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Advances in Antibiotic-Loaded Nanofibers for the Treatment of Bone Infections: A Review

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ABSTRACT

Antibiotic-loaded nanofiber-based drug delivery systems offer a solution for treating complex bone infections, particularly osteomyelitis caused by Methicillin-resistant *Staphylococcus aureus* (MRSA). The incidence of MRSA infections has risen during the COVID-19 pandemic, driven by factors such as increased antibiotic use, healthcare disruptions, and extended hospital stays, which have facilitated the spread of resistant strains. These nanofiber systems enable localized, sustained drug release, reducing systemic side effects and mitigating the development of resistance. This review highlights recent advancements in electrospun nanofibers, particularly those using biodegradable polymers like Poly(lactic-co-glycolic acid) (PLGA) and Polycaprolactone (PCL), which ensure controlled release and support bone regeneration. A systematic review following PRISMA guidelines identified 42 relevant studies from ScienceDirect and ACS Publications databases (2020-2024). The incorporation of bioactive agents, such as hydroxyapatite, enhances antibacterial properties and accelerates tissue regeneration. These findings suggest that antibiotic-loaded nanofibers offer a targeted, effective alternative to conventional treatments, especially for osteomyelitis and other challenging bone infections. Future research will focus on optimizing nanofiber formulations to better address clinical needs and improve personalized treatment strategies for bone infections.

INTRODUCTION

Nanotechnology has significantly impacted various fields in pharmacy, particularly in drug delivery, with nanofibers emerging as a promising platform. Nanofibers, especially those produced via electrospinning techniques, have shown substantial potential in medical applications, such as drug delivery and tissue engineering (Bishnoi et al., 2023; Chou et al., 2022). The structure of nanofibers, resembling the extracellular matrix (ECM), is beneficial for supporting cell adhesion, proliferation, and differentiation, thereby enhancing the healing process of damaged tissues (Bishnoi et al., 2023; Gill et al., 2023).

Bone infections, such as osteomyelitis, often caused by *Staphylococcus aureus*, pose significant clinical challenges due to bacterial resistance to antibiotics and their ability to form biofilms. These biofilms protect bacteria from the effects of conventional antibiotic therapies (Yekani et al., 2023). As a result, systemic antibiotic administration approaches often ineffective and can lead to significant side effects, including the risk of antibiotic resistance and the risk of toxicity (Boncu et al., 2020; Kamal et al., 2022). Antibiotic resistance, notably MRSA, escalated during and after the COVID-19 pandemic. Prolonged antibiotic use, extended hospital stays, and disruptions in healthcare

systems contributed to the emergence and proliferation of resistant strains, including MRSA, complicating infection management and therapeutic interventions (Aslam et al., 2023).

Nanofibers loaded with antibiotics offer a solution for controlled and localized drug release in infected areas. Biodegradable polymers, such as poly(D, L-lactide-co-glycolate) (PLGA) and poly(ε-caprolactone) (PCL), are frequently selected for the fabrication of these nanofibers due to their biocompatibility, biodegradability, and flexibility (Boncu et al., 2020; Sun et al., 2023). For instance, PLGA decomposes into lactic acid and glycolic acid, which are naturally metabolized by the body, making it highly suitable for long-term drug delivery systems in treating bone infections (Buck et al., 2018; Téllez Corral et al., 2024).

Research indicates that PLGA-based nanofibers loaded with antibiotics exhibit effective antibacterial activity, even against resistant strains like MRSA, a common cause of chronic osteomyelitis (Gao et al., 2016; Yekani et al., 2023). Incorporating PLGA in nanofibers allows for sustained drug release, maintaining therapeutic concentrations at the infection site for several days to weeks, thereby enhancing therapeutic efficacy without requiring repeated antibiotic administration (Silva et al., 2022)

In addition to PLGA, other polymers, such as PCL, are also widely utilized in this application. PCL possesses good mechanical strength and can be combined with osteoinductive materials such as hydroxyapatite to support bone regeneration while treating infections (Dehkordi et al., 2022; Rezk et al., 2019). The combination of PLGA, hydroxyapatite and linezolid provides dual benefits, addressing the infection while accelerating the healing process of damaged bone tissue (Ke re mu et al., 2024). Electrospinning has produced nanofibers with various tunable properties, such as fiber diameter, porosity, and drug release profiles (Hartatiek et al., 2020; Raizaday & Chakma, 2024). This technology facilitates the integration of drugs and growth factors into the nanofiber structure, creating a highly effective drug delivery system for treating chronic or hard-to-heal bone infections (Silva et al., 2023). The use of antibiotic nanofibers in the treatment of osteomyelitis offers significant advantages over systemic approaches. Localized drug release reduces the risk of side effects and minimizes the likelihood of antibiotic resistance due to more controlled and targeted drug exposure (Silva et al., 2022, 2023).

This narrative review aims to explore recent advancements in the use of biodegradable polymer-based nanofibers for the treatment of bone infections. The primary focus is on innovations in nanofiber technology as an antibiotic drug delivery system, electrospinning processes, and the characterization of nanofiber formulations, as well as drug release mechanisms. By integrating findings from various studies, this review seeks to provide an in-depth understanding of the potential of nanofibers as a more effective and innovative approach to bone infection treatment.

METHODS

The literature search for this narrative review was conducted using two primary databases, ScienceDirect and ACS Publications, covering the period from 2020 to 2024. This period was chosen to reflect the surge in antibiotic resistance cases observed during and after the COVID-19 pandemi. A total of 1,034 articles were found in ScienceDirect and 302 in ACS Publications. During the identification stage, 159 articles relevant to the topic were selected. Further selection was done using inclusion and exclusion criteria, excluding journals that did not address antibiotics, did not involve biodegradable polymers, or were solely narrative reviews, leaving 42 relevant articles for review.

The PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) approach was employed in the literature selection and review process. Each article in the screening phase was assessed based on its relevance to the established keywords: nanofiber, antibiotics, biodegradable, and bone infections. The inclusion phase was performed to identify research articles focusing on developing antibiotic-loaded nanofibers as an alternative treatment for bone infections. The exclusion process eliminated articles that did not meet the criteria, such as those that did not use biodegradable polymers or did not include antibiotics as a primary component of the nanofibers. The results of this process are summarized in a PRISMA flow diagram, illustrating the number of articles at each selection stage, as shown in **Figure 1.**

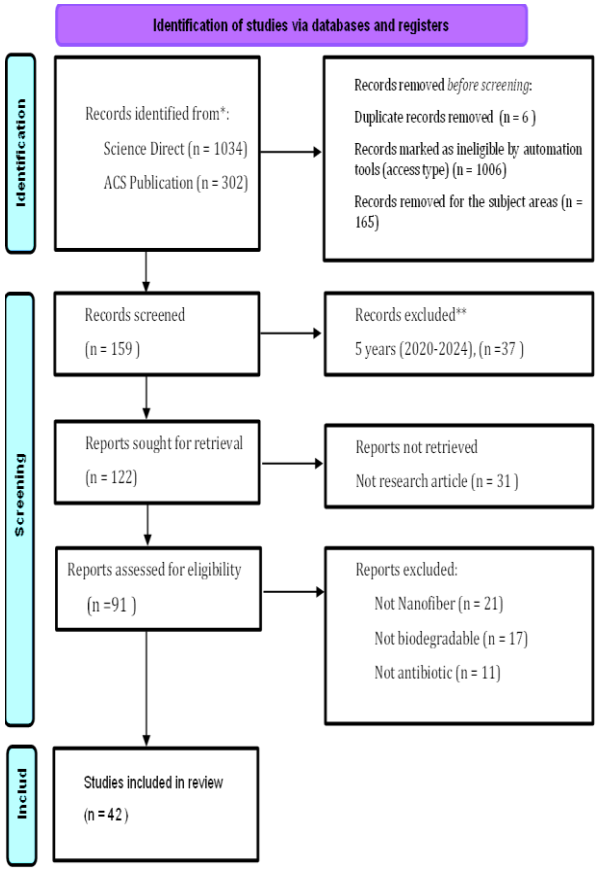

Figure 1. Review Strategy Scheme

RESULT AND DISCUSSION

Nanofibers as a Replacement for Extracellular Matrix (ECM)

Nanofibers have emerged as promising substitutes for the extracellular matrix (ECM) in bone infection treatments, owing to their ability to replicate the natural ECM's complex nanoscale structure, which is essential for cell adhesion, proliferation, and differentiation during tissue regeneration (Gill et al., 2023). The ECM serves as a scaffold for cellular interactions and biochemical signaling, crucial for tissue regeneration. Engineered nanofibers can mimic these functions, with the added advantage of being customizable to meet the biological and mechanical requirements of bone tissue (Niveditha et al., 2024; Raizaday & Chakma, 2024)

Nanofibers, with sizes similar to collagen fibrils in the ECM, promote cell adhesion more effectively than conventional materials. For instance, PCL-based electrospun nanofibers, known for their biocompatibility and biodegradability, hold significant promise in bone regeneration, though their hydrophobicity can limit cell adhesion (Chandika et al., 2021). This limitation is addressed by incorporating bioactive materials like hydroxyapatite (HAp), which enhances osteoconductive properties and accelerates bone healing (Udomluck et al., 2020; Xiang et al., 2022).

Studies have shown that incorporating nanomaterials into nanofiber matrices improves their functionality in supporting bone regeneration. For example, vanadium and strontium co-doped HAp in PCL nanofibers improves mechanical strength and promotes cell adhesion and proliferation. Additionally, metal ions provide antibacterial properties, preventing bacterial colonization and supporting tissue regeneration in infected bone areas (Megha et al., 2024). Nanofibers are capable of imitating the functional characteristics of the ECM, such as controlled drug release. Antibiotic-loaded nanofibers, including those with Vancomycin, inhibit bacterial growth while promoting bone healing (Yekani et al., 2023).

Table 1 summarizes studies on nanofibers used as ECM substitutes in bone regeneration and infection treatment. These studies explore the use of synthetic and natural polymers combined with bioactive agents like antibiotics or antimicrobial peptides to enhance nanofiber functionality in tissue growth. Additionally, cell compatibility tests ensure the biocompatibility of these materials, confirming their potential for clinical application in bone healing and infection management.

Antibiotic Nanofibers as an Alternative Treatment for Infections

Antibiotic nanofibers offer an effective solution for treating osteomyelitis by enabling targeted drug delivery through controlled release, reducing the need for systemic antibiotics. Vancomycin-loaded Eudragit nanofibers have shown success in inhibiting bacteria linked to osteomyelitis(Abdel-Rahman et al., 2020). In addition to Vancomycin, other studies have demonstrated that cephalexin loaded in polyhydroxy butyrate-co-hydroxy valerate (PHBV) nanofibers provides significant inhibition against *Staphylococcus aureus* (Kamal et al., 2022).

One of the primary challenges in treating osteomyelitis is the need to avoid reoperations for implant removal after healing. Biodegradable antibiotic nanofibers, such as those made from PCL, offer a solution with their ability to naturally degrade within the body after

delivering the necessary antibiotic dosage (Zafari et al., 2020). In the context of osteomyelitis, antibiotic nanofibers enable the implementation of single-use implants that do not require further surgery for removal due to their biodegradable nature and long-term therapeutic effectiveness, particularly in cases of chronic infections (Silva et al., 2022). With further development, these antibiotic-based nanofibers have the potential to revolutionize the treatment of osteomyelitis, offering more practical and convenient therapeutic solutions for patients.

Table 1. Summary of Studies Utilizing Nanofibers as ECM Substitutes in Bone Regeneration and Infection Treatment

Nanofiber Material	Application	Advantages as ECM Mimic	Cell Compatibility Results	Refference
Polycaprolactone (PCL) + Hydroxyapatite (HAp) co-doped with Vanadium and Strontium	Bone tissue engineering, osteoconductivity enhancement	Improving mechanical strength, osteoconductivity, and cell adhesion	Rat bone marrow stromal cells (rBMSC): Enhanced ALP activity and cell adhesion	(Megha et al., 2024)
Eudragit-based nanofiber + Vancomycin	Antibacterial wound healing, tuneable drug release	Controlled drug release, antibacterial properties to prevent infection	Enhanced wound healing efficacy with antibacterial activity	(Abdel-Rahman et al., 2020)
Polyvinyl Alcohol (PVA) + Chitosan + β-Cyclodextrin capped Zinc Sulphide (ZnS) nanoparticles	Antibacterial, antifungal, antioxidant properties for wound healing	Accelerating wound healing, mimicking structural and functional properties of ECM	NIH3T3 cells: Enhanced cell migration, promoting wound healing activity	(Niveditha et al., 2024)
Chitosan nanofibers	Wound healing, drug delivery	High biocompatibility, promoting tissue regeneration	Fibroblast cells: Enhanced tissue regeneration	(Kumar et al., 2023)
Polycaprolactone (PCL) + Carrageenan + Microalgal peptides	Antibacterial and wound healing	Promoting cell proliferation with antimicrobial peptides	HEK 293 cells: Increased cell viability, high biocompatibility	(Raghunathan et al., 2024)
Silk Fibroin + Copper nanoparticles	Bone regeneration, antibacterial scaffold	Enhancing osteoconductivity and antibacterial activity	Osteoblast cells: Enhanced bone regeneration and antibacterial properties	(Khan et al., 2024)
Polyvinylpyrrolidone (PVP) and Cyclodextrin (CD)	Antibacterial and wound healing	antibacterial activity	human dermal fibroblasts (HFF-1)	(Alsulami et al., 2024)

Nanofibers Qualities for Bone Infections

At least for quality nanofibers must possess in treating bone infections such as osteomyelitis in clinical settings. Biocompatibility is one of the most essential properties, it ensures the material can integrate with biological tissues without eliciting adverse immune reactions. For example, polymer-based nanofibers like PLGA and PCL have been shown to support cell growth while possessing properties that promote bone tissue regeneration (Boncu et al., 2020; Qian et al., 2019). Combining PLGA with Chitosan, for instance, has enhanced cell adhesion and accelerated the healing process in infected wounds (Ajalloueian et al., 2014).

Biodegradability is also an essential characteristic. PLGA-based nanofibers can be degraded in the body eliminating further surgeries to remove implants after complete healing (Badaraev et al., 2023). The hydrolytic

degradation of PLGA occurs in four stages: (1) hydration, where water penetrates the copolymer and disrupts hydrogen bonds; (2) initial degradation, where covalent bonds break, reducing molecular weight; (3) constant degradation, where further bond cleavage from the polymer backbone leads to mass loss and decreased integrity; and (4) solubilization, where polymer fragments are broken down and dissolved in the surrounding aqueous medium. PLGA with high molecular weight and an amorphous structure are effective drug carriers, enabling sustained release over one to six months (Badaraev et al., 2023).

The incorporation of multiple polymers into nanofibers can enhance porosity and their ability to support tissue regeneration (Kumar et al., 2023; Udomluck et al., 2020). Moreover, the nanofiber must be strong enough to mechanically support damaged tissue, especially in bone applications. The combination of PLGA or PCL with materials such as hydroxyapatite (HAp) has significantly enhanced the mechanical strength of nanofibers while preserving the flexibility essential for bone regeneration (Megha et al., 2024). Similarly, composite materials, including combinations of PCL and silk fibroin or those augmented with dopant materials such as strontium, have demonstrated improvements in structural strength while simultaneously supporting bone tissue regeneration. Although biodegradable polymers commonly employed in nanofiber fabrication exhibit lower mechanical strength compared to non-degradable materials. Overall, the characteristics of quality nanofibers include biocompatibility, biodegradability, porosity, controlled drug delivery capability, and mechanical strength. Nanofibers designed with these characteristics provide superior solutions for treating bone infections and supporting tissue regeneration in clinical applications.

Electrospinning Method in Nanofiber Production

The electrospinning method has become a widely utilized technique for fabricating nanofibers in various biomedical applications, including tissue regeneration and drug delivery. This process involves the application of a high voltage that draws a polymer solution to form fibers with diameters ranging from nanometers to micrometers, creating nanofibers with high surface area and controllable porosity (Hsiung et al., 2023). Research by Zhao et al.(2021) has shown that nanofibers produced via electrospinning are highly effective in supporting cell proliferation and tissue regeneration, particularly when combined with bioactive agents such as antibiotics and growth factors. The addition of black phosphorus nanosheets to PCL-based nanofibers has been found to provide antimicrobial properties (X. Zhang et al., 2023).

Polymers such as PCL and PLGA are widely employed in the treatment of bone infections and tissue regeneration. Scaffolds made from PLGA support bone tissue regeneration and deliver drugs locally to address infections. PLGA-based nanofibers modified with gentamicin have effectively controlled antibiotic release and supported faster wound healing. Modifying the morphology of fibers by adjusting parameters such as voltage, flow rate, and the distance between the needle and collector plays a crucial role in the structure of the resulting nanofibers. Higher voltages typically produce finer fibers with better porosity, which is particularly beneficial for bone regeneration (Sun et al., 2023). The electrospinning process and characteristics of antibiotic-based nanofibers can be seen in **Table 2.**

The **Table 2** presents the characteristics of antibiotic-based nanofibers produced via the electrospinning process. The polymers used include Eudragit, PHBV, PCL, PLA, PLGA, and their composites, exhibiting properties such as controlled drug release (Vancomycin-Eudragit, PVA/PEO), rapid degradation (Cephalexin-PHBV), and high biocompatibility (Metronidazole-PLA stereo complex). PLGA demonstrates high mechanical strength (Amoxicillin) and sustained drug release (Linezolid). Process parameters vary, including flow rates (0.2–2.8 mL/h), voltage (10–30 kV), and distance (8–20 cm). Key characterization instruments are SEM, FTIR, and DSC, revealing surface morphology, chemical structure, and thermal properties. This study highlights the potential of biodegradable nanofibers for sustained antibiotic release and effective infection control.

Table 2. Electrospinning Process and Characteristics of Antibiotic-Based Nanofibers

Antibiotic	Polymer	Flow rate (mL/h)	Voltage (kV)	Distance (cm)	Mechanical Strength (MPa)	Biodegradability of Polymer	Nanofiber Characteristics	Characterization Instrument	References
Vancomycin	Eudragit	1.0	20	15	0.724	Moderate	Controlled drug release, antibacterial	SEM	(Abdel-Rahman et al., 2020)
Cephalexin	PHBV	0.5	17	15	4.2-8.4	High	Fast degradation, antibacterial	SEM, FTIR	(Kamal et al., 2022)
Azithromycin	PCL	1.5-2.8	19-21	10-13	10.68-19.26	Moderate	Sustained drug release	SEM, FTIR	(Alimohammadi et al., 2022)
Metronidazole	PLA stereocomplex	1.0	15	15	3.9-12.9	Moderate	Biodegradable and good biocompatibility	SEM, DSC, FTIR	(Srithep et al., 2021)
Linezolid	PLGA and PLGA/PCL	0.75-2.0	12-14	15	2.56-3.02	Moderate	Sustained release, strong antibacterial	SEM, DSC	(Boncu et al., 2020)
Amoxicillin	PLGA	0.5	18	15	1250	High	Biodegradable, effective for long-term infection control	SEM, FTIR	(Chou et al., 2022))
Vancomycin	PVA, PEO	0.2-1.5	10-30	8-20	NA	Moderate	Controlled and Sustained release	SEM, FTIR, TGA	(Serpelloni et al., 2024)
Vancomycin	PLA	0.5	18.5	10	NA	Moderate	Sustained drug release, antibacterial	SEM, FTIR	(Silva et al., 2023)

The electrospinning technique used to create core-shell structured nanofibers provides better control over drug release, particularly in clinical applications. Nanofibers with this structure allow for drug delivery within the core layer of the fiber, while the outer layer offers protection that prevents rapid drug release (Lopes Gama e Silva et al., 2023). These scaffolds are essential in treating bone infections like osteomyelitis, as they facilitate better bone regeneration without requiring scaffold removal through additional surgery (X. Zhang et al., 2023). A depiction of the electrospinning process is illustrated in **Figure 2.**

Utilization of Biodegradable Polymers as Nanofiber Matrices

The use of biodegradable polymers in developing nanofiber matrices has become a major focus in biomaterial research, particularly for biomedical applications such as tissue regeneration and drug delivery. Biodegradable polymers, such PLGA and PCL, have the primary advantage of being able to degrade within the body into non-toxic products, thus eliminating the need for further surgery to remove scaffolds after therapy completion (Qian et al., 2018). In this context, biodegradable polymers serve as ideal matrices for nanofiber applications designed for localized drug delivery and tissue regeneration, especially in treating bone infections like osteomyelitis.

PCL is often utilized due to its slow degradation rate, allowing PCL-based scaffolds to remain stable during tissue regeneration. Additionally, PCL exhibits good biological compatibility, supporting cell growth, and can be modified with various bioactive materials to enhance its antimicrobial and osteogenic properties (Afshar et al., 2024; Sam et al., 2023). The incorporation of antibiotics such as gentamicin into PCL-based nanofibers through the electrospinning method has proven effective in controlling localized infections and accelerating wound healing (Sun et al., 2023). On the other hand, PLGA is known for its faster degradation profile compared to PCL, making it frequently used for applications requiring more rapid drug delivery.

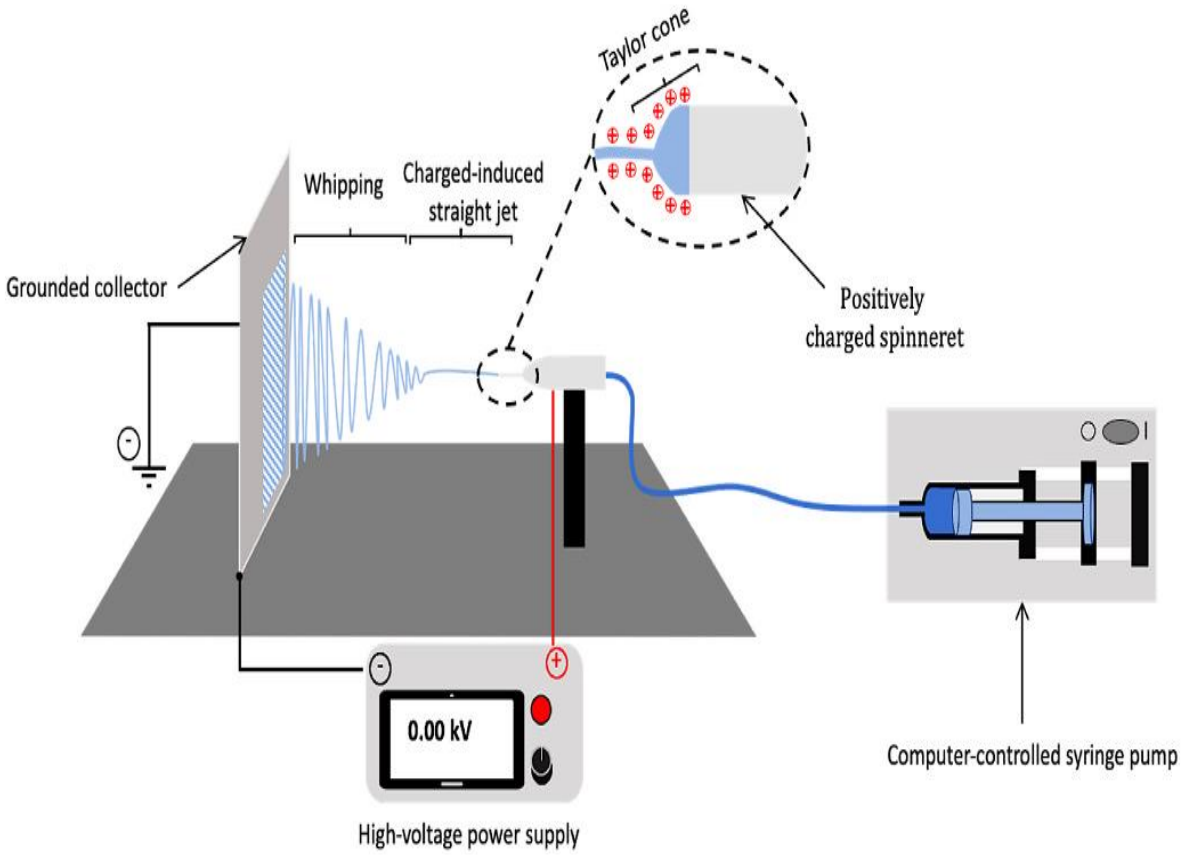

Figure 2. Nanofiber Fabrication Using the Electrospinning Method (Abdulhussain et al., 2023)

The utilization of biodegradable polymers also involves various modifications to enhance therapeutic efficacy. For instance, the incorporation of essential oils and vitamin A palmitate into cellulose acetate-based nanofiber matrices has significantly improved antibacterial properties and wound healing (Akturk, 2023). Another study by Sen (Sen et al., 2023) indicated that the use of smart hydrogels applied to biodegradable polymer-based nanofibers can provide responses to infections and accelerate wound healing more dynamically. Overall, using biodegradable polymers in nanofiber development shows great potential in enhancing biomedical therapy. The combination of biodegradability with the ability to modify matrices to incorporate various bioactive substances, such as antibiotics and wound healing agents, makes polymers like PCL and PLGA ideal candidates for tissue regeneration and localized drug delivery applications. The characteristics and applications of biodegradable polymers can be seen in **Table 3.**

Table 3. Characteristics and Applications of Biodegradable Polymers

Polymer	Biodegradation Rate	Degradation By products	Biocompatibility	Biodegradability Characteristics	Applications	References
Polycaprolactone (PCL)	Slow (months to 1 year)	CO_2, H_2O	Excellent	Slow degradation, suitable for long-term scaffold applications	Bone Tissue Engineering, Drug Delivery	(Dehkordi et al., 2022; X. Zhang et al., 2023)
Poly(lactic-co-glycolic acid) (PLGA)	Moderate (months to 1 year)	Lactic Acid, Glycolic Acid	Good	Moderate degradation, ideal for localized drug delivery	Wound Healing, Drug Delivery, Bone Regeneration	(Gentile et al., 2014; Téllez Corral et al., 2024)
Polylactic Acid (PLA)	Moderate (months)	Lactic Acid	Good	Biodegradable, degrades into lactic acid	Wound Healing, Drug Delivery	(Al-Wafi et al., 2021)
Polyhydroxybutyrate (PHB)	Moderate (months to 1 year)	Hydroxybutyric Acid	Good	Moderate degradation, biocompatible for clinical use	Drug Delivery, Sutures	(Mohammadalipour, Asadolahi, et al., 2022; Mohammadalipour, Karbasi, et al., 2022)
Cellulose Acetate	Fast (weeks)	CO_2, H_2O	Excellent	Rapid degradation, environmentally friendly, plant-based	Wound Healing, Drug Delivery	(Akturk, 2023; Sofi et al., 2021)
Gelatin	Fast (weeks)	Amino Acids	Good	Fast degradation, suitable for temporary applications	Tissue Scaffolds, Wound Healing	(Yekani et al., 2023)
Chitosan	Moderate (weeks to months)	Glucosamine	Moderate	Moderate degradation, biodegradable, supports cell adhesion	Tissue Engineering, Wound Healing	(Lin et al., 2022; S. Zhang et al., 2024)

Table 3 provides a comprehensive overview of the characteristics and applications of various biodegradable polymers used in biomedical engineering and related fields. Polymers such as PCL, PLGA, and Polylactic Acid (PLA) exhibit differing biodegradation rates, ranging from slow (2-3 years) to moderate (months to 1 year), producing byproducts such as CO2, H2O, lactic acid, and glycolic acid. These byproducts are non-toxic, contributing to the excellent biocompatibility of the polymers, making them ideal for various medical applications. For

instance, PCL's slow degradation rate makes it suitable for long-term scaffold applications in bone tissue engineering, while the moderate degradation rates of PLGA and PLA favor their use in drug delivery systems and wound healing. Fast-degrading polymers like cellulose acetate and gelatin are preferred for temporary medical applications such as wound dressings and tissue scaffolds. These polymers' ability to degrade into non-toxic byproducts while supporting cell adhesion and regeneration underscores their potential for advancing regenerative medicine and drug delivery technologies.

Effectiveness of Nanofibers in Addressing Osteomyelitis and MRSA

The treatment of osteomyelitis, particularly in cases of bone fractures, poses significant challenges in the medical field. Bone infections, especially those caused by MRSA, are difficult to manage due to the presence of bacterial biofilms that protect the pathogens from antibiotics. The use of nanofibers in this therapy offers an effective solution due to their ability to provide targeted and controlled drug release in infected areas, as well as their capacity to penetrate bacterial biofilms (Silva et al., 2022).

In cases of bone fractures accompanied by osteomyelitis, nanofibers can serve as biodegradable scaffolds that not only deliver antibiotics such as Vancomycin and gentamicin but also support the regeneration of infected bone. For instance, studies have shown that antibiotic-modified scaffolds based on PCL and PLGA are capable of addressing infections while simultaneously stimulating bone regeneration (Boncu et al., 2020; Qian et al., 2018). The main advantage of this drug delivery system is its ability to maintain effective antibiotic concentrations at the infection site over extended periods, without the need for systemic antibiotic administration, which is often associated with side effects.

In fractures accompanied by osteomyelitis, nanofibers modified with metal nanoparticles such as silver or copper have also proven effective. Research indicates that PCL-based nanofiber membranes modified with silver nanoparticles (AgNPs) not only deliver antibiotics but also leverage the antibacterial effects of the nanoparticles themselves, which can disrupt biofilms and kill infection-causing bacteria (Menazea et al., 2020; Zhao et al., 2023). Additionally, the photothermal properties of these materials can be utilized to activate local immune responses and stimulate bacterial killing through controlled heat, without damaging healthy bone tissue.

The ability of nanofibers to degrade naturally also presents a significant advantage in the treatment of osteomyelitis related to bone fractures. After the drug delivery process is complete and healing progresses, polymer-based nanofiber scaffolds such as PLGA gradually degrade without the need for additional surgical intervention to remove the material. Moreover, these biodegradable polymers also support osseointegration, or the biological integration of new bone with the scaffold, which is critical in cases of fractures accompanied by infection (Silva et al., 2022). Overall, nanofibers provide a comprehensive solution for the treatment of osteomyelitis in cases of bone fractures. With their ability to deliver antibiotics in a targeted manner, disrupt biofilms, and support bone regeneration, nanofibers present an innovative approach that is more effective than conventional antibiotic therapies.

Analysis of Drug Release from Nanofibers

The kinetics of drug release from nanofibers is a critical aspect in determining the effectiveness of drug delivery systems, particularly in controlling the gradual release of the drug. This release profile is influenced by various factors such as the type of polymer, molecular weight, drug concentration, and the electrospinning conditions used. Drug release from nanofibers can follow several kinetic models, including the Higuchi model, Korsmeyer-Peppas model, and zero-order release model, which provide insights into the drug release mechanisms.

The Korsmeyer-Peppas model is frequently employed to evaluate the drug release behavior from nanofiber systems. The exponent value 'n' from this model is used to predict the release mechanism. For example, if the value of 'n' approaches 0.5, Fickian diffusion dominates the release, while values close to 1.0 indicate that the release mechanism is controlled by polymer erosion (Taghe et al., 2024). The mechanisms governing drug release from nanofibrous membranes typically include surface desorption of drug molecules, diffusion through the nanofiber matrix into the surrounding environment, and the degradation of the fibers themselves. These processes play a crucial role in shaping the drug release kinetics over the

entire release duration. The initial rapid release, often observed in nanofibrous membranes, primarily arises from the desorption of drug molecules adhered to the nanofiber surfaces. Moreover, the primary driving force for drug diffusion is the concentration gradient established between the membrane's interconnected nanopores and the surrounding medium (Alimohammadi et al., 2022).

The polymer composition within nanofibers significantly affects the drug release profile. For example, variations in the ratio of PCL to polyethylene oxide (PEO) in composite nanofibers significantly influence the degradation rate and, consequently, the drug release profile. Fibers with a higher PCL content tend to have a slower degradation rate, resulting in a slower drug release (Martin et al., 2022). Similarly, the degradation rate of the PLGA polymer can be modified by adjusting the ratio of lactic acid to glycolic acid. A higher glycolic acid content accelerates degradation and, therefore, enhances drug release (Téllez Corral et al., 2024). The selection of polymer composition allows for precise control over the drug release rate, which is crucial for specific medical conditions requiring rapid or prolonged drug exposure.

The development of biodegradable polymers as nanofiber matrices involves several critical challenges. Selecting suitable polymers with optimal mechanical properties and controlled degradation rates for specific applications remains a complex task. The fabrication process, particularly electrospinning, requires precise control of parameters to achieve uniform fiber morphology. Environmental factors, such as changes in humidity or temperature, can hinder solvent evaporation, causing deformation or bead formation on nanofibers. Ray-leigh's instability may also contribute to bead formation due to disruptions in surface tension at the needle tip (Silva et al., 2023). Nanofibers designed for the treatment of bone infections must possess adequate mechanical strength to ensure their effectiveness in load-bearing applications. A significant limitation of biodegradable polymers commonly utilized in nanofiber fabrication is their comparatively lower mechanical strength relative to non-degradable materials. Managing degradation rates is challenging as they depend on environmental factors such as pH and enzymatic activity. Ensuring the biocompatibility of degradation products is essential, especially for biomedical applications. Furthermore, high production costs and scalability issues hinder broader industrial adoption.

CONCLUSIONS

Nanotechnology, particularly in the form of antibiotic-loaded nanofibers, has introduced innovative solutions for the treatment of chronic bone infections such as osteomyelitis caused by resistant pathogens like MRSA. Nanofibers, designed through the electrospinning method, not only enable localized and controlled drug delivery but also support bone regeneration. The use of biodegradable polymers such as PLGA and PCL enhances the potential of nanofibers in these medical applications due to their biodegradability, which allows for sustained drug release without the need for scaffold removal surgery. Additional modifications with bioactive materials such as hydroxyapatite, Vancomycin, and metal nanoparticles further improve the effectiveness of nanofibers in disrupting bacterial biofilms while supporting tissue healing. With advancements in this drug delivery technology, nanofibers present an attractive and effective alternative in addressing the challenges of treating bone infections, particularly those accompanied by antibiotic resistance and other clinical complications.

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AUTHORS' CONTRIBUTIONS

TI conducted the narrative review, which involved comprehensive literature collection, critical analysis of relevant studies, and drafting the manuscript. NSS, KZ, and TNSS provided supervisory roles, offering guidance and oversight throughout the research process.

CONFLICT OF INTERESTS

The author declare that there is no conflict of interest regarding the publication of this article.

ETHICAL CONSIDERATION

Ethical issues (including plagiarism, data fabrication, double publication, etc) have been completely observed by the author.

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