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# Electrospun Nanofibers in Wound Healing: Advancements, Antibacterial Properties, and Clinical Potential

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## ABSTRACT

The exploration of electrospun nanofibers has gained significant attention in wound healing due to their unique structural properties and potential to enhance therapeutic efficacy. This review examines the development and application of electrospun nanofibers, focusing on their antibacterial properties and biocompatibility, which are essential for effective wound management. Electrospinning techniques enable the production of nanofibers with high surface-area-to-volume ratios, tunable porosity, and controlled release profiles of therapeutic agents, making them ideal for wound dressings. We explore various biopolymers and synthetic polymers used in electrospun nanofiber fabrication, emphasizing their contributions to antibacterial effects and biocompatibility. The incorporation of antimicrobial agents, such as silver nanoparticles and essential oils, enhances infection prevention and promotes healing. Additionally, challenges related to the scalability of electrospinning processes and the need for standardized evaluation methods are discussed. The review also highlights the influence of nanofiber architecture such as fiber diameter, alignment, and surface modifications on cellular response and tissue integration. The findings underscore the potential of electrospun nanofibers to not only serve as passive wound dressings but also actively facilitate healing through antibacterial action and favorable biological interactions. Future research should focus on optimizing fabrication techniques, enhancing functional properties, and conducting in vivo studies to fully realize the clinical potential of these materials in wound care applications.

**Keywords**: Electrospun, nanofibers, wound healing, antibacterial and biocompatibility

## INTRODUCTION

Electrospun nanofibers have gained significant attention as a promising material for wound healing applications due to their unique structural properties, which closely mimic the extracellular matrix (ECM) of human skin. These nanofibers possess a high surface-area-to-volume ratio, tunable porosity, and the capability to incorporate bioactive agents, making them ideal for promoting tissue regeneration and preventing infections [1]. Electrospinning technology, an affordable and versatile method for fabricating ultra-fine fibers with specialized properties, has been extensively utilized in biomedical applications, including tissue engineering scaffolds, wound dressings, and drug delivery systems. Among these, wound dressing materials designed to accelerate wound closure and enhance the healing process are in high demand [2]. Electrospun nanofibrous materials offer exceptional potential in wound care due to their large surface area, superior mimicry of the native ECM, adjustable waterproofness and breathability, and programmable drug delivery capabilities. By integrating antimicrobial agents and ensuring biocompatibility with human tissue, these nanofibers represent a cutting-edge solution for advanced wound care technology, addressing both functional and therapeutic needs in modern medicine [3]. The advent of novel polymers and advanced fabrication techniques has revolutionized wound dressings, enabling the development of materials with tunable functionalities alongside excellent structural and mechanical properties. Bio-based polymeric materials are particularly favored for skin regeneration, serving as functional skin substitutes, wound healing patches, and dressings for various wound types [4]. A broad spectrum of natural biopolymers, including cellulose, chitosan, gelatin, hyaluronic acid, and collagen, has been employed in the electrospinning of nanofibers to replicate the native tissue matrix and support wound healing. In addition, synthetic bio-based polymers such as polylactides (PLAs) and polyhydroxyalkanoates (PHAs) are widely used in the fabrication of electrospun wound dressings. The mechanical, degradation, and morphological properties of these dressings can be precisely tailored using coaxial, multi-nozzle, or blend electrospinning techniques, combining natural and synthetic bio-based polymers to enhance functionality [5].



This review explores the application of electrospun nanofibers in wound healing, with a focus on their antibacterial properties and biocompatibility. The discussion highlights the potential of these materials to serve as advanced wound care solutions, bridging the gap between innovation and clinical efficacy.

## METHODOLOGY

This review methodologically synthesizes current research on the application of electrospun nanofibers in wound healing, with a specific focus on their antibacterial properties and biocompatibility. Studies from various biomedical and materials science journals were systematically analyzed, with a focus on research involving electrospinning techniques, polymer selection, and the incorporation of bioactive agents. Articles were selected based on their relevance to wound healing, tissue regeneration, and advanced drug delivery systems. Key themes discussed include electrospinning methodologies, clinical validation of electrospun nanofibers, tissue engineering applications, and the integration of bioactive agents such as antimicrobial compounds. Comparative studies on antibacterial agents incorporated into electrospun nanofibers were also evaluated.

### Electrospun Nanofibers for Wound Healing Application

Wound healing, the complex biological process through which cells regenerate and repair damaged tissues, is critical to restoring skin integrity and functionality [6]. Electrospun nanofibers have garnered significant attention in recent years due to their ability to replicate the architecture of the natural extracellular matrix (ECM), providing unique structural and functional benefits. As highlighted by [7], these nanofibers offer a high surface area-to-volume ratio, tunable porosity, and superior mechanical properties, which collectively promote cell adhesion, proliferation, and differentiation. These attributes facilitate three-dimensional tissue formation, making electrospun nanofibers highly effective as wound dressings. Electrospinning, a versatile and widely adopted method, allows for the production of nanofibrous structures from diverse materials, with customizable features, compositions, shapes, and morphologies [6]. Compared to traditional wound dressings, nanofibrous materials demonstrate enhanced wound healing efficiency due to their superior ability to mimic the ECM. Additionally, they provide a conducive microenvironment for tissue regeneration by enabling moisture retention, gas exchange, and the controlled delivery of therapeutic agents. In the medical and biomedical domains, electrospun nanofibers are particularly valuable in applications such as tissue engineering and drug delivery systems. For wound healing specifically, they serve as scaffolds to support cellular growth and as carriers for bioactive molecules, including antibiotics, growth factors, and anti-inflammatory agents. These functionalities underscore their transformative potential in advancing wound care and improving patient outcomes.

### Clinical Validation of Electrospun Nanofibers

This work aims to consolidate the current state of knowledge regarding electrospun nanofibers for wound healing applications while highlighting the lack of extensive clinical data on their usage. Clinical studies are crucial for evaluating the feasibility, effectiveness, and safety of these materials, particularly in critical wound care scenarios. According to Memic et al. (2019), electrospun nanofibers, due to their structural similarity to the natural extracellular matrix (ECM), can facilitate cell attachment and proliferation. However, the authors emphasize the necessity of validating these properties in situ within wounded environments to assess their practical applicability. Similarly, Dabiri et al. (2016) point out that materials intended for wound healing must undergo rigorous evaluation through Phase III clinical trials. Such trials are essential not only to confirm their efficacy in promoting wound repair but also to identify and mitigate potential adverse effects, such as infections or immune system hyperactivity. Future research must focus on translating laboratory findings into real-world medical applications. This includes conducting comprehensive clinical trials, pilot studies, and sound validation tests to ensure the reliability and safety of electrospun nanofibers for widespread clinical adoption. Bridging this gap between experimental discoveries and clinical practice will be pivotal in realizing the full potential of electrospun nanofibers in advanced wound care.



## Tissue Engineering with Electrospun Nanofibers

Electrospinning is an efficient and versatile technique for manufacturing tissue scaffolds, producing non-woven meshes of micron- to submicron-sized fibers. Electrospun nanofibers are employed to repair, replace, and enhance tissue properties, offering significant potential in tissue engineering applications. Numerous electrospun polymer fibers have been effectively applied in this field, demonstrating advancements in scaffold design and functionalization.

## Core/Shell Nanofiber Structures

Core/shell nanofibers exhibit exceptional versatility in tissue engineering due to their ability to encapsulate biologically relevant molecules and nanocomposites, as well as to modify electrospun fiber surfaces. The electrical and mechanical properties of these nanofibers are critical in designing effective scaffolds. For instance, conductive electrospun scaffolds fabricated using biodegradable poly (lactic acid) (PLA) mixed with single-wall carbon nanotubes (SWNTs) have been shown to support cellular growth without adverse effects on cell proliferation [2]. Further innovations include collagen surface-coated poly(ε-caprolactone) (PCL) fibers synthesized via coaxial electrospinning, which demonstrated improved cell-scaffold interactions when tested with human dermal fibroblasts for skin tissue engineering applications [8]. These advancements highlight the potential of core/shell nanofibers in creating functional scaffolds tailored for specific tissue regeneration needs.

## Mechanical Properties and Biocompatibility

The mechanical properties and biocompatibility of electrospun nanofibers are pivotal for their application in tissue engineering. Research in [9] demonstrated that composite electrospun nanofibrous membranes exhibited superior tensile strength and Young's modulus compared to traditional electrospun PLGA membranes during degradation. Additionally, cell culture experiments revealed that PLGA-chitosan/PVA composite membranes enhanced the adhesion of human embryo skin fibroblasts. Another study by [10] successfully fabricated hybrid PLGA/chitosan nanofibrous membranes using dual-source and dual-power electrospinning. The introduction of varying amounts of hydrophilic chitosan (ranging from 32.3% to 86.5%) significantly enhanced the structural and mechanical properties, as well as the cytocompatibility, of these scaffolds. The interaction between endometrial stromal fibroblasts (hESFs) and the hybrid membranes demonstrated their efficiency as scaffolds for skin tissue engineering. Furthermore, multi-layer electrospun PCL microfiber scaffolds, as developed in [11], incorporated nanofiber layers with optimized balances between nanofiber and microfiber components, presenting significant potential for 3D tissue engineering. These multilayer scaffolds exhibited reduced cellular infiltration under static and dynamic culture conditions, offering a refined approach to scaffold design.

## Long-Term Stability and Degradation

The long-term stability and degradation of electrospun nanofibers remain critical challenges in optimizing their performance for wound healing applications. Research in [3] highlighted that while the mechanical properties of PLGA-chitosan/PVA membranes diminished over time, they remained suitable for cell attachment and growth during the early healing stages. However, detailed degradation profiles for other materials, such as PCL/chitosan blends, are limited. Although materials like cellulose have demonstrated biocompatibility and effective moisture retention [12], their long-term stability in dynamic biological environments, particularly in chronic wound healing, requires further investigation. Future research should focus on understanding the enzymatic stability and biophysical integrity of these materials over prolonged healing periods, ensuring their efficacy in both acute and chronic wound scenarios.

## Medication Delivery Systems Using Electrospun Nanofibers

Electrospun fibers offer a unique advantage in medication delivery systems due to their ability to preserve the integrity and bioactivity of drug molecules, facilitated by mild processing conditions. The use of these fibers in localized drug delivery for wound treatment significantly reduces systemic absorption of the drug, minimizing side effects while enhancing therapeutic efficacy through targeted treatment [13].

## Core/Shell Electrospun Fibers for Drug Delivery

Core/shell electrospun fibers are widely utilized in drug delivery applications because of their ability to encapsulate drug molecules within a protective core. This structure not only safeguards therapeutic agents but also prevents external factors, such as enzymes and growth factors, from denaturing during processing [14-15]. As a result, the bioactivity and structural integrity of the therapeutic agents remain intact until they are released at the target site. For instance, Yang [17] investigated the bioreactivity and structural stability of PDLLA (Poly-D, L-lactic acid) ultrafine nanofibers using lysozyme as a model protein. Scanning electron microscopy (SEM) revealed that the fibers exhibited a highly porous and bead-free core/shell structure. This architecture makes them suitable for encapsulating a wide range of therapeutic compounds for controlled drug delivery.



### Encapsulation Techniques and Drug Release Patterns

The encapsulation of drugs into electrospun fibers can be achieved through two primary methods:

1. **Blending:** In this straightforward technique, drug molecules are blended with the polymer and electrospun together to form encapsulated fibers. According to [13], fibers with larger diameters displayed zero-order kinetics, meaning that the drug was released at a constant rate [18]. Since the drug molecules are located near the surface of the fibers, this method is relatively simple to execute.
2. **Core/Shell Structure:** Using a coaxial spinneret, core/shell fibers are fabricated to achieve controlled drug release. Studies by [17] demonstrated that drugs delivered through this method exhibit an initial burst release followed by stabilization at a constant release rate [19]. This pattern ensures an immediate therapeutic effect followed by sustained delivery over time.

### Advantages and Challenges

The localized delivery of drugs using electrospun fibers enhances treatment efficacy by concentrating therapeutic agents at the wound site, reducing systemic exposure and potential side effects. However, complexities in processing parameters, such as controlling the mode of encapsulation and the architecture of the fibers, pose challenges. These factors must be optimized to achieve desirable drug release profiles, tailored to specific medical needs [13]. In summary, electrospun fibers represent a promising platform for advanced medication delivery systems, particularly in wound healing. Ongoing research and technological advancements will further refine their capabilities, ensuring greater clinical applicability and improved patient outcomes.

### Antibacterial and Biocompatibility Properties of Electrospun Nanofibers

Numerous studies have highlighted the critical role of wound dressings in enhancing the healing process. Effective wound care relies on selecting the appropriate dressing for each specific wound type [6, 20]. A proper dressing should offer excellent biocompatibility while providing efficient protection against bacterial infections [21, 22].

### Antibacterial Properties

Wound infections represent a significant global health challenge, and designing antibacterial products for wound healing has become a major focus of research [23]. To prevent the harmful effects of infections in injured areas, wound dressings must be capable of blocking bacterial penetration, inhibiting microbial colonization, and promoting skin regeneration [24]. Electrospun scaffolds with antibacterial properties can help prevent wound infections by incorporating antimicrobial agents during the electrospinning process [4]. Various antimicrobial agents, such as antibiotics, metallic nanoparticles, and natural extracts, are incorporated into electrospun nanofibers to enhance their antibacterial properties. Metallic nanomaterials, particularly silver nanoparticles (AgNPs), are well-known for their efficiency in treating wound infections. Their high surface-to-volume ratio significantly boosts the antibacterial activity of electrospun wound dressings [25, 23]. Additionally, recent strategies have focused on using polymers with intrinsic antibacterial properties, which rely on physical, chemical, or morphological factors to prevent bacterial colonization and biofilm formation. Bio-based and biopolymer materials offer significant promise in this area.

### Comparative Analysis of Antibacterial Agents

Electrospun nanofibers have been enhanced with silver nanoparticles (AgNPs) and natural extracts to improve their wound healing properties. However, the current literature lacks clear guidance on which of these agents is superior or which carries more potential side effects. According to [22, 21], while AgNPs demonstrate strong antibacterial properties, they also present toxicity issues at higher concentrations, which can harm healthy skin cells. In contrast, natural extracts and bio-based agents like chitosan are reported to have lower toxicity and higher biocompatibility than metallic nanoparticles, though they exhibit less antibacterial effectiveness. A detailed comparison of these agents, considering their modes of action, longevity, and biocompatibility, would be valuable in identifying the most suitable antibacterial agents for different types of wounds.

### Biocompatibility of Electrospun Nanofibers

Bio-based polymers, or biopolymers, are organic macromolecules synthesized by living organisms. Biopolymers sourced from plants (cellulose, lignin), animals (collagen, chitin, chitosan), microorganisms (bacterial cellulose, PHA), and biotechnological processes (polylactides) have shown significant promise in biomedical applications, including drug delivery, tissue engineering, and wound healing due to their unique properties. Many biopolymers possess characteristics such as antibacterial, antifungal, antiviral, low immunogenicity, renewability, biodegradability, and excellent biocompatibility [26]. Cellulose is a natural, biodegradable, environmentally friendly biopolymer that plays a crucial role in a variety of biomedical applications, including tissue repair scaffolds, wound dressings, artificial tissue/skin, controlled drug delivery, blood purification, and cell culture materials [12, 27]. Its moisture-retaining properties are especially beneficial in wound care, as moist wounds heal faster by supporting the delivery of growth factors essential for tissue regeneration. The porous structure of cellulose also aids in tissue regeneration by mimicking the extracellular matrix (ECM) of the skin [28].



### Role of Bio-Based Polymers in Wound Healing

Electrospinning is a promising technique for producing cellulose nanofibers or various polymer/cellulose blends, including blends with nanoparticles. This method enhances the functional properties, particularly antimicrobial activity, to prevent wound site infections [29]. Nanofibrous nonwovens have a high surface area and highly interconnected porous structures, which are naturally suitable for wound healing applications. These structures facilitate a high capacity for exudate absorption and adequate gas exchange [30,31]. Additionally, cellulose scaffolds can carry bioactive components such as anti-inflammatory and antimicrobial agents, which further enhance their healing potential. Chitin and chitosan, the deacetylated form of chitin, are polysaccharides with well-documented antimicrobial, biocompatible, and hemostatic properties [32,33]. Chitosan accelerates the wound-healing process through macrophage activation. It also helps develop granulation tissue by promoting the migration of polymorphonuclear neutrophils (PMNs) early in the healing process. Min et al. used electrospinning to fabricate chitin and chitosan nanofibrous matrices for wound dressing applications, employing 1,1,1,3,3,3-hexafluoro-2-propanol (HFIP) as a spinning solvent. However, the mechanical properties of pure electrospun chitosan are insufficient, limiting its application [28]. Blend electrospinning is a solution to overcome this limitation, allowing for improved mechanical characteristics [34].

### Environmental and Cost Implications

The use of PLA (polylactic acid) or PCL (polycaprolactone) in electrospun nanofiber formation presents both environmental and cost challenges. While cellulose and chitosan are environmentally sustainable, being renewable and biodegradable, concerns remain regarding the raw materials used, as they may be non-renewable. Additionally, by-products from the synthesis process could be harmful. Researchers have indicated that while these synthesized materials exhibit superior mechanical properties, the environmental footprint and sustainability issues still need to be addressed [27]. Furthermore, [4] emphasized the importance of developing a cost-efficient method for large-scale production of electrospun nanofibers to enable more widespread clinical applications. To achieve a more sustainable and cost-effective approach in developing these materials, future studies should focus on conducting life-cycle assessments and evaluating costs as the foundation for advancing these technologies.

### Advanced Functionalization Techniques

The electrospinning process offers significant flexibility for incorporating bioactive agents and enhancing the functionality of nanofibers. However, the current article does not provide much detail on novel methods such as stimuli-responsive materials or the integration of growth factors. For example, [34] proposed blending chitosan with agarose, which could enhance the properties of the resulting fibers. In another study, [17] demonstrated that core-shell structures could effectively protect and release drugs in a controlled manner. Temporary structures, such as temperature-sensitive or pH-responsive fibers, hold great promise for creating versatile wound dressings that can adapt to the dynamic conditions of the wound healing process. Moreover, directly incorporating bioactive molecules such as anti-inflammatory agents or growth factors into the electrospun fibers could significantly improve their therapeutic performance, advancing wound healing outcomes [20].

### Patient-Specific Applications

One area not fully addressed in the article is the development of wound healing materials tailored for individual patients. Specific wounds, such as diabetic ulcers, burns, or other chronic wounds, require dressings with specialized characteristics, such as enhanced bactericidal activity or increased hydrophilicity. Yang et al. demonstrated that electrospun nanofibers are well-suited for fabricating stimuli-sensitive scaffolds with tunable pore size, drug delivery capabilities, and mechanical properties. Additionally, the study by [18] suggests that the fiber diameter and composition can be modulated to meet specific wound care needs, including minimizing scar formation or promoting angiogenesis. This highlights the potential for personalized wound care, where integrating patient-specific design requirements—such as through 3D printing techniques or altering polymer blends—could transform electrospun nanofibers into highly versatile wound healing solutions.

### Findings

1. **Electrospun Nanofibers for Wound Healing**: These nanofibers exhibit exceptional properties that replicate the ECM, enhancing cell adhesion, proliferation, and differentiation, crucial for tissue regeneration. Their ability to mimic the ECM structure provides an ideal scaffold for wound healing.
2. **Core/Shell Nanofiber Structures**: Core/shell electrospun fibers have emerged as valuable platforms for drug delivery systems. These fibers protect and release therapeutic agents such as antibiotics and growth factors, offering controlled and sustained delivery, enhancing wound healing efficacy.

3. **Antibacterial and Biocompatibility Properties**: Electrospun nanofibers enhanced with antimicrobial agents, particularly silver nanoparticles (AgNPs), demonstrate superior antibacterial activity. However, concerns about toxicity at higher concentrations necessitate further investigation. Natural biopolymers such as chitosan and cellulose show excellent biocompatibility and promise for infection prevention with minimal toxicity.
4. **Challenges in Clinical Validation**: Although electrospun nanofibers exhibit promising results in preclinical studies, the lack of extensive clinical trials poses a barrier to their widespread adoption in clinical settings. Phase III trials are essential to assess their safety, efficacy, and practicality in wound care.
5. **Mechanical Properties and Long-Term Stability**: The mechanical properties of electrospun nanofibers, including tensile strength and degradation rates, are crucial for their long-term effectiveness in wound healing. While some materials maintain suitable properties for the early stages of healing, long-term stability, especially in chronic wounds, remains a challenge.



## CONCLUSION

Electrospun nanofibers represent a groundbreaking advancement in wound care, offering enhanced tissue regeneration, antibacterial properties, and the potential for controlled drug delivery. Their ability to mimic the extracellular matrix (ECM), integrate bioactive agents, and provide a conducive healing environment makes them promising candidates for modern wound care solutions. However, challenges such as a lack of comprehensive clinical data, long-term stability, and optimization of drug delivery systems remain. This review emphasizes the potential of electrospun nanofibers in enhancing cell growth, attachment, and differentiation, while also addressing key limitations that must be overcome for clinical application. Further clinical trials are required to confirm their safety and effectiveness, as well as to better define their long-term stability and degradation characteristics in dynamic physiological environments. There is also a need for more comparative studies on the efficacy, toxicity, and mechanisms of various antimicrobial agents incorporated into the nanofibers. Environmental and cost considerations in the production of electrospun nanofibers have not been sufficiently addressed and warrant further investigation. Additionally, the development of advanced functionalization strategies, including redox-sensitive, pH-sensitive, and growth-factor-incorporated nanofibers, could expand their applications in personalized medicine. The potential for using electrospun nanofibers in chronic wound therapy and various tissue healing needs presents promising avenues for future development. Finally, while electrospun nanofibers show significant promise in wound healing, closing existing gaps particularly in clinical use, environmental impact, and individual variations will be crucial for maximizing their potential and revolutionizing regenerative medicine. Future research should focus on these aspects to ensure the widespread, effective use of electrospun nanofibers in wound care.

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