

REVIEW PAPER

Antimicrobial nanoparticle-based wound dressings: from theory to clinical applications

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ABSTRACT

Chronic and infected wounds continue to represent a substantial clinical burden, particularly in the context of escalating antibiotic resistance, where conventional dressings frequently fail to provide adequate antimicrobial protection or to promote efficient tissue repair. Nanoparticles have emerged as promising antibacterial and wound-healing agents due to their distinctive physicochemical properties, including high surface area and controlled ion release. Among these, silver nanoparticles exhibit the most potent antimicrobial activity, whereas polymeric and lipid-based systems offer enhanced biocompatibility and sustained release characteristics. This review presents an updated and comparative analysis of antimicrobial nanoparticle-based wound dressings, encompassing metallic, polymeric, lipid-based, carbon-based, and hybrid nanomaterials. It examines their antibacterial mechanisms of action, fabrication strategies (including hydrogels, electrospinning, and three-dimensional printing), and clinical applicability. In addition, the review critically evaluates toxicity thresholds, biocompatibility considerations, regulatory frameworks, and translational challenges. By integrating recent evidence (2020–2024), including clinical case reports, this review bridges experimental findings with clinical practice and outlines future perspectives, such as the development of smart, stimuli-responsive, and environmentally sustainable nanoparticle systems for next-generation wound management.

Keywords: Antibacterial agents; Nanomedicine; Nanoparticles; Wound dressings; Wound healing

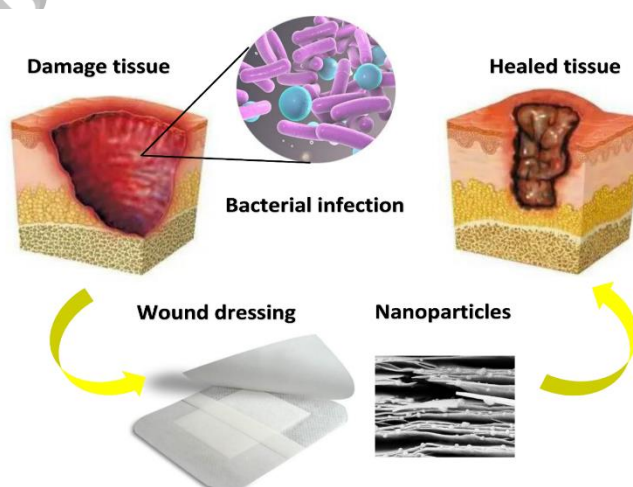
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Abbreviations

NPs: nano particles ; **TiO₂:** Titanium Dioxide ; **ZnO:** Zinc Oxide ; **CNT:** Carbon Nano Tube ; **SLN:** Solid Lipid Nano particles ; **HNTs:** Halloysite Nanotubes ; **PVA:** Polyvinyl Alcohol ; **PCL:** Polycaprolactone ; **PSI:** Poly-Succinimide ; **HH:** Hydrazine Hydrate ; **PGA:** Polygalacturonic Acid ; **EPL:** Poly-L-Lysine ; **PAHY:** Poly-Asparhydrazone ; **TEM:** Transmission Electron Microscopy ; **SEM:** Secondary Electron Microscopy ; **H₂O₂:** Hydrogen Peroxide

Graphical Abstract



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INTRODUCTION

Bacterial infection remains a major impediment to effective wound healing. Microorganisms can readily invade disrupted skin barriers or underlying tissues, leading to local or systemic infections that delay tissue repair and increase the risk of serious complications. The escalating prevalence of antibiotic-resistant strains has further intensified this challenge, necessitating the development and broader implementation of antimicrobial materials as a strategic approach for the prevention and management of wound-associated infections [1, 2]. Antibiotic resistance constitutes a critical global health concern, undermining the effectiveness of existing therapeutic regimens and contributing to prolonged illness and increased mortality. According to the World Health Organization (WHO), approximately 700,000 deaths annually are attributed to antimicrobial-resistant infections, with projections suggesting this figure could reach 10 million by 2050 if no effective interventions are implemented. Beyond its clinical impact, antimicrobial resistance also imposes substantial economic burdens on healthcare systems worldwide [3, 4].

Despite substantial advances in nanotechnology and materials science, critical knowledge gaps remain regarding the precise mechanisms of antibacterial action, optimal incorporation strategies, and long-term clinical performance of nanoparticle-based wound dressings. For instance, although silver nanoparticles (AgNPs) are extensively integrated into commercially available wound care products, issues related to controlled release kinetics and potential cytotoxic effects have not been fully resolved [5]. Likewise, the comparative effectiveness of polymeric and lipid-based nanoparticles—such as chitosan-based systems and liposomal formulations—relative to conventional wound care approaches warrants further systematic investigation. Nanoparticles, typically ranging from 1 to 100 nm in diameter, possess distinctive physicochemical characteristics, including high surface-to-volume ratios, increased surface reactivity, and the capacity to interact at molecular and cellular scales, which collectively underpin their therapeutic potential in wound management [6].

Wound healing is a complex biological process that proceeds through a series of overlapping and coordinated stages following skin injury. Initially, hemostasis occurs to prevent excessive bleeding. Arterial vessels constrict immediately after injury to reduce blood flow, leading to localized hypoxia and acidosis [7]. Shortly thereafter, the vessels dilate, and chemical mediators such as nitric oxide and

histamine are released, increasing vascular permeability and promoting the recruitment of inflammatory cells to the wound site. This phase involves three principal mechanisms: the intrinsic and extrinsic coagulation pathways, as well as platelet activation. The second stage, inflammation, primarily functions to prevent infection. Neutrophils are the first immune responders and eliminate pathogens and foreign particles through three principal mechanisms: (1) phagocytosis, (2) the release of antimicrobial substances such as lactoferrin, proteases, and cathepsins, and (3) the formation of neutrophil extracellular traps (NETs), which capture and destroy bacteria. Reactive oxygen species generated during this phase further contribute to microbial killing. After fulfilling their function, neutrophils undergo apoptosis or are cleared by macrophages.

Once hemostasis is established and the wound is cleared of pathogens, the proliferative phase begins. This phase includes angiogenesis (formation of new blood vessels), collagen deposition (reinforcement of tissue structure), granulation tissue formation, epithelialization (re-epithelialization of the wound surface), and wound contraction [8]. Finally, the remodeling phase restores tissue integrity and may persist for up to two years. During this stage, collagen and other extracellular matrix components are progressively reorganized, with type III collagen gradually replaced by type I collagen. Although the wound does not fully recover its original tensile strength, scar maturation is characterized by reduced vascularity and a gradual color transition from red to gray [9]. Given the complexity and interdependence of these stages, strategies that can simultaneously prevent infection and actively promote tissue repair are essential. Nanoparticle-based wound dressings have emerged as promising approaches to address these challenges by exerting antibacterial effects, modulating inflammatory responses, and supporting tissue regeneration. This review aims to provide a comprehensive overview of recent advances in nanoparticle-based antibacterial wound dressings, including the types of nanoparticles utilized, their mechanisms of action, methods of incorporation into wound care systems, and their clinical applications.

Types of wound dressings: Classification and applications in wound management

Although the body typically initiates self-repair following injury, this capacity can be compromised by conditions such as infection, diabetes, and other systemic factors. Effective wound management

requires a precise evaluation of the wound type, the extent and severity of tissue damage, wound color and morphology, the level of exudate, and anatomical location. To optimize wound healing outcomes, various types of wound dressings and bandages may be employed. An ideal wound dressing should minimize the risk of infection, maintain a moist wound environment, and prevent excessive dehydration. It should provide resistance to external mechanical stress, protect the wound from secondary injury, and facilitate cellular migration. Additionally, it should allow adequate gas exchange while remaining impermeable to

bacteria and other foreign contaminants. The dressing should possess non-adherent properties to enable atraumatic removal without causing pain or discomfort to the patient. Furthermore, it should be non-allergenic, non-toxic, and cost-effective [10]. To achieve these characteristics and enhance the healing process, wound dressings are manufactured in various forms according to material composition, mechanism of action, and intended duration of use. Table 1 provides a general classification of traditional and modern wound dressings.

Table 1. Types of wound dressings: composition, clinical applications, and performance characteristics

Dressing Type	Composition/Materials	Advantages	Disadvantages	Application	Ref.
Traditional	Cotton, rayon, polyester, natural or synthetic bandages	Inexpensive, widely available, suitable for many wounds	Drying out, painful removal, requires frequent changes	Primary or secondary dressing	[12]
Hydrocolloid	Two-layer structure: inner colloid layer (carboxymethyl cellulose, gelatin, pectin, elastomers, adhesives), outer waterproof layer	Creates a moist environment, promotes collagen synthesis, fibroblast proliferation, and epithelialization; painless removal; impermeable to bacteria	Opaque (requires removal for wound inspection), leaves gel residue that may be mistaken for infection, unpleasant odor after removal, may reduce oxygen to wound causing inflammation	removal, may reduce oxygen to wound causing inflammation, Suitable for wounds with low to moderate exudate, such as pressure ulcers and burns; not suitable for highly exudative or neuropathic wounds	[13]
Foam (Sponge) Dressings	Porous polyurethane or silicone, synthesized in sponge-like form	High absorption capacity, absorption rate controlled by pore size and thickness, maintain moist balance, can be produced in different sizes and thicknesses	Limited transparency (wound inspection requires removal), not ideal for wounds with low exudate	Suitable for highly exuding wounds, best used in early inflammatory phase, postoperative wounds, superficial wounds, and as fillers in cavity wounds; used as primary dressings without the need for secondary ones	[14]
Hydrogel Dressings	Three-dimensional networks of hydrophilic polymers (e.g., gelatin, polysaccharides), up to 95% water content	High water retention, elastic and flexible texture, non-irritating, reduce inflammatory reactions, cooling effect relieves pain	Not suitable for highly exuding or infected wounds, may require secondary dressing	Suitable for low to moderately exuding wounds; available as gels, thin films, or sheets; promote faster healing by maintaining a moist environment	[15]
Alginate Dressings	Natural polysaccharide from red seaweed; linear chains of uronic, mannuronic, and glucuronic acids; form calcium alginate in presence of Ca^{2+}	High absorption capacity, gel formation upon Ca^{2+}/Na^{+} ion exchange, maintains moist environment, aids hemostasis, easy removal, supports fibroblast proliferation and keratinocyte migration	Not recommended for burn wounds; may require secondary dressing; less effective for dry wounds	Suitable for moderately exuding wounds; useful in wound healing and tissue engineering; also act as hemostatic dressings	[15]

Dressing Type	Composition/Materials	Advantages	Disadvantages	Application	Ref.
Film Dressings	Thin, transparent polyurethane or copolyester with adhesive and porous structure	Allows gas exchange (O ₂ , CO ₂ , water vapor), impermeable to bacteria, transparent for wound observation, waterproof, flexible	Not suitable for heavily exuding wounds; may cause maceration if exudate accumulates; limited absorption capacity	Suitable for superficial wounds with low exudate; can be used as secondary dressing when waterproof coverage is required	[16]
Smart dressing	Sensors (biological/physical), Antibacterial agents (antibiotics, nanoparticles), Stimuli-responsive elements, Base materials (hydrogels, absorptive materials), Communication system (wireless)	Real-time wound monitoring, Controlled drug release, Provides reports to physicians	Still experimental, High cost, Requires advanced technology	Chronic wounds such as diabetic wounds	[17]
Bioactive wound dressings	Natural or synthetic biomaterials (collagen, hyaluronic acid, chitosan, sometimes antimicrobial agents)	Better performance than conventional dressings (hydrogels, gauze)	Usually expensive	Promote wound healing	[16]
Antimicrobial Dressings	Antibiotics (tetracycline, ciprofloxacin, cephalixin, gentamicin, etc.), natural agents (honey, essential oils, chitosan), or nanoparticles (Ag, Au, Cu, Maxin, etc.)	Can be one of the common dressing types while providing antibacterial and antibiofilm properties; enhanced wound healing	Can be expensive; potential for antibiotic resistance	Wound healing, especially infected wounds or wounds prone to biofilm formation	[15]

Types of Nanoparticles Applied to Dressings for Wounds

As a result of significant advances in nanoscience and nanotechnology, increasing attention has been directed toward nanoparticles as key components in the development of advanced wound dressings. These nanoparticles possess a broad range of applications in wound

management and can substantially enhance the performance of wound dressings owing to their unique physicochemical properties (Figure 1) [11]. This section reviews the various types of nanoparticles employed in wound dressings and examines their advantages, characteristics, and applications.

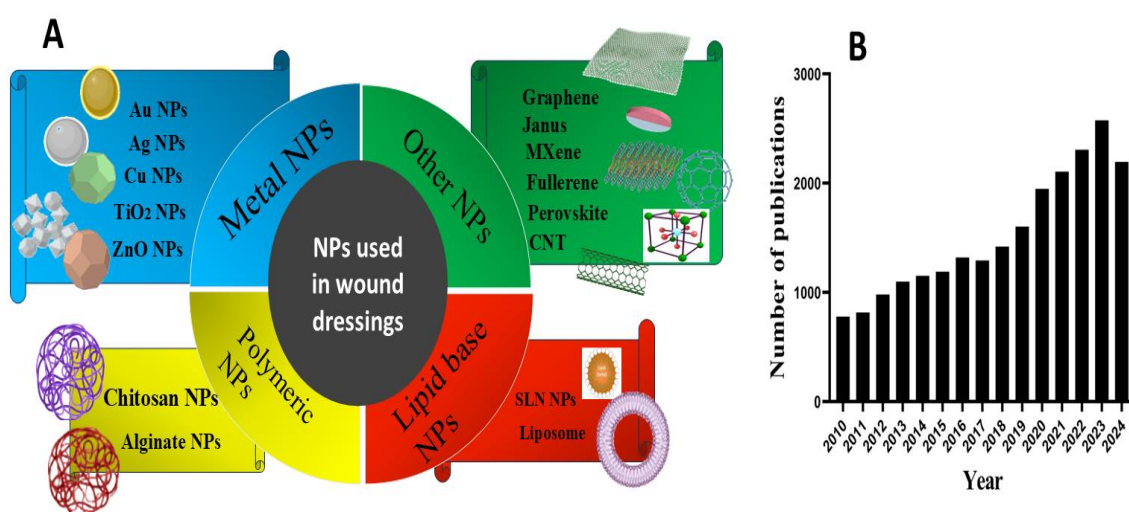


Fig. 1. (A) Types of nanoparticles used in wound dressing. (B) The number of published articles based on the keyword "wound dressing" in the Pub Med database. (create with power point).

Metal nanoparticles

Silver nanoparticles (AgNPs)

Silver nanoparticles (AgNPs) are among the most extensively studied metallic nanomaterials in wound care due to their potent and broad-spectrum antibacterial activity. AgNPs exert antimicrobial effects through multiple mechanisms, including interactions with bacterial thiol groups, disruption of cell membranes, increased membrane permeability, and the generation of reactive oxygen species (ROS). They may also bind to bacterial DNA, thereby interfering with replication processes and contributing to bacterial cell death [12]. Recent studies (2020–2024) highlight the growing integration of AgNPs into advanced wound dressings. Konop et al. (2020) successfully incorporated AgNPs into keratin-based dressings, achieving significant inhibition of *S. aureus* and *E. coli* [13]. Liu et al. (2022) developed a chitosan–curcumin–AgNP composite that exhibited synergistic antibacterial and wound-healing effects, enhancing re-epithelialization in vivo models [14]. Bîrcă et al. (2023) employed a microfluidic

approach to fabricate alginate-based AgNP dressings that effectively suppressed biofilm formation while maintaining keratinocyte biocompatibility [15]. Zhang et al. (2024) fabricated AgNP-loaded poly (asparahydrazide) (PAHY) hydrogel dressings via in situ nanoparticle formation during electrospinning. The resulting hydrogels contained uniformly distributed AgNPs (10–70 nm), demonstrated strong antibacterial activity (99.99% inhibition against *S. aureus* and *E. coli*), and exhibited excellent biocompatibility in human dermal fibroblasts. In vivo studies confirmed enhanced collagen deposition and accelerated wound closure compared with standard gauze dressings (Figure 2) [16]. Similarly, Vijayakumar et al. (2024) synthesized AgNPs using a green synthesis approach with fungal extracts, producing approximately 50 nm nanoparticles with potent antibacterial activity against *S. aureus* and *E. coli*. When incorporated into PVA/PGA nanofibers, these AgNPs promoted wound closure in scratch assays and demonstrated notable antimicrobial performance [17].

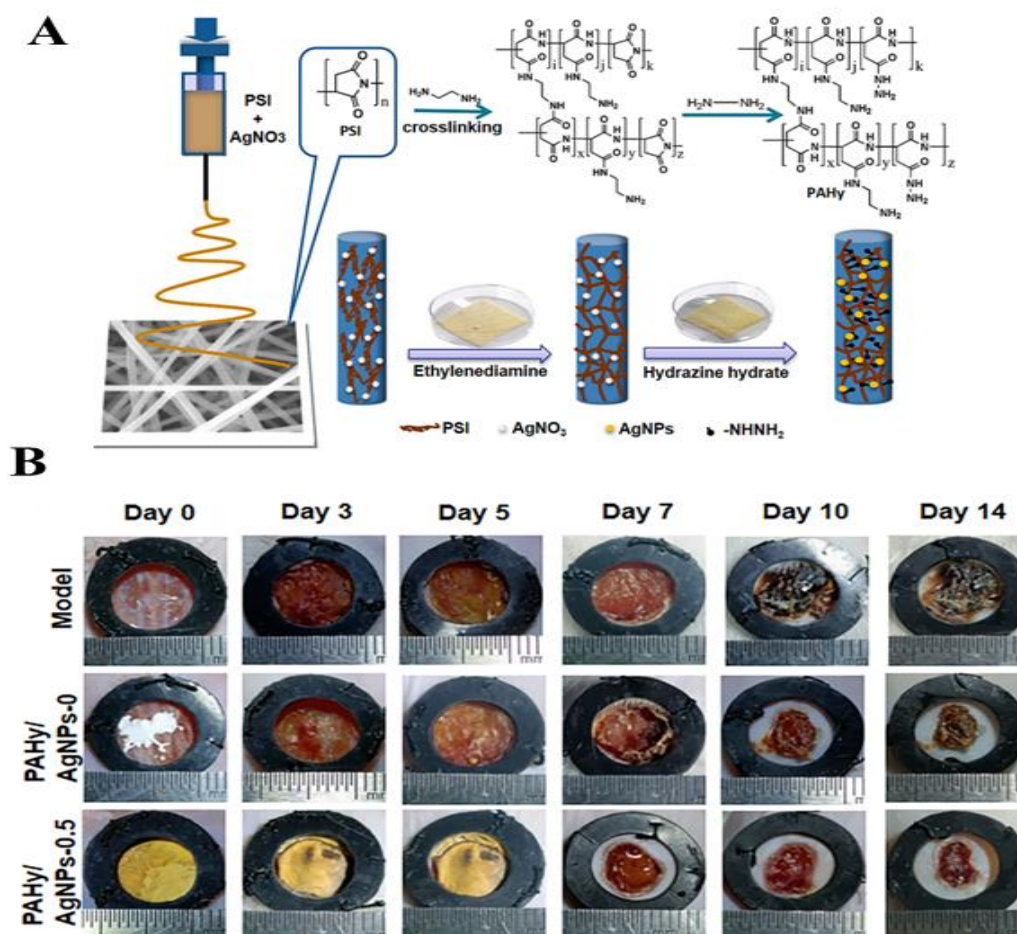


Fig. 2. The process of creating PAHY/AgNPs nanofiber hydrogel wound dressings using a mix of electrospinning and post-processing procedures is schematically represented. (A). (B) Digital photos of the wound sites taken on days 0, 3, 5, 7, 10, and 14 for three distinct groups wearing PAHY/AgNPs wound dressings and the control group. Ref [1], used with permission.

In summary, AgNPs remain among the most effective metallic nanomaterials for wound dressings owing to their potent antimicrobial mechanisms, biofilm-disrupting capacity, and compatibility with hydrogels, nanofibers, and microfluidic technologies. However, their long-term cytotoxicity and silver ion release profiles require careful optimization.

Gold nanoparticles (AuNPs)

Gold nanoparticles (AuNPs) have attracted increasing attention in wound care owing to their excellent chemical stability, biocompatibility, and anti-inflammatory properties. Although AuNPs inherently exhibit weaker antibacterial activity than silver or zinc oxide nanoparticles, their biological performance can be markedly enhanced through green synthesis approaches or surface functionalization. Functionalized AuNPs have been shown to disrupt bacterial membranes, induce reactive oxygen species (ROS) production, and interfere with microbial metabolic pathways. Recent studies have incorporated AuNPs into multifunctional wound dressings to improve antimicrobial efficacy and promote tissue regeneration. For instance, AuNP–chitosan and AuNP–silver hybrid systems have demonstrated synergistic antibacterial activity and accelerated wound closure in preclinical models. In addition, AuNPs functionalized with gelatin or 2-mercapto-1-methylimidazole exhibited strong activity against methicillin-resistant *Staphylococcus aureus* (MRSA), underscoring their potential for the treatment of drug-resistant infections. AuNPs combined with natural compounds such as capsaicin have also shown enhanced anti-inflammatory effects and improved epithelial regeneration in vivo [18]. In 2023, Zhao et al. incorporated AuNPs into halloysite nanotube (HNT)-based hydrogels, enabling photothermal antibacterial therapy. The synthesized AuNPs (5–10 nm) effectively eradicated *S. aureus* and *E. coli* upon infrared irradiation and achieved nearly 80% wound closure by day 7 in infected murine models [19]. Similarly, in 2023, Liu et al. developed hybrid Fe₃O₄–MOF–Au nanozymes with pronounced peroxidase-like catalytic activity. These nanozymes generated hydroxyl radicals (•OH) from H₂O₂, resulting in potent antibacterial effects and more than 80% wound closure within three days in *S. aureus*-infected models, while maintaining excellent cytocompatibility [20]. In summary, AuNP-based systems offer promising multifunctional capabilities, including anti-inflammatory activity, ROS-mediated antibacterial effects, and compatibility with photothermal and

catalytic therapies. Although their intrinsic antibacterial potency is generally lower than that of AgNPs or ZnO nanoparticles, AuNPs demonstrate particular advantages in promoting tissue regeneration and facilitating advanced stimuli-responsive wound dressings.

Copper nanoparticles (CuNPs)

Copper nanoparticles (CuNPs) have emerged as potent antimicrobial agents with considerable potential in wound management. Historically, copper has been recognized as an effective disinfectant and, compared with noble metals such as silver, provides strong antibacterial activity at a lower cost [35,36]. Copper is also an essential trace element involved in more than 30 biological proteins and enzymes, including lysyl oxidase and superoxide dismutase, which play critical roles in tissue repair and oxidative homeostasis. CuNPs exert pronounced antibacterial effects by disrupting bacterial membranes, generating reactive oxygen species (ROS), and altering metal ion homeostasis, thereby inhibiting the growth of both Gram-positive and Gram-negative bacteria, including drug-resistant strains such as *S. aureus* and *P. aeruginosa* [21]. Enhanced nitric oxide release has also been linked to their improved antibacterial efficacy. Copper-containing surfaces have demonstrated promise in reducing hospital-acquired infections by effectively suppressing pathogens such as *Acinetobacter* spp. and *S. aureus*. Beyond their antimicrobial activity, CuNPs actively contribute to wound healing by promoting collagen and fibrinogen expression, stimulating fibroblast proliferation, and enhancing angiogenesis [22]. Importantly, several studies have reported that copper-based dressings exhibit lower cytotoxicity than silver-based formulations, thereby rendering them attractive candidates for clinical application [23]. Polymeric wound dressings incorporating copper oxide nanoparticles have demonstrated potent antibacterial activity with minimal cytotoxic effects on human fibroblasts [24]. Dual-layer wound dressings incorporating CuNPs, polyvinyl alcohol (PVA), and chitosan have demonstrated accelerated wound closure in vivo [25]. Similarly, electrospun polyurethane nanofibers embedded with carbon-coated CuNPs enhanced tissue regeneration while maintaining strong antibacterial activity [21]. Recent advances have further reinforced the therapeutic potential of CuNP-based dressings. Ajalli et al. (2023) fabricated a composite nanofibrous dressing composed of graphene oxide, CuNPs, and PVA, achieving a remarkable 92% wound closure within 14 days in animal models [26]. Johari et al. (2024) reported

that chitosan–alginate hydrogels enriched with CuNPs effectively inhibited *E. coli* and *S. aureus* growth [27]. In another study, Zhou et al. (2023) developed polydopamine-coated copper–TMB antibacterial nanoparticles (Cu-TMB@PDA), which promoted fibroblast proliferation, reduced hemolysis, disrupted bacterial membranes, and significantly accelerated wound healing by day 7 [28]. Addressing chronic diabetic wounds, Zhao et al. (2023) synthesized copper-based nanozymes (Cu-CPNs) that mimic the enzymatic activities of superoxide dismutase (SOD) and glutathione peroxidase (GPx). When combined with poly-L-lysine, the Cu-CPNs@EPL system exhibited enhanced antibacterial and antioxidant effects [45]. In MRSA-infected diabetic murine models, these nanozymes achieved nearly complete wound healing within 12 days, underscoring their substantial therapeutic potential [29].

Titanium dioxide nanoparticles (TiO₂ NPs)

Titanium dioxide (TiO₂) nanoparticles have attracted considerable attention in biomedical applications owing to their chemical stability, low toxicity, cost-effectiveness, and FDA-approved status for use in pharmaceuticals, cosmetics, and food products [30]. TiO₂ exhibits notable photocatalytic properties, generating reactive oxygen species (ROS) under UV or visible light irradiation, which damage bacterial membranes and inactivate both Gram-positive and Gram-negative bacteria, including *E. coli* and *S. aureus*

[31]. Metal doping enhances visible light absorption, thereby reducing reliance on UV irradiation and minimizing potential tissue damage. The incorporation of TiO₂ nanoparticles into polymeric wound dressings and hydrogels has demonstrated significant antimicrobial and wound-healing benefits. PMMA–TiO₂ nanocomposites inhibited *Lactobacillus acidophilus*, *S. mutans*, and *C. albicans*, while TiO₂–gellan gum biofilm dressings suppressed *S. aureus* and *E. coli* and promoted complete wound closure within 14 days. Chitosan–polypropylene glycol hydrogels containing TiO₂ exhibited strong antibacterial activity [32], and 3D-printed hydrogel dressings incorporating TiO₂ and silver nanoparticles effectively inhibited *P. aeruginosa* and *S. aureus* [33]. Recent studies have further explored TiO₂ in combination with natural polymers and bioactive agents. Gelatin–polycaprolactone–silk fibroin–TiO₂ scaffolds enhanced infection control and tissue regeneration, while PVA–sodium alginate films containing 3 wt% TiO₂ nanoparticles improved antibacterial activity against Gram-positive bacteria and supported human dermal fibroblast viability. Multilayer PAN nanofiber dressings functionalized with TiO₂ and gelatin promoted fibroblast attachment and proliferation and inhibited a broad spectrum of bacteria, including *Klebsiella pneumoniae*, *S. aureus*, and *E. coli*, demonstrating both biocompatibility and antimicrobial efficacy (Figure 3) [34].

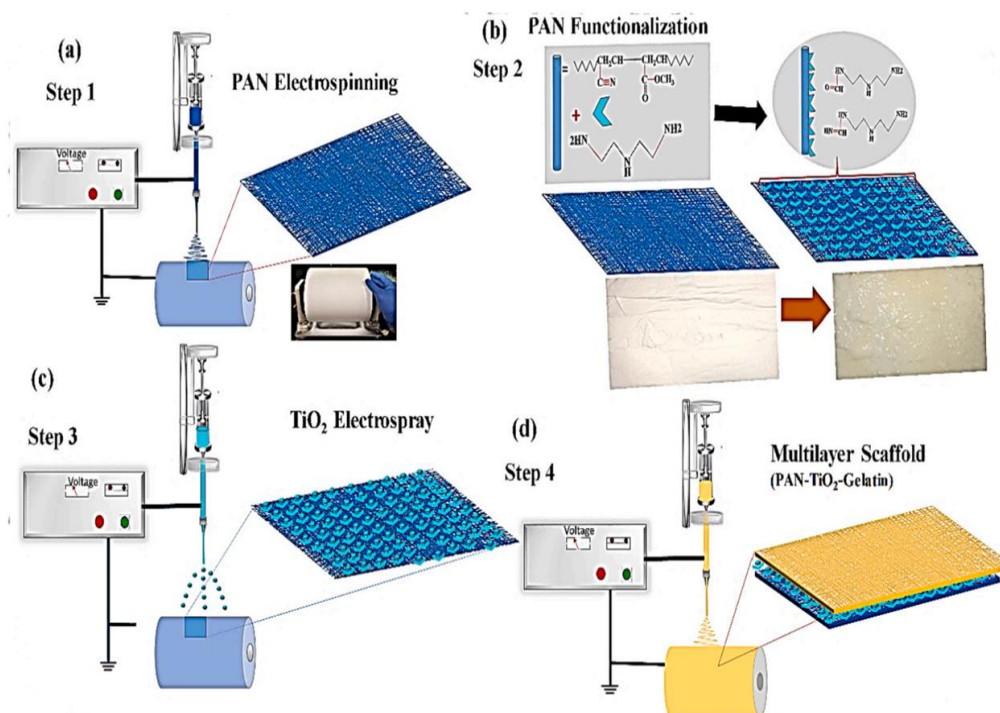


Fig. 3. (A) Schematic of the step-by-step synthesis of multi-layered nanofibrous wound dressings. From ref [2] with permission.

Overall, these findings underscore TiO₂ nanoparticles as promising candidates for next-generation antimicrobial wound dressings, combining photocatalytic antibacterial activity with tissue compatibility and minimal cytotoxicity. Nevertheless, further optimization is required to achieve comprehensive broad-spectrum pathogen control.

Zinc oxide nanoparticles (ZnO NPs)

Zinc oxide nanoparticles (ZnO NPs) are widely recognized for their potent antibacterial, antioxidant, and wound-healing properties. Zinc plays a critical biological role as a structural component of zinc-finger proteins and numerous enzymes essential for cellular function [35]. ZnO NPs exhibit strong antimicrobial activity against both Gram-positive and Gram-negative bacteria owing to their ability to generate reactive oxygen species (ROS), disrupt bacterial membranes, and inhibit biofilm formation, particularly in pathogens such as *S. aureus* and *P. aeruginosa*. Their antibacterial effects can be further enhanced under UV irradiation, and rod-shaped ZnO NPs have demonstrated superior antimicrobial activity compared with other morphologies [36]. ZnO NPs have been extensively incorporated into advanced wound dressing systems due to their biocompatibility and multifunctional properties. Aleetus et al. (2020) developed 3D-printed sodium alginate scaffolds containing ZnO NPs, which inhibited *S. epidermidis* without inducing cytotoxicity in fibroblasts [37]. Mosallanezhad et al. (2022) fabricated polycaprolactone–chitosan nanofibers enriched with ZnO NPs and curcumin, demonstrating strong antibacterial activity against *E. coli* and *S. aureus* [38]. In another study, Khorasani et al. (2021) incorporated heparinized ZnO NPs into PVA–chitosan hydrogels, accelerating wound closure in murine models [39]. Further developments include composite dressings composed of chitosan, glycogen, and ZnO NPs derived from cotton–polyester fibers, which effectively inhibited *P. aeruginosa* and *S. aureus* and enhanced wound healing in vivo [40]. Homaeigohar et al. (2023) introduced ZnO-loaded polyacrylonitrile (PAN) nanofiber coatings cross-linked with L-carnosine. These modified nanocoatings promoted fibroblast and endothelial cell proliferation, improved cell adhesion through optimized surface chemistry, and exhibited stronger antibacterial activity than pure PAN fibers.

L-carnosine–functionalized ZnO NPs also supported cellular rejuvenation by maintaining telomere stability and enhancing F-actin organization [41]. Overall, ZnO nanoparticles demonstrate a robust combination of antibacterial efficacy, antioxidant activity, and wound-repair benefits, positioning them as promising candidates for next-generation wound dressing technologies.

In the following section, the comparative profiles of the five metal-based nanoparticles (Ag, Au, Cu, ZnO, and TiO₂) are summarized in Figure 4. These data reflect the intrinsic properties of the nanoparticles themselves but provide insight into their anticipated antibacterial and biological behavior when incorporated into wound dressings. Among these nanomaterials, Ag exhibits the most potent antibacterial activity. Cu and ZnO demonstrate moderate antibacterial effects, whereas Au shows comparatively lower antibacterial activity but superior biocompatibility. All five nanoparticles share common antibacterial mechanisms, including ROS generation, disruption of bacterial membranes, and DNA damage. TiO₂ additionally displays photoactive properties, with its antibacterial activity enhanced under light irradiation. These distinctions underscore the importance of appropriate nanoparticle selection for optimizing wound dressing performance.

Polymeric nanoparticles: Biocompatibility, drug delivery capabilities, and applications in wound dressings

Chitosan nanoparticles (Chitosan NPs)

Chitosan is a cationic biopolymer derived from chitin and is widely recognized for its biocompatibility, biodegradability, and intrinsic antibacterial properties. Although insoluble in water, it dissolves in acidic media and exhibits pronounced mucoadhesive behavior, making it suitable for drug delivery, gene transport, and various biomedical applications. Chitosan nanoparticles (CS-NPs) further enhance these inherent properties, demonstrating notable antibacterial, anti-inflammatory, and even anticancer activities. Their primary antibacterial mechanism involves electrostatic interactions with negatively charged bacterial membranes, leading to membrane disruption and subsequent cell death. These effects can be synergistically enhanced through the incorporation of metal ions such as zinc or silver, as well as bioactive plant extracts, including cinnamon or cardamom.

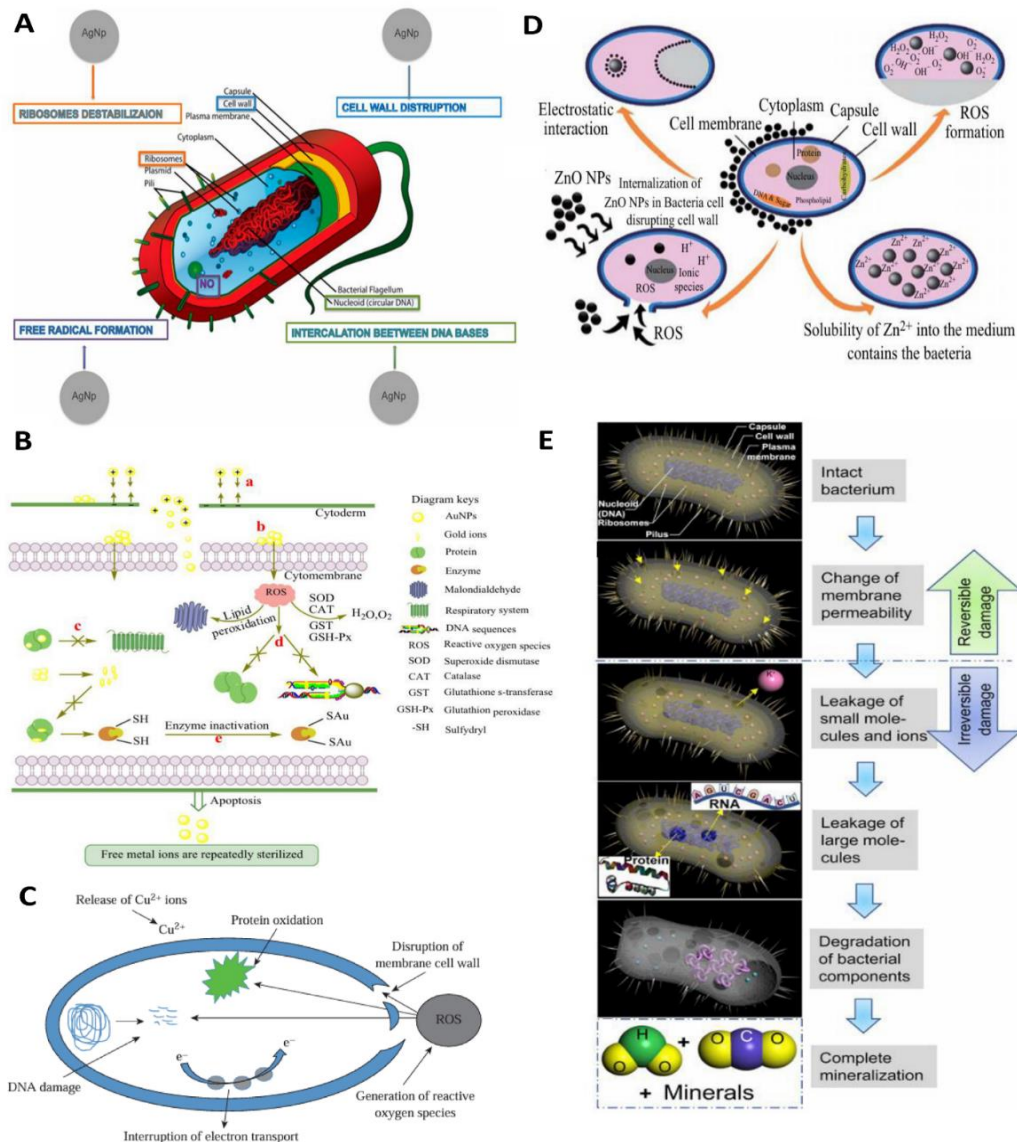


Fig. 4. Comparative responses of five metal-based nanoparticles: (A) AgNP [3]. (B) AuNP [4]. (C) CuNP [5]. (D) ZnO NP [6] and (E) TiO_2 NP [7]. Images reproduced with permission

Recent studies have highlighted the broad versatility of CS-NPs in wound care applications. Fahimirad et al. (2021) incorporated curcumin-loaded chitosan nanoparticles into polycaprolactone dressings, achieving potent antibacterial activity against methicillin-resistant *S. aureus* and significant acceleration of wound healing in vivo [47]. Similarly, Zhang et al. (2021) designed dual-layer hydrogel dressings containing metal-organic frameworks (MOFs) and silver-loaded CS-NPs, which effectively inhibited *S. aureus* and *E. coli*, promoted hemostasis, and enhanced tissue regeneration in animal models [48]. In 2024, Shunlai Shang et al. developed hydrogel wound dressings incorporating chitosan nanoparticles loaded with exosomes (Figure 5). These dressings demonstrated over 90% suppression of *E. coli* and *S. aureus* and stimulated angiogenesis when

combined with bioactive glass and TiO_2 nanoparticles. These treatments markedly accelerated the healing of burn and diabetic lesions in murine models [49]. Furthermore, El Naggar et al. (2023) reported strong antibiofilm activity from CS-NPs synthesized using *Lavandula angustifolia* extract, resulting in more than 90% disruption of *P. aeruginosa* biofilms and observable morphological damage under SEM analysis [50].

Collectively, these studies demonstrate that chitosan nanoparticles provide a highly biocompatible and multifunctional platform for wound dressings, combining potent antibacterial activity, enhanced biofilm disruption, and significant regenerative potential. Their tunability through metal incorporation, natural extracts, or bioactive cargo further expands their applicability as next-generation wound healing materials.

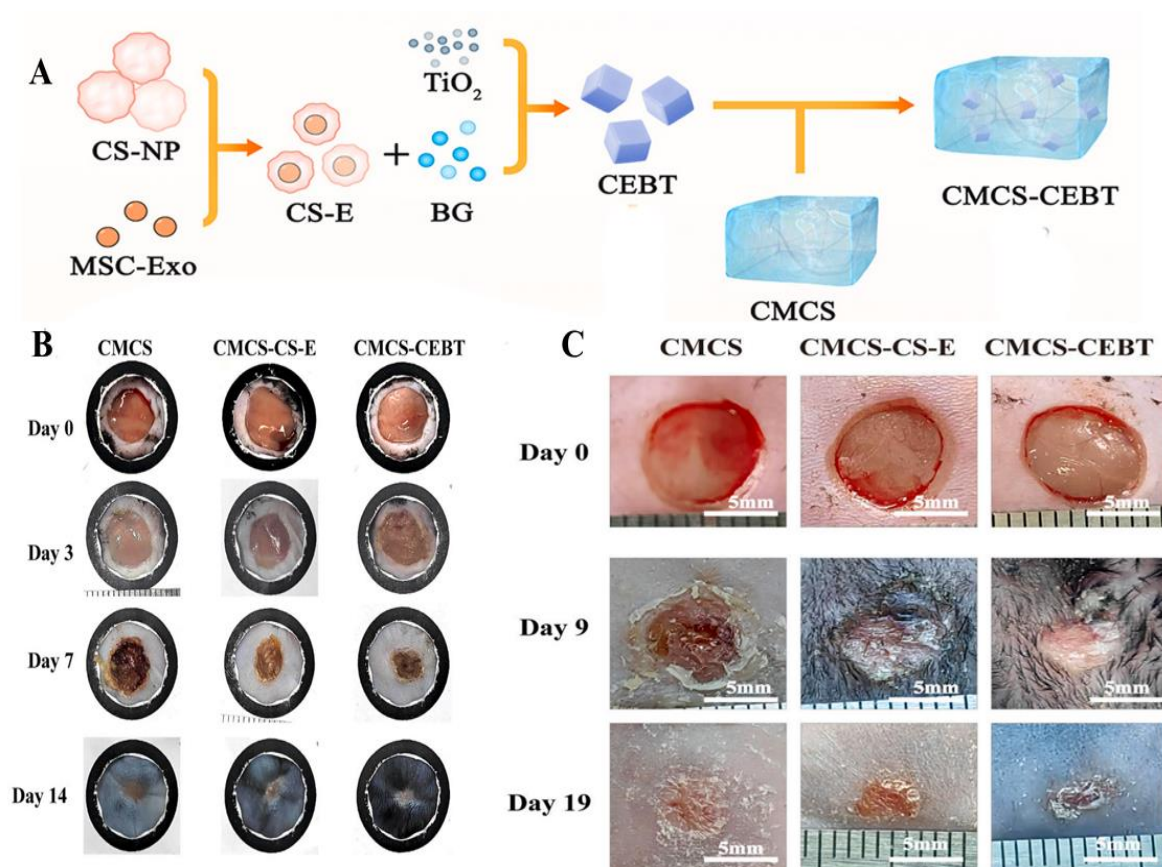


Fig. 5. (A) Schematic of the synthesis of hydrogel dressings containing chitosan nanoparticles loaded with exosomes derived from mesenchymal stem cells. (B) Images of treated diabetic wounds after 14 days. (C) Images of treated burn wounds after 19 days. From ref [8] with permission.

Alginate nanoparticles (Alginate NPs)

Alginate is an anionic polysaccharide composed of linear mannuronic (M) and guluronic (G) acid residues, primarily extracted from brown seaweeds such as *Laminaria digitata* and *Laminaria japonica*. It is water-soluble but remains insoluble in alcohol and most organic solvents. The therapeutic application of alginate dates back to the 1940s, as first documented by Major George Blein, and since its introduction as an encapsulation material in 1980, it has attracted broad interest across biomedical and industrial fields. Due to its mucilaginous characteristics and strong mucoadhesive properties—often considered superior to those of polymers such as chitosan—alginate is widely employed in gastrointestinal drug delivery, tissue engineering, and wound repair applications [51].

Alginate's biocompatibility, cost-effectiveness, ease of chemical modification, and strong ion-mediated gelation capacity render it a versatile biomaterial. Recent studies have also highlighted its potential for antibacterial applications. Alginate hydrogels, which structurally resemble the natural extracellular matrix, can be engineered with

tunable physical and biochemical properties, making them suitable for drug delivery, cell transplantation, regenerative medicine, and wound healing. In wound dressings, alginate provides a moist healing environment capable of absorbing substantial amounts of wound exudate, thereby reducing infection risk and promoting accelerated tissue regeneration. Upon contact with sodium ions present in wound fluid, alginate fibers are converted into soluble sodium alginate, forming a protective gel layer at the wound surface. The absorption capacity and mechanical properties of alginate-based dressings depend on several factors, including the M/G ratio, fiber composition, and ionic content—where a higher mannuronic acid content typically increases absorbency despite slightly reduced fiber strength. Recent research has further explored alginate nanoparticles as advanced antimicrobial systems. For example, alginate nanoparticles encapsulating meta-bromothiolactone were shown in 2022 to significantly inhibit *Pseudomonas aeruginosa* growth in vitro, demonstrating alginate's potential as a nano-enabled antibacterial platform [52].

Overall, alginate-based materials—whether in the form of hydrogels, fibers, or nanoparticles—provide a biocompatible, highly absorbent, and customizable platform for wound dressings, with growing evidence supporting their antibacterial and therapeutic potential.

Lipid-based nanoparticles: Encapsulation efficiency, antibacterial properties, and clinical relevance in wound healing

Liposomes

Liposomes, first introduced in 1965 by British hematologist Alec Bangham in Cambridge, are spherical vesicles composed of one or more phospholipid bilayers, marking the beginning of their development as advanced drug delivery systems [53, 54]. Owing to their biocompatibility, biodegradability, straightforward fabrication, high drug-loading capacity, and ability to provide controlled and sustained release, liposomes have become widely employed carriers for antimicrobial and wound-healing applications. Significant advances in recent years have further demonstrated the therapeutic potential of liposomal formulations in wound management. In 2020, Aytekin et al. developed a topical liposomal system incorporating propolis, a natural bee-derived antimicrobial agent. This formulation exhibited potent antibacterial and antioxidant activity, effectively scavenging free radicals and inhibiting the growth of bacterial and fungal pathogens commonly associated with wound sites [55]. In 2021, Ahani et al. engineered a sheep wool-based wound dressing containing polyhexamethylene biguanide (PHMB) encapsulated within cationic nanoliposomes. The liposomal system disrupted bacterial membranes and induced cell death through controlled PHMB release, resulting in potent antibacterial activity [56]. Further innovations were reported in 2023 when Pandey et al. introduced a liposomal Carbopol hydrogel for the treatment of diabetic foot ulcers. Their *in vivo* studies demonstrated significantly accelerated wound closure, enhanced collagen deposition, improved epithelialization by day nine, and increased glycosaminoglycan levels, along with reduced blood glucose concentrations—highlighting the formulation's dual therapeutic and metabolic benefits [57]. To enhance curcumin's limited solubility and improve its antimicrobial activity, Poornima et al. (2024) developed curcumin-loaded liposomes that exhibited sustained drug release and significantly enhanced antibacterial activity against *S. aureus* and *E. coli* *in vitro* [58]. In the same year, Schulte-Werning et al. developed environmentally friendly wound dressings using a green electrospinning approach with

polyethylene oxide (PEO) and pectin. Liposomes loaded with chloramphenicol were embedded within the fibers, achieving sustained antibiotic release, excellent biocompatibility, and potent antibacterial activity against *E. coli* and *S. aureus*, compared with non-liposomal control fibers [59]. Collectively, recent studies underscore liposomes as highly effective and versatile nanocarriers for wound dressings, offering controlled drug release, favorable biocompatibility, and potent antimicrobial activity, thereby positioning them as promising platforms for advanced wound care.

Solid Lipid Nanoparticles (SLN)

Solid lipid nanoparticles (SLNs), first introduced in 1991, have emerged as promising alternatives to traditional colloidal drug carriers such as liposomes and emulsions. Their advantages—including low toxicity, uniform particle distribution, nanoscale dimensions, high drug-loading capacity, and excellent biocompatibility—have driven their widespread application in biomedical fields. Composed of solid lipid cores dispersed within an aqueous phase and stabilized by surfactants, SLNs can efficiently encapsulate hydrophilic, lipophilic, and even large biomolecules, making them suitable candidates for advanced wound dressings and antimicrobial delivery systems [60–62]. SLN-based wound treatments have demonstrated significant antibacterial activity across various formulations. For instance, sponge dressings incorporating SLNs exhibited strong inhibitory effects against common wound pathogens, including *P. aeruginosa*, *S. aureus*, *S. pyogenes*, and *E. coli*. Nanofibers embedded with SLNs and plant-derived essential oils further enhanced antibacterial efficacy, achieving approximately 90% inhibition against *S. aureus* and 60% against *P. aeruginosa*, thereby outperforming conventional formulations. Additionally, gels containing SLNs have been reported to suppress infections caused by *S. aureus* and *E. coli* while promoting wound healing without inducing inflammatory responses [63, 64]. Recent advances have highlighted the versatility of SLNs as delivery vehicles for next-generation antimicrobials. In 2023, Aoibhín Ryan et al. developed SLNs loaded with lactocin 3147, a potent bacteriocin produced by *Lactococcus lactis*. The formulation, prepared using a lipid–surfactant–co-surfactant matrix followed by incorporation of a lactocin solution, exhibited strong inhibitory activity against methicillin-resistant *S. aureus* (MRSA), even at low concentrations. The study employed an Ultrez 10–based gel to compare free lactocin with SLN-encapsulated lactocin. Both formulations significantly reduced bacterial growth; however, the SLN-loaded system achieved superior

sustained release and more pronounced antibacterial activity. In an ex vivo porcine skin infection model challenged with fluorescent *S. aureus*, SLN formulations resulted in a marked reduction in bacterial bioluminescence, confirming their potent anti-MRSA efficacy [65].

Overall, SLNs represent a highly effective, biocompatible, and versatile platform for antimicrobial delivery in wound dressings, offering controlled drug release, enhanced physicochemical stability, and potent antibacterial activity against drug-resistant pathogens.

Other nanoparticles (e.g., Janus, MXene, carbon-based): Multifunctional properties and emerging applications in wound dressings.

Carbon-based nanoparticles

Carbon-based nanomaterials—particularly carbon nanotubes (CNTs), fullerenes, and graphene—represent a major class of advanced antibacterial platforms owing to their unique physicochemical properties, high surface reactivity, and strong interactions with biological systems. Among these, CNTs are among the most extensively investigated nanocarbon structures. First described by Iijima (1991), CNTs consist of cylindrical graphene sheets and exist in single-walled (SWCNTs) and multi-walled (MWCNTs) forms. Their exceptional mechanical strength, electrical conductivity, and ability to interact with biomolecules such as DNA and enzymes have facilitated their application in antimicrobial and wound-healing technologies. Several studies have demonstrated that CNT-based composites—particularly those incorporating MWCNTs with silver or polyaniline—effectively inhibit both *S. aureus* and *E. coli*, underscoring their potent antibacterial potential [66, 67]. Recent advances include the 2024 study by O. Zeynep Guner Yilmaz et al., who synthesized SWCNTs via chemical vapor deposition (CVD) and functionalized them with iron oxide nanoparticles to produce magnetic SWCNTs. When incorporated into hydrogels, these nanocomposites enabled controlled drug release and exhibited no detectable cytotoxicity, suggesting substantial promise for wound-healing applications [68].

Fullerenes represent another major class of nanocarbon materials. Since their discovery by Smalley's group in 1985, fullerene molecules—particularly C_{60} —have attracted considerable attention owing to their unique cage-like geometry and capacity to generate reactive oxygen species (ROS). Their antibacterial activity is primarily attributed to lipid peroxidation and disruption of bacterial membranes [69]. In 2023, Xuan Chen et al. functionalized C_{60} fullerenes with polydopamine (PDA) to enhance solubility and biocompatibility,

forming C_{60} &PDA nanocomposites. These nanocomposites were incorporated into hydrogels that exhibited strong antioxidant and antimicrobial activity against *S. aureus* and *E. coli*. In vivo experiments demonstrated significantly accelerated wound healing, with complete recovery achieved by day 14, underscoring the therapeutic potential of fullerene-based dressings [70].

Graphene-based materials—including graphene sheets, graphene oxide (GO), and reduced graphene oxide (rGO)—represent one of the most rapidly expanding areas in nanomedicine. Since the discovery of graphene in 2004, its exceptional two-dimensional structure, high surface area, photothermal responsiveness, and potent antimicrobial activity have made it an attractive component in advanced wound dressings. Its antibacterial activity is attributed to membrane disruption, oxidative stress, and near-infrared (NIR)-enhanced photothermal effects [71–73]. For example, in 2021, Lin Mei demonstrated that graphene oxide functionalized with tetraaminophthalocyanine effectively inactivated *S. aureus* and *E. coli* under 680 nm irradiation [74]. Similarly, polyurethane/GO nanocomposites developed in 2020 exhibited enhanced antibacterial activity and improved wound closure in vivo [75]. In 2022, GO-loaded chitosan–gelatin nanofibers demonstrated 50% and 80% inhibition of *E. coli* and *S. aureus*, respectively, without inducing cytotoxicity [76].

More recent research has advanced the clinical potential of graphene-based dressings. In 2023, Aslam Khan et al. engineered hydrogel dressings by functionalizing GO with bacterial cellulose via a hydrothermal process. These hydrogels exhibited robust antibacterial activity against *S. aureus*, *E. coli*, and *P. aeruginosa*, while also promoting cell adhesion, proliferation, and blood clotting, with minimal hemolysis [77]. Priyadarshani Choudhary et al. (2023) synthesized reduced graphene oxide (rGO) using a modified Hummers' method and combined it with silver nanoparticles to form rGO-Ag nanocomposites. These nanocomposites were incorporated into chitosan-based hydrogel dressings functionalized with poly-L-lysine (Figure 6). The resulting dressings achieved a 99.999% reduction in *E. coli* and *S. aureus* bacterial populations, compared to only 90% with chitosan alone. Hemocompatibility tests indicated lower hemolysis and better cell attachment in these dressings, which also promoted angiogenesis and faster wound healing in Wistar rat models. After 14 days, wounds treated with the CGAPL dressings showed a 93.08% size reduction, outperforming commercial dressings like Tegaderm and Fibroheal silver, which achieved reductions of 72.06% and 84.59%, respectively [78].

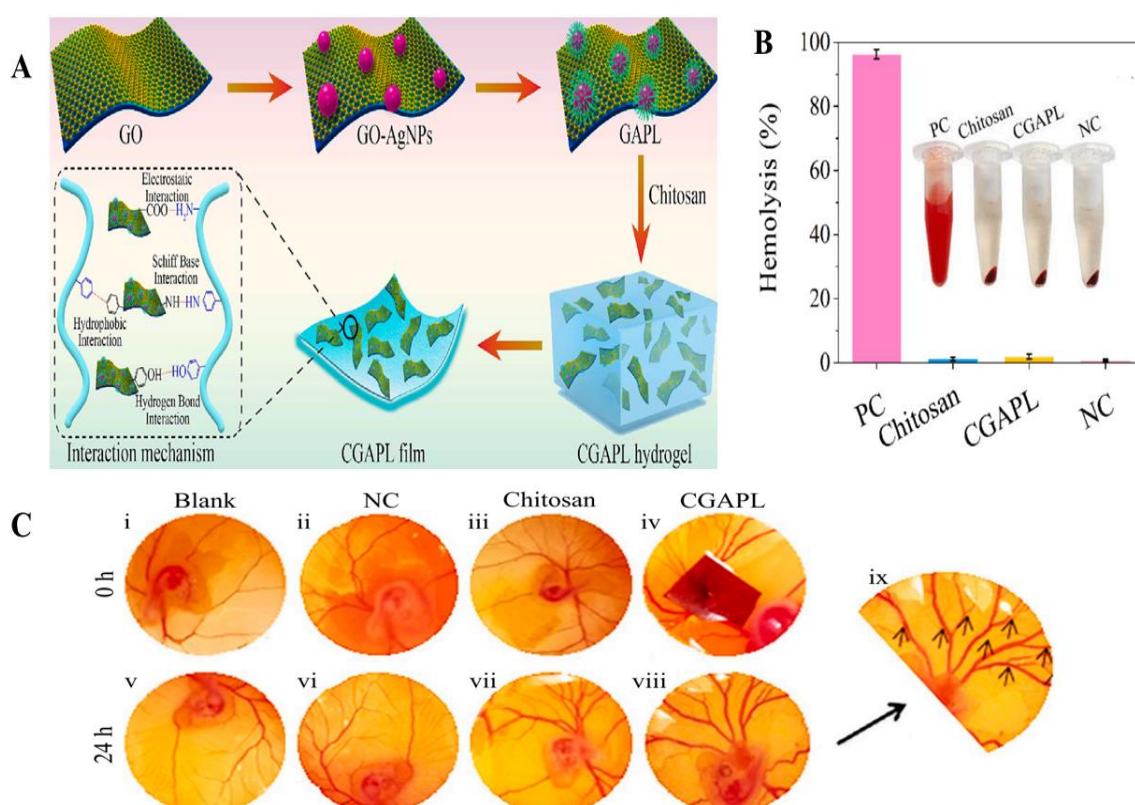


Fig. 6. (A) Schematic illustration of the synthesis of graphene oxide by the modified Hummer method, its combination with silver nanoparticles and hydrogel synthesis with the help of chitosan. (B) Hemolysis test results for hydrogel wound dressing using red blood cells. (C) Images of pro-angiogenesis assay using chorioallantoic membrane. From ref [9] with permission.

Overall, CNTs, fullerenes, and graphene-based nanomaterials demonstrate potent antibacterial activity, biocompatibility, and multifunctionality, making them highly promising candidates for next-generation wound dressings and regenerative therapies

MXene nanoparticles

MXenes, two-dimensional nanoparticles composed of metal carbides or nitrides, were first discovered in 2011, which are generally represented by the formula $Mn+1XnTx$ [79, 80]. These nanoparticles exhibit exceptional photothermal properties, catalytic activity, electrical conductivity, and structural tunability, making them promising candidates for drug-free antibacterial therapies [81, 82]. MXenes efficiently interact with bacterial membranes, causing membrane disruption, oxidative stress, and DNA exposure, while their antibacterial activity can be further enhanced under near-infrared (NIR) irradiation [83, 84]. Recent studies have indicated the therapeutic potential of MXene-based wound dressings. For example, Li et al. (2023) fabricated composite hydrogels by incorporating MXenes with silver nanoparticles in a PVA matrix, which exhibited potent antibacterial activity and inhibited

93% of *S. aureus* and 95% of *E. coli* [85]. Similarly, Park et al. (2023) developed hydrogel wound dressings by integrating MXenes into a sodium alginate solution along with ciprofloxacin. The dressings showed enhanced antibacterial activity under NIR irradiation, effectively reducing *E. coli* and *S. aureus* growth. In vivo experiments showed a 90% improvement in wound healing within 14 days, with histological analyses confirming enhanced tissue regeneration, collagen deposition, and angiogenesis [86]. Hai Zhou et al. (2024) designed a sponge-like wound dressing using decellularized pig skin matrix (PADM) and hydroxypropyl chitosan (HPCS), integrating MXene nanoparticles to enhance the material's properties (Figure 7). The sponge exhibited high biocompatibility, with minimal cytotoxicity, and demonstrated strong antibacterial activity, killing 97.21% of *E. coli* and 98.89% of *S. aureus* after 36 hours. The sponge also showed excellent hemostasis, outperforming commercial collagen sponges in blood absorption and clot formation. The MXene-based sponge significantly promoted wound healing in a rat model simulating visceral injuries, achieving an 87% healing rate in diabetic wounds after 14 days [87].

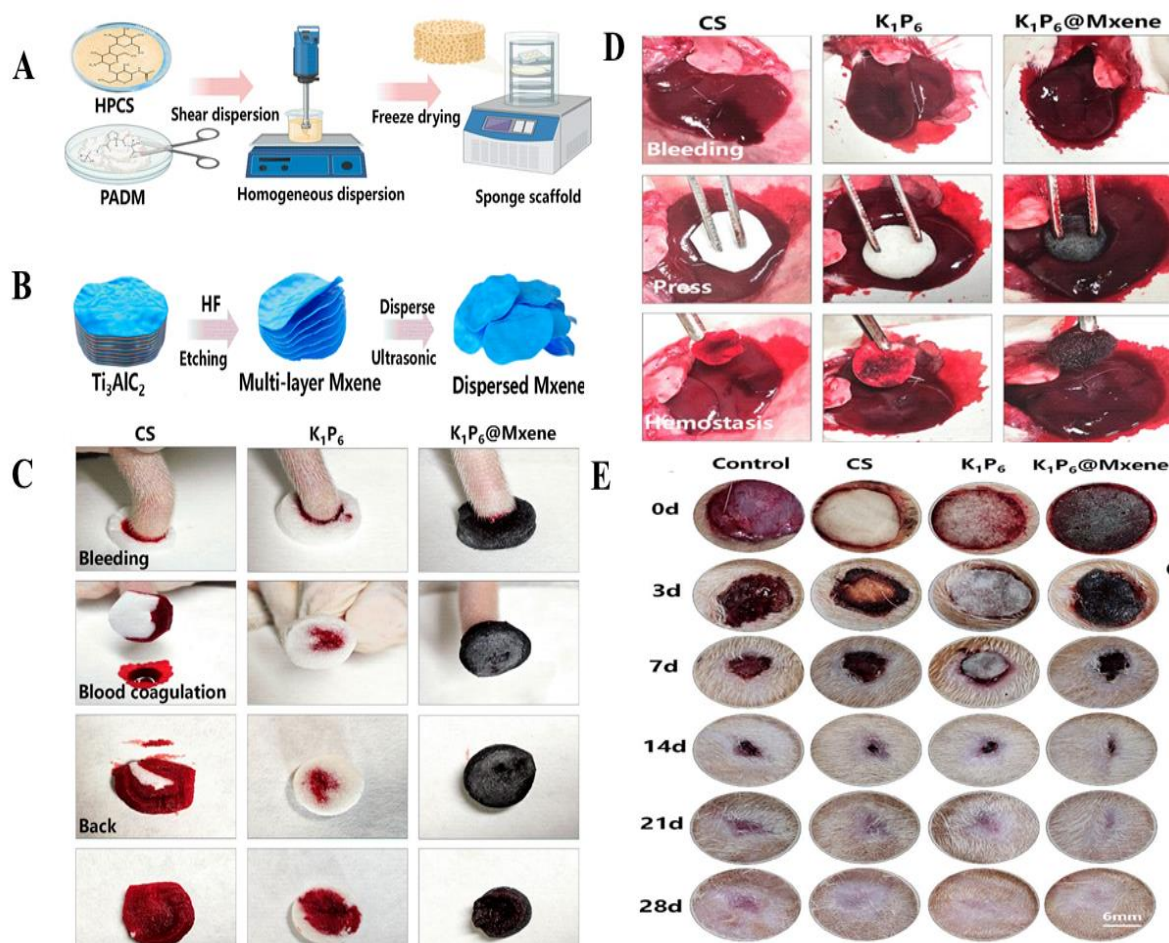


Fig. 7. (A) Schematic of hydrogel wound dressing synthesis using HPCS and PADM. (B) Schematic of MXene synthesis by etching method. Images of hemostatic function of wound-dressing in an animal model with bleeding caused by (C) tail amputation and (D) liver damage. (E) Performance of wound dressing in the treatment of diabetic wounds. From ref [10]. With permission.

Perovskite nanoparticles

Perovskites are a class of hybrid nanomaterials known for their unique structural, optical, and functional properties. The first perovskite, calcium titanate ($CaTiO_3$), was discovered in 1839 and named after the Russian scientist Count Lev Alekseyevich Perovskiy, which generally follow the formula ABO_3 , where A and B are cations of different sizes and charges. Substituting A and B with various metal ions allows tunable surface and functional properties, making perovskite nanoparticles highly versatile. Perovskites can be synthesized in zero-, one-, two-, and three-dimensional configurations using methods such as sol-gel, hydrothermal, co-precipitation, solid-state processes, and electrospinning. Their excellent thermal stability, optical properties, and bandgap tunability (3–4 eV) make them suitable for biomedical imaging applications when produced as zero-dimensional particles like quantum dots. Beyond imaging, perovskite nanoparticles demonstrate significant antibacterial activity, which has been exploited in wound dressing

applications. For instance, Góra et al. (2020) incorporated $Ag_{0.3}Na_{1.7}La_2Ti_3O_{10}$ perovskite nanoparticles into PLGA nanofibers, producing scaffolds, inhibiting *K. pneumoniae*, *E. coli*, *P. aeruginosa*, *S. saprophyticus*, and *C. albicans*. These nanofibers also exhibited mechanical properties similar to human skin and promoted human fibroblast proliferation while maintaining native protein expression [88]. Further advancements were reported in 2023. Kandoth et al. developed $Cs_3Bi_2Br_9$ perovskite nanoparticles functionalized with TiO_2 , which generated reactive oxygen species (ROS) under light exposure and effectively eradicated biofilms formed by *C. jejuni* and methicillin-resistant *S. aureus* (MRSA) [89]. In the same year, Thurnkul et al. synthesized near-spherical $ZnTiO_3$ perovskites, achieving 100% suppression of *S. aureus* colonies and highlighting their potent antibacterial potential [90].

Overall, perovskite nanoparticles combine structural tunability, strong antibacterial activity, and biocompatibility, positioning them as

promising candidates for next-generation antimicrobial wound dressings.

Janus nanoparticles

Janus nanoparticles (JNPs), first studied by Pierre-Gilles de Gennes in 1991, are anisotropic nanoparticles characterized by asymmetric structures with two distinct regions of differing polarity or amphiphilic properties, combining hydrophilic and hydrophobic segments [145–147]. The unique non-central properties of JNPs make synthesis challenging, but methods such as phase separation, masking, self-assembly, controlled nucleation, lithography, and microfluidics allow for diverse nanoparticle shapes, including octopus, spherical, discoidal, cylindrical, hamburger, raspberry, and snowman forms [91]. The structural asymmetry of Janus nanoparticles enables their use in a wide range of biomedical applications, including antibacterial therapy, drug delivery, imaging, hemostasis, and cancer treatment. For instance, Yang et al. (2020) synthesized Janus nanofibers using polyvinylpyrrolidone (PVP) and ethyl cellulose (EC) polymers for antibacterial applications. Ciprofloxacin was loaded into the PVP solution, silver nanoparticles into the EC solution, and the fibers were subsequently coated with gold. These nanofibers exhibited significant antibacterial activity against *S. aureus* and *E. coli* [92]. JNPs have

also been investigated for hemostasis and wound management. Chen et al. (2021) developed mesoporous silica nanoparticles (MSN) loaded with silver and tannic acid, which are enhanced by calcium ions (Ca-TA-MSN@Ag) and demonstrate superior hemostatic performance and significantly reduced bleeding times in mouse liver and femoral artery injury models. These nanoparticles also showed potent antibacterial effects, achieving over 99% inhibition of *S. aureus* and *E. coli* [93]. In wound dressing applications, Shi et al. (2023) created a bilayer PLGA-based dressing containing copper sulfide (CuS) nanoparticles and antibiotics, which provided sustained drug release, strong antibacterial activity (96.3% for *E. coli* and 97.8% for *S. aureus*), and accelerated healing of MRSA-infected wounds, especially when combined with laser treatment [94]. Similarly, Tao Zhou et al. (2024) created a two-layer Janus nanofiber wound dressing with gelatin, magnesium oxide (MgO) nanoparticles, polycaprolactone (PCL), and polylactic acid (PLLA) (Figure 8). The optimal MgO concentration significantly improved wound healing, reduced inflammation, and promoted angiogenesis and collagen formation. Moreover, the dressing demonstrated potent antibacterial effects, particularly against *E. coli*, due to the generation of reactive oxygen species (ROS) by MgO nanoparticles [95].

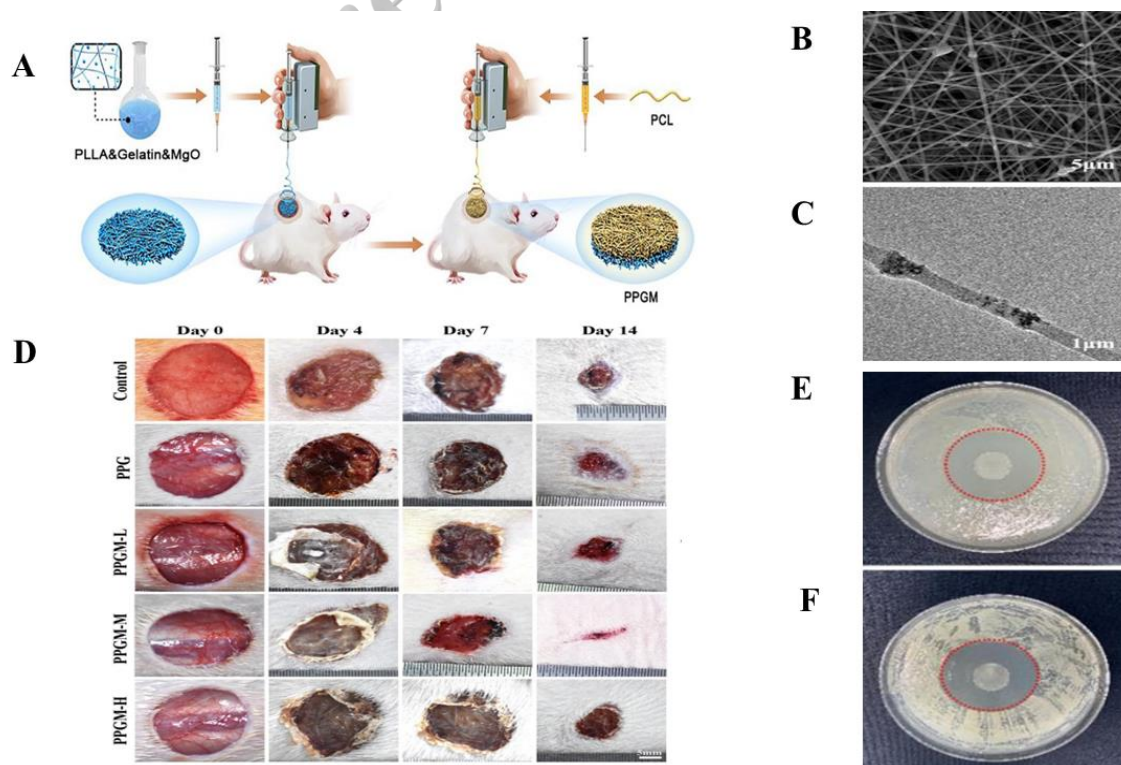


Fig. 8. (A) Schematic of the synthesis of two-layer Janus dressing. (B) SEM and (C) TEM images of the two-layer wound dressing. (D) Images of Janus dressing function. Antimicrobial performance of double-layer wound dressing against bacteria (E) *E. coli* and (F) *S. aureus*. From ref [11] with permission.

Overall, Janus nanoparticles combine structural asymmetry, potent antibacterial effects, and enhanced wound healing capabilities, making them promising candidates for next-generation wound dressings and biomedical applications.

Table 2 reports the detailed types of nanoparticles involved in the synthesis of wound dressings in treating microbial wounds.

Table 2. Types of nanoparticles with antibacterial properties used in wound dressing design, summarizing nanoparticle category, composition, wound dressing type, in vitro and in vivo antibacterial efficacy, target bacterial species, and key references

Category	Nanoparticles	Components	Wound dressing design	In vitro	In vivo	type of bacteria	Ref.
Metal nanoparticles	Ag NPs	Ag NPs	Spray containing nanoparticles	*	*	<i>P. aeruginosa</i> <i>S. aureus</i>	[18]
Metal nanoparticles	Ag NPs	Ag NPs, PVA, alginate, chitosan	Hydrogel	*		<i>S. aureus</i> <i>E. coli</i>	[19]
Metal nanoparticles	Ag NPs	Ag NPs, PVA, PCL and gum arabic	Nanofiber	*		<i>P. aeruginosa</i> <i>S. aureus</i> <i>E. coli</i>	[20]
Metal nanoparticles	Ag NPs	Ag NPs, sodium alginate, gelatin	Hydrogel	*	*	<i>P. aeruginosa</i> <i>S. aureus</i>	[21]
Metal nanoparticles	Ag NPs	Ag NPs, PCL, gelatin	Nanofiber	*	*	<i>E. coli</i>	[22]
Metal nanoparticles	Ag NPs	Ag NPs, metronidazole, gelatin, polyethylene glycol	Sponge	*		<i>S. epidermidis</i> , <i>P. aeruginosa</i> , <i>S. aureus</i> , <i>E. coli</i> , <i>P. vulgaris</i> <i>P. aeruginosa</i> , <i>S. aureus</i> , <i>E. coli</i>	[23]
Metal nanoparticles	Ag NPs	Ag NPs, chitosan, PCL	Nanofiber	*		<i>S. aureus</i> , <i>E. coli</i>	[24]
Metal nanoparticles	Au NPs	AuNPs, arginine-modified chitosan	Film	*	*	<i>S. aureus</i> <i>E. coli</i>	[25]
Metal nanoparticles	Au NPs	AuNPs, chitosan, PVA	Film	*		<i>S. aureus</i>	[26]
Metal nanoparticles	Cu NPs	Cu NPs and hydroxy-propyl-methyl-cellulose	Hydrogel	*		<i>S. aureus</i> <i>E. coli</i>	[27]
Metal nanoparticles	Cu NPs	Cu NPs and sodium alginate	Membrane	*		<i>S. aureus</i>	[28]
Metal nanoparticles	ZnO	ZnO NPs, polyurethane, gelatin, honey	Nanofiber	*		<i>P. aeruginosa</i> <i>S. aureus</i> <i>B. subtilis</i>	[29]
Metal nanoparticles	TiO ₂	TiO ₂ , silver, PVA, starch, graphite carbon nitride	Hydrogel	*	*	<i>S. aureus</i> <i>E. coli</i>	[30]
Metal nanoparticles	TiO ₂	TiO ₂ , silver, PVA	Hydrogel	*		<i>S. aureus</i> <i>E. coli</i>	[30]
Polymer nanoparticles	Chitosan	Chitosan nanoparticles, PVA, hyaluronic acid, pullulan	Hydrogel	*	*	<i>P. aeruginosa</i> <i>S. aureus</i> <i>E. coli</i>	[31]
Lipid nanoparticles	Nanoliposome	Nanoliposome containing lycopene loaded with tobramycin, gelatin	Hydrogel	*	*	<i>S. aureus</i> <i>E. coli</i>	[32]
Lipid nanoparticles	Nanoliposome	Nanoliposome containing Amoxicillin, Polyethylene Glycol, Cyclodextrin, Acryl Omid	Hydrogel	*		<i>S. aureus</i>	[33]
Lipid nanoparticles	SLN	SLN containing Mentha pulegium essential oil	Gel	*	*	<i>S. epidermidis</i> <i>S. aureus</i> <i>Listeria monocytogenes</i> <i>P. aeruginosa</i> <i>E. coli</i>	[34]
Other nanoparticles	CNT	CNT, Chitosan	Hydrogel	*	*	<i>P. aeruginosa</i> , <i>S. aureus</i> , and <i>S. pyogenes</i> , <i>S. aureus</i>	[35]
Other nanoparticles	CNT	CNT, gelatin	Hydrogel	*		<i>S. aureus</i>	[36]

Category	Nanoparticles	Components	Wound dressing design	In vitro	In vivo	type of bacteria	Ref.
Other nanoparticles	CNT	CNT, poly(acrylamide), Chitosan	Hydrogel		*		[37]
Other nanoparticles	Fullerene	Fullerene, Ag NPs		*		<i>S. aureus</i>	[38]
Other nanoparticles	Graphene	Graphene oxide, zein, tetracycline hydrochloride	Nanofiber	*		<i>S. aureus</i> <i>E. coli</i>	[39]
Other nanoparticles	Graphene	Graphene oxide, polyurethane	Double layer membrane	*	*	<i>S. aureus</i> <i>E. coli</i>	[40]
Other nanoparticles	MXene	Mxene, PCA, Gelatin	Nanofiber	*	*	<i>S. aureus</i> <i>E. coli</i>	[41]
Other nanoparticles	MXene	Mxene, Alginate, lysozyme	Hydrogel	*	*	<i>S. aureus</i>	[42]
Other nanoparticles	MXene	Mxene, Chitosan	Hydrogel	*		<i>S. aureus</i>	[43]
Other nanoparticles	Perovskite	Silica-coated Cs3Bi2Br9 QDs@SiO2, cotton fibers	Cotton fabric	*		<i>S. aureus</i> <i>E. coli</i>	[44]
Other nanoparticles	Perovskite	SrSnO3	SrSnO3	*		<i>S. aureus</i> <i>E. coli</i>	[45]
Other nanoparticles	Perovskite	CsPb2Br7	CsPb2Br7	*		<i>E. coli</i>	[46]
Other nanoparticles	Perovskite	LaCoO3	LaCoO3	*		<i>E. coli</i>	[47]
Other nanoparticles	Janus	Alginate, Chitosan, Ag, L-Arginine	Hydrogel		*		[48]
Other nanoparticles	Janus	Au NR, TiO ₂		*		<i>S. aureus</i>	[49]
Other nanoparticles	Janus	PLA, oxacillin, phenol red, polyacrylonitrile	Nanofiber	*	*	<i>S. aureus</i>	[50]
Other nanoparticles	Janus	polyvinylidene fluoride, polydopamine, AgNPs	Nanofiber	*	*	<i>S. aureus</i> <i>E. coli</i>	[51]

Figure 9 compares the antimicrobial mechanisms of metallic, polymeric, and carbon-based nanoparticles, facilitating conceptual understanding.

Clinical studies

Recent investigations have indicated that silver nanoparticles are the primary focus in contemporary wound-healing dressings, particularly for their antibacterial properties. These nanoparticles have become standard in commercially available dressings due to their efficacy in combating infections. For instance, JiHui Chen et al. (2021) treated 58 pemphigus vulgaris patients, comparing silver dressings with wet povidone-iodine dressings. Patients treated with silver dressings reported higher satisfaction and shorter hospital stays [96]. However, not all findings favor silver nanoparticle dressings. A study by Parvaneh Asgari et al. (2022) on paraplegic patients with pressure ulcers found that hydrocolloid dressings outperformed silver nanoparticle dressings in terms of healing outcomes [97]. In the same year, Miner et al.

studied the effects of silver hydrogel dressings on post-surgery scar tissue formation in foot and ankle injuries. Their findings showed a significant reduction in scar tissue over 12 weeks in the group treated with silver dressings [98]. Additionally, Ze-Yao Shi et al. (2022) treated an umbilical infection in a newborn with a combination of antibiotics and silver dressings. The treatment effectively controlled the methicillin-resistant *S. aureus* (MRSA) infection by day 14, demonstrating the antibacterial efficacy of silver dressings in critical cases [99]. Another study by Rui Wang et al. (2022) found that silver dressings significantly promoted wound healing in chronic wound patients by maintaining a moist environment on the wound surface and reducing the frequency of dressing changes [100]. Finally, Dong Zhang et al. (2022) investigated the use of thermoplastic polyurethane dressings with silver nanoparticles on 98 diabetic patients with open lower limb fractures. This study demonstrated that these dressings inhibited bacterial growth in vitro and enhanced healing and shortened hospital stays in vivo [101].

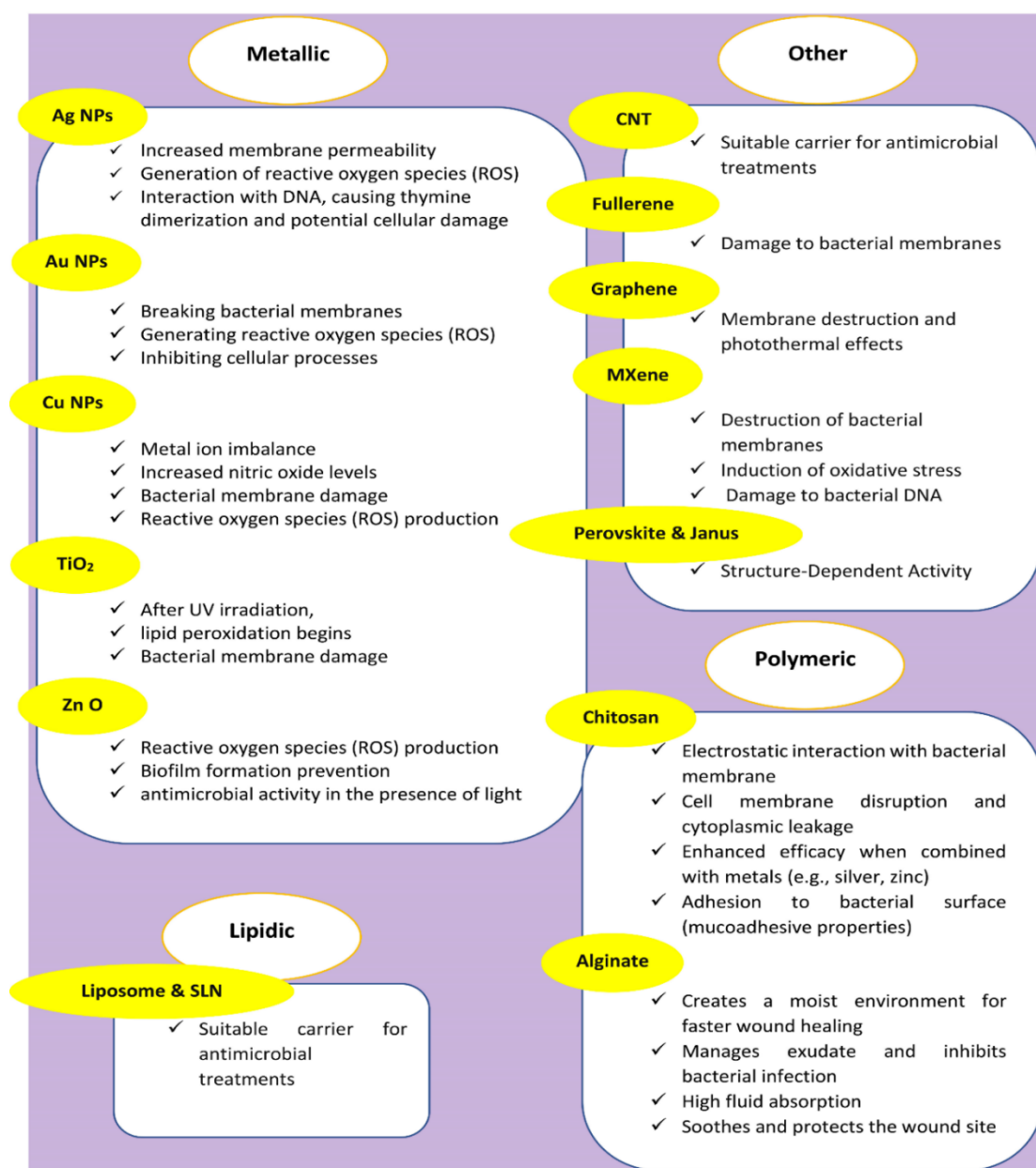


Fig. 9. Comparative mechanisms of antimicrobial action of nanoparticles: Overview of antibacterial strategies. (create with power point).

The clinical evidence outlined above has paved the way for the commercialization and regulatory approval of several silver nanoparticle-based wound dressings. These products have been evaluated through the U.S. Food and Drug Administration (FDA) clearance process or CE

certification in Europe, ensuring both their safety and efficacy for patient use. Table 3 summarizes the key silver-containing dressings, which are currently approved and available on the market, along with their clinical and regulatory status.

Table 3. FDA and CE approved nanoparticle-based wound dressings, including product name, regulatory approval, key features and reference.

Product Name	Approval	Key Features	Address	Ref.
ACTICOAT®	FDA (510(k))	Nanocrystalline silver antimicrobial barrier dressing	Data obtained from FDA 510(k) Summary and official product page	[52]
CovaClear Ag™	FDA (510(k))	Collagen with silver; for chronic and post-surgical wounds	CovaClear Ag™: FDA 510(k) Summary, CovaClear Ag™ (K221218)	-
BCT Silver Bandage	FDA (510(k))	Silver dressing for chronic and acute wounds	BCT Silver Bandage: FDA 510(k) Summary, BCT Silver Bandage (K140147)	-
Silver Calcium Alginate	FDA cleared	Silver + calcium alginate; maintains moisture and antibacterial	Silver Calcium Alginate: FDA 510(k) Summary, Silver Calcium Alginate (K053590)	-

Pros, toxicity, and Translational Considerations of Nanoparticles

In this section, the advantages and limitations of various nanoparticles used in wound dressings were critically analyzed with a focus on efficacy, toxicity, and translational considerations.

Nanoparticles can penetrate the body through multiple entry points, such as the skin, eyes, and respiratory system, due to their minuscule size and travel to various organs including the brain, liver, kidneys, and lungs. For instance, prolonged exposure to silver nanoparticles has been associated with argyria. This condition was identified as early as 1647, where skin and eye pigmentation changes due to nanoparticle accumulation. Moreover, nanoparticles introduced through the olfactory system can impair macrophage function, leading to particle buildup in the body. The potential cytotoxic effects of these particles extend beyond bacteria because nanoparticles have been shown to adversely affect healthy cells. In addition, their interaction with mitochondria can disrupt the respiratory chain, resulting in excessive ROS production, DNA damage, and ultimately cell death. Zinc oxide nanoparticles, in particular, pose a significant health risk by triggering severe lung inflammation. Furthermore, research has demonstrated that other nanoparticles, such as gold and TiO₂, can accumulate in organs like the liver and spleen, leading to extensive tissue damage. Additionally, the emerging class of two-dimensional nanoparticles, such as MXenes, raises concerns about their synthesis processes. Methods like etching introduce functional groups such as fluoride and chloride, which can lead to toxicity in both humans and the environment. Beyond toxicity, the cost of nanoparticle production and integration into wound dressings remains a critical factor. For example, gold nanoparticles (AuNPs) are prohibitively expensive for large-scale use, although highly effective in certain applications. In contrast, chitosan-based nanoparticles offer biocompatibility and biodegradability at a lower cost, but their efficacy is often limited compared to metallic nanoparticles [102].

Other inherent challenges with nanoparticles, such as poor chemical and thermal stability, limited bioavailability, inadequate biodegradability, and low water solubility, further complicate their safe and effective application in medical settings [103]. Despite these substantial challenges, the future of antimicrobial nanomaterials in wound care remains

promising. Thus, continued research is essential to optimize their safety and efficacy. The integration of smart technologies, including stimuli-responsive nanoparticles and personalized medicine approaches, can significantly revolutionize wound treatment by delivering tailored therapies to individual patients. As the field evolves, nanoparticle-based wound dressings could become pivotal in improving patient outcomes and alleviating the global burden of wound infections. Nevertheless, achieving this future may require a cautious and well-regulated approach to mitigate potential health risks and environmental concerns. Table 4 summarizes the key advantages and limitations of different nanoparticles, including considerations for clinical translation and commercialization.

Scalability and commercialization

Nanotechnology, as a transformative innovation, holds great potential for addressing fundamental human challenges in fields such as health, energy, environment, and food, with generated extensive commercial opportunities over the past three decades. The development of nano-based medical products, particularly advanced wound dressings, can play a significant role in improving quality of life. However, the transition of nanomaterials from laboratory-scale synthesis to industrial production and effective commercialization remains challenging [104]. One of the major obstacles is large-scale production to meet commercial demands. Moreover, maintaining and precisely controlling the unique characteristics of nanomaterials, such as size, morphology, and surface chemistry, which critically influence their efficiency and biocompatibility, becomes increasingly difficult at industrial scales. This issue is particularly critical in nano-based wound dressings because slight variations in the particle size of silver or copper can affect their antibacterial effects and safety. Additionally, many common synthesis methods such as sol-gel, chemical vapor deposition, and hydrothermal processes are not suitable for mass production and are associated with problems like low reproducibility, complex processing, and high costs. Moreover, integrating nanomaterials into conventional production lines is a major barrier due to the need for specialized equipment and process redesign [105].

Table 4. Comparative summary of different categories of nanoparticles used in wound dressing design, highlighting their advantages, disadvantages, cost, clinical relevance, and key references.

Category	Nanoparticles	advantages	disadvantages	Cost	Notes / Clinical relevance	Ref.
Metal	Ag NPs	Strong antibacterial; helps heal wounds	Cytotoxicity at high doses; possibility of resistance development	Moderate to High	Widely used in commercial wound dressings	[1, 53]
Metal	Au NPs	Biocompatible; surface modification possible; low toxicity	Weak antibacterial effect alone; expensive	High	Often combined with other factors	[54]
Metal	Cu NPs	Antibacterial; Stimulates angiogenesis	Cytotoxic at high concentrations; stability issues	Moderate	Can be used in hydrogel dressings	[55]
Metal	TiO ₂	Photocatalytic antibacterial; promotes healing	Potential cytotoxicity under UV; aggregation	Moderate	Investigated in composite wound dressings	[56, 57]
Metal	ZnO	Antibacterial; UV protection; promotes cell proliferation	Cytotoxicity at high doses; aggregation	Low to Moderate	Common in nanocomposite dressings	[58]
Polymer nanoparticles	Chitosan	Biodegradable; antibacterial; promotes healing	Poor mechanical strength alone; pH-sensitive	Low	Often combined with other polymers	[59]
Polymer nanoparticles	Alginate	Biocompatible; gel-forming; maintains moist environment	Limited antibacterial effect alone	Low	Common in hydrogel dressings	[58, 60]
Lipid nanoparticles	Nanoliposome	Biocompatible; drug encapsulation; controlled release	Short-term stability; expensive	High	Suitable for drug delivery in wounds	[61, 62]
Lipid nanoparticles	SLN	Controlled drug release; biocompatible	Limited loading capacity; aggregation	Moderate	Experimental wound dressings	[63]
Other nanoparticles	Graphene	Strong antibacterial; mechanical reinforcement	Potential cytotoxicity; complex production	High	Used in advanced wound dressings	[64]
Other nanoparticles	MXene	Broad-spectrum antibacterial; biodegradable	Limited studies; cost	High	Experimental stage	[65]
Other nanoparticles	Janus	Multi-functional; antibacterial + drug delivery	Complex synthesis; limited in vivo data	Very High	Novel approach; under research	[66]
Other nanoparticles	Perovskite	Multifunctional; tunable properties	Limited biological studies; potential toxicity	Very High	Early-stage research	[52]

Alongside these technical challenges, economic and infrastructural limitations also complicate the path to commercialization. The production of nanomaterials requires expensive precursors, costly purification processes, and specialized packaging, all of which increase the final product cost and restrict its entry into price-sensitive markets such as medical devices. The absence of comprehensive international standards for production and quality control further hesitate industries and regulatory bodies in accepting these

products. Additionally, the lack of advanced infrastructure, skilled workforce, bureaucratic hurdles in patent registration, and the "valley of death" between laboratory achievements and financial support for prototyping are major barriers in developing the nano-based products. Environmental and health concerns, along with negative publicity, can also challenge social acceptance [106]. Despite these obstacles, there are valuable opportunities for the commercialization of nano-based products. High

societal expectations for emerging technologies, market demand for innovative products, and the potential to develop a wide range of applications create favorable conditions for growth in this field. Commercialization models show that this process begins with identifying market needs and research and development, followed by stages such as patent registration, licensing, revenue generation, product improvement based on feedback, and ultimately standardization. In this process, factors such as product innovation, market size, and economic conditions play a key role. Ultimately, effective scaling up and commercializing nanoproducts, including advanced wound dressings, requires a multifaceted approach. Developing green and scalable synthesis methods, establishing international standards, investing in specialized infrastructure, training skilled personnel, and applying technologies like automation and artificial intelligence in process monitoring can facilitate the entry of these products into practical and clinical markets. Such measures enhance quality and safety and enable the supply of more efficient and cost-effective products [107].

CONCLUSION

Nanotechnology has significantly transformed wound care, offering innovative strategies to address bacterial infections and antibiotic resistance. Among antimicrobial nanomaterials, silver and zinc oxide nanoparticles demonstrate the highest antibacterial efficacy, whereas polymeric and lipid-based nanoparticles provide enhanced biocompatibility and controlled release profiles, supporting tissue regeneration. Carbon-based nanoparticles, such as graphene oxide, disrupt bacterial membranes via physical interactions and ROS production. These nanoparticles hold considerable potential for integration into advanced wound care technologies, including smart, stimuli-responsive, and eco-friendly dressings. Nevertheless, careful evaluation of their long-term safety, environmental impact, and clinical translation remains essential. This review offers practical guidance for researchers, clinicians, and industry stakeholders aiming to develop effective and safe nanoparticle-based wound dressings by providing a comparative overview of nanoparticle types, mechanisms, and applications.

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Conflict of interest

The authors declare no conflicts of interest.

Author contribution

T S T and T S T: Investigation, Writing – original draft. V Sh: Conceptualization, Investigation, Methodology, Validation, Supervision, Project administration, Writing – review & editing.

Artificial Intelligence (AI)

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