unspecified)
33	[52]	China	ROS-responsive, bacteria-targeted moxifloxacin nanoparticle for moxifloxacin delivery (MXF@UiO-UBI-PEGTK)	Biologically derived	<i>S. aureus</i> , and MRSA	Experimental	ROS-responsive moxifloxacin (MXF) release improved biofilm penetration in vitro and treated endophthalmitis in vivo	ROS-cleavable poly (ethylene glycol)-thioketal (PEG-TK) triggers MXF release in high ROS; UBI _{29–41} targets bacteria/biofilms; MXF blocks DNA gyrase and topoisomerase	Outperformed free moxifloxacin in biofilm penetration, ROS-responsive targeted delivery, and in vivo infection resolution with reduced inflammation	-	In vivo (animal model)
34	[53]	India	Silver oxide (Ag ₂ O) nanoparticles	Metal-oxide-based	MRSA	Experimental	Demonstrated potent antibacterial activity against MRSA, with a 17.6 ± 0.5 mm inhibition zone	Ag ₂ O nanoparticle production may be enzyme-mediated	Ag ₂ O nanoparticles are freely dispersed, enhancing their effectiveness	-	In vivo (animal model)
35	[54]	Egypt	AgNPs	Metal-based	<i>S. aureus</i>	Experimental	Showed strong activity vs. MDR bacteria (MIC 31–250 µg/mL, MBC 125–500 µg/mL)	Disruption of bacterial cell membrane structure, leakage of intracellular contents	AgNPs (S4) showed superior antibacterial activity compared to AgNO ₃ and ginger extract alone	-	Preclinical (unspecified)

Table 1. Summary of nanomaterial-based antimicrobials targeting Gram-positive bacteria. (continued)

S/N	Citation	Country	Nanomaterial type used	Nanomaterials class	Pathogen (s) targeted	Study type	Key findings	Mechanism of action	Advantages over conventional agents	Limitations	Translational stage/clinical phase
36	[55]	India	Iron oxide nanoparticles (FeONPs)	Metal-oxide-based	<i>S. aureus</i>	Experimental	Strong antibacterial/antifungal activity; rapid synthesis verified by UV-Vis, XRD, SEM, TEM	Act through direct contact with bacterial cell walls	Enhance membrane permeability and cell destruction	-	Preclinical (unspecified)
37	[56]	India	AgNPs	Metal-based	<i>S. aureus</i>	Experimental	Produced 27 mm and 32 mm zones vs. MDR <i>S. aureus</i>	Disrupts the outer membrane, binds thiols, impairs replication, and generates ROS, causing damage and enzyme inhibition	AgNPs showed 27 mm (<i>S. aureus</i>), far exceeding antibiotics (≤ 5 mm)	-	Preclinical (unspecified)
38	[57]	Malaysia	AgNPs	Metal-based	MRSA	Experimental	-	Phyto-AgNPs are antibacterial, and with antibiotics, greatly increase MRSA inhibition zones	AgNP-antibiotic combinations showed significantly larger inhibition zones compared to antibiotics or AgNPs alone	The precise mechanism of action for nanoparticles remains unclear	Preclinical (unspecified)
39	[58]	Lithuania	Nisin-loaded iron oxide magnetic nanoparticles (IONPs)	Metal oxide/biologically derived	<i>B. subtilis</i> ATCC 6633	Experimental	Nisin-magnetic nanoparticles combined with pulsed electric field (PEF)/pulsed electromagnetic field (PEMF) boost antimicrobial action and resistance synergistically	Nisin resistance mechanisms were identified in Gram-positive bacteria	Nanomaterials enhance the stability and activity of antimicrobial agents	Mechanism not fully understood and requires further investigation	Preclinical (unspecified)
40	[59]	Ethiopia	Copper oxide nanoparticles (CONPs)	Metal-oxide-based	<i>S. aureus</i>	Experimental	Active against Gram-positive diabetic foot isolates, with <i>S. aureus</i> showing the largest zone (16 mm)	CONPs adhere to bacterial surfaces and penetrate cells, destroying bacterial biomolecules and structures	CONPs possess strong antioxidant potential compared to conventional agents	Still needs some modifications on CONPs concerning ascorbic acid activity	Preclinical (unspecified)
41	[60]	Iran	AgNPs	Metal-based	<i>S. aureus</i>	Experimental	Strong activity MIC ≈ 0.1 $\mu\text{g/mL}$ for <i>S. aureus</i> and degraded pollutants photocatalytically	Membrane penetration/disruption, thiol binding, DNA replication inhibition, and ROS generation	AgNPs@SI had lower MICs than ciprofloxacin for some strains and were eco-friendly synthesized without toxic chemicals	-	Preclinical (unspecified)
42	[61]	Egypt	AgNPs	Metal-based	<i>Streptococcus agalactiae</i>	Experimental	Showed antimicrobial activity against MDR mastitis pathogens	AgNPs act by disrupting microbial membranes, causing rupture and content leakage	Effective against MDR pathogens with lower cytotoxicity and an alternative to antibiotics in mastitis treatment	No in vivo studies support the clinical use of these compounds	Clinical
43	[62]	Iran	Chitosan-based nanofibrous mats embedded with silver, copper oxide, and zinc oxide nanoparticles (CS-nACZ)	Metal oxide-polymeric based	<i>S. aureus</i>	Experimental	Strong antimicrobial action, healed wounds in vivo, and were non-toxic to fibroblasts	-	Active against MDR bacteria (unlike single NPs), promoted healing, and was non-cytotoxic	-	In vivo (animal model)
44	[63]	Lithuania	Methionine-capped ultra-small gold (Au@Met) nanoparticles and methionine-stabilized magnetite-gold (Fe ₃ O ₄ @Au@Met) nanoparticles	Metal/biologically derived	MRSA, <i>Micrococcus luteus</i>	Experimental	Showed 89.1–75.7% against Gram-positive bacteria at 70 mg/L concentration	The presence of Au ⁺ ions causes interaction with bacterial membranes and metabolic imbalance	High biocompatibility, non-toxicity, effective at low concentration, and activity against MDR pathogens	-	In vivo (animal model)

Table 1. Summary of nanomaterial-based antimicrobials targeting Gram-positive bacteria. (continued)

S/N	Citation	Country	Nanomaterial type used	Nanomaterials class	Pathogen (s) targeted	Study type	Key findings	Mechanism of action	Advantages over conventional agents	Limitations	Translational stage/clinical phase
45	[64]	Iran	Chitosan NPs and TiO ₂ NPs	Polymer/Metal-based	<i>Streptococcus mutans</i>	Experimental	Experimental group showed marked <i>Streptococcus mutans</i> reduction at 1 day, 2 months, and 6 months, highest in the upper second premolars at 6 months	-	-	-	Preclinical (unspecified)
46	[65]	Brazil	Tea tree oil and low molecular weight chitosan (TTO-CH) nanoparticles	Biologically derived polymeric-based	<i>Streptococcus sanguinis</i>	Experimental	TTO-CH showed strong antimicrobial activity and had synergistic effects, matching azithromycin against mono- and mixed biofilms	Attributed to terpinen-4-ol and terpinene in TTO, the mechanism involves membrane disruption and metabolic interference	TTO-CH combination matched azithromycin in activity against oral biofilms and offers a natural alternative to antibiotics	Further studies are required to confirm efficacy in vivo and explore potential clinical applications	Clinical
47	[66]	India	AgNPs	Metal-based	<i>S. aureus</i>	Experimental	Exhibited up to 92.41% inhibition of <i>S. aureus</i> biofilms; anti-adhesion and biofilm disruption effects	Disrupt bacterial cell membranes, generate ROS, and interfere with cellular functions to inhibit biofilm formation	Exhibit stronger biofilm inhibition and penetration against antibiotics; plant-based eco-synthesis improves biocompatibility	-	Preclinical (unspecified)
48	[67]	China	Epigallocatechin gallate-gold nanoparticles (E-Au NPs)	Metal/Biologically derived	MRSA and <i>S. aureus</i>	Experimental	NIR-triggered, achieved > 90% MRSA biofilm destruction, strong antibacterial/antibiofilm effects, and promoted wound/keratitis healing with high biocompatibility	Combines mild photothermal therapy (PTT), ROS, quinoprotein formation, gene downregulation, and cell wall disruption	Highly biocompatible with minimal side effects; synergistic photothermal-polyphenol action boosts efficacy against MDR MRSA; suitable for eye and skin infections	-	In vivo (animal model)
49	[68]	China	Nano-Germanium dioxide (GeO ₂) /cetyltrimethylammonium bromide (CTAB) complex (nano-GeO ₂ /CTAB complex)	Biologically derived	<i>S. aureus</i>	Experimental	Nano-GeO ₂ /CTAB complex showed stronger Gram+ antibacterial activity than the individual components	-	-	More research is needed on long-term efficacy and environmental safety before use	Preclinical (unspecified)
50	[69]	Iran	α-Fe ₂ O ₃ nanoparticles (α-Fe ₂ O ₃ -NPs)	Metal oxide/biologically derived	<i>S. aureus</i> and <i>B. cereus</i>	Experimental	Exhibited significant antibacterial activity with MIC values between 0.625–5 µg/mL and MBC values between 5–20 µg/mL	ROS generation causes membrane damage and cell death, with minimal metal ion release, distinguishing them from other metal NPs	-	Requires further clinical trials and safety evaluations before medical application	Clinical
51	[70]	India	Erythromycin-loaded PLGA nanoparticles (PLGA-Ery NPs)	Polymer-based	<i>S. aureus</i>	Experimental	Enhanced antibacterial activity (1.5–2.1× MIC) against <i>S. aureus</i> , biofilm inhibition	Provided sustained drug release, better cell penetration, disrupted cell walls, and lowered efflux activity	Improved efficacy against resistant strains, biofilm inhibition, sustained drug release, and reduced toxicity	-	Preclinical (unspecified)
52	[71]	Iran	PEG-coated UIO-66-NH ₂ nanoparticles loaded with vancomycin and amikacin (VAN/AMK-UIO-66-NH ₂ @PEG)	Biologically derived	Vancomycin-resistant <i>S. aureus</i> (VRSA)	Experimental	Stronger antibacterial/antibiofilm effects downregulated <i>mecA</i> , <i>vanA</i> , <i>icaA</i> , <i>icaD</i> ; showed potent antioxidant activity	Inhibits biofilm and MDR gene expression (<i>mecA</i> , <i>vanA</i> , <i>icaA</i> , <i>icaD</i>); PEGylation enhances drug retention and delivery	Lower MIC/MBC than free VAN/AMK or VAN/AMK-UIO-66; sustained release, better stability, encapsulation, and bioavailability	Future in vivo studies are needed to assess safety, efficacy, and clinical use of these nanoparticles	Clinical

Table 1. Summary of nanomaterial-based antimicrobials targeting Gram-positive bacteria. (continued)

S/N	Citation	Country	Nanomaterial type used	Nanomaterials class	Pathogen (s) targeted	Study type	Key findings	Mechanism of action	Advantages over conventional agents	Limitations	Translational stage/clinical phase
53	[72]	Nigeria	AgNPs, AuNPs, and bimetallic gold-silver nanoparticles	Metal-based	<i>S. aureus</i> (ATCC 25923)	Experimental	Showed strong antibacterial activity against <i>S. aureus</i> , with a MIC of 1.953 µg/mL	Metal ions are liberated into the cells by oxidation and produce ROS that attack the bacterial cells and cause cell death	Offer a potential indigenous alternative to combat antibiotic resistance	-	Preclinical (unspecified)
54	[73]	China	Copper-doped hollow mesoporous cerium oxide (Cu-HMCE) nanozyme	Biologically derived	<i>S. aureus</i>	Experimental	Exhibited strong antibacterial properties against <i>S. aureus</i>	HMCE reduces bacterial viability via oxidative stress and disrupted nutrient transport	Shows promise for treating acidified chronic refractory wounds with infections	Further research is needed on its biosafety and vascularization mechanism	Preclinical (unspecified)
55	[74]	China	Bacteria-activated macrophage membrane coated ROS-responsive vancomycin nanoparticles (Sa-MM@Van-NPs)	Biologically derived	MRSA	Experimental	Efficiently targeted infected sites and released vancomycin to eliminate bacteria, facilitating faster wound healing	Targets infections via receptor interactions and releases antibiotics in high ROS to kill bacteria	ROS-responsive release of antibiotics improves antibacterial efficacy	-	Preclinical (unspecified)
56	[75]	Iraq	AgNPs	Biologically derived	<i>S. sciuri</i> and <i>S. lentus</i>	Experimental	Strong Gram+ activity by disrupting membranes and causing nucleic acid/protein leakage	Damaged bacterial membranes cause DNA, RNA, and protein leakage	-	Studies are needed to clarify mechanisms and assess in vivo safety	In vivo (animal model)
57	[76]	China	Polypeptide-based carbon nanoparticles	Carbon-based	<i>S. aureus</i> , and MRSA	Experimental	Achieved 99%+ inhibition of <i>S. aureus</i> and ~99% healing in MRSA wound infections	Nanozyme's peroxidase, oxidase, catalase, and glutathione peroxidase (GPx)-like activities regulate ROS for bacterial inhibition	Showed high inhibition against Gram-positive <i>S. aureus</i> planktonic bacteria	-	Preclinical (unspecified)
58	[77]	Egypt	Vancomycin functionalized silver nanoparticles (Ag-VanNPs)	Metal/Biologically derived	MRSA	Experimental	Lowered MIC/MBC with fractional inhibitory concentration/ fractional bactericidal concentration (FIC/FBC) ≤ 0.5, indicating synergistic action and fewer side effects	-	Synergistic action, better targeting, and much lower MIC/MBC than pure vancomycin	-	Preclinical (unspecified)
59	[78]	India	CuNPs	Metal	<i>S. aureus</i>	Experimental	CuNPs showed broad antimicrobial activity, with the strongest effect against <i>Staphylococcus aureus</i> (27 ± 1.00 mm).	-	Outperformed vancomycin with synergistic action, lower MIC/MBC, and better targeting	-	Preclinical (unspecified)
60	[79]	India	Sarsaparilla root extract fabricated silver nanoparticles (sAgNPs)	Metal/Biologically derived	<i>S. aureus</i> and MRSA	Experimental	Showed MICs 125 µM <i>S. aureus</i> , MRSA, and protected zebrafish from infection	At 1× MIC, sAgNPs generate excess ROS and disrupt membranes, causing depolarization	Potential to act as nanocatalysts and nano-drugs in addressing key challenges in medical and environmental research	-	Preclinical (unspecified)
61	[80]	Pakistan	ZnO NPs and aluminum-doped ZnO NPs (Zn _{1-x} Al _x O NCs)	Biologically derived	<i>S. aureus</i>	Experimental	Possess largest inhibition zones (notably vs. <i>B. cereus</i>), with strong antimicrobial effects, low toxicity, and high biocompatibility	Zn ²⁺ and ROS damage membranes/DNA, inhibit enzymes, and block biofilm formation	Al-doping increases antimicrobial activity through enhanced ROS generation	-	Preclinical (unspecified)

Table 1. Summary of nanomaterial-based antimicrobials targeting Gram-positive bacteria. (continued)

S/N	Citation	Country	Nanomaterial type used	Nanomaterials class	Pathogen (s) targeted	Study type	Key findings	Mechanism of action	Advantages over conventional agents	Limitations	Translational stage/clinical phase
62	[81]	Iran	Chitosan, ZnO, and ZnO– <i>Urtica dioica</i> (ZnO– <i>U. dioica</i>) NPs	Polymer and metal-oxide-based	<i>S. aureus</i>	Experimental	The zone of inhibition for was greater for aqueous leaf extract against <i>S. aureus</i>	Interact with microbial membranes, results in structural damage, protein denaturation, and generation of ROS leading to cell death	Showed enhanced antimicrobial efficacy over crude extracts and were environmentally friendly	-	Preclinical (unspecified)
63	[82]	Italy	Surface active maghemite nanoparticles (SAMN), colloidal iron oxide NPs with oxyhydroxide-like surface	Biologically derived	<i>Listeria</i> spp.	Experimental	Captured 100% of bacteria in wastewater without agitation and bound stably, non-toxically to polysaccharides and cells	Bind peptidoglycan and polysaccharides via chelation and electrostatic interactions	Non-toxic, reusable, and highly stable, and enables physical removal of Gram (+) bacteria as an alternative to antibiotics	-	Preclinical (unspecified)
64	[83]	China	Nickel oxide nanoparticles (NiOx NPs)	Metal oxide	MRSA	Experimental	Eradicated MRSA and biofilms in vitro and in vivo and promoted wound healing, collagen deposition, and tissue regeneration in animal models	Oxygen vacancies boost ROS and photothermal effects; NiOx mimics oxidase/peroxidase to generate •OH and damage membranes, DNA, and proteins	Non-antibiotic dual-action strategy; effective against drug-resistant biofilms with high biosafety, biocompatibility, and regenerative properties	The long-term effects of NiOx NPs were not addressed.	In vivo (animal model)
65	[84]	Nigeria	Green-synthesized AgNPs using <i>Vitex grandifolia</i> leaves extract	Biologically derived	<i>Streptococcus pyogenes</i> and <i>S. aureus</i>	Experimental	Significant antibacterial activity against MDR pathogens; inhibition zones up to 15 mm at 100 µg/mL; concentration-dependent response	Ag ⁺ release disrupts membranes, inactivates enzymes, generates ROS, and blocks DNA/protein synthesis	-	Further research is needed to confirm safety and biocompatibility	Preclinical (unspecified)
66	[85]	Thailand	Ag/AgCl-NPs	Metal/Metal oxide based	<i>S. haemolyticus</i>	Experimental	MIC/MBC 7.8–15.6 µg/mL; reduced biofilm biomass ~95% and viability ~78%; caused visible cell damage	ROS-driven membrane damage, morphological changes, and reduced viability in the biofilm strain	The synthesized Ag/AgCl-NPs show an enhanced antibacterial and antibiofilm agent against <i>S. haemolyticus</i>	-	Preclinical (unspecified)
67	[86]	India	ZnO NPs	Metal oxide	<i>S. aureus</i> and <i>Streptococcus pyogenes</i>	Experimental	Inhibited bacterial growth and biofilms in a dose-dependent manner, confirmed by SEM and CFU reduction	Antibacterial and antibiofilm effects stem from membrane disruption and ROS-induced stress	Antibiotic-loaded ZnO NPs showed stronger antibacterial activity than Li-ZnO NPs or ciprofloxacin alone	-	Preclinical (unspecified)
68	[87]	Iraq	AgNPs	Metal-based	MDR bacteria (not specified)	Experimental	AgNPs showed significant dose-dependent antibacterial activity	-	AgNPs exhibited antibacterial activity against MDR bacteria compared to conventional agents	Nanotoxicology studies are needed to find doses balancing antibacterial efficacy and low human toxicity	In vivo (animal model)
69	[88]	Saudi Arabia	Nickel ferrite nanoparticles (NiFe ₂ O ₄ NPs)	Metal-oxide-based	MRSA	Experimental	MIC 1.6–2 mg/mL, reduced biofilm formation ~50%, eradicated mature biofilms 50–76%	Membrane disruption and structural damage, blocked biofilm adherence with visible membrane deformation	NiFe ₂ O ₄ NPs not only prevent the formation of biofilm, but also eliminate existing mature biofilms by 50.5–75.79%	-	Preclinical (unspecified)
70	[89]	Portugal	Photo-crosslinked chitosan/methacrylated hyaluronic acid nanoparticles (HAMA/CS NPs)	Polymer-based	<i>S. aureus</i> , MRSA, and <i>S. epidermidis</i>	Experimental	Showed strong antibacterial/antibiofilm effects and boosted mammalian cell growth	Inhibit growth via contact, cut biofilms, and improve delivery/diffusion for antibacterial action at 37°C	Strong antibacterial/antibiofilm effects in wounds, supports cell growth, is non-cytotoxic, and enables targeted antibiotic delivery	-	Preclinical (unspecified)

Table 1. Summary of nanomaterial-based antimicrobials targeting Gram-positive bacteria. (continued)

S/N	Citation	Country	Nanomaterial type used	Nanomaterials class	Pathogen (s) targeted	Study type	Key findings	Mechanism of action	Advantages over conventional agents	Limitations	Translational stage/clinical phase
71	[90]	Germany	PLGA-based NPs	Polymer-based	MRSA	Experimental	The efficacy against MSSA and MRSA strains was demonstrated in vitro in several bacteria strains and in vivo in the <i>G. mellonella</i> model	SV7-loaded nanoparticles target intracellular MRSA infections effectively	SV7-loaded nanoparticles show a safe profile at all tested concentrations	Further in vivo mouse studies are needed to optimize post-infection regimens in complex environment	In vivo (animal model)
72	[91]	Egypt	ZnO NPs	Metal oxide	<i>S. aureus</i>	Experimental	Showed inhibitory percentages ranging from 12.0% to 39.1%, with extract ranging from 28.0% to 52.2%	GyrB inhibition stops bacterial DNA replication, leading to bacterial death	Zinc nanoparticles exhibit potential antibacterial and anticancer properties	-	Preclinical (unspecified)
73	[92]	India	In situ aqueous nanosuspension of PPEF.3HCl (IsPPEF.3HCl-NS)	Biologically derived	MRSA	Experimental	Inhibited bacterial growth, showing promise against intracellular MRSA	Blocks DNA rejoining and disrupts enzymatic processes as a poison inhibitor	IsPPEF.3HCl-NS enhanced log CFU reduction in <i>S. aureus</i> -induced murine sepsis model	-	Preclinical (unspecified)
74	[93]	Romania	AgNPs	Metal-based	<i>S. aureus</i> (ATCC 29213), MRSA, <i>E. faecalis</i> (ATCC 29212)	Experimental	Exhibit strong antibacterial effects by damaging bacterial cell membranes and generating oxidative stress	Ag ⁺ ions disrupt membranes, trigger ROS and oxidative stress, block ATP synthesis, alter gene expression, and inhibit respiration	Nanomaterials offer enhanced antibacterial efficacy against MDR bacteria	More in vivo studies are needed for satisfactory results	Preclinical (unspecified)
75	[94]	China	Silver- and zinc-doped silica nanoparticles synthesized using the sol-gel [Ag/Zn-SiO ₂ NPs (sol-gel)]	Metal/Biologically derived	<i>S. aureus</i> , <i>E. faecalis</i>	Experimental	Demonstrated antibacterial and antifungal properties against all the tested strains	Released Ag ⁺ , Cu ²⁺ , and Zn ²⁺ ions damage bacterial membranes and inhibit growth	Ag- and Zn-doped silica NPs were found effective against periodontitis microbe	-	In vivo (animal model)
76	[95]	China	DMY-AgNPs (silver nanoparticles synthesized using dihydromyricetin)	Metal/Biologically derived	MRSA	Experimental	Showed the highest antibacterial activity with inhibition zones of 1.92 mm (<i>S. aureus</i>) and 1.75 mm (MRSA)	-	The antibacterial efficacy of DMY-AgNPs surpassed that of other green-synthesized AgNPs	High AgNPs concentrations impacted zebrafish embryo development	In vivo (animal model)
77	[96]	Pakistan	Levofloxacin loaded chitosan and poly-lactic-co-glycolic acid nano-particles (LVX-CS-III PLGA-I NPs)	Polymer-based	<i>S. aureus</i>	Experimental	Better antibacterial potency against gram+ve bacteria	CS-NPs enhance antibiotic delivery and pharmacokinetic profiles	Improved antibiotic sensitivity without compromising patient safety; enhanced zone of inhibition compared to free LVX	Conflicting reports exist on mass ratios affecting nanoparticle characteristics	Preclinical (unspecified)
78	[97]	Pakistan	AgNPs	Metal-based	<i>S. aureus</i>	Experimental	AgNPs exhibited significant antibacterial and antifungal activities	-	Aqueous extract of AgNPs provides a safer alternative to conventional antibacterial agents	-	Preclinical (unspecified)
79	[98]	India	AgNP-antibiotic combinations (SACs) synthesized using <i>Streptococcus pneumoniae</i> ATCC 49619	Metal-based	<i>Enterococcus faecium</i> , <i>S. aureus</i>	Experimental	SACs synergized with antibiotics, cutting required doses up to 32× and showing growth inhibition and bactericidal effects	AgNPs in SACs boost local Ag ⁺ release, forming membrane pores, causing leakage, and killing bacteria	Up to 32-fold enhanced antibacterial activity, effective against biofilms, non-cytotoxic to normal cells	-	Preclinical (unspecified)

Table 1. Summary of nanomaterial-based antimicrobials targeting Gram-positive bacteria. (continued)

S/N	Citation	Country	Nanomaterial type used	Nanomaterials class	Pathogen (s) targeted	Study type	Key findings	Mechanism of action	Advantages over conventional agents	Limitations	Translational stage/clinical phase
80	[99]	China	Epigallocatechin gallate-ferric (EGCG-Fe) complex nanoparticles	Biologically derived	<i>S. aureus</i>	Experimental	Uses photothermal conversion to enhance antibacterial effects on <i>S. aureus</i> , prevent/destroy biofilms, and aid wound healing in vivo	Photothermal effect disrupts bacterial membranes and enhances antibacterial performance upon NIR laser irradiation	Shows photothermal enhanced antibacterial and wound healing effects compared to conventional agents	-	In vivo (animal model)
81	[100]	Argentina	AgNPs	Metal-based	<i>S. aureus</i>	Experimental	AgNPs with a diameter of around 11 nm exhibited high antibacterial activity against both tested bacteria	The AgNPs increased intracellular ROS levels in both bacteria and caused membrane damage	AgNPs showed high antibacterial activity against <i>S. aureus</i>	-	Preclinical (unspecified)
82	[101]	Saudi Arabia	AuNPs	Metal-based	<i>S. aureus</i>	Experimental	Strong antimicrobial activity, especially at 20 µg/vol; inhibited Gram-positive bacteria	Nilavembu choornam-gold nanoparticles (NC-GNPs) disrupt bacterial membrane integrity, leading to cell death	NC-GNPs enhance drug efficacy and combat antibiotic resistance	Variations in drug delivery rates limit therapeutic efficacy	In vivo (animal model)
83	[102]	Indonesia	AuNPs	Metal-based	<i>S. aureus</i> and MRSA	Experimental	Showed antibacterial activity; higher metal ion levels increased efficiency	Damaged bacterial cell walls, disrupted metabolism, and ROS generation	-	-	Preclinical (unspecified)
84	[103]	Bangladesh	Green synthesized chitosan nanoparticles (ChiNPs)	Biologically derived	<i>S. aureus</i> strains	Experimental	Reduced zones of inhibition against methicillin-resistant (<i>mecA</i>) and penicillin-resistant (<i>blaZ</i>) <i>S. aureus</i>	Positively charged nanomaterials interact with negatively charged bacterial cell walls through electrostatic interaction	-	The antiviral as well as antifungal activity of the yielded nanoparticles needs to be verified before field application	Preclinical (unspecified)
85	[104]	New Zealand	AuNPs	Metal-based	<i>S. aureus</i> (MRSA ATCC 33593)	Experimental	Showed strong antimicrobial activity (0.13–1.25 µM), inhibited 90% of initial biofilms, and reduced 80% of preformed biofilms	-	The conjugates were stable in rat serum and not toxic to representative mammalian cell lines in vitro (≤ 64 µM) and in vivo (≤ 100 µM)	-	Preclinical (unspecified)
86	[105]	Iraq	AgNPs	Metal-based	<i>Streptococcus mitis</i>	Experimental	Synergistic effect in the inhibition when combining AgNPs with some antibiotics	-	Clear synergistic effect in the inhibition of <i>Streptococcus mitis</i>	-	Preclinical (unspecified)
87	[106]	Egypt	Streptomycin (Str) and Moringa oleifera leaf extract (MOLe)-loaded ZnONPs (Str/MOLe@ZnONPs)	Biologically derived	<i>E. faecalis</i>	Experimental	Strongly inhibited <i>E. faecalis</i> growth and biofilm formation	Enhance delivery by bacterial binding, blocking efflux pumps, and disrupting membranes	Nanoparticles enhance antibiotic binding to bacteria, improving efficacy	-	Preclinical (unspecified)
88	[107]	China	Phenylboronic acid-functionalized BSA@CuS@PpIX (BSA@CuS@PpIX@PBA; BCPP) nanoparticles	Biologically derived	<i>S. aureus</i>	Experimental	BCPP exhibited good bacteria-targeting properties for both <i>S. aureus</i>	Produces ROS, amplifying Str's bactericidal action	BCPP shows good hemocompatibility and low cytotoxicity compared to conventional agents	Photodynamic therapy (PDT) is restricted by poor photosensitizer solubility and a short half-life	Preclinical (unspecified)

Table 1. Summary of nanomaterial-based antimicrobials targeting Gram-positive bacteria. (continued)

S/N	Citation	Country	Nanomaterial type used	Nanomaterials class	Pathogen (s) targeted	Study type	Key findings	Mechanism of action	Advantages over conventional agents	Limitations	Translational stage/clinical phase
89	[108]	Egypt	TiO ₂ , magnesium oxide (MgO), calcium oxide (CaO), and ZnO nanoparticles	Metal/Metal oxide-based	<i>S. aureus</i>	Experimental	Showed significant antibacterial effects, particularly MgO- and ZnO-hydrogel types	Generated free radicals and ROS that damage membranes, proteins, and DNA, causing bacterial death	Embedding nanoparticles in hydrogels prevents aggregation and boosts antibacterial synergy	-	Preclinical (unspecified)
90	[109]	Egypt	Myricetin-coated zinc oxide/polyvinyl alcohol nanocomposites (MYR-loaded ZnO/PVA NCs)	Biologically derived	<i>Clostridium (C.) perfringens</i>	Experimental	<i>C. perfringens</i> isolates were most sensitive to MYR-loaded ZnO/PVA, with MICs of 0.125–2 µg/mL	MYR inhibits α-hemolysin-induced cell damage without inhibiting bacterial growth	Nanomaterials exhibit enhanced antimicrobial activity compared to conventional agents	In vivo studies are needed for validation	In vivo (animal model)
91	[110]	Egypt	Ciprofloxacin hydrochloride (CIP) encapsulated in PLGA nanoparticles coated with chitosan (CIP-CS-PLGA-NPs)	Polymer-based	<i>E. faecalis</i>	Experimental	Enabled controlled release, boosted antibacterial/antibiofilm effects, and improved healing	-	Exhibited greater antibacterial and anti-biofilm activity than free ciprofloxacin and calcium hydroxide	There is a need to link current findings to short- and long-term periapical healing	Preclinical (unspecified)
92	[111]	Iran	Silver nanoparticles and propolis (AgNPs@propolis)	Biologically derived	<i>S. aureus</i> and <i>E. faecalis</i>	Experimental	Possesses a low toxic effect on the cell and has a high effect in inhibiting the growth of various bacteria	Membrane damage, energy transfer disruption, ROS generation, and toxic element release	Green synthesis reduces toxic effects compared to conventional methods	-	Preclinical (unspecified)
93	[112]	Czech Republic	TiO ₂ NPs	Metal-oxide-based	<i>S. aureus</i>	Experimental	Offer a promising alternative to antibiotics, particularly for controlling MDR	Disrupts cell wall integrity, leading to cell death	TiO ₂ NPs exhibit enhanced antimicrobial properties against resistant strains	More studies are required to explore full applications and possible hazards	Preclinical (unspecified)
94	[113]	Algeria	Silver carbonate nanoparticles (BioAg ₂ CO ₃ NPs)	Biologically derived	<i>S. aureus</i>	Experimental	Displayed good antibacterial and antibiofilm activity	Protein inactivation, production of ROS, and formation of free radicals	Pathogens fail to develop resistance to BioAg ₂ CO ₃ NPs, unlike conventional antimicrobials	-	Preclinical (unspecified)
95	[114]	Turkey	Biogenic AgNPs	Biologically derived	<i>S. aureus</i>	Experimental	Showed antibacterial activity against <i>S. aureus</i>	-	The synergistic effects increased antibacterial effectiveness	-	Preclinical (unspecified)
96	[115]	USA	PVP- or PEG-coated Ga ₂ (HPO ₄) ₃ nanoparticles	Biologically derived	<i>S. aureus</i>	Experimental	Exhibit potent antimicrobial activity that is comparable to Ga(NO ₃) ₃	-	Showed no bacterial resistance after 30 days, unlike Ga(NO ₃) ₃ and ciprofloxacin	Ineffective against Gram-positive <i>S. aureus</i> even at high concentrations	In vivo (animal model)
97	[116]	Ethiopia	Silver and cobalt oxide nanoparticles (Ag/Co ₃ O ₄ NPs)	Metal-metal oxide-based	<i>S. aureus</i> and <i>E. faecalis</i>	Experimental	Showed promising antibacterial activities, with Ag NPs exhibiting the best inhibition	Disintegration of bacterial cell membranes results in pathogen death	High specific surface area of the nanoparticles enhances antibacterial performance	-	Preclinical (unspecified)
98	[117]	Saudi Arabia	Saponin-derived AgNPs (AgNPs-S)	Biologically derived	MTCC-121 (<i>B. subtilis</i>), MTCC-439 (<i>E. faecalis</i>), and MTCC-96 (<i>S. aureus</i>)	Experimental	Exhibited potent antibacterial activity against both Gram-positive and Gram-negative bacteria	Damaged bacterial membranes, causing DNA, RNA, and protein leakage	-	Further investigations to elucidate the possible mechanism involved and safety concerns	Preclinical (unspecified)

Table 1. Summary of nanomaterial-based antimicrobials targeting Gram-positive bacteria. (continued)

S/N	Citation	Country	Nanomaterial type used	Nanomaterials class	Pathogen (s) targeted	Study type	Key findings	Mechanism of action	Advantages over conventional agents	Limitations	Translational stage/clinical phase
99	[118]	USA	AgNPs	Metal-based	<i>S. aureus</i>	Experimental	Kenaf-based activated carbon (KAC)-chitosan (CS)-AgNPs exhibited a strong bactericidal effect with an MIC of 43.6 µg/mL for <i>S. aureus</i>	Disruption of bacterial cell walls, generation of ROS, interaction with sulfur and phosphorus of DNA, and cell death	Environmentally friendly synthesis method compared to conventional agents	-	Preclinical (unspecified)
100	[119]	United Arab Emirates	CuO, ZnO, and tungsten trioxide (WO ₃) nanoparticles	Metal-oxide-based	<i>S. aureus</i> and MRSA	Experimental	Exhibited significant antimicrobial effects under dark incubation, while photoactivated WO ₃ NPs reduced viable cells by 75%	Lipid peroxidation due to ROS generation and cell membrane disruption, as shown by MDA production and live/dead staining	Nanomaterials exhibit > 90% antimicrobial activity at low concentrations	Varying results based on the NPs size	Preclinical (unspecified)
101	[120]	Spain	AuNPs	Metal-based	<i>S. aureus</i>	Experimental	The antibiotic as an enhancer of amoxicillin was demonstrated, causing the precursors and the NPs to act quickly, and favor microbial death with a small amount of antibiotic	Internalization into bacteria, damage to the bacterial surface, production of ROS, and disruption of biosynthetic machinery led to microbial death	Acts quickly, favoring microbial death with a small antibiotic, thereby combating resistance and avoiding side effects derived from high doses	Further investigations to identify possible long-term adverse effects	In vivo (animal model)
102	[121]	Spain	Silver, gold, zinc, and copper nanoparticles (Ag, Au, Zn, and Cu NPs)	Metal-based	<i>Enterococcus</i> spp.	Experimental	Effectively inhibit planktonic cells and biofilm formation at low concentrations, affects preformed biofilms, and destabilizes their structure	-	Represent a good alternative to avoid the spread of MDR bacteria and minimize the selective pressure by systemic antibiotics or disinfectants	Further studies are required to confirm the compatibility and cytotoxicity of the most successful combinations	In vivo (animal model)
103	[122]	Egypt	Liposomal nanoparticles (LNPs)	Lipid-based	MRSA	Experimental	Combination therapies (AuNPs/AgNPs) and traditional antibiotics, provided enhanced antimicrobial efficacy and inhibited biofilm formation	-	This combination may overcome resistance and restore sensitivity in MDR bacteria	Further investigations are necessary to establish the safety and cytotoxicity profiles of these nanocomplexes	Preclinical (unspecified)
104	[123]	Egypt	ZnONPs	Metal-oxide-based	<i>Enterococcus</i> spp. and MRSA	Experimental	Exhibited a synergistic antibacterial effect, showing enhanced inhibition compared to individual NPs	Based on the generation of ROS, leading to lipid peroxidation and membrane damage	Offers a non-toxic, non-invasive, and cost-effective alternative to conventional antimicrobials	Further in vivo investigations are required to validate the safety and efficacy	In vivo (animal model)
105	[124]	Australia	(Rif)-loaded MSN and organo-modified (ethylene-bridged) MSN (MON)	Inorganic based	<i>S. aureus</i>	Experimental	The combined effects reduced the CFU of intracellular SCV-SA 28 times and 65 times compared to MSN-Rif and non-encapsulated Rif, respectively	Increased uptake of MON is five-fold compared to MSN	MON reduced CFU of intracellular SCV-SA significantly compared to MSN-Rif	Further in vivo validation would be required	In vivo (animal model)

Table 1. Summary of nanomaterial-based antimicrobials targeting Gram-positive bacteria. (continued)

S/N	Citation	Country	Nanomaterial type used	Nanomaterials class	Pathogen (s) targeted	Study type	Key findings	Mechanism of action	Advantages over conventional agents	Limitations	Translational stage/clinical phase
106	[125]	Spain	Silica MSNs	Inorganic-based	<i>S. aureus</i> and <i>E. faecalis</i>	Experimental	Displayed antibacterial activity against <i>S. aureus</i> with Ag-containing materials, showing the highest effectiveness	Bacterial death, including interactions with the outer and inner membranes, and alterations in the cytoplasmic membrane	Act as carriers of antibiotics, increasing their ability to penetrate the biofilm bacteria often developed to conventional antibiotics	Further in vivo studies will be necessary to validate their biomedical application	In vivo (animal model)
107	[126]	Romania	ZnO NPs	Metal-oxide-based	<i>S. aureus</i>	Experimental	The hydrogels containing 4% and 5% ZnO NPs, respectively, showed good antimicrobial activity	Direct contact of ZnO NP with the cell wall results in the bacterial cell's integrity destruction and the release of antimicrobial ions (Zn ²⁺ ions)	-	The biocomposites present some degree of toxicity towards HSF normal cells, depending on the quantity	Preclinical (unspecified)
108	[127]	USA	AgNPs	Metal-based	MRSA	Experimental	Promising clinical application as a potential stand-alone therapy or antibiotic adjuvant	-	Synergy with clinically relevant antibiotics reduced the MIC of aminoglycosides by approximately 22-fold	Exhibits cytotoxicity, which could limit its application as a broad oral antimicrobial	Clinical
109	[128]	India	ZnO NPs	Metal-oxide-based	<i>B. cereus</i>	Experimental	Exhibited high antibiofilm activity against <i>B. cereus</i> with minimum biofilm inhibitory concentration (MBIC) of ZnO NPs at 46.8 µg/mL. Exhibited high antibiofilm activity against <i>B. cereus</i> with MBIC of ZnO NPs at 46.8 µg/mL and 93.7 µg/mL	ZnO NPs target the cell membrane-induced ROS generation as a bactericidal mechanism	ZnO NPs reduced the bacterial cell viability and eradicate the biofilms	-	Preclinical (unspecified)
110	[129]	Saudi Arabia	AgNPs	Metal-based	<i>S. aureus</i>	Experimental	Enhanced antibacterial activity by increasing inhibition zones and reducing MIC values compared to lincomycin or AgNPs alone	The ROS, along with free radicals, damaged the bacterial cell wall and also inhibited the respiratory enzymes	Enhanced antibacterial efficacy compared to lincomycin alone, reducing MIC and increasing inhibition zone diameters	Lincomycin has restricted Gram-positive antibacterial activity and is developing resistance	Preclinical (unspecified)
111	[130]	Iran	Ag Np conjugated to chitosan (Ag Np and Chitosan Np)	Inorganic metal-based	MRSA	Experimental	Ag Np-chitosan exhibits great antibacterial and anti-biofilm effects against CRAB and MRSA isolates	-	Ag Np-chitosan conjugation, an ideal alternative for ineffective antibiotics	-	Preclinical (unspecified)
112	[131]	Saudi Arabia	CNPs	Polymer-based	<i>Streptococcus pneumoniae</i>	Experimental	Enhanced antibacterial activity compared to C3-005 alone	C3-005 reduces ATP generation in <i>Streptococcus pneumoniae</i>	Precise mechanism of haemolysis reduction by CNPs has not been determined	-	Preclinical (unspecified)
113	[132]	Saudi Arabia	AgNPs	Metal-based	MRSA	Experimental	Exhibited high antimicrobial activity and a synergistic effect with penicillin against MRSA strains	AgNPs enhance antibiotic efficiency through synergistic effects with penicillin	AgNPs exhibited high antimicrobial activity and a synergistic effect with penicillin against MRSA strains	Phenotype from healthcare-associated (HA)-MRSA lacks plasmid DNA, limiting resistance understanding	Preclinical (unspecified)

Table 1. Summary of nanomaterial-based antimicrobials targeting Gram-positive bacteria. (continued)

S/N	Citation	Country	Nanomaterial type used	Nanomaterials class	Pathogen (s) targeted	Study type	Key findings	Mechanism of action	Advantages over conventional agents	Limitations	Translational stage/clinical phase
114	[133]	China	AgNPs	Metal-based	<i>Streptococcus suis</i>	Experimental	Significantly inhibited the growth of MDR <i>Streptococcus suis</i> , disrupted bacterial morphology and cell walls, and destroyed biofilm structures	ROS overproduction inhibited peptidoglycan biosynthesis, downregulated bacterial division proteins, and interfered with quorum sensing	AgNPs are effective against MDR bacteria, unlike conventional antibiotics	Insufficient antioxidant enzyme expression to eliminate excessive ROS effectively	Preclinical (unspecified)
115	[134]	South Korea	C2-coated ZnONPs (C2-ZnONPs)	Inorganic based	<i>S. aureus</i>	Experimental	C2-ZnONPs inhibited biofilm and virulence of <i>S. aureus</i>	Lam-AuNPs disrupt mature biofilm structures in a dose-dependent manner	Lam-AuNPs effectively control biofilm and virulence in pathogens	The need to unravel the molecular mechanism of biofilm and virulence attenuation	Preclinical (unspecified)
116	[135]	USA	Ag NPs	Metal based	<i>S. aureus</i>	Experimental	Ag NPs do not exhibit cytotoxicity up to 50 µg/mL in each solution	-	Ag NPs/methylene blue (MB) were shown to be more effective than MB and Ag NPs alone	To evaluate its effectiveness against pathogens that cause prosthetic joint infection	Preclinical (unspecified)
117	[136]	China	Ti ₃ C ₂ T _x MXene loaded with indocyanine green nanoparticles (ICG@Ti ₃ C ₂ T _x MXene NPs)	Biologically derived	<i>Streptococcus mutans</i>	Experimental	ICG-MXene under NIR irradiation killed MRSA; no antibacterial effect without NIR	Combination of the photothermal effect of MXene and the photodynamic effect of ICG	ICG-MXene has a great synergistic PTT/PDT effect against MRSA	-	Preclinical (unspecified)
118	[137]	India	Zn and Mg substituted β-tricalcium phosphate/functionalized multiwalled carbon nanotube (f-MWCNT) nanocomposites	Metal based	MRSA	Experimental	The in-vitro cell viability and anti-biofilm results of zinc (5%) rich nanocomposite confirmed that prepared nanocomposite has biocompatible and enhanced anti-biofilm property, which will be beneficial candidate for biomedical applications	-	Nanocomposites have the ability to enhance the bioactivity of commercial antibiotics by means of a decrease in drug resistance	-	Preclinical (unspecified)
119	[138]	Jordan	Tryasine-AgNPs	Metal-based/biologically derived	MRSA	Experimental	More effective with MICs ranging from 30 to 100 µM, while at 100 µM caused only 1% haemolysis on human erythrocytes after 30 min of incubation	Tryasine enters the bacterial cell wall outer membrane, increasing its permeability, and the antibiotic impact of AgNPs	Strong activity against resistant bacteria while exhibiting low haemolytic activity and cytotoxicity	Potential toxicity not extensively evaluated beyond hemolytic assay	Preclinical (unspecified)
120	[139]	Iraq	AgNPs	Metal-based	<i>S. aureus</i> , <i>S. epidermidis</i>	Experimental	Broad-spectrum antibacterial activity. Synergistic effect with multiple antibiotics, increasing the inhibition fold area	Generation of ROS, disruption of the electron transport chain, decreased ATP levels, interference with the plasma membrane, and inhibition of DNA unwinding	Synergistic combination of AgNPs with conventional antibiotics enhances antibacterial efficacy against resistant strains	Further investigations (e.g., checkerboard assay, cytotoxicity, and blood compatibility studies) are required	Preclinical (unspecified)

Table 1. Summary of nanomaterial-based antimicrobials targeting Gram-positive bacteria. (continued)

S/N	Citation	Country	Nanomaterial type used	Nanomaterials class	Pathogen (s) targeted	Study type	Key findings	Mechanism of action	Advantages over conventional agents	Limitations	Translational stage/clinical phase
121	[140]	Saudi Arabia	AgNPs	Metal-based	<i>S. aureus</i> , <i>S. saprophyticus</i> , <i>S. sciuri</i> , and <i>S. epidermidis</i>	Experimental	AgNPs (15–25 nm) were not effective against Gram-positive strains (MIC 256 µg/mL).	AgNPs mediate antimicrobial effects via the generation of ROS, direct interaction with and rupture of bacterial membranes	Enhances antimicrobial efficacy, reduces required antibiotic doses, and minimizes toxicity against AMR strains	To evaluate potential cytotoxicity and confirm in vivo effectiveness	In vivo (animal model)
122	[141]	Turkey	Ag–Pt nanoparticles	Metal based	<i>S. aureus</i> , <i>B. subtilis</i> , <i>S. epidermidis</i>	Experimental	Antimicrobial activity at 25, 50, and 100 µg/mL, with 100 µg/mL achieving low bacterial viability (22.58–29.67%)	Oxidative dissolution leads to the release of silver ions (Ag ⁺), which initiates the antibacterial effect	Propolis in nanoparticle synthesis helps prevent industrial synthesis methods that consume more resources and induce side effects	-	Preclinical (unspecified)
123	[142]	Brazil	Biogenically synthesized silver nanoparticles using <i>Fusarium oxysporum</i> (BioAgNP)	Biologically derived	MRSA	Experimental	BioAgNP and thymol exhibited synergistic antibacterial activity, inhibited biofilm, and prevented the development of MDR	Membrane disruption, leakage of intracellular contents, oxidative stress (ROS, lipid peroxidation)	Combination prevented resistance development, faster antibacterial action, and reduced MIC values	Limited to specific bacterial strains tested in the study.	Preclinical (unspecified)
124	[143]	South Korea	Thymol-zinc oxide nanocomposite (ZnO NCs)	Metal oxide/biologically derived	<i>Staphylococcus</i> spp.	Experimental	Highly selective and bactericidal against <i>S. epidermidis</i> ; MIC 2–32-fold lower than THO alone	Membrane rupture, suppression of biofilm, modulation of cell wall and protein synthesis pathways	Bioconjugation improves the efficacy of natural antibacterial compounds	Thymol has low antibacterial activity and non-selectivity	Preclinical (unspecified)
125	[144]	Saudi Arabia	Chitosan silver and gold nanoparticles (CS-Ag-Au NPs)	Metal/Polymer-based	<i>B. subtilis</i> and <i>S. aureus</i>	Experimental	Chitosan (Ch)-AgNPs showed strong antibacterial and antibiofilm activities; ch-AuNPs showed moderate to weak activity	Biofilm formation aids bacterial colonization on surfaces	Biogenic nanoparticles do not require rigorous conditions for synthesis like conventional agents	-	In vivo (animal model)
126	[145]	Mexico	AgNPs	Metal-based	<i>S. aureus</i>	Experimental	Increased susceptibility to antibiotics by 20% (without efflux effect) and 3% (with efflux effect). Decreased isolates with efflux effect by 17.5%	Decreases the portion of bacterial isolates exhibiting efflux activity, indirectly restoring antibiotic susceptibility	AgNPs can restore antibiotic activity and reduce treatment duration	-	Preclinical (unspecified)
127	[146]	India	AgNPs	Metal-based	<i>S. aureus</i>	Experimental	Best synergistic antibacterial activity against planktonic <i>S. aureus</i> despite lower drug release compared to AgNP-trisodium citrate (TSC)-tannic acid (TA)	AgNPs with mupirocin and antibiofilm agents enhance activity against <i>S. aureus</i>	Nanoparticles enhance antibiotic concentrations at infection sites	-	Preclinical (unspecified)
128	[147]	Jordan	Tobramycin-chitosan nanoparticles (TOB-CS NPs) coated with zinc oxide nanoparticles (ZnO NPs)	Biologically derived	<i>S. aureus</i>	Experimental	Enhanced antimicrobial activity against <i>S. aureus</i> compared to TOB-CS NPs or ZnO NPs alone	Generated oxidative stress and damage bacterial membranes; TOB inhibits protein synthesis	Nanoparticles can improve drug entrapment efficiency significantly	No MIC data for <i>S. aureus</i> ATCC 29215 was found	Preclinical (unspecified)
129	[148]	Saudi Arabia	Ceftriaxone-loaded gold nanoparticles (CGNPs)	Metal-based	<i>S. aureus</i>	Experimental	Showed MIC ₅₀ values 2× lower compared to pure ceftriaxone and enhanced antibacterial potency	CGNPs increase ceftriaxone concentration by attachment	CGNPs showed two times better antibacterial efficacy compared to pure ceftriaxone	In vivo studies on CGNPs' fate and toxicity are needed	Preclinical (unspecified)

Table 1. Summary of nanomaterial-based antimicrobials targeting Gram-positive bacteria. (continued)

S/N	Citation	Country	Nanomaterial type used	Nanomaterials class	Pathogen (s) targeted	Study type	Key findings	Mechanism of action	Advantages over conventional agents	Limitations	Translational stage/clinical phase
130	[149]	Czech Republic	AgNPs	Metal-based	<i>S. aureus</i>	Experimental	TMPyP and AgNPs showed a synergistic antimicrobial effect, a promising alternative against MDR	Penetrate the bacterial cell and release Ag ions, which attack the respiratory chain, sulfur-containing proteins, and phosphorus-containing compounds such as DNA	Effective fight against MDR	lack of development in new molecules with antibacterial properties	Preclinical (unspecified)
131	[150]	Iran	Zinc sulfide (ZnS) nanoparticles	Metal-based	<i>Streptococcus pyogenes</i>	Experimental	Antibacterial effects dependent on concentration; 150 µg/mL had the highest antibacterial effect	-	Nanoparticles exhibit enhanced antibacterial effects compared to conventional agents	-	In vivo (animal model)

-: No details. MDR: multidrug-resistant; MRSA: methicillin-resistant *Staphylococcus aureus*; XRD: X-ray diffraction patterns; SEM: scanning electron microscopy; TEM: transmission electron microscopy.

Mechanisms of action of nanomaterials

Nanoparticles exert antimicrobial and therapeutic effects against Gram-positive bacteria through multiple physical, chemical, and biological mechanisms (Table 1). The most frequently reported mechanism is bacterial membrane disruption, which increases permeability, causes leakage of cytoplasmic components (e.g., DNA, ions, proteins), and ultimately leads to cell lysis [20, 29, 31, 37, 45, 60, 61]. ROS generation is another key mechanism, inducing oxidative stress that damages lipids, proteins, and DNA, resulting in significant bacterial mortality [24, 31, 42, 86, 93, 100, 113, 118, 140]. Intracellular interference by nanoparticles can inhibit replication, transcription, and protein synthesis, often through DNA interaction or ATP depletion [50, 69, 125]. Some nanoparticles disrupt bacterial enzymes and metabolic pathways, causing energy depletion and cell death [24, 139]. For biofilm prevention and eradication, particularly in persistent infections like MRSA, nanoparticles prevent surface adhesion, degrade the EPS matrix, and downregulate biofilm-associated genes [31, 47, 52, 133, 146]. Stimulus-responsive drug delivery allows nanoparticles to release therapeutic agents in response to bacterial cues such as enzymes, pH, enhancing specificity and minimizing side effects [30, 71, 74]. The release of metal ions (Ag^+ , Zn^{2+} , Cu^{2+}) further disrupts thiol-containing proteins, inhibits enzymes, and generates ROS, intensifying antibacterial activity [33, 80, 94, 98, 149]. Additionally, some nanoparticles cause localized physical damage via photothermal or electromagnetic effects, leading to protein denaturation and membrane rupture [60, 99, 136].

Toxicity assessment in included studies

Forty-five of the included 131 studies reported toxicity assessments or safety considerations at either cellular, preclinical, or in vivo levels. Most of these involved in vitro cytotoxicity assays on mammalian cell lines, while a smaller number examined hemolytic activity or animal model safety. A recurring finding was dose-dependent toxicity, where nanoparticles were biocompatible at lower concentrations but cytotoxic at higher doses [23, 28, 86, 98, 134, 140]. Metal-based nanoparticles, particularly silver and CuO, were most frequently associated with such safety concerns [28, 41, 87, 98, 121, 140], whereas polymeric and lipid-based formulations generally showed better tolerance. Despite these encouraging results, standardized protocols and long-term safety studies remain scarce.

Advantages of nanomaterial-based antimicrobial agents over conventional methods

Green-synthesized nanoparticles offer biocompatibility, lower toxicity, and environmental safety, making them a sustainable alternative to conventional antibiotics [48, 79, 112, 113]. They exhibit strong activity against MDR Gram-positive bacteria, including MRSA and *Enterococcus faecalis*, even in strains resistant to vancomycin and β -lactams [21, 48, 111, 117]. Their broad-spectrum efficacy arises from simultaneous targeting of multiple bacterial components, such as membranes, DNA, and intracellular proteins, effectively overcoming resistance mechanisms [77, 111, 117]. Studies show minimal resistance development after repeated bacterial exposure, highlighting a lower propensity for resistance compared to traditional antibiotics [120, 122, 142]. Synergistic combinations of nanoparticles with conventional antibiotics can restore sensitivity in resistant strains [48], enhance antibacterial efficacy [65], reduce MICs [57], and allow lower drug dosages, thereby minimizing toxicity [45]. Unlike standard antibiotics, which often fail against biofilms, nanoparticles, especially ROS-generating types, effectively prevent biofilm formation and disrupt preformed biofilms [79, 133, 146]. Beyond antimicrobial activity, some nanoparticles promote wound healing and tissue regeneration, such as epigallocatechin gallate-ferric complex nanoparticles and photocrosslinked chitosan/methacrylate hyaluronic acid nanoparticles [44, 99]. AuNPs and SWCNTs@mSiO₂TSD@Ag also support tissue repair while maintaining antibacterial potency [33]. Several nanoparticles additionally enhance therapeutic value through targeted drug delivery, biosensing, or imaging [48, 70, 86]. Stimuli-responsive nanoparticles release drugs in response to bacterial cues such as pH shifts, enzymes, or oxidative stress, allowing precise delivery to infection sites with minimal impact on healthy tissues [30, 52, 71, 74].

Discussion

The integration of nanomaterials into biomedical strategies has shown promise in combating AMR among Gram-positive bacteria, enhancing antimicrobial efficacy, drug delivery, and tissue regeneration. Among nanomaterials, AgNPs are widely studied for their strong antimicrobial and antibiofilm activity, with mechanisms including ROS generation, membrane disruption, ATP depletion, DNA damage, and inhibition of protein synthesis [152]. Green-synthesized and curcumin-stabilized AgNPs demonstrate superior biofilm inhibition and suppression of resistance genes in pathogens like MRSA. However, the statement simplifies the diversity of action and omits key nuances, such as nanoparticle size, shape, and surface charge, as emphasized by More et al. [152] (2023) and Dube et al. [153] (2025), that smaller, spherical AgNPs exhibit stronger activity. When combined with conventional antibiotics, AgNPs further enhance antimicrobial efficacy [154, 155]. Metal-based nanoparticles such as AuNPs, Al-ZnO, CuO, PdNPs, and iron oxide derivatives exhibit broad-spectrum antimicrobial activity and versatility in clinical scenarios. As supported by the studies of Nawaz et al. [21] (2021) and Brown et al. [156] (2012), AuNPs combined with antibiotics like ciprofloxacin and ampicillin enhance membrane disruption, inhibit metabolic processes, reduce MICs, and effectively subvert resistance mechanisms. Al-doped ZnO improves activity against *S. aureus*, as corroborated by Asif et al. [80] (2024) and Chidhambaram [157] (2019), CuO NPs support wound healing in diabetic models, as further shown by Shehabeldine et al. [158] (2025), and Cannabis sativa extracts have demonstrated their ability to mediate the green synthesis of metal nanoparticles, particularly AgNPs, which exhibit strong antibacterial effects against various human pathogens in tandem with Csakvari et al. [159] (2021), emphasizing its value for clinical safety and environmental sustainability. As shown by Fatih et al. [69] (2024), iron oxide nanoparticles, including Fe₃O₄-SiO₂ and α -Fe₂O₃ offer dual antimicrobial and magnetic properties for targeted drug delivery and biofilm penetration, while nickel ferrite nanoparticles show efficacy against polymicrobial biofilms, which was supported by the study of Ansari and Alomary [88] (2024), highlighting their broader-spectrum potential, a vital feature in immunocompromised or critical care settings [114].

Bimetallic nanoparticles (Ag-Au, Ag-Cu, Ag-Pt) provide synergistic effects, enhance antibacterial potency, broaden antimicrobial spectra, and reduce the likelihood of resistance development due to multi-target interactions. Recent research also suggests that these particles may interfere with both intracellular and extracellular bacterial processes simultaneously, thus outpacing traditional antibiotics [160, 161].

Photocatalytic nanomaterials such as TiO₂ and WO₃ also demonstrate significant antimicrobial activity. As reported by Ahmed et al. [162] (2022), these materials effectively reduce microbial load and infection risk on various surfaces, including air purifiers, hospital textiles, surgical masks, and wound dressings. Their prolonged antimicrobial action supports their utility in infection prevention and environmental sanitation. MSNs loaded with antibiotics, liposomal metal nanoparticles, and PEGylated MOFs demonstrate controlled drug release, enhanced biofilm penetration, and suppression of resistance genes. These findings align with studies by Jambhrunkar et al. [124] (2023), Ghaffar et al. [163] (2019), Pinho et al. [164] (2024), Aguilar-Colomer et al. [165] (2020), and Subramaniam et al. [166] (2019). In addition, SeNPs, particularly those functionalized with quercetin or poly-L-lysine, have exhibited potent bactericidal effects via ATP depletion and ROS generation, without inducing resistance. Polymeric carriers such as chitosan nanoparticles and PLGA-based systems have also outperformed traditional antibiotics, offering superior biofilm inhibition and targeted delivery, as demonstrated by Derakhshan-Sefidi et al. [167] (2024). Although most evidence remains *in vitro*, preclinical *in vivo* studies validate efficacy with minimal toxicity. Green-synthesized NPs using biological agents (*Azadirachta indica*, *Aloe vera*, *Crocus sativus*) demonstrate strong activity and low toxicity [168, 169], while tulsimediated ZnO NPs show no liver or kidney toxicity over 20 days [170]. However, variability in particle size and reproducibility persists [171, 172]. Photodynamic, sonodynamic, and MOF-based nanoparticles accelerate bacterial eradication and wound healing in murine models [173–175], and preliminary studies using clinical isolates suggest translational potential [176, 177]. Yet, clinical validation remains a key knowledge gap, as human trials confirming safety and efficacy are lacking [176, 178].

Clinical translation and policy pathways

Widespread implementation requires integration into national and global AMR frameworks. World Health Organization (WHO), Centres for Disease Control and Prevention, and the European Medicines Agency should include nanomedicine strategies in upcoming AMR action plans, with the 2026 WHO Global Action Plan offering a key opportunity to integrate these innovations into policy [179]. A Global Nanomedicine Regulation and Evaluation Framework, modelled after International Council for Harmonization and the International Coalition of Medicines Regulatory Authorities guidelines, could harmonize safety, efficacy, and quality standards [180–182]. Establishing good manufacturing practice (GMP)-compliant nanomedicine hubs and mobile synthesis labs will support scalable production, as demonstrated by Sri Lanka Institute of Nanotechnology and African mRNA tech hubs [183]. Pooled procurement mechanisms such as the PAHO Revolving Fund and EAC framework can enhance access and affordability [184, 185].

Translational barriers and future recommendations

Major translational barriers include the lack of standardized toxicity protocols, limited pharmacokinetic-pharmacodynamic data, and variability in nanomaterial synthesis. Although microfluidic and GMP-compliant platforms improve reproducibility, their use is still constrained by cost and infrastructure [186, 187]. Regulatory frameworks are also emerging slowly, with no universally defined approval pathways for nano-antimicrobials [188, 189]. Current research highlights the promise of nanomaterial-based antimicrobials in combating Gram-positive AMR, particularly through their ability to target biofilms and evade traditional resistance mechanisms [190, 191]. However, significant challenges remain, including the lack of standardized manufacturing processes, which leads to heterogeneity in nanoparticle synthesis, size, and functionalization, ultimately hampering reproducibility and cross-study comparisons [192, 193]. The need for scalable, cost-effective, and standardized production methods supported by international guidelines is emphasized to improve quality control and accelerate clinical translation, while also addressing economic feasibility and access in low resource settings [194, 195].

There is growing concern that bacteria may develop resistance to nanomaterials themselves, as sub-lethal exposure can induce adaptive responses such as biofilm reinforcement, efflux pump upregulation, and antioxidant defense activation [196, 197]. Long-term surveillance, nanoparticle rotation, combination therapies, and stimuli-responsive delivery systems are proposed strategies to mitigate this risk [193, 198].

Comprehensive toxicity studies, including long-term and environmental effects, are also needed under standardized protocols to ensure safety risk [198]. Translation to clinical use will also require well-designed trials with standardized endpoints that compare nanoparticle therapies directly with existing antibiotics [199]. Ultimately, coordinated efforts across scientific, medical, policy, and industrial sectors, along with the establishment of international regulatory frameworks and GMP-compliant hubs, are seen as essential for harmonizing safety and efficacy standards and ensuring global access to these advanced therapies [195].

Abbreviations

AMR: antimicrobial resistance

GMP: good manufacturing practice

MDR: multidrug-resistant

MRSA: methicillin-resistant *Staphylococcus aureus*

PLGA: poly(lactic-co-glycolic acid)

PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses

ROS: reactive oxygen species

WHO: World Health Organization

Supplementary materials

The supplementary table for this article is available at: https://www.explorationpub.com/uploads/Article/file/1008144_sup_1.pdf.

Declarations

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The authors declare that they have no conflicts of interest.

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Not applicable.

Consent to participate

Not applicable.

Consent to publication

Not applicable.

Availability of data and materials

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