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SideroGuard: Overview of Siderophore-Enhanced Nanofiber Systems for Biofilm Prevention and Control

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Abstract

In recent years, there has been an incredible increase in scientific innovation in curing biofilms on chronic wounds. Microbial biofilm is an aggregate of microbial cells surrounded by a polymer matrix that may or may not adhere to surfaces, but present in the tissues or secretions. The free iron involves in biofilm formation, delayed wound healing, and may even be responsible for destruction of connective tissue. To minimize the free iron on wound sites to avoid biofilm formation, the use of siderophores and their derivatives were focused. To address this requirement, researchers have developed various techniques such as non-electrospinning and electrospinning techniques for the formation of nanofibers. Electrospinning has confirmed to be an excellent method for the fabrication of nanofibers which gained the interest of biomedical applications. Electrospinning is a current technique in which electric fields are used to produce fine fibers wherein diameter can be reduced to nanometers which has wide application in the field of medicine. The review aims to discuss the importance of electrospun siderophore-based nanofibers as nanohealers for wound biofilm formation.

Keywords: Siderophore, Electrospinning, Nanofibers, Biofilms, Chronic Wounds

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1. Introduction

A wound is a damage to the body's tissues, involving in breaking of skin or underlying structures. Wounds vary in severity, from minor scrapes to more serious injuries like lacerations, puncture wounds, or burns. The causes of wounds can include accidents, trauma, surgical procedures, or medical conditions (1,2). During the past few decades, despite advancements in therapies and wound dressing, the prevalence of chronic wounds continues to rise, especially among populations with conditions like diabetes mellitus or those undergoing immuno-suppressive treatments and biofilm formation of the wound regions. Chronic wounds fail to heal, in the expected time which might take a couple of weeks in some cases (3–6). Alterations of cytokines, growth factors and ECM components at the wound site may also lead to the formation of chronic wounds. Moreover, factors like oxidative damage of free radicals, infection, ischemia and the accumulation of necrotic tissue are also other causes of many non-healing wounds (7,8). Several studies have demonstrated that increased levels of microbial load and microbial biofilm formation distinguish chronic wounds (9). It's evident that biofilm-related issues pose significant challenges in wound healing and connecting the gap between laboratory research and clinical practice is crucial for improving patient outcomes (10–14). While the field lacks a clear standard of clinical practice, several promising strategies are being explored for biofilm management (15). These strategies help to study the advantages and limitations of electrospun nanofibers (11,16). This paper highlights the importance of microbial siderophore nanofibers as effective nanohealers for biofilm formation.

2. Importance of biofilm in wound healing

Biofilms were first reported as animalcules by Anton von Leeuwenhoek. But later it was observed as a suitable surface that facilitates microbial growth wherein, the biological activities were greatly accelerated. Studies on microbial varieties revealed the physical arrangement of the shiny layer which was later named “slime” paved the way for a wider perspective of biofilm interaction. Bill Costerton in 2002 was the first to coin the term “biofilm” which was described as group of microorganisms covered within a self-produced matrix of extracellular polymeric substances (EPS)(17). Extracellular Polymeric Substances are produced by microorganisms to form a defensive and supportive structure around themselves. It is made up of polysaccharides, proteins, nucleic acids, lipids, and other macromolecules. The composition also varies for

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microbial species in relation to environmental conditions, and the stage of biofilm development. This biofilm mainly protects the bacteria from the host immune response and environmental factors like antibiotics, disinfectants, and dehydration. This resistance makes it challenging to eradicate the bacteria causing chronic wounds. Biofilm offers a habitat for microorganisms by establishing a protective environment against the host. Microbes existing in biofilms are more resistant to antibiotics because of gene transfer which provides inter-cellular communication and encourages growth. Biofilm bacteria release the toxins and enzymes that damage host tissues and interfere with cellular signaling pathways involved in wound repair. Chronic inflammation caused by persistent infection further delays healing. Biofilm-associated infections are often recalcitrant to conventional treatments. Traditional antibiotics are less effective against biofilm bacteria due to their limited penetration into the biofilm matrix and the presence of dormant cells within the biofilm (17–19).

Iron plays a vital role in multiple stages of biofilm formation by acting as an important regulator of microbial metabolism, adhesion, quorum sensing, and extracellular polymeric substance (EPS) production. During the initial stage (stage 1–2), iron exists predominantly as ferric iron (Fe^{3+}) bound to host proteins such as transferrin, ferritin, and heme-containing molecules released from damaged tissue. The Surface-associated Fe^{3+} increases microbial attachment thereby increase electrostatic interactions between bacterial cell surfaces and host extracellular matrix components. Several pathogens, including Pseudomonas aeruginosa and Staphylococcus aureus, sense iron availability via iron-responsive regulatory systems (e.g., Fur regulon), which upregulate adhesins and surface proteins essential for irreversible attachment (20,21). During the stage -3 the microcolony formation occurs which requires iron for as a metabolic cofactor, DNA synthesis, respiration, redox homeostasis. At this stage, bacteria actively secrete siderophores which are high-affinity chelators that specifically bind Fe^{3+} from host sources. The iron–siderophore complexes are transported into the bacterial cell through specific outer membrane receptors which supports rapid cell division and also facilitates interspecies competition, as siderophore production limits iron availability to competing microbes, thereby shaping biofilm community structure(22–24). At the of stage 4–5, iron availability directly acts on EPS synthesis and biofilm architecture wherein the elevated levels of Fe^{3+} stimulate the production of polysaccharides such as alginate, Psl, and Pel, which increase biofilm thickness and mechanical stability. Iron also promotes quorum sensing–mediated gene expression, and increases the coordinated biofilm behaviors including

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virulence factor secretion and stress tolerance. In mature biofilms iron undergoes redox cycling between Fe^{3+} and ferrous iron (Fe^{2+}) particularly in chronic wounds.Fe^{2+} generates reactive oxygen species (ROS) which cause host tissue damage and further impair wound healing, while biofilm bacteria remain protected within the EPS matrix (24).In stage 6, iron limitation, often induced by host sequestration mechanisms or therapeutic chelation which downregulates EPS synthesis and promotes motility and planktonic behaviour, facilitating dissemination to new sites. Microbial siderophores such as pyoverdine, Enterobactin, and Desferrioxamine form stable complexes with Fe^{3+} by removing iron from host proteins. Incorporation of siderophore-based systems into wound dressings exploits this mechanism by sequestering free ferric iron at the wound site, thereby reduce biofilm-forming bacteria of an essential micronutrient. This iron restriction disrupts biofilm establishment, reduces EPS production, attenuates virulence, and increase the bacterial susceptibility to host immune defence and antimicrobial agents.

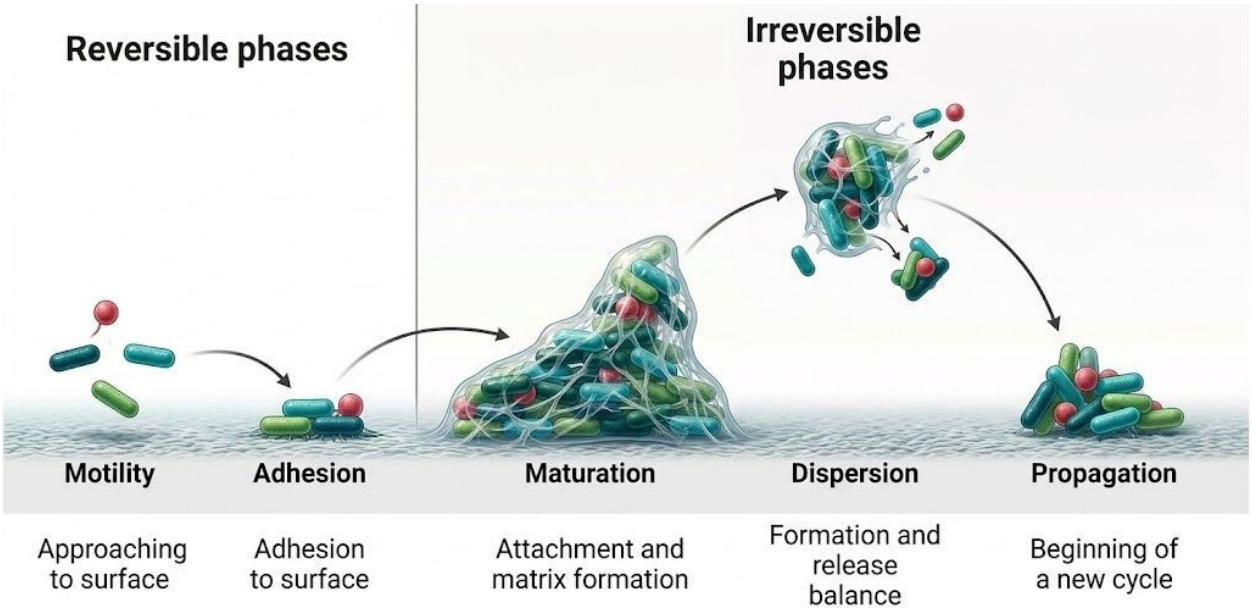

Fig.1. Stages of biofilm formation highlighting iron-dependent maturation relevant to chronic wound environments. Reproduced from Ref. [9] with permission from Frontiers, copyright 2022.

The stages of biofilm are summarized in Fig.1. The more mature biofilms are heterogeneous, having characteristics similar to those of multicellular organisms. Studies reported that formation of biofilms is mainly attributed to the presence of free iron which leads to connective tissue destruction. Iron is an essential micronutrient for cellular processes; however, excess of free iron can pose unique challenges in delaying wound healing(12,13).

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Iron chelators incorporated in the wound dressing materials may hasten the wound healing. Studies reveal that Lactoferrin, an iron chelator in mammals inhibit the formation of biofilms. Similar reports were obtained with synthetic iron chelators (13). The use of microbial siderophore as an iron chelator regulates the biofilm formation. The research reports suggest that incorporation of siderophore-based nanofibers for wound dressings controls the bacterial growth and biofilm formation on chronic wounds (25).

3. Consensus for management of biofilms

Control of biofilms on the wound sites involves a complex method due to their flexibility and capability to resist traditional treatments. The prevention of biofilm is often more effective than treating established biofilms which involves in maintaining good hygiene practices, proper sterilization procedures, and regular cleaning of surfaces to remove biofilm precursors (25). The mechanical methods like brushing, scraping, or flushing, physically disrupt biofilms and are effective for biofilms on surfaces like teeth, medical implants, or industrial equipment (15). The chemical agents are used to break down the biofilm matrix and kills the embedded bacteria which includes enzymes, surfactants, chelating agents, and disinfectants. However, selection of an appropriate agent is crucial as these biofilms are resistant to many antimicrobial compounds. Antibiotics or antimicrobial agents are used to target bacteria within the biofilm (13,16). However, penetration of these agents into the biofilm matrix are limited, and bacteria within biofilms often exhibit increased resistance to antibiotics compared to planktonic (free-floating) bacteria. By combining the different approaches, like physical removal with chemical disruption or antimicrobial therapy, reduce the risk of resistance development. In some cases, using materials that resist biofilm formation can be beneficial (2,16,17). For example, certain coatings or surface modifications discourage bacterial attachment and biofilm formation. One such modification includes the use of microbial siderophore nanofibers as biofilm inhibitors (17). The microbial siderophores hunts the iron components and disrupt the biofilm formation on the wounds. This biofilm wound care is an effective approach to biofilm management which enhances the reduction of microbial load and biofilm burden at the wound sites (18,19).

4. Microbial siderophore types and their chemistry

The types of siderophores are based on the chemical group utilization for iron coordination, leading to three primary classes: catecholates, hydroxamates, and (α-hydroxy-) carboxylates, with

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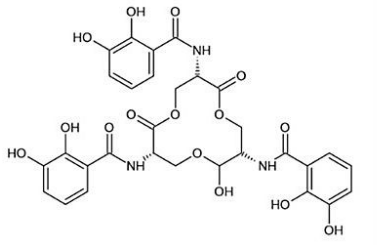
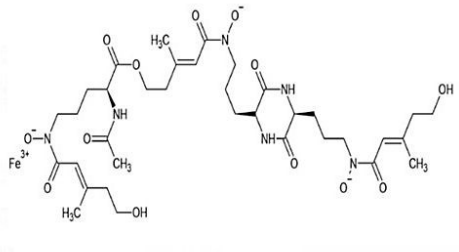
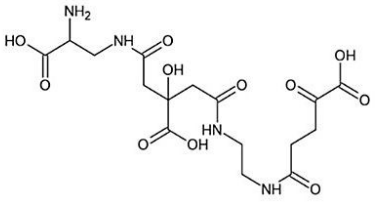
a fourth "Mixed type" incorporating combinations of these groups Fig.2. Catecholate siderophores are a class of siderophores mainly produced by bacteria which contains either mono or dihydroxybenzoic acid residues, which are utilized to chelate iron. These residues are obtained from dihydroxybenzoic acid (20,21). The two main types of catecholate siderophores include monocatecholates, wherein these siderophores contain a single dihydroxybenzoic acid residue used for ferric iron chelation and dicarboxylates siderophores feature two dihydroxybenzoic acid residues for ferric iron binding. Enterobactin is the most well-known example of catecholate siderophores, which fall under the dicarboxylate type (20,22). The hydroxamate siderophores are another class involved in iron acquisition, characterized by hydroxamic acid groups used for ferric iron chelation. These hydroxamic acid were typically derived from amines like lysine or ornithine. There are two main types of hydroxamate siderophores namely monohydroxamate and dihydroxamate (23).



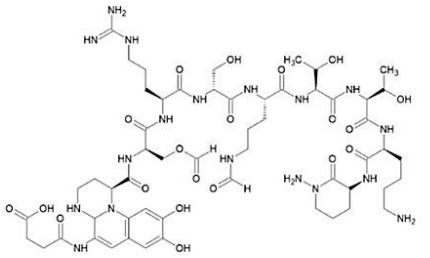
a) Catechol type : Enterobactin



b) Hydroxamate type: Coprogen



c) Carboxylate type: Staphyloferrin



d) Mixed type : pyoverdine

Fig. 2. Structural classification of siderophores and their iron-chelating relevance in biofilm inhibition.

The monohydroxamate siderophores mainly contains single hydroxamic acid group used for iron chelation. These siderophores naturally contain one hydroxamic acid moiety derivative from amino acids such as lysine or ornithine. The examples of monohydroxamate siderophores include ferrichrome, which is produced by various fungi and certain bacteria, for example the

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monohydroxamate rhizobactin 1021 were produced by rhizobia bacteria. These siderophores show a vital role in iron acquisition and are vital for the existence and virulence of many microorganisms. The dihydroxamate siderophores contains two hydroxamic acid groups used for iron chelation. These siderophores contain two hydroxamic acid moieties derived from amino acids such as lysine or ornithine (23). The examples of dihydroxamate siderophores include aerobactin, schizokinen, and alcaligin. Aerobactin is produced by various Gram-negative bacteria which are associated with virulence in certain pathogens. Schizokinen type siderophores are produced by soil-dwelling plant symbionts, while alcaligin type siderophore is produced by certain bacteria and is involved in iron acquisition in both host-associated and environmental contexts. The carboxylate type is characterized by the presence of carboxyl functional groups, which act as oxygen donor atoms to bind iron.

The examples of carboxylate siderophores includes rhizobactin DM415, staphyloferrin A and B, vibrioferrin, fungal rhizoferrin, and bacterial rhizoferrin (24). The mixed-type siderophores are a different class of siderophores which incorporates the different chemical groups for iron chelation. Unlike single-class siderophores like catecholates, hydroxamates, or carboxylates, mixed-type siderophores utilizes the mixture of these groups in their structure(22,23). These class of siderophores determines the versatility of iron coordination, potentially enhancing their efficacy in iron acquisition. However, specific examples and features of mixed-type siderophores vary widely due to their diverse chemical compositions and structural variations (24).

5. Siderophore: Natural iron chelators as a biofilm inhibitor

The history of siderophores is so fascinating for several decades of scientific inquiry and discovery. Siderophores were first discovered in the mid-20th century when researchers observed that microorganisms, particularly bacteria, and fungi, secreted compounds to scavenge iron from their environment. These compounds were termed siderophore ("sidero" for iron and "phore" for carrier) which have small organic molecules with a high affinity for iron to acquire iron from their environment. The siderophores bind tightly to iron ions, forming stable complexes that can be observed by the microbes through the specific transport system on the cell membranes, effectively “stealing” iron from their environment (26). The research work by Jacques Monod and Andre Lwoffon in 1950s revealed that the siderophore produced by microbes to scavenge iron from their surrounding and help them to transport it into the cell, which are very important for their survival

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and growth (27). As research progressed, the biological significance of siderophores became increasingly evident and found to play crucial roles in microbial iron acquisition and also in various ecological processes, including competition between microorganisms for limited iron resources.

Siderophore has drawn attraction to their function in microbial physiology because of their uses in environmental remediation, biotechnology, and medicine. Siderophore-based strategies, have been found to improve wound healing applications and function as innovative antimicrobial agents that target the iron metabolism of bacteria (28). In recent years, siderophores research had continued more than a decade, with a focus on uncovering novel siderophores, explaining their roles in microbial communities, and discovering their latent therapeutic applications, including as antimicrobial agents or as carriers for controlling biofilm formation. The research reports had revealed that Enterobactin (siderophore) produced by *E.coli* were subjected to extensive investigation due to its remarkable ability to bind iron. Its structure features have three catecholate units arranged in C3 symmetry, branching from a chiral triserine lactone backbone. The metal binding units, of siderophore play pivotal roles in forming metal binding complexes was highlighted by the research studies of Pollack et al. in 1970. The macrocyclic structure of the siderophore backbone was elucidated and provided a preorganization that enhances its metal binding ability. which lowers the pH and reducing proton competition, thereby facilitating stable complex formation. The ability of siderophore to form stable complexes with metals had encouraged researchers to explore their potential applications in wound applications (28). Certain research studies reveal that these stable complexes would deplete the availability of iron in the wound area paving a way to reduce the biofilm formation. By harnessing its metal binding capabilities, siderophore holds promise for novel approaches in eliminating the microbial load on wound regions and also eradicating biofilm formation (29). Combining electrospinning with siderophores could involve incorporating siderophores into the polymer solution or melting before electrospinning. This result in the production of nanofibers with siderophores immobilized within the polymer matrix. These nanofibers can be used to capture metal ions from aqueous solutions or as components in wound dressings or tissue engineering scaffolds with enhanced biofilm inhibitor properties due to the iron-chelating ability of siderophores. This approach needs a careful analysis of the compatibility between the siderophores and the polymer used for electrospinning, as well as optimization of the electrospinning process to ensure uniform distribution of the siderophores (30).

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6. Microbial siderophore focus and targeting on biofilm formation

As iron-chelating molecules, siderophores plays an important role in biofilm formation, affecting microbial survival. These molecules scavenge iron from the environment, limiting the bacteria in biofilm of these essential nutrients. By limiting iron availability, siderophores can delay the initial attachment of bacteria to surfaces and consequent biofilm development. At lower concentrations, siderophores primarily inhibit initial bacterial attachment and early biofilm development, while higher concentrations disrupt biofilm maturation, EPS production, and quorum sensing–regulated pathways. Their antibiofilm efficacy is most pronounced under iron-limited conditions, closely resembling host environments. Siderophores also influence bacterial communication systems like quorum sensing, which directs the biofilm formation (31–34). Quorum sensing depends on signaling molecule production and detection to co-ordinate microbial activities such as biofilm growth. Siderophore disrupts the quorum sensing pathways, affecting biofilm formation or structure (34).

As iron-chelating molecules, siderophores plays an important role in biofilm formation, affecting microbial survival by scavenging iron from the environment and limiting the bacteria in biofilm environment. By reducing iron availability, siderophores can delay the initial attachment of bacteria to surfaces and consequent biofilm development. At lower concentrations, siderophore inhibit initial bacterial attachment while at higher concentrations they exhibit the disruption of biofilm maturation, EPS production, and quorum sensing–regulated pathways. Their antibiofilm efficacy is most pronounced under iron-limited conditions, closely resembling host environments. Siderophores also influence bacterial communication systems like quorum sensing, which directs the biofilm formation (31–33). Quorum sensing depends on signaling molecule production and detection to co-ordinate microbial activities such as biofilm growth. Siderophore disrupts the quorum sensing pathways, affecting biofilm formation or structure (34).

In the host environment, iron is tightly controlled as part of nutritional immunity to restrict microbial growth. Pathogenic bacteria-produced siderophores can compete with host iron-binding proteins for iron uptake. The spectrum of activity of siderophores is broad but variable. In bacterial biofilm siderophore can alter the microbial composition and dynamics, causing changes in biofilm structure and their stability. According to various research investigations, it is reported that siderophore-mediated iron uptake is mostly responsible for the antibiofilm activities against Gram-

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negative bacteria such Pseudomonas aeruginosa, Acinetobacter baumannii, and Escherichia coli. Siderophores affect competition and biofilm stability in polymicrobial biofilms by changing the availability of iron. Bacteria manage the host defenses and promote the production of biofilms in host tissues through siderophore-mediated iron uptake. Interactions among the different microbial species are important for biofilm formation influencing interspecies interactions by modulating the iron availability and microbial competition within the biofilm community (35).

Compared with traditional antibiotics these siderophores function as anti-virulence agents by limiting iron thereby killing bacteria and lowering the selective pressure for resistance while exhibiting limited effectiveness against mature biofilms. Siderophores exhibit better biocompatibility and higher iron selectivity than the metal chelators like EDTA, which may unintentionally promote the growth of infections that use siderophores. The quorum sensing inhibitors shows a dual effect on iron metabolism and cell–cell signaling their activity is influenced by environmental iron levels.

Electrospinning nanofiber incorporated with siderophore compounds have good potential to offer numerous benefits wherein these nanofibers physically disrupt the structure of biofilms and making them more susceptible to treatment (36). The siderophores present in the nanofibers chelate iron ions, depriving the biofilm-forming bacteria of their essential nutrient and inhibiting their growth and biofilm formation (37,38). By targeting iron chelation, these nanofibers have a good potential to interfere with bacterial virulence, reducing their pathogenicity and the severity of infections (38).

These siderophores show a promising strategy for antibiofilm control, particularly when it is incorporated into nanofiber-based delivery systems and also when used in combination with antibiotics or enzymatic agents. Their ability to target iron-dependent virulence pathways shows a biologically relevant approach to manage biofilm-associated infections and also recognizing the need for optimized dosing and combination therapies. This approach proves to be more valuable in biofilm-related infections, which often focus on conventional antimicrobial therapies due to the protective nature of the biofilm matrix (39).

7. Medicated nanofibers for biofilm healing

Medicated nanofibers provide an excellent platform for studying biofilm formation. Their properties make them ideal substrates for mimicking various surfaces encountered in medical

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settings (40,41). Researchers use these nanofibers to investigate the initial attachment of microbes, kinetics, and the influence of surface topography on biofilm architecture. The advancement in wound dressing strategies and availability of a wide variety of biomaterials provides impetus in developing wound dressing materials for our desired needs. Such ideal wound dressing strategies include electrospun nanofibers. Nanofibers have gathered significant interest and found numerous applications in medicine and healthcare due to their unique versatility (41,42).

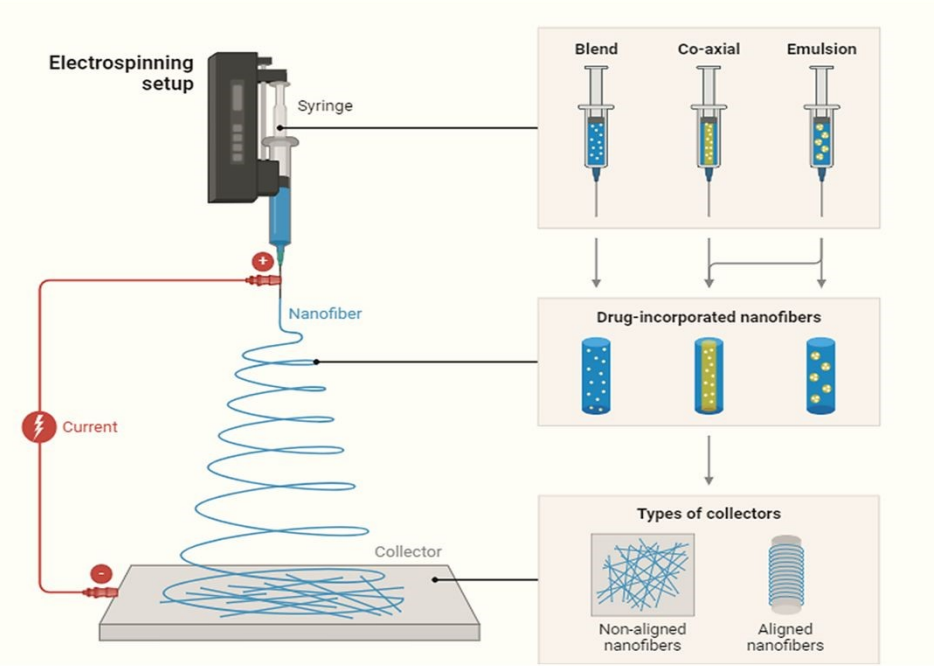

Fig. 3. Schematic representation of electrospinning-based fabrication of siderophore-loaded nanofibers for wound biofilm control.

Nanofibers offer an innovative solution for all medical diagnostic tools. Their unique versatile applications hold great promise for addressing unmet medical needs and improving patient outcomes in varied healthcare settings (32). The history of nanofibers started in the early 17th-19th centuries wherein they observed the formation of fibers when certain materials were subjected to mechanical or electrical forces. However, in the early mid-20th century, significant progress was made in the development of polymer fibers, including synthetic polymers such as nylon and polyester (43,44). Techniques for producing macro-scale fibers were refined, laying the groundwork for nanoscale fiber production. Nanofibers can be prepared from a variety of substances, depending on the desired properties and application. Synthetic polymers like

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polyacrylonitrile (PAN), polyvinyl alcohol (PVA), polyethylene oxide (PEO), polycaprolactone (PCL), and polylactic acid (PLA) are frequently used due to their flexibility and tunable properties (45,46). Proteins like collagen or gelatin serve as a fundamental building block in the human body, making up a significant portion of connective tissues such as skin, bones, tendons, and ligaments. It provides structural support, elasticity, and strength to various tissues and organs (47,48). In recent years, collagen has gained significant attention in the field of nanofibers research and applications. Nanofibers made from collagen offer several advantages namely biocompatibility and biomimic properties providing an ideal environment for cell adhesion, proliferation, and cell differentiation (49). Certain biopolymers like cellulose, chitosan, and silk fibroin are used for their sustainability (50)[51]. The production of nanofibers can be achieved through various techniques and one such recent technique is application of electrospinning which offers unique advantages and is suitable for different applications in the field of medicine Fig. 3.(51,52).

8. Fabrication of siderophore–loaded nanofibers

Fabrication of siderophore-loaded nanofibers involves several key steps, which are important in ensuring th11e successful integration of siderophores into the nanofiber matrix and the production of fibres with desirable properties (53). The choice of polymer is important for the fabrication of siderophore-loaded nanofibers. The commonly used polymers include PVA, PCL and PEO, where these polymers are used for fabrication of siderophore-loaded nanofibers through electrospinning which is a promising technique for biofilm management (32). These fibers are used in medical, industrial, and environmental applications, offering a novel method to prevent biofilm formation (48). The fabrication of siderophore-loaded nanofibers using PCL by electrospinning is a suitable technique for biofilm management. PCL is a biodegradable polymer known for its excellent mechanical properties and biocompatibility and making it suitable for fabricating siderophore-loaded nanofibers for biofilm applications. These fibres have a good potential in the field of medical, industrial, and environmental applications and offers a novel method to prevent biofilm formation (41,42).

Polyethylene Oxide (PEO) are water-soluble polymer which known for biocompatibility and non-toxicity and making it an excellent candidate for fabricating siderophore-loaded nanofibers for biofilm applications. The fabrication of siderophore-loaded nanofibers using PEO via electrospinning is a promising technique for biofilm management. These fibers hold significant

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potential in medical, industrial, and environmental applications, offering a novel method to disrupt and prevent biofilm formation(42).

9. Electrospun nanofibers as a nanohealers

Electrospinning has become progressively fascinating in recent decades, by attracting much attention to versatility and extensive applicability, particularly within disciplines such as biomaterials science, and nanotechnology (54). Electrospinning has its roots in the early 20th century (39,47). In 1902, British engineer Sir William Thomson (also known as Lord Kelvin) patented a method for the electrostatic spinning of fibers. However, it wasn't until the 1930s that further progresses were made (35,49). In the 1930s, Anton Formhals, an American physicist, made an important contribution to the progress of electrospinning technology (39,55). He developed a method for producing ultra-fine fibers using electrostatic forces. The research work of Formhal *et al*. work also laid a good the foundation for modern electrospinning techniques in mid-20th century (54,55). During this period, researchers discovered various aspects of the process, including the effects of different parameters such as voltage, polymer solution properties, and collector configurations on fiber morphology (39,56). This development gained its importance in late 1990s and early 2000s in the field of materials science and nanotechnology for various applications (55,57,58). Researchers began to explore the potential of electrospinning for producing nanoscale fibers with detailed control over their properties. In the past few decades, electrospinning shown a rapid progress by developing coaxial electrospinning and near-field electrospinning to enhance the versatility and capabilities of the process(39,59,60). The history of electrospinning shows (Table 1) the journey of investigation, innovation and technological advancement, with each milestone by contributing to our understanding of the process and expanding its potential applications.

The electrospinning setup comprises key components such as a syringe pump, a high-voltage power supply, and a metal collecting plate(61,62). The syringe pump directs a consistent flow of polymer solution, while a high voltage generates an electrically charged polymer jet from the nozzle. The setup generates an electric field at the nozzle, typically 1 to 50 kV per meter, initiatin.g the progress and also leads to electrostatic repulsion forces to overcome the liquid's surface tension, collecting high-voltage electrical charges and also the liquid reforms into a cone formation known as the Taylor cone, expelling a charged jet from its tip (56,61,62). The trajectory of the jet experiences bending variabilities which leads to whipping and oscillation as it progresses.

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As the jet stretches into thinner diameters, it swiftly solidifies, depositing solid fibers onto a grounded collector plate. Various collector designs like plates, drums, mandrels, and discs, can be utilized. In some cases, residual solvent may remain in the nanofibrous mat, imposing post-processing adjustments (54,56).

Table 1. The Evolution of Electrospinning: Landmark Discoveries and Technological Advances

Types	Inventors & Year	Applications	Ref.
Mono-axial	Cooley and Morton (1902)	Drug delivery	(52)
Co-axial	Sun et.al (2003)	Modelling Drug Release	(63)
Multi-jet	Ding et.al (2004)	Nanosensors	(64)
Magnetic field	Yarin et.al (2004)	Textile Industries	(65)
Roller	Jirsak et.al (2005)	Skin Tissue Engineering	(66)
Porous tube	Dosunmu et.al (2006)	Waste Water Treatment	(67)
Bubble	Liu et.al (2008)	Therapeutic and Diagnostic tools	(68)
Tri-axial	Kalra et.al (2009)	Loading of Multiple Drugs	(69)
Ball	Miloh et.al (2009)	Water Purification	(70)
Disk	Niu et.al (2009)	Drug delivery	(71)
Wet 3D	Yokoyama et.al (2009)	Waste Water Treatment	(72)
Cone	Lu et.al (2010)	Biomedical and Food Applications	(73)
Spiral Coil	Wang et.al (2012)	Electrodes For Batteries	(74)
Beaded Chain	Liu et.al (2008)	Energy Catalysis	(68)
Cold Plate3D	Sheikh et.al (2015)	Skin Damage and Diabetic Ulcers	(50)
3 Dimensional	Vong et.al (2018)	Cell infiltration and Wound Healing	(61)

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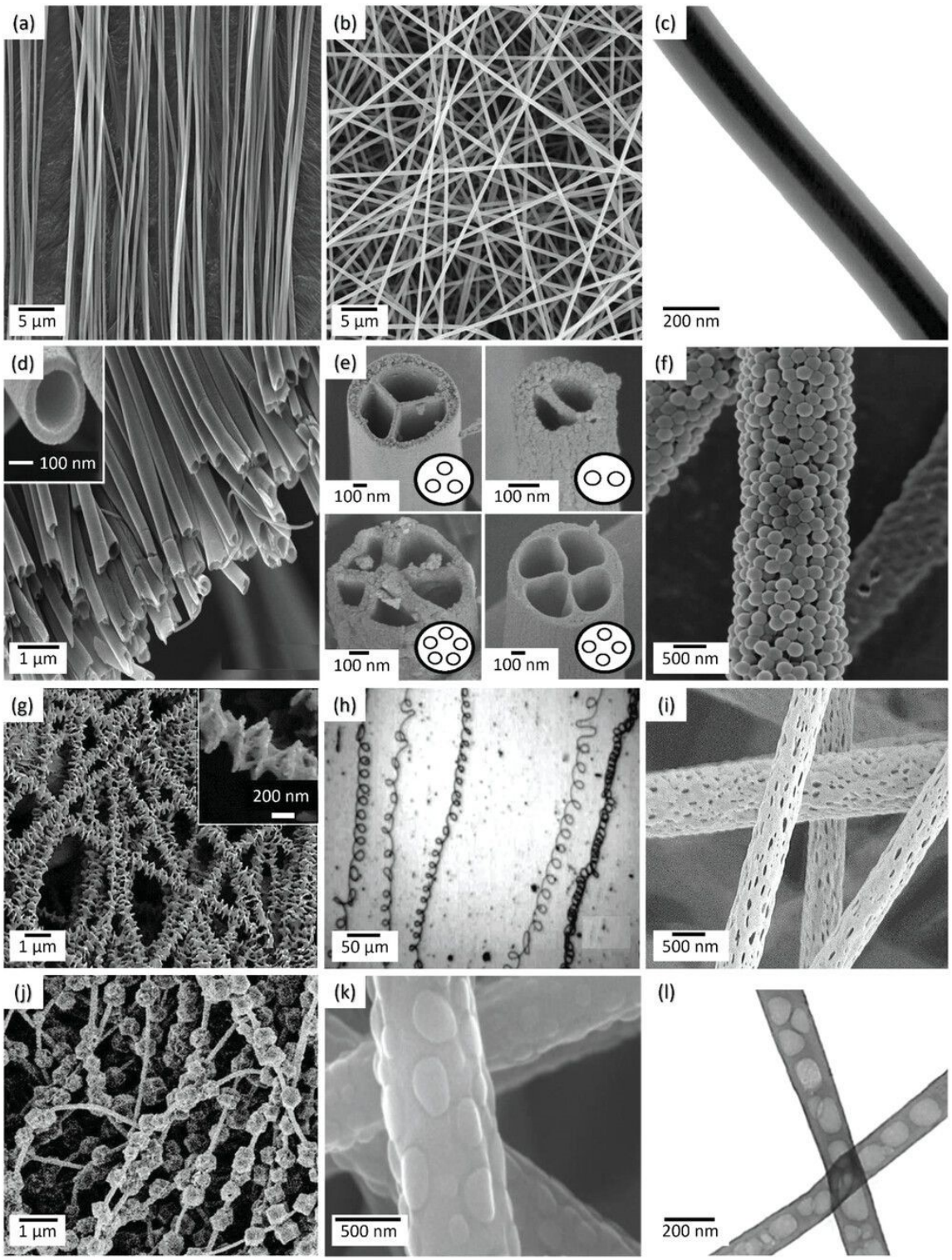

Fig. 4. Various structure of electrospun fiber morphologies: (a) aligned, (b) randomly oriented, (c) core/shell, (d) hollow, (e) multi-channel microtubes, (f) colloidal nanoparticle-decorated, (g) shish-kebab, (h) helical, (i) porous, (j) necklace-like, and (k) island-like. (a-c, i) Reproduced from

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The electrospinning process includes charging a liquid droplet with electricity, forming a Taylor cone or cone-shaped jet, extending the jet in a straight path, thinning the jet using an electric field, increasing electrical bending instability (also known as whipping instability), and ultimately solidifying and collecting the jet as solid fibers on a grounded collector The electrospinning process involves charging a liquid droplet with electricity, forming a Taylor cone or cone-shaped jet, extending the jet in a straight path, thinning the jet using an electric field, increasing electrical bending instability (also known as whipping instability), and ultimately solidifying and collecting the jet as solid fibers on a grounded collector Among the various morphologies shown in Fig. 4, porous and core–shell nanofibers are particularly suitable for siderophore delivery and sustained iron chelation in wound environments (55). Different polymer matrices exhibit distinct physicochemical and biological properties that influence siderophore loading efficiency, release behavior, and antibiofilm performance (55,59,75–81).

10. Current investigations and future directions

The preparation of nanofibers from microbial siderophore by electrospinning process gain a positive approach in addressing the challenges related to biofilms. Their ability to interrupt the biofilm and also the combined benefits of electrospinning technology, makes them suitable for various applications, like healing medical wounds and also preventing industrial biofilms (23,82). According to research reports, the stability of nanofibers leads to increased degradation of biofilms at wound sites. Since siderophores occur naturally, the biocompatibility of the entire nanofiber system confirms their safety for medical use. It is important to develop electrospinning processes that are cost-effective and scalable for the commercialization of nanofibers loaded with siderophores.

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Biphasic scaffolds prepared from the University of Nebraska was a fascinating method in drug delivery and antimicrobial therapy(72,83). The researchers combined the nanofiber mats with microneedle arrays and developed a delivery system to target bacterial biofilms. The usage of coaxial type to make the scaffolds had a good control over the structure thereby enhancing the transfer of antimicrobial agents. The use of polyvinylpyrrolidone (PVP) microneedle arrays and Pluronic F-127-poly (ε-caprolactone) nanofiber mats also enhance the function of the scaffold. The distribution of antimicrobial agents through a scaffold helps in the killing mechanism and results in synergistic efficacy against the biofilms. This approach had an important promise for treating infections associated with biofilm formation, which are often challenging to eradicate the conventional therapies. The successful demonstration of the antimicrobial delivery on human skin highlights their potential on clinical application in treating the wounds infected with bacterial biofilms. The research and development in this area could lead to the development of novel therapies for combating antibiotic-resistant infections and improving patient outcomes(84).

The current invention of core-shell nanofibers incorporated with PEO, chitosan (CS), PVP, and gelatin gains the progress in the study of dual drug delivery of vancomycin and Primaxin (imipenem/cilastatin)(85). These nanofibers, with an average diameter ranging from 218 to 342 nm, were used in diabetic foot ulcer infections, particularly in methicillin-resistant *Staphylococcus aureus* (MRSA). By incorpating the antibiotics into these nanofibers allowed a controlled release of drugs which target on bacterial strains like MRSA, *Escherichia coli* and *Pseudomonas aeruginosa*(86). The approach minimizes the risk which are associated with traditional drug delivery methods, such as nephrotoxicity and cytotoxicity(87). The work also focused on fabricating the electrospun nanofibers with anti-inflammatory and antipyretic properties. This research also highlights the importance for nanofiber-based therapies to address complex medical challenges while minimizing systemic side effects (71,88). Fig. 5. The comparative studies of polymers are summarized in the table 2.

The combination of copper sulfide with PVP and gelatin nanofibers gives several beneficial medical properties wherein, Copper sulfide was recognized for its antimicrobial properties that helps to kill microbes, while PVP and gelatin offer structural support and biocompatibility. PVP are often used in medical field for their ability to form films and fibers and making it an excellent substance for creating nanofibers. Gelatin obtained from collagen act as a biodegradable material

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and were widely used in wound healing applications. By blending these materials into composite nanofibers, Liu et al. achieved a co-operative effect, where each and every compound contributes its unique properties and enhance the material's overall performance. This approach demonstrated the innovation and gained the importance for various biomedical applications, including wound dressings and antimicrobial coatings(89,90).

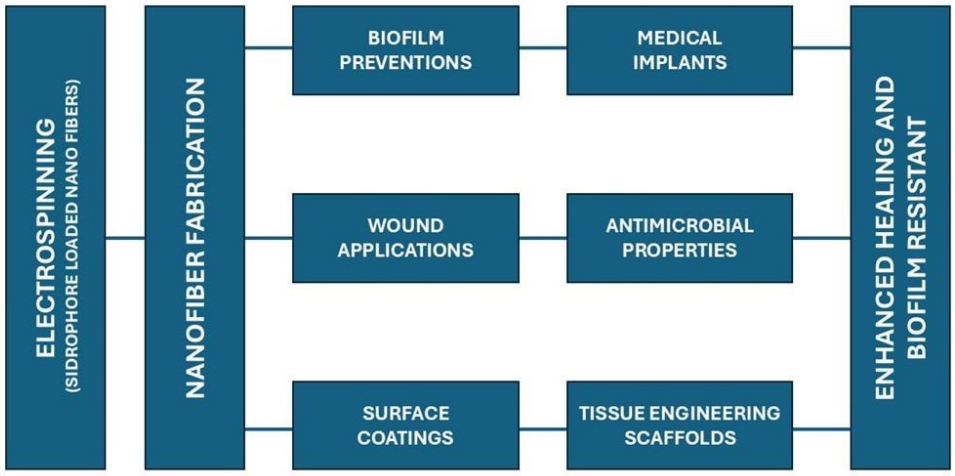

Fig. 5. Schematic representation of electrospun nanofiber-based wound healing systems with corrected chemical proportions.

Table 2. Polymers in Wound Dressings: A Comparative Study of Material Properties and Performance Parameters

S.No	Parameter	PCL	PVA	PEO
1	**Polymer Type**	Hydrophobic aliphatic polyester (91)	Hydrophilic water-soluble polymer	Hydrophilic non-ionic polymer
2	**Fabrication Methods**	Electrospinning, solvent casting, nanoparticles, core–shell fibers	Electrospinning, hydrogels, freeze-drying	Hydrophilic matrix/tablets, hydrogels
3	**Typical Siderophore Type Studied**	Few direct reports (inferred from drug/antibiotic models)	Few direct reports (hydrogel matrices) (92)	Not commonly reported for siderophores, used in controlled release

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4	**Loading Efficiency/Mechanism**	Compatible with hydrophobic drugs or hydrophobicmodifications of siderophores when encapsulated in particles (93,94)	Good entrapment with hydrophilic drugs; rapid release for water-soluble siderophores (94)	Facilitates diffusion-controlled release due toswelling/erosion(95)
5	**Release Profile**	Sustained, slow release over weeks/months due to hydrophobicity and crystallinity (96)	Burst or rapid release depending on gel/swelling; tunable via crosslinking	Fast release with hydrophilic swelling; slower with high MW grades
6	**Mechanical/Physical Properties**	Good mechanical strength; slow biodegradation suitable for implants (97)	Flexible hydrogel; water solubility can limit mechanical integrity unless crosslinked	High water uptake; matrix can erode rapidly, weaker mechanical strength
7	**Advantages for Siderophore Delivery**	Sustained release ideal for prolonged antimicrobial action; strong network for protective encapsulation (98)	High loading for hydrophilic siderophores; tunable porosity & swelling (6)	Enhanced diffusivity; rapid release useful for acute siderophore payloads (99)
8	**Limitations**	Hydrophobicity may impede loading of hydrophilic siderophores; slow degradation	Rapid initial release ("burst") may limit duration; water solubility may lead to fast clearance	Rapid erosion/swelling may undermine controlled, long-term delivery
9	**Best Use Cases**	Long-term localized delivery (e.g., implanted coatings, nanofiber mats)	Hydrogel pads/films for wound or topical delivery	Oral/implant hydrophilic matrix where rapid release is acceptable

All these innovations and studies related to nanofibers paved the way for a solution of biofilm formation. Electrospun nanofibers can mimic the architecture of natural extracellular

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matrices, making them suitable for medical applications. These nanofibers give a good environment for cell adhesion, proliferation, and differentiation (97,100). They are used in the regeneration of various tissues and organs, including skin, bone, cartilage, nerve, and blood vessels (53,101). Electrospun nanofibers also serve as carriers for controlled and targeted drug delivery. Researchers attained sustained release profiles, improved drug stability, and enhanced therapeutic efficacy by incorporating drugs, growth factors, or other bioactive molecules into the polymer matrix during electrospinning. Studies also proved that electrospun nanofibers-based drug delivery systems are effective for applications in cancer therapy, wound healing, and treatment of infections (102–104).The schematic representation are illustrated in Fig.

11. Conclusion

Electrospun microbial siderophore-based nanofibers represents as an innovative strategy to witness the challenges faced in biofilm-associated chronic wounds. By using this iron sequestration to disrupt microbial metabolism, quorum sensing, and biofilm maturation, these nano-engineered dressings offer the advantage over a traditional antimicrobial, including reduced risk of resistance development and multifunctional wound support. The ability of electrospinning to generate nanofibrous matrices with tunable architecture, high surface area, and controlled release profiles further strengthens the potential of siderophore-loaded systems as advanced wound care platforms that simultaneously promote antimicrobial activity, modulate inflammation, facilitate granulation tissue formation, and support cell adhesion and proliferation. Despite these promising attributes, the translation of siderophore-based nanofibers from bench to bedside are controlled by several challenges. The current studies are limited to in vitro or short-term in vivo models due to inefficiency of long-term biocompatibility, immunogenicity, iron homeostasis disruption and host–microbiome interactions. The variability in siderophore source, stability under physiological wound conditions and controlled release kinetics within complex wound environments require optimization. Regulatory and clinical considerations further complicate translation, as siderophore-based dressings may be classified as combination products, necessitating rigorous safety, toxicity, and efficacy evaluations. Future research should therefore prioritize standardized in vivo wound models, long-term safety assessments, and comparative studies against existing clinical dressings. Integrating smart or stimuli-responsive nanofiber

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systems, synergistic combinations with growth factors or probiotics, and advanced delivery strategies may further enhance therapeutic outcomes.

To conclude, the microbial siderophore-based electrospun nanofibers holds a substantial promise as next-generation "nanohealers" for biofilm-infected chronic wounds and their clinical realization will depend on interdisciplinary efforts that bridge materials science, microbiology, pharmacology, and regulatory science. Addressing these translational gaps, it would be essential to harness their therapeutic potential and to advance these systems toward safe, effective, and clinically viable wound care solutions.

Data Availability

The datasets generated and analyzed during this study are available from the corresponding author upon reasonable request.

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Ethical approval

Ethical approval was not applicable for this study.

Clinical Trial Number

Not Applicable.

Declarations Conflict of interest

The authors declared no conflict of interest.

Author Contributions

Sitalakshmi Thyagarajan & Senthamil Selvi Poongavanam contributed to the conception, literature review, manuscript preparation, and final approval of the article and acted as the corresponding author.

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References

1. Percival NJ. Classification of wounds and their management. Surgery [Internet]. 2002 May;20(5):114–7. Available from: http://dx.doi.org/10.1383/surg.20.5.114.14626

2. Lazarus GS, Cooper DM, Knighton DR, Margolis DJ, Percoraro RE, Rodeheaver G, et al. Definitions and guidelines for assessment of wounds and evaluation of healing. Wound Repair Regen [Internet]. 1994 July;2(3):165–70. Available from: http://dx.doi.org/10.1046/j.1524-475x.1994.20305.x

3. Thyagarajan SL, Kandhasamy S, Ramanathan G, Sivagnanam UT, Perumal PT. Evaluation of stress-induced microbial siderophore from Pseudomonas aeruginosa strain S1 as a potential matrix metalloproteinase inhibitor in wound healing applications. Curr Microbiol [Internet]. 2016 May;72(5):583–8. Available from: http://dx.doi.org/10.1007/s00284-016-0988-x

4. Mir M, Ali MN, Barakullah A, Gulzar A, Arshad M, Fatima S, et al. Synthetic polymeric biomaterials for wound healing: a review. Prog Biomater [Internet]. 2018 Mar;7(1):1–21. Available from: http://dx.doi.org/10.1007/s40204-018-0083-4

5. Thyagarajan SL, Ramanathan G, Singaravelu S, Kandhasamy S, Perumal PT, Sivagnanam UT. Microbial Siderophore as MMP inhibitor:An interactive approach on wound healing application. Wound Med [Internet]. 2017 Mar;16:7–14. Available from: http://dx.doi.org/10.1016/j.wndm.2016.12.002

6. Thyagarajan SL, Ramanathan G, Singaravelu S, Kandhasamy S, Perumal PT, Sivagnanam UT. Characterization and evaluation of siderophore-loaded gelatin microspheres: a potent tool for wound-dressing material. Polym Bull (Berl) [Internet]. 2017 June;74(6):2349–63. Available from: http://dx.doi.org/10.1007/s00289-016-1840-y

7. Ramanathan G, Thyagarajan S, Sivagnanam UT. Accelerated wound healing and its promoting effects of biomimetic collagen matrices with siderophore loaded gelatin microspheres in tissue engineering. Mater Sci Eng C Mater Biol Appl [Internet]. 2018 Dec;93:455–64. Available from: http://dx.doi.org/10.1016/j.msec.2018.08.026

8. Demir A, Cevher E. Biopolymers as wound healing materials: Challenges and new strategies. In: Biomaterials Applications for Nanomedicine [Internet]. InTech; 2011. Available from: http://dx.doi.org/10.5772/25177

9. Shaffique S, Imran M, Wani SH, Khan MA, Kang S-M, Adhikari A, et al. Evaluating the adhesive potential of the newly isolated bacterial strains in research exploitation of plant

View Article Online
DOI: 10.1039/D5PM00300H

microbial interaction. Front Plant Sci [Internet]. 2022 Oct 21;13:1004331. Available from: http://dx.doi.org/10.3389/fpls.2022.1004331

10. Lappin-Scott H, Burton S, Stoodley P. Revealing a world of biofilms — the pioneering research of Bill Costerton. Nat Rev Microbiol [Internet]. 2014 Nov;12(11):781–7. Available from: http://dx.doi.org/10.1038/nrmicro3343

11. McLean RJC, Lam JS, Graham LL. Training the biofilm generation—a tribute to J. w. costerton. J Bacteriol [Internet]. 2012 Dec 15;194(24):6706–11. Available from: http://dx.doi.org/10.1128/jb.01252-12

12. Stoodley P, Hall-Stoodley L, Costerton B, DeMeo P, Shirtliff M, Gawalt E, et al. Biofilms, biomaterials, and device-related infections. In: Handbook of Polymer Applications in Medicine and Medical Devices [Internet]. Elsevier; 2013. p. 77–101. Available from: http://dx.doi.org/10.1016/b978-0-323-22805-3.00005-0

13. Miethke M, Marahiel MA. Siderophore-based iron acquisition and pathogen control. Microbiol Mol Biol Rev [Internet]. 2007 Sept;71(3):413–51. Available from: http://dx.doi.org/10.1128/mmbr.00012-07

14. Hofmann M, Heine T, Malik L, Hofmann S, Joffroy K, Senges CHR, et al. Screening for microbial metal-chelating siderophores for the removal of metal ions from solutions. Microorganisms [Internet]. 2021 Jan 5;9(1):111. Available from: http://dx.doi.org/10.3390/microorganisms9010111

15. Haesler E, Swanson T, Ousey K, Carville K. Clinical indicators of wound infection and biofilm: reaching international consensus. J Wound Care [Internet]. 2019 Mar 2;28(Sup3b):s4–12. Available from: http://dx.doi.org/10.12968/jowc.2019.28.sup3b.s4

16. Szomolay B, Klapper I, Dockery J, Stewart PS. Adaptive responses to antimicrobial agents in biofilms. Environ Microbiol [Internet]. 2005 Aug;7(8):1186–91. Available from: http://dx.doi.org/10.1111/j.1462-2920.2005.00797.x

17. Srinivasan R, Santhakumari S, Poonguzhali P, Geetha M, Dyavaiah M, Xiangmin L. Bacterial biofilm inhibition: A focused review on recent therapeutic strategies for combating the biofilm mediated infections. Front Microbiol [Internet]. 2021 May 12;12:676458. Available from: http://dx.doi.org/10.3389/fmicb.2021.676458

18. Ishida S, Arai M, Niikawa H, Kobayashi M. Inhibitory effect of cyclic trihydroxamate siderophore, desferrioxamine E, on the biofilm formation of Mycobacterium species. Biol Pharm Bull [Internet]. 2011;34(6):917–20. Available from: http://dx.doi.org/10.1248/bpb.34.917

19. Schaudinn C, Costerton B, Stoodley P, Robinson D, Webster P, Baum M, et al. Bacterial biofilms, other structures seen as mainstream concepts. Microbe Wash DC [Internet]. 2007 May 1;2(5):231–7. Available from: http://dx.doi.org/10.1128/microbe.2.231.1

View Article Online
DOI: 10.1039/D5PM00300H

20. Sharman GJ, Williams DH, Ewing DF, Ratledge C. Isolation, purification and structure of exochelin MS, the extracellular siderophore from *Mycobacterium smegmatis*. Biochem J [Internet]. 1995 Jan 1;305(1):187–96. Available from: http://dx.doi.org/10.1042/bj3050187

21. Patel AK, Deshattiwar MK, Chaudhari BL, Chincholkar SB. Production, purification and chemical characterization of the catecholate siderophore from potent probiotic strains of Bacillus spp. Bioresour Technol [Internet]. 2009 Jan;100(1):368–73. Available from: http://dx.doi.org/10.1016/j.biortech.2008.05.008

22. Sah S, Singh R. Siderophore: Structural and functional characterisation – A comprehensive review. Agriculture [Internet]. 2015 Sept 1;61(3):97–114. Available from: http://dx.doi.org/10.1515/agri-2015-0015

23. Khan A, Singh P, Srivastava A. Synthesis, nature and utility of universal iron chelator – Siderophore: A review. Microbiol Res [Internet]. 2018 July;212–213:103–11. Available from: http://dx.doi.org/10.1016/j.micres.2017.10.012

24. Gledhill M, McCormack P, Ussher S, Achterberg EP, Mantoura RFC, Worsfold PJ. Production of siderophore type chelates by mixed bacterioplankton populations in nutrient enriched seawater incubations. Mar Chem [Internet]. 2004 Aug;88(1–2):75–83. Available from: http://dx.doi.org/10.1016/j.marchem.2004.03.003

25. Bianchi T, Wolcott RD, Peghetti A, Leaper D, Cutting K, Polignano R, et al. Recommendations for the management of biofilm: a consensus document. J Wound Care [Internet]. 2016 June 2;25(6):305–17. Available from: http://dx.doi.org/10.12968/jowc.2016.25.6.305

26. Niehus R, Picot A, Oliveira NM, Mitri S, Foster KR. The evolution of siderophore production as a competitive trait. Evolution [Internet]. 2017 June;71(6):1443–55. Available from: http://dx.doi.org/10.1111/evo.13230

27. Schwyn B, Neilands JB. Universal chemical assay for the detection and determination of siderophores. Anal Biochem [Internet]. 1987 Jan;160(1):47–56. Available from: http://dx.doi.org/10.1016/0003-2697(87)90612-9

28. Ali S, Vidhale NN. Bacterial Siderohore and their Application: A review. IntJCurrMicrobiolAppSci. 2013;2:303–12.

29. Sadaf F, Saleem R, Ahmed M, Ahmad SI, Navaid-ul-Zafar. Healing potential of cream containing extract of Sphaeranthus indicus on dermal wounds in Guinea pigs. J Ethnopharmacol [Internet]. 2006 Sept;107(2):161–3. Available from: http://dx.doi.org/10.1016/j.jep.2006.02.022

30. Ojha A, Hatfull GF. The role of iron in *Mycobacterium smegmatis* biofilm formation: the exochelin siderophore is essential in limiting iron conditions for biofilm formation but not for planktonic growth. Mol Microbiol [Internet]. 2007 Oct;66(2):468–83. Available from: http://dx.doi.org/10.1111/j.1365-2958.2007.05935.x

View Article Online
DOI: 10.1039/D5PM00300H

31. Su Y, McCarthy A, Wong SL, Hollins RR, Wang G, Xie J. Simultaneous delivery of multiple antimicrobial agents by biphasic scaffolds for effective treatment of wound biofilms. Adv Healthc Mater [Internet]. 2021 June;10(12). Available from: http://dx.doi.org/10.1002/adhm.202100135

32. Su Y, Yrastorza JT, Matis M, Cusick J, Zhao S, Wang G, et al. Biofilms: Formation, research models, potential targets, and methods for prevention and treatment. Adv Sci (Weinh) [Internet]. 2022 Oct;9(29). Available from: http://dx.doi.org/10.1002/advs.202203291

33. Su Y, Mainardi VL, Wang H, McCarthy A, Zhang YS, Chen S, et al. Dissolvable microneedles coupled with nanofiber dressings eradicate biofilms *via* effectively delivering a database-designed antimicrobial peptide. ACS Nano [Internet]. 2020 Sept 22;14(9):11775–86. Available from: http://dx.doi.org/10.1021/acsnano.0c04527

34. Rajput A, Kaur K, Kumar M. SigMol: repertoire of quorum sensing signaling molecules in prokaryotes. Nucleic Acids Res [Internet]. 2016 Jan 4;44(D1):D634–9. Available from: http://dx.doi.org/10.1093/nar/gkv1076

35. Chen J, Sun Z, Jin J, Wang F, Yang Q, Yu H, et al. Role of siderophore in Pseudomonas fluorescens biofilm formation and spoilage potential function. Food Microbiol [Internet]. 2023 Feb;109(104151):104151. Available from: http://dx.doi.org/10.1016/j.fm.2022.104151

36. Ahire JJ, Dicks LMT. Nisin incorporated with 2,3-dihydroxybenzoic acid in nanofibers inhibits biofilm formation by a methicillin-resistant strain of staphylococcus aureus. Probiotics Antimicrob Proteins [Internet]. 2015 Mar;7(1):52–9. Available from: http://dx.doi.org/10.1007/s12602-014-9171-5

37. Adeli-Sardou M, Torkzadeh-Mahani M, Yaghoobi M, Dodel M. Antibacterial and Anti-biofilm Investigation of Electrospun PCL/gelatin/Lawsone Nano Fiber Scaffolds against Biofilm Producing Bacteria. Biomacromolecular Journal [Internet]. 2018 Apr 1 [cited 2025 Oct 22];4(1):46–57. Available from: https://www.bmmj.org/article_34368.html

38. Kamoun EA, Loutfy SA, Hussein Y, Kenawy E-RS. Recent advances in PVA-polysaccharide based hydrogels and electrospun nanofibers in biomedical applications: A review. Int J Biol Macromol [Internet]. 2021 Sept;187:755–68. Available from: http://dx.doi.org/10.1016/j.ijbiomac.2021.08.002

39. Xue C-H, Guo X-J, Zhang M-M, Ma J-Z, Jia S-T. Fabrication of robust superhydrophobic surfaces by modification of chemically roughened fibers via thiol–ene click chemistry. J Mater Chem A Mater Energy Sustain [Internet]. 2015;3(43):21797–804. Available from: http://dx.doi.org/10.1039/c5ta04802h

40. Ye Q, Chen W, Huang H, Tang Y, Wang W, Meng F, et al. Iron and zinc ions, potent weapons against multidrug-resistant bacteria. Appl Microbiol Biotechnol [Internet]. 2020 June;104(12):5213–27. Available from: http://dx.doi.org/10.1007/s00253-020-10600-4

View Article Online
DOI: 10.1039/D5PM00300H

41. Hamdan N, Yamin A, Hamid SA, Khodir WKWA, Guarino V. Functionalized antimicrobial nanofibers: Design criteria and recent advances. J Funct Biomater [Internet]. 2021 Oct 28;12(4):59. Available from: http://dx.doi.org/10.3390/jfb12040059

42. Daneshmand S, Shahraki O, Hosseynipour H, Roshan F, Miri MA. Piperine-loaded Zein electrospun nanofibers: Development, characterization and antibacterial application. Bionanoscience [Internet]. 2024 Mar;14(1):11–26. Available from: http://dx.doi.org/10.1007/s12668-023-01246-3

43. Ghafoor B, Aleem A, Najabat Ali M, Mir M. Review of the fabrication techniques and applications of polymeric electrospun nanofibers for drug delivery systems. J Drug Deliv Sci Technol [Internet]. 2018 Dec;48:82–7. Available from: http://dx.doi.org/10.1016/j.jddst.2018.09.005

44. Mukherjee A, Bose S, Shaoo A, Das SK. Nanotechnology based therapeutic approaches: an advanced strategy to target the biofilm of ESKAPE pathogens. Mater Adv [Internet]. 2023;4(12):2544–72. Available from: http://dx.doi.org/10.1039/d2ma00846g

45. Torres-Giner S, Gimeno-Alcañiz JV, Ocio MJ, Lagaron JM. Comparative performance of electrospun collagen nanofibers cross-linked by means of different methods. ACS Appl Mater Interfaces [Internet]. 2009 Jan 28;1(1):218–23. Available from: http://dx.doi.org/10.1021/am800063x

46. Law JX, Liau LL, Saim A, Yang Y, Idrus R. Electrospun collagen nanofibers and their applications in skin tissue engineering. Tissue Eng Regen Med [Internet]. 2017 Dec;14(6):699–718. Available from: http://dx.doi.org/10.1007/s13770-017-0075-9

47. Mbese Z, Alven S, Aderibigbe BA. Collagen-based nanofibers for skin regeneration and wound dressing applications. Polymers (Basel) [Internet]. 2021 Dec 13;13(24):4368. Available from: http://dx.doi.org/10.3390/polym13244368

48. Place ES, George JH, Williams CK, Stevens MM. Synthetic polymer scaffolds for tissue engineering. Chem Soc Rev [Internet]. 2009;38(4):1139. Available from: http://dx.doi.org/10.1039/b811392k

49. Luo J, Han H, Wu J, Wang X, Feng J, Toan S, et al. Excellent photocatalytic activity of MoO3-adorned g-C3N4 systems: Construction of S-scheme heterojunction. Appl Surf Sci [Internet]. 2022 Dec;604(154512):154512. Available from: http://dx.doi.org/10.1016/j.apsusc.2022.154512

50. Sheikh FA, Ju HW, Lee JM, Moon BM, Park HJ, Lee OJ, et al. 3D electrospun silk fibroin nanofibers for fabrication of artificial skin. Nanomedicine [Internet]. 2015 Apr;11(3):681–91. Available from: http://dx.doi.org/10.1016/j.nano.2014.11.007

51. Huang Z-M, Zhang Y-Z, Kotaki M, Ramakrishna S. A review on polymer nanofibers by electrospinning and their applications in nanocomposites. Compos Sci Technol [Internet]. 2003 Nov;63(15):2223–53. Available from: http://dx.doi.org/10.1016/s0266-3538(03)00178-7

View Article Online
DOI: 10.1039/D5PM00300H

52. Cooley JF, Eastman C. Apparatus for electrically dispersing fluids. United States patent US 692,631. 1902.

53. Huang C-K, Zhang K, Gong Q, Yu D-G, Wang J, Tan X, et al. Ethylcellulose-based drug nano depots fabricated using a modified triaxial electrospinning. Int J Biol Macromol [Internet]. 2020 June;152:68–76. Available from: http://dx.doi.org/10.1016/j.ijbiomac.2020.02.239

54. Zhou Y, Yang H, Liu X, Mao J, Gu S, Xu W. Electrospinning of carboxyethyl chitosan/poly(vinyl alcohol)/silk fibroin nanoparticles for wound dressings. Int J Biol Macromol [Internet]. 2013 Feb;53:88–92. Available from: http://dx.doi.org/10.1016/j.ijbiomac.2012.11.013

55. Zhao Y, Cao X, Jiang L. Bio-mimic multichannel microtubes by a facile method. J Am Chem Soc [Internet]. 2007 Jan 1;129(4):764–5. Available from: http://dx.doi.org/10.1021/ja068165g

56. Zhang Y, Luo J, Zhang Q, Deng T. Growth factors, as biological macromolecules in bioactivity enhancing of electrospun wound dressings for diabetic wound healing: A review. Int J Biol Macromol [Internet]. 2021 Dec;193:205–18. Available from: http://dx.doi.org/10.1016/j.ijbiomac.2021.09.210

57. Long Z, Li R, Dai Z, Shi C, Wu C, Wei Q, et al. Necklace-like $NiCo_2O_4$@carbon composite nanofibers derived from metal–organic framework compounds for high-rate lithium storage. Mater Chem Front [Internet]. 2021;5(15):5726–37. Available from: http://dx.doi.org/10.1039/d1qm00398d

58. Xu T, Yang H, Yang D, Yu Z-Z. Polylactic acid nanofiber scaffold decorated with chitosan islandlike topography for bone tissue engineering. ACS Appl Mater Interfaces [Internet]. 2017 June 28;9(25):21094–104. Available from: http://dx.doi.org/10.1021/acsami.7b01176

59. Keirouz A, Radacsi N, Ren Q, Dommann A, Beldi G, Maniura-Weber K, et al. Nylon-6/chitosan core/shell antimicrobial nanofibers for the prevention of mesh-associated surgical site infection. J Nanobiotechnology [Internet]. 2020 Dec;18(1). Available from: http://dx.doi.org/10.1186/s12951-020-00602-9

60. Boys CV. On the Production, Properties, and some suggested Uses of the Finest Threads. Proc Phys Soc Lond [Internet]. 1887 Apr [cited 2025 Oct 22];9(1):8–19. Available from: https://api.semanticscholar.org/CorpusID:138887096

61. Vong M, Speirs E, Klomkliang C, Akinwumi I, Nuansing W, Radacsi N. Controlled three-dimensional polystyrene micro- and nano-structures fabricated by three-dimensional electrospinning. RSC Adv [Internet]. 2018;8(28):15501–12. Available from: http://dx.doi.org/10.1039/c7ra13278f

62. Disintegration of water drops in an electric field. Proc R Soc Lond [Internet]. 1964 July 28;280(1382):383–97. Available from: http://dx.doi.org/10.1098/rspa.1964.0151

View Article Online
DOI: 10.1039/D5PM00300H

63. Sun Z, Zussman E, Yarin AL, Wendorff JH, Greiner A. Compound core–shell polymer nanofibers by co-electrospinning. Adv Mater [Internet]. 2003 Nov 17;15(22):1929–32. Available from: http://dx.doi.org/10.1002/adma.200305136

64. Ding B, Kimura E, Sato T, Fujita S, Shiratori S. Fabrication of blend biodegradable nanofibrous nonwoven mats via multi-jet electrospinning. Polymer (Guildf) [Internet]. 2004 Mar;45(6):1895–902. Available from: http://dx.doi.org/10.1016/j.polymer.2004.01.026

65. Yarin AL, Zussman E. Upward needleless electrospinning of multiple nanofibers. Polymer (Guildf) [Internet]. 2004 Apr;45(9):2977–80. Available from: http://dx.doi.org/10.1016/j.polymer.2004.02.066

66. Trokhymchuk A, Nezbeda I, Jirsák J, Henderson D. Hard-sphere radial distribution function again. J Chem Phys [Internet]. 2005 July 8;123(2). Available from: http://dx.doi.org/10.1063/1.1979488

67. Dosunmu OO, Chase GG, Kataphinan W, Reneker DH. Electrospinning of polymer nanofibres from multiple jets on a porous tubular surface. Nanotechnology [Internet]. 2006 Feb 28;17(4):1123–7. Available from: http://dx.doi.org/10.1088/0957-4484/17/4/046

68. Liu Y, He J-H, Yu J-Y. Bubble-electrospinning: a novel method for making nanofibers. J Phys Conf Ser [Internet]. 2008 Feb 1;96:012001. Available from: http://dx.doi.org/10.1088/1742-6596/96/1/012001

69. Kalra V, Lee JH, Park JH, Marquez M, Joo YL. Confined assembly of asymmetric block-copolymer nanofibers via multiaxial jet electrospinning. Small [Internet]. 2009 Oct 16;5(20):2323–32. Available from: http://dx.doi.org/10.1002/smll.200900157

70. Miloh T, Spivak B, Yarin AL. Needleless electrospinning: Electrically driven instability and multiple jetting from the free surface of a spherical liquid layer. J Appl Phys [Internet]. 2009 Dec 1;106(11). Available from: http://dx.doi.org/10.1063/1.3264884

71. Niu H, Lin T. Fiber generators in needleless electrospinning. J Nanomater [Internet]. 2012 Jan;2012(1). Available from: http://dx.doi.org/10.1155/2012/725950

72. Yokoyama Y, Hattori S, Yoshikawa C, Yasuda Y, Koyama H, Takato T, et al. Novel wet electrospinning system for fabrication of spongiform nanofiber 3-dimensional fabric. Mater Lett [Internet]. 2009 Apr;63(9–10):754–6. Available from: http://dx.doi.org/10.1016/j.matlet.2008.12.042

73. Lu B, Wang Y, Liu Y, Duan H, Zhou J, Zhang Z, et al. Superhigh-throughput needleless electrospinning using a rotary cone as spinneret. Small [Internet]. 2010 Aug 2;6(15):1612–6. Available from: http://dx.doi.org/10.1002/smll.201000454

74. Wang X, Niu H, Wang X, Lin T. Needleless electrospinning of uniform nanofibers using spiral coil spinnerets. J Nanomater [Internet]. 2012 Jan;2012(1). Available from: http://dx.doi.org/10.1155/2012/785920

View Article Online
DOI: 10.1039/D5PM00300H

75. Li D, Xia Y. Direct fabrication of composite and ceramic hollow nanofibers by electrospinning. Nano letters. 2004 May 12;4:933–8.

76. Yuan W, Zhang K-Q. Structural evolution of electrospun composite fibers from the blend of polyvinyl alcohol and polymer nanoparticles. Langmuir [Internet]. 2012 Oct 30;28(43):15418–24. Available from: http://dx.doi.org/10.1021/la303312q

77. Wang ZL. Triboelectric nanogenerators as new energy technology for self-powered systems and as active mechanical and chemical sensors. ACS Nano [Internet]. 2013 Nov 26;7(11):9533–57. Available from: http://dx.doi.org/10.1021/nn404614z

78. Yu J, Qiu Y, Zha X, Yu M, Yu J, Rafique J, et al. Production of aligned helical polymer nanofibers by electrospinning. Eur Polym J [Internet]. 2008 Sept;44(9):2838–44. Available from: http://dx.doi.org/10.1016/j.eurpolymj.2008.05.020

79. Xu T, Yang H, Yang D, Yu ZZ. Polylactic acid nanofiber scaffold decorated with chitosan islandlike topography for bone tissue engineering. ACS applied materials & interfaces. 2017 June 28;9:21094–104.

80. Long Z, Li R, Dai Z, Shi C, Wu C, Wei Q, et al. Necklace-like NiCo 2 O 4@ carbon composite nanofibers derived from metal-organic framework compounds for high-rate lithium storage. Materials Chemistry Frontiers. 2021;5(15):5726–37.

81. Li D, Xia Y. Direct fabrication of composite and ceramic hollow nanofibers by electrospinning. Nano Lett [Internet]. 2004 May 1;4(5):933–8. Available from: http://dx.doi.org/10.1021/nl049590f

82. Ghosh SK, Bera T, Chakrabarty AM. Microbial siderophore – A boon to agricultural sciences. Biol Control [Internet]. 2020 May;144(104214):104214. Available from: http://dx.doi.org/10.1016/j.biocontrol.2020.104214

83. Gutschmidt D, Hazra RS, Zhou X, Xu X, Sabzi M, Jiang L. Electrospun, sepiolite-loaded poly(vinyl alcohol)/soy protein isolate nanofibers: Preparation, characterization, and their drug release behavior. Int J Pharm [Internet]. 2021 Feb;594(120172):120172. Available from: http://dx.doi.org/10.1016/j.ijpharm.2020.120172

84. Guadagno FM, Revellino P. Debris avalanches and debris flows of the Campania Region (southern Italy). In: Debris-flow Hazards and Related Phenomena [Internet]. Berlin, Heidelberg: Springer Berlin Heidelberg; 2007. p. 489–518. (Springer Praxis Books). Available from: http://dx.doi.org/10.1007/3-540-27129-5_19

85. Adeli H, Khorasani MT, Parvazinia M. Wound dressing based on electrospun PVA/chitosan/starch nanofibrous mats: Fabrication, antibacterial and cytocompatibility evaluation and in vitro healing assay. Int J Biol Macromol [Internet]. 2019 Feb;122:238–54. Available from: http://dx.doi.org/10.1016/j.ijbiomac.2018.10.115

View Article Online
DOI: 10.1039/D5PM00300H

86. Sahay R, Thavasi V, Ramakrishna S. Design modifications in electrospinning setup for advanced applications. J Nanomater [Internet]. 2011;2011:1–17. Available from: http://dx.doi.org/10.1155/2011/317673

87. Qin Z-Y, Jia X-W, Liu Q, Kong B-H, Wang H. Fast dissolving oral films for drug delivery prepared from chitosan/pullulan electrospinning nanofibers. Int J Biol Macromol [Internet]. 2019 Sept;137:224–31. Available from: http://dx.doi.org/10.1016/j.ijbiomac.2019.06.224

88. Davani F, Alishahi M, Sabzi M, Khorram M, Arastehfar A, Zomorodian K. Dual drug delivery of vancomycin and imipenem/cilastatin by coaxial nanofibers for treatment of diabetic foot ulcer infections. Mater Sci Eng C Mater Biol Appl [Internet]. 2021 Apr;123(111975):111975. Available from: http://dx.doi.org/10.1016/j.msec.2021.111975

89. Bai Y, Dou Y, Xie L-H, Rutledge W, Li J-R, Zhou H-C. Zr-based metal–organic frameworks: design, synthesis, structure, and applications. Chem Soc Rev [Internet]. 2016;45(8):2327–67. Available from: http://dx.doi.org/10.1039/c5cs00837a

90. Bai Y, Wang D, Zhang Z, Pan J, Cui Z, Yu D-G, et al. Testing of fast dissolution of ibuprofen from its electrospun hydrophilic polymer nanocomposites. Polym Test [Internet]. 2021 Jan;93(106872):106872. Available from: http://dx.doi.org/10.1016/j.polymertesting.2020.106872

91. Begines B, Ortiz T, Pérez-Aranda M, Martínez G, Merinero M, Argüelles-Arias F, et al. Polymeric nanoparticles for drug delivery: Recent developments and future prospects. Nanomaterials. 2020 July 19;10(7).

92. Hetrick EM, Schoenfisch MH. Reducing implant-related infections: Active release strategies. ChemInform [Internet]. 2006 Nov 28;37(48). Available from: http://dx.doi.org/10.1002/chin.200648272

93. Liang X, Zhong H-J, Ding H, Yu B, Ma X, Liu X, et al. Polyvinyl alcohol (PVA)-based hydrogels: Recent progress in fabrication, properties, and multifunctional applications. Polymers (Basel) [Internet]. 2024 Sept 29;16(19):2755. Available from: http://dx.doi.org/10.3390/polym16192755

94. Peppas NA, Merrill EW. Poly (vinyl alcohol) hydrogels: reinforcement of radiation-crosslinked networks by crystallization. Journal of Polymer Science: Polymer Chemistry Edition. 1976 Feb;14(2):441–57.

95. Dash TK, Konkimalla VB. Poly-ϵ-caprolactone based formulations for drug delivery and tissue engineering: A review. J Control Release [Internet]. 2012 Feb 28;158(1):15–33. Available from: http://dx.doi.org/10.1016/j.jconrel.2011.09.064

96. Bolívar-Monsalve EJ, Alvarez MM, Hosseini S, Espinosa-Hernandez MA, Ceballos-González CF, Sanchez-Dominguez M, et al. Engineering bioactive synthetic polymers for biomedical applications: a review with emphasis on tissue engineering and controlled release. Mater Adv [Internet]. 2021;2(14):4447–78. Available from: http://dx.doi.org/10.1039/d1ma00092f

View Article Online
DOI: 10.1039/D5PM00300H

97. Sill TJ, von Recum HA. Electrospinning: Applications in drug delivery and tissue engineering. Biomaterials [Internet]. 2008 May;29(13):1989–2006. Available from: http://dx.doi.org/10.1016/j.biomaterials.2008.01.011

98. Soares Í, Faria J, Marques A, Ribeiro IAC, Baleizão C, Bettencourt A, et al. Drug delivery from PCL/chitosan multilayer coatings for metallic implants. ACS Omega [Internet]. 2022 July 12;7(27):23096–106. Available from: http://dx.doi.org/10.1021/acsomega.2c00504

99. Mayegowda SB, Gadilingappa MN. Microbial siderophores: A new insight on healthcare applications. BME Front [Internet]. 2025 Mar 21;6:0112. Available from: http://dx.doi.org/10.34133/bmef.0112

100. Liu X-F, Zhang J, Liu J-J, Zhou Q-H, Liu Z, Hu P-Y, et al. Bifunctional CuS composite nanofibers via in situ electrospinning for outdoor rapid hemostasis and simultaneous ablating superbug. Chem Eng J [Internet]. 2020 Dec;401(126096):126096. Available from: http://dx.doi.org/10.1016/j.cej.2020.126096

101. Khalf A, Madihally SV. Recent advances in multiaxial electrospinning for drug delivery. Eur J Pharm Biopharm [Internet]. 2017 Mar;112:1–17. Available from: http://dx.doi.org/10.1016/j.ejpb.2016.11.010

102. Hemamalini T, Giri Dev VR. Comprehensive review on electrospinning of starch polymer for biomedical applications. Int J Biol Macromol [Internet]. 2018 Jan;106:712–8. Available from: http://dx.doi.org/10.1016/j.ijbiomac.2017.08.079

103. Jadidi Kouhbanani MA, Mosleh-Shirazi S, Beheshtkhoo N, Kasaee SR, Nekouian S, Alshehery S, et al. Investigation through the antimicrobial activity of electrospun PCL nanofiber mats with green synthesized Ag–Fe nanoparticles. J Drug Deliv Sci Technol [Internet]. 2023 Aug;85(104541):104541. Available from: http://dx.doi.org/10.1016/j.jddst.2023.104541

104. Asl MA, Karbasi S, Beigi-Boroujeni S, Zamanlui Benisi S, Saeed M. Evaluation of the effects of starch on polyhydroxybutyrate electrospun scaffolds for bone tissue engineering applications. Int J Biol Macromol [Internet]. 2021 Nov;191:500–13. Available from: http://dx.doi.org/10.1016/j.ijbiomac.2021.09.078

Data Availability Statement

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The datasets generated and analyzed during this study are available from the corresponding author upon reasonable request.