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Integrating piezoelectric dressings with botanicals as emerging smart dressings for diabetic wound healing

Yaqi Yue, Ruodan Xu * and Ning Li *

Diabetic foot ulcers (DFUs) are a common type of chronic wound characterized by slow healing, susceptibility to infection, and high amputation rates, causing significant suffering and economic burden to patients. Unfortunately, existing first-line treatments often fail to deliver desired outcomes, highlighting the urgent need for more effective solutions. Appropriate wound dressings can provide a favorable microenvironment for healing, making them an essential component of effective DFU management. Currently, novel dressings based on piezoelectric materials have gradually attracted attention. This review focuses on the remarkable advantages of these piezoelectric dressings and their applications in treating chronic wounds, particularly DFUs. Piezoelectric dressings facilitate tissue repair through electrical stimulation and achieve antibacterial effects *via* piezoelectric catalysis. Moreover, they allow for the controlled and on-demand release of therapeutic agents, addressing wound healing from multiple aspects. Additionally, botanicals, which provide a rich source of biochemicals, are safe and cost-effective and have shown significant efficacy in clinical applications for chronic wounds. However, investigations into integrating botanicals with piezoelectric materials in wound dressings are still in their infancy. Following presentations of the mechanisms by which botanicals can enhance DFU treatment, this review proposes that the development of piezoelectric dressings loaded with botanicals will fully harness their synergistic effects, paving the way for more effective treatment options for DFUs and other chronic wounds. Future research should further emphasize optimizing the design and functionality of these advanced dressings to significantly enhance their clinical impact.

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1. Introduction

Diabetic Foot Ulcers (DFUs) represent one of the most common and serious complications in diabetic patients.[1] With a high incidence rate and a tendency to resist healing, DFUs can severely affect the patient's quality of life while also imposing a substantial economic burden on individuals and society. The management of DFUs is fraught with challenges, including prolonged healing times, a heightened risk of infection, and escalating treatment costs.

An Indian study from 2011 to 2018 found that DFUs in Asian Indians had a median healing time of 3 months, with 43.4% requiring amputation and 42.4% recurring. These findings demonstrate the limited efficacy of current first-line therapies and underscore the critical need for early intervention to prevent severe outcomes like amputation.[2] Wound dressings are essential in the treatment of DFUs, as they provide an optimal microenvironment conducive to healing. Despite extensive studies on wound dressings, many available options are prohibitively expensive and lack robust clinical evidence of their efficacy, leading to ongoing challenges in treatment. A meta-analysis has found that sucrose octasulfate and hydrogels can improve healing in non-infected neuropathic DFUs when compared to standard care. However, the quality of evidence is only "moderate" due to the reliance on limited, single-center, low-quality trials. This suggests that many advanced dressings lack strong evidence of efficacy, and the effectiveness of existing advanced wound dressings still needs to be validated.[3] Therefore, the urgent need to develop novel, cost-effective, and efficient wound dressings cannot be overstated.

In recent years, piezoelectric materials have emerged as a focus in the biomedical field due to their unique physicochemical properties. However, their application in wound dressings remains largely unexplored. This study aims to explore new strategies for developing wound dressings utilizing piezoelectric materials. By advancing this approach, we aim to significantly improve the clinical treatment of DFUs, offering substantial theoretical insights and practical solutions that can transform patient care and enhance clinical outcomes.

Department of Biomedical Engineering and Technology, Institute of Basic Theory for Chinese Medicine, China Academy of Chinese Medical Sciences, Beijing, 100700, China. E-mail: lili.li.ning@gmail.com, ruodanxu@gmail.com

2. Hard-to-heal diabetic foot ulcers

Various factors influence the healing process of DFUs, and the challenges associated with their healing arise from a complex cycle of interconnected issues. The primary cause of these ulcers involves a harmful cycle characterized by reduced blood flow, impaired nerve function, suppressed immune responses, and weakened cellular repair, all triggered by hyperglycemia and exacerbated by infections and external stressors.[4] In particular, DFUs are often accompanied by the formation of biofilms, which are complex microbial communities encased in a polysaccharide matrix secreted by microorganisms. The presence of biofilms contributes to high levels of drug resistance, allowing pathogens to evade the host immune system and complicating conventional antibiotic treatments, making wound healing more difficult.[5] To break this cycle, effective management of DFUs requires a comprehensive approach that simultaneously addresses blood circulation, revascularization, infection control, and the regulation of hyperglycemia and its associated microenvironment.

Dressings play a key role in DFU interventions, providing protection and facilitating healing. Commonly used wound dressings in clinical practice include conventional passive dressings, antimicrobial active dressings, and bioactive dressings.[6] While these dressings offer sufficient moisture retention and the ability to absorb exudates, several gaps remain in meeting the clinical requirements. For instance, passive dressings only cover the wounds and do not actively respond to the wound's microenvironment. Moreover, traditional antimicrobial agents often struggle to penetrate biofilm, leading to recurrent infections. Additionally, externally supplied growth factors intended to support vascular regeneration are prone to degradation, failing to sustainably activate the signaling necessary for neovascularization. To address the limitations of current dressings, there is an urgent need to develop multifunctional wound dressings that integrate to promote healing, combat infection, enable controlled drug release, and dynamically respond to the microenvironment to revolutionize the management of DFUs.

3. Piezoelectric materials

Piezoelectric materials are special substances that convert energy between mechanical and electrical forms. When these materials experience mechanical stress, they exhibit electrical polarization, generating charges on their surfaces in a phenomenon known as the piezoelectric effect. Conversely, when exposed to an electric field, these materials undergo mechanical deformation, which is referred to as the converse piezoelectric effect. The origin of the piezoelectric effect lies in the non-centrosymmetric crystal structure of the material. When subjected to stretching, twisting, bending, or compression, these materials generate a net dipole moment, forming electric charges on their surfaces. This feature allows piezoelectric scaffolds to autonomously generate electrical stimulation (ES) through mechanical deformation without needing an external power source.[7]

3.1 Advantages of piezoelectric dressings for wound healing

One critical application of piezoelectric materials in tissue engineering is the promotion of wound healing. Piezoelectric dressings are a novel type of medical dressing that harnesses the piezoelectric effect to convert mechanical energy into electrical energy. This process promotes wound healing, catalyzes antibacterial activity, and enables precise, on-demand drug release (Fig. 1). The use of piezoelectric dressings can shorten wound healing times and reduce the risk of infection, demonstrating broad application potential in the realm of wound care.

3.1.1 ES promotes tissue repair. The skin itself demonstrates piezoelectric properties, primarily due to the presence of collagen and keratin. In 1986, Rossi *et al.* discovered that the piezoelectricity of the dermis originates from collagen,

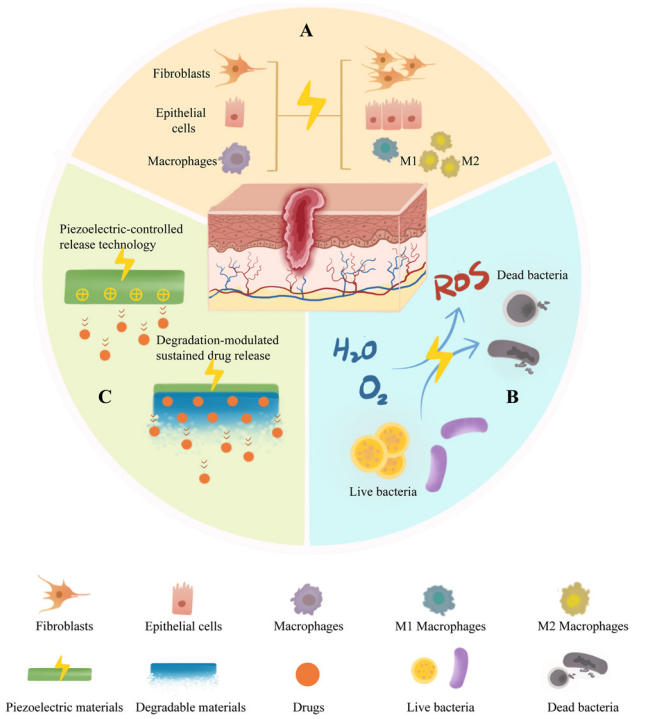

Fig. 1 Three aspects that piezoelectric materials promote wound healing. (A) Electrical stimulation promotes tissue repair through a dual mechanism: directly activating the migration, proliferation, and extracellular matrix synthesis functions of epithelial cells and fibroblasts; modulating the immune microenvironment by promoting the transformation of macrophages from the pro-inflammatory M1 phenotype to the anti-inflammatory M2 phenotype, thereby accelerating inflammation resolution and tissue regeneration. (B) The electric fields generated by piezoelectric materials under mechanical stress can catalyze the redox reactions of water molecules and oxygen, and the resulting reactive oxygen species can efficiently kill bacteria. (C) Piezoelectric dressings integrate drugs through two key strategies: one uses charge repulsion induced by the piezoelectric effect for on-demand controlled release of therapeutics; the other incorporates biodegradable materials to achieve sustained drug release during degradation.

while the epidermis and stratum corneum gain their piezoelectric properties from keratin.[8] At wound sites in human skin, as well as in the cornea and skin of rodents, consistent and sustained outward electric currents are observed. Cells can respond to weak electric fields,[9] and ES therapy plays a crucial role in all stages of wound healing. During the hemostasis phase, ES enhances the generation of platelet-derived microparticles and activates pro-coagulant markers on the platelet surface.[10] In the inflammatory phase, it strengthens the phagocytic capacity of macrophages,[11] suppresses the M1 inflammatory phenotype, and enhances polarization of macrophages towards the M2 phenotype, thereby mitigating inflammation at the wound site.[12] During the proliferation phase, ES promotes the proliferation and differentiation of keratinocytes, which increases keratin deposition and the migration rate of keratinocytes.[13] Even in the remodeling phase, ES enhances the contractility of myofibroblasts and facilitates the substitution of type III collagen with type I collagen, improving tissue maturity through increased tensile strength.[14]

During wound healing, electrical signals act as primary directional cues for guiding and stimulating the migration of inflammatory cells, fibroblasts, and epithelial cells. Two critical regulators of electric-field-induced cell migration and wound healing are phosphatidylinositol-3-OH kinase-γ (PI(3)Kγ) and phosphatase and tensin homolog (PTEN). PI(3)Kγ promotes electrotaxis by activating downstream signaling pathways, while PTEN acts as a negative regulator, fine-tuning the cell's response to electrical cues.[15] By promoting the migration and proliferation of epithelial cells, the re-epithelialization process of the wound is accelerated, reducing exposure time, lowering the risk of infection, and facilitating rapid wound closure. Fibroblasts are crucial in wound healing by producing the extracellular matrix (ECM), including collagen, to fill the wound and form new tissue. Enhancing fibroblast activity accelerates the deposition of the ECM, improving both the speed and quality of wound closure. In diabetic wounds, the hyperglycemic environment hinders the transformation of macrophages from the pro-inflammatory M1 phenotype to the anti-inflammatory M2 phenotype, resulting in the accumulation of M1 macrophages. This accumulation produces excessive inflammatory factors, creating an unfavorable microenvironment characterized by oxidative stress, enhanced proteolysis, and cell damage, which delays wound healing. Therefore, regulating macrophage polarization has become a key strategy for promoting diabetic wound healing. Collectively, these effects improved the wound healing rates, reduced scar areas, and significantly enhanced levels of vascularization, collagen synthesis, and the formation of visible hair follicle structures in regenerated skin tissue, ultimately restoring skin functionality (Fig. 1A).

However, traditional ES typically requires external power sources, which can lead to poor portability and discomfort for patients. Using transdermal electrodes requires sterilization to prevent infections and may cause secondary damage to the wounds. Even non-invasive patch electrodes must avoid direct contact with the wound, as prolonged or concentrated current application can lead to burns or allergic reactions. These limitations currently restrict the clinical application of ES in wound healing and skin tissue regeneration. Integrating piezoelectric materials into dressings provides a solution by converting external mechanical stimuli into electrical energy, thus overcoming the constraints of traditional ES therapies. Piezoelectric materials can generate ES by bearing mechanical loads during patient movement or through ultrasound irradiation. Such processes stimulate the proliferation or differentiation of various types of cells, effectively promoting the development and regeneration of tissues including bone, ligament, cartilage, tendon, skin, hair, outer hair cells, cornea, and sclera.[16] The exogenous ES generated by piezoelectric materials can mimic endogenous bioelectricity, promoting the migration of key cells, influencing intercellular signaling, and accelerating various stages of wound healing. This includes reducing edema, promoting cell migration, regulating collagen deposition, and stimulating nerve and vascular regeneration.[17] This collective function serves as the fundamental principle behind the application of piezoelectric materials to wound healing.

3.1.2 Antibacterial mechanisms and applications of piezocatalytic medicine. Piezocatalytic medicine (PCM) utilizes electric fields generated by piezoelectric materials under mechanical stress to catalyze redox reactions. This process produces reactive species, including reactive oxygen species (ROS), which have potential biomedical applications. Current applications of PCM include tumor therapy, antibacterial activity, degradation of organic compounds, tissue repair and regeneration, and biosensing.[18] The production of ROS and electron enrichment *via* piezoelectric materials through non-invasive stimulation offers significant advantages in antibacterial treatment, making it highly efficient and distinct from traditional antibiotics. This approach addresses typical issues related to antibiotic resistance and cytotoxicity. When mechanically stimulated, piezoelectric materials can catalyze the redox reactions of water molecules and oxygen, generating ROS such as hydroxyl radicals ($^{\bullet}OH$), superoxide anions (O_2^-), singlet oxygen ($^1O_2$), and hydrogen peroxide (H_2O_2). These ROS are powerful oxidizing agents that can attack and damage bacterial cell membranes and walls. They oxidize the lipid bilayer, disrupt membrane integrity, and cause leakage of cellular contents, ultimately leading to bacterial death. Additionally, ROS can inhibit the electron transport chain of bacterial metabolism, disrupt normal bacterial metabolic processes, and modulate immune responses to enhance the bactericidal activity of immune cells. For instance, they can shift the polarization state of macrophages from the anti-inflammatory M2 type to the pro-inflammatory M1 type, thereby enhancing macrophages' ability to clear bacteria.[19] More importantly, the amount of ROS generated is safe for normal mammalian cells[20] (Fig. 1B).

3.1.3 Drug loading and release mechanisms of piezoelectric dressings. Drug-loaded piezoelectric dressings can simultaneously exert the electrical stimulation effects of piezoelectric materials and the synergistic therapeutic effects of drugs.

Piezoelectric dressings incorporate drugs through two main strategies: one utilizes charge repulsion induced by the piezoelectric effect for on-demand controlled release of therapeutic agents, while the other integrates biodegradable materials to enable sustained drug release during their degradation process (Fig. 1C).

3.2 How to design suitable piezoelectric wound dressings?

Choosing the right piezoelectric materials for medical applications is crucial, as it involves several essential factors that can significantly impact patient outcomes. Biocompatibility is paramount; materials must not provoke an immune response or cause tissue damage when used inside or on the body. Moreover, flexibility and bendability are vital to accommodate the complex physiological structures and movement needs of the human body. For implantable or internal applications, biodegradability becomes particularly advantageous, as it removes the burden of secondary surgeries to retrieve implants. This enhances patient comfort, reduces risks, and provides environmental benefits.

In the field of biomedicine, four main categories of piezoelectric materials can be identified (Table 1). (1) Biological piezoelectric materials, such as amino acids, peptides, proteins, and polysaccharides. These materials are known for their excellent biocompatibility, biosafety, and biodegradability among all types of piezoelectric materials. However, they exhibit poor piezoelectric properties and lack adequate chemical stability. (2) Organic piezoelectric materials, like polyvinylidene fluoride (PVDF), demonstrate good biocompatibility along with excellent processability and plasticity. Nevertheless, some organic materials are non-biodegradable, and their piezoelectric constants are generally lower than those of inorganic piezoelectric materials. (3) Inorganic piezoelectric materials, including barium titanate ($BaTiO_3$, BTO), zinc oxide (ZnO), and aluminum nitride, are recognized for their outstanding piezoelectric properties, including high piezoelectric constants and good environmental stability. However, they tend to have inferior biocompatibility and biodegradability compared to natural materials. (4) Composite materials, including PVDF/$BaTiO_3$ and poly(vinylidene fluoride-trifluoroethylene) [P(VDF-TrFE)] can combine the advantages of each component.[21]

Selecting piezoelectric materials for medical applications also requires carefully balancing several key factors. While traditional lead-containing piezoelectric ceramics are highly efficient in converting mechanical to electrical energy, their toxic lead content makes them unsuitable for biomedicine.[22] On the other hand, while natural amino acids are biocompatible, their weak piezoelectric properties and low charge conversion efficiency pose limitations.[23] This is where composite piezoelectric materials offer advantages. By integrating the benefits of various materials through specialized processes, they are gaining significant attention in research. In developing piezoelectric materials that meet specific medical needs, researchers prioritize biocompatibility, piezoelectric properties, biodegradability, mechanical properties, and long-term stability. This holistic approach facilitates the effective application of piezoelectric materials across diverse fields, including tissue engineering, drug delivery, biosensing, energy harvesting, and piezoelectric catalysis in biomedicine.

3.3 Piezoelectric dressings

Dressings can be prepared in various forms, such as nanofiber membranes, hydrogel composites, and multilayer structured dressings, using different processing methods like electrospinning, coating, and 3D printing. These dressings can be customized to meet the specific needs of a wound, taking into account its size, depth, and location (Table 2).

3.3.1 Piezoelectric electrospun dressings. Electrospinning is a process that utilizes a high-voltage electric field to charge polymer solutions or melts, forming jet streams that eventually solidify into nanofibers or microfibers. The nanofibrous structure prepared by electrospinning typically has fiber diameters ranging from the nanoscale to the microscale, with intercon-

Table 1 Advantages and disadvantages of various piezoelectric materials

Types of piezoelectric materials	Representative materials	Biocompatibility	Piezoelectric properties	Advantages	Disadvantages
Biological	Amino acids, peptides and proteins	Fully biocompatible	Poor	1. Best in biocompatibility, biosafety, and biodegradability	1. Poor piezoelectric properties and chemical stability
Organic synthetic	PVDF and its copolymer	Good biocompatibility	Good	1. Good biocompatibility 2. Excellent processability and plasticity	1. Some materials are non-biodegradable 2. Piezoelectric constants are lower than those of inorganic piezoelectric materials
Inorganic	Pb-free piezoelectric ceramic materials: $BaTiO_3$, ZnO	Safety under long-term exposure remains to be verified	Excellent	1. High piezoelectric constants 2. Good environmental stability	1. Biocompatibility and biodegradability are not as good as natural materials
Composite	N/A	N/A	N/A	1. Combine the advantages of each component	N/A

Table 2 Comparative analysis of the morphological advantages and disadvantages of different forms of piezoelectric dressings

Different forms of piezoelectric dressings	Advantages	Disadvantages
Electrospinning	1. High specific surface areas, porosity, and good permeability	1. Low adhesion to wounds, requiring external dressings for fixation 2. Unable to provide a moist environment for wound healing
Hydrogel	1. Creating a moist wound environment 2. Absorbing tissue exudates 3. Good adhesion	1. Inferior piezoelectric properties compared to electrospun thin films
Multilayer structure	Combines the advantages of each component	N/A

nected porous network structures formed between the fibers. It can mimic the extracellular matrix (ECM) of natural tissues. This biomimetic property provides an ideal microenvironment for cell adhesion, proliferation, and migration, thereby promoting wound healing. The high specific surface area and interconnected porous structure facilitate efficient gas exchange and can also accommodate a certain amount of tissue exudate (Table 2).

PVDF is a piezoelectric organic synthetic polymer that is recognized for its high flexibility, non-cytotoxicity, and stability in both chemical and physical aspects. This makes it widely used in the biomedical field. PVDF can be prepared into nanofiber membranes through electrospinning technology, which is particularly advantageous for wound dressings. The piezoelectric properties of PVDF are primarily attributed to its polar crystalline phases, particularly the β phase. The proportion of the β phase in PVDF correlates with its degree of crystallinity. The mechanical properties of PVDF can be optimized by modifying the polymer chain composition and adjusting the degree of crystallinity. Guo *et al.* successfully converted the crystal phase of PVDF from the non-piezoelectric α phase to the piezoelectric β phase through electrospinning technology, preparing a PVDF/polyurethane (PU) membrane as a wound scaffold. By adjusting the polymer ratio to 1 : 1, they achieved a balance between mechanical and piezoelectric properties. Both *in vivo* and *in vitro* studies demonstrated that piezoelectric stimulation significantly enhances fibroblasts' migration, adhesion, and secretion capabilities, highlighting the effectiveness of piezoelectric dressings in promoting wound healing.[24]

P(VDF-TrFE) exhibits significant alterations in its crystalline structure and properties due to the incorporation of tetrafluoroethylene units. Compared with other piezoelectric polymers, such as nylon, polylactic acid (PLA), or polyhydroxybutyrate, P(VDF-TrFE) demonstrates superior piezoelectric performance. Unlike PVDF, P(VDF-TrFE) maintains an all-*trans* configuration without requiring mechanical stretching. Additionally, polarization treatment, like corona poling or electrode poling, can further enhance the piezoelectric properties of materials. The piezoelectricity and ferroelectricity of P(VDF-TrFE) vary with the intensity of polarization, allowing for controllable surface potential by adjusting the applied voltage. In the study by Zhiyuan Zhou, electric field strengths for polarization were applied at +50 V μm^{-1}, +100 V μm^{-1} (positive poling), as well as −50 V μm^{-1}, −100 V μm^{-1} (negative poling), alongside a control group. The high-voltage poled P(VDF-TrFE) films (both +100 V μm^{-1} and −100 V μm^{-1}) exhibited approximately 4% higher β-phase content compared to the control group, along with enhanced surface potential and improved piezoelectric response.[25] Aochen Wang *et al.* used P(VDF-TrFE) as the primary piezoelectric material and optimized the electrospinning conditions along with annealing to enhance its piezoelectric properties. *In vitro* cell proliferation experiments showed a 60% increase in the fibroblast proliferation rate due to piezoelectric stimulation, with fibroblasts showing better elongation and alignment along the direction of the nanofiber scaffold compared to the control group. *In vivo* experiments further confirmed the potential of this application for wound healing.[26]

While PVDF is not fully biodegradable, which may pose potential environmental impacts and limit its applications in the biomedical field, combining PVDF with other biodegradable materials such as PLA or polyvinyl alcohol allows for the creation of dressings with partial biodegradability, thus reducing their environmental impact. Biodegradable dressings often exhibit favorable biocompatibility and can gradually degrade alongside the wound healing process, minimizing damages to newly formed tissues caused by the frequent replacement of traditional dressings. Although natural biopolymer-based piezoelectric dressings exhibit excellent biocompatibility, they often have relatively low piezoelectric performance. This performance can be further enhanced by incorporating plasticizers or nanoparticles, like ZnO, which improve the materials' crystallinity and piezoelectric properties. For instance, Xiaoyang Yue *et al.* developed a biodegradable piezoelectric nanofiber scaffold based on silk fibroin (SF) *via* electrospinning technology. They created a composite scaffold incorporating lithium niobate (LN) nanoparticles and multiwalled carbon nanotubes (MWCNTs) to enhance its piezoelectric properties. This composite scaffold significantly promoted cell proliferation and wound healing under dynamic stimulation, with *in vitro* experiments indicating a 43% enhancement in cell proliferation. Correspondingly, *in vivo* experiments exhibited a greater number of new blood vessels and more intact lumen structures in the skin tissue, indicating better healing outcomes (Fig. 2A).[27]

The piezoelectric effect can also help reduce scar formation and promote high-quality healing of skin wounds, achieving scarless repair. Chao Zhang and colleagues discovered that an improper design of the static physical properties of materials can lead to a pro-fibrotic effect. In contrast, when piezoelectric

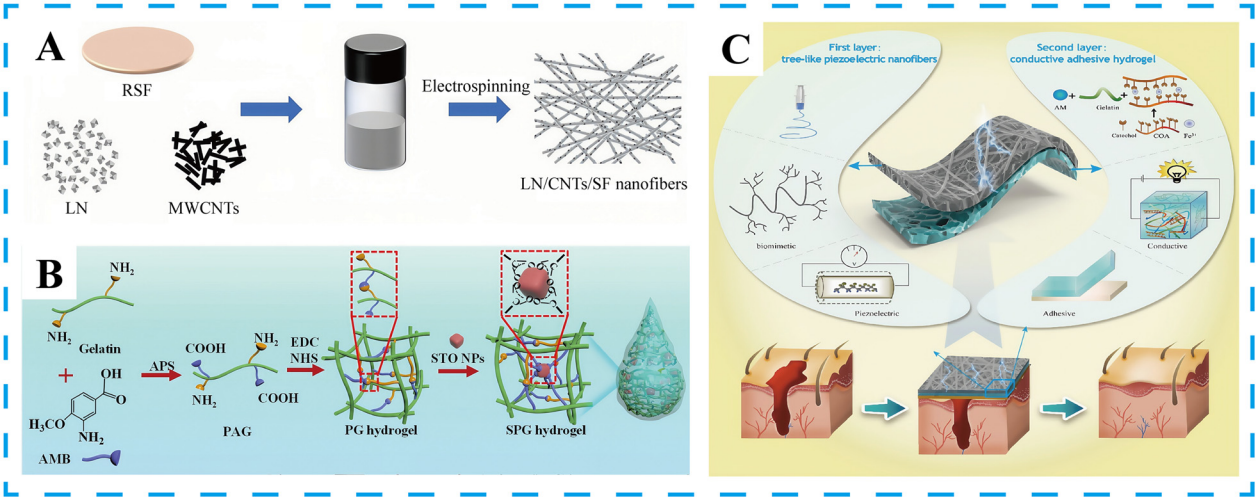

Fig. 2 Design of material structures for piezoelectric wound dressings. (A) Preparation of piezoelectric wound dressings *via* electrospinning technology. Reproduced from ref. 27 with permission from the Royal Society of Chemistry Publishing Group, copyright 2023. (B) Hydrogel piezoelectric wound dressings. Reproduced from ref. 30 with permission from the Elsevier Publishing Group, copyright 2025. (C) Piezoelectric dressings with composite structures. Reproduced from ref. 33 with permission from the American Chemical Society Publishing Group, copyright 2023.

dressings are stimulated by ultrasound, they generate a stable electrical output that inhibits the transforming growth factor-β (TGF-β) signaling pathway. This significantly decreases fibroblast proliferation, suppresses their over-activation, and reduces the excessive secretion of type I collagen, which is the primary component of scar tissue. Meanwhile, these dressings increase the secretion of type III collagen, thereby reducing scar formation. Additionally, piezoelectric dressings support the regeneration of hair follicles, blood vessels, and nerves, aiding in the restoration of normal skin function and achieving scarless healing along with functional tissue regeneration.[28]

3.3.2 Piezoelectric hydrogel dressings. Hydrogel dressings are advanced wound care materials characterized by their softness, flexibility, and biocompatibility. Notably, they exhibit exceptional adhesion and moisture retention compared to electrospun dressings. These properties enable them to maintain a moist wound environment that closely resembles the ECM, effectively reducing secondary tissue disruption that can occur with traditional dry dressings (Table 2).

Hydrogels create an optimal microenvironment for wound healing. They showcase piezoelectric properties, allowing them to convert mechanical stimuli from wound movement into bioelectrical signals, which activate repair processes like cell proliferation and angiogenesis. The synergy of these properties enhances wound healing. One strategy for designing piezoelectric hydrogels is to create them with intrinsic piezoelectric properties. Materials such as SF, chitosan (CS), chitin, and collagen can facilitate the formation of piezoelectric hydrogels through self-assembly or sol–gel mechanisms. While these materials offer excellent biocompatibility, their piezoelectric response coefficients remain relatively low.

Another method is to incorporate piezoelectric nanoparticles into the hydrogel.[29] However, these piezoelectric nanoparticles often agglomerate within the hydrogel matrix, and their low electrical conductivity hinders effective electron transfer, significantly diminishing the piezoelectric effect. Yunyun Wu and colleagues developed a multifunctional hydrogel integrating piezoelectricity, conductivity, and injectability. By leveraging the coordination interaction between titanium ions and carboxyl groups, strontium titanate ($SrTiO_3$) nanoparticles were evenly immobilized within the conductive hydrogel network through coordination bonds. This approach effectively addressed the tendency of piezoelectric materials to aggregate within the matrix and significantly improved the uniformity and electrical conductivity of the hydrogel (Fig. 2B).[30]

A promising strategy involves designing a bilayer dressing that combines a piezoelectric layer with a conductive hydrogel layer. Anjana Sharma *et al.* prepared a skin patch utilizing PVDF as the piezoelectric layer to generate ES, alongside carbonized polydopamine as the conductive hydrogel layer. This dual-layer, self-powered hydrogel efficiently accelerates the healing of DFUs and exhibits excellent antibacterial properties.[31] Tianyi Lu and colleagues have designed a "band-aid" style dressing that incorporates a CS/graphene oxide hydrogel matrix and a piezoelectric nanogenerator patch based on electrospun PVDF nanofibers.[32] Additionally, a team led by Yining Chen integrated bionic dendritic piezoelectric nanofibers with an adhesive hydrogel that showcases bio-inspired electrical activity (Fig. 2C).[33] In this bilayer configuration, the self-adhesive hydrogel ensures a tight fit to the wound dressing at the wound site. The embedded piezoelectric nanofiber layer captures slight biomechanical energy from tissue movements and converts it into continuous electrical signals, generating real-time electric fields that promote tissue regeneration. Detailed parameters of piezoelectric dressings are listed in Table 3.

Table 3 Dimension and piezoelectric properties of piezoelectric dressings

Piezoelectric materials	Dimension (μm)	Piezoelectric properties: Piezoelectric coefficient (pC N^{-1})	Electrical output: Output voltage (V)/ current (nA)	Experimental conditions	Ref.
PU/PVDF	1.41	d_{33} = 13.96	N/A	N/A	24
P(VDF-TrFE)	50	d_{33} = 25.90	N/A	N/A	25
P(VDF-TrFE)	0.51	d_{31} = 15.73	N/A	N/A	26
SF/LN	0.35	N/A	0.6/15	N/A	27
PLA/$BaTiO_3$	2.00	N/A	3	N/A	28
$SrTiO_3$	0.12	d_{33} = 26.82	N/A	N/A	30
PVDF	0.08	N/A	0.04/60	Pressure: 13 kPa; frequency: 5 Hz	31
PVDF	N/A	N/A	2/6	N/A	32
P(VDF-TrFE)	0.19 (trunk) 0.03 (branch)	N/A	2.7	Force: 2 N	33

3.3.3 Long-term safety risks and solutions of piezoelectric dressings. While PVDF demonstrates favorable short-term biocompatibility, its long-term use raises concerns regarding potential impacts on biological systems. The non-biodegradability of PVDF may lead to gradual accumulation in the body, resulting in local irritation and potentially triggering chronic inflammatory responses. To enhance the piezoelectric properties of wound dressings, dopants such as $BaTiO_3$ and ZnO nanoparticles, well-known for their excellent stability, high piezoelectric performance, and general non-toxicity, are frequently utilized. Additionally, carbon nanotubes are also frequently incorporated to improve conductivity. However, our understanding of their toxicity and distribution of these materials is primarily based on studies involving short-term exposure; there is limited research on the toxic effects of chronic exposure. Recent studies suggest that long-term exposure to nanoparticles may pose toxic risks. These particles can enter the human body through various pathways, including inhalation, oral ingestion, and skin contact, leading to cellular accumulation and potentially causing organ-specific toxicity. For instance, carbon nanotubes have been shown to cause harm to healthy tissues following long-term exposure.[34]

To reduce the risks associated with toxicity, several key strategies can be employed, including property regulation, surface modification, and the development of biodegradable composites. It is advisable to avoid nanoparticles that are excessively small, rod-shaped, plate-like, or long and fibrous, and instead favor biocompatible spherical forms. Neutral nanoparticles tend to exhibit better biocompatibility compared to positively charged variants, which can be cytotoxic. Additionally, surface coatings like poly(ethylene glycol) can modify protein interactions to help reduce toxicity. The combination of inorganic piezoelectric materials with biodegradable polymers, such as PLA and polycaprolactone, creates a balance between degradation rates and performance.[35]

In summary, it is essential to thoroughly assess the long-term toxic risks of piezoelectric dressings under prolonged exposure to ensure their safety in biomedical applications.

3.4 Piezoelectric catalytic antibacterial action

3.4.1 Bacterial eradication *via* reactive oxygen species generation. Wu *et al.* designed gold nanoparticle-decorated $BaTiO_3$ (BTO) nanocubes that produce $^{\bullet}OH$ and $^1O_2$ under ultrasound stimulation. Their antibacterial efficiency against Gram-negative *Escherichia coli* (*E. coli*) and Gram-positive *Staphylococcus aureus* (*S. aureus*) reached 99.23% and 99.94%, respectively, demonstrating highly efficient antibacterial capabilities. Electron microscopy revealed that the treated bacterial cells exhibited significant morphological changes, such as wrinkled and deformed surfaces, indicating that ROS had destroyed the bacterial cell membranes, releasing intracellular components such as proteins and nucleic acids, which led to notable antibacterial effects.[36] Dun Liu *et al.* embedded BTO nanoparticles into a hydrogel (Gel) to form BTO-Gel, which rapidly generates ROS under ultrasound stimulation. *In vitro* antibacterial experiments showed that just after 10 minutes of ultrasound exposure, the proportion of dead *E. coli* and *S. aureus* in the BTO-Gel group reached as high as 98.5% and 97.4%, respectively, with virtually no surviving bacteria on the dressing, showcasing excellent antibacterial performance (Fig. 3A).[37]

3.4.2 Adaptive-response piezoelectric smart dressings for stage-specific therapy of diabetic wounds. Diabetic wounds, characterized by persistent hyperglycemia-induced oxidative stress and chronic inflammation, are often complicated by bacterial infections and impaired tissue repair. While piezoelectric materials can generate ROS *via* sonodynamic therapy to eliminate pathogens, excessive residual ROS exacerbates oxidative damage, prolongs inflammatory cycles, and impedes healing. Recent innovations have given rise to smart dressings that can self-adapt to the changing conditions of wound microenvironments. These dynamic-response smart dressings cater to the specific needs of the inflammatory, reparative, and remodeling phases of diabetic foot ulcers. This stage-specific synergistic therapy targets antibacterial, anti-inflammatory, and pro-regenerative needs, thus addressing the limitations of conventional dressings, which typically offer single functionality and poor adaptability to complex pathological conditions.

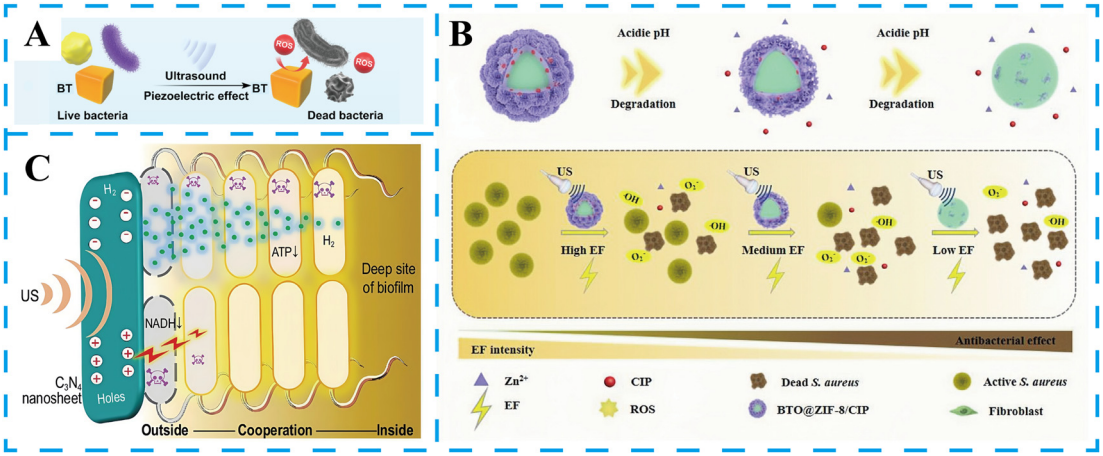

Fig. 3 Antibacterial effects of piezoelectric dressings. (A) Sterilization of piezoelectric dressings *via* ROS generation under ultrasound irradiation. Reproduced from ref. 37 with permission from the KeAi Publishing Group, copyright 2023. (B) Adaptive-response piezoelectric smart dressings. Reproduced from ref. 39 with permission from the Elsevier Publishing Group, copyright 2023. (C) Mechanism of antibiofilm action of piezoelectric dressings. Reproduced from ref. 40 with permission from the Oxford University Press Publishing Group, copyright 2023.

This innovative approach presents a transformative strategy for managing diabetic wounds. The piezoelectric microfibers developed by Xianli Wang *et al.* are made from lithium (Li)-doped ZnO/PLA microfibers coated with the antioxidant 4-octyl itaconate (4OI). These microfibers exhibit therapeutic effects that vary depending on the specific conditions present. The antioxidant 4OI upregulates the expression of downstream genes that possess antioxidant properties. When subjected to sonodynamic therapy, these microfibers can eliminate over 94.2% of *S. aureus* within just 15 minutes. After this antibacterial phase, the microfibers actively scavenge residual ROS through a combination of sustained release of 4OI, Li/ZnO catalytic modulation, and regulation of the immune microenvironment. This process facilitates the reprogramming of macrophages, restores mitochondrial functionality, reestablishes homeostasis, and shortens inflammatory cycles. As the wound progresses to the healing stage, bioactive Zn^{2+} and Li^{+} ions are continuously released to enhance cellular recruitment. Additionally, piezoelectric stimulation promotes neurovascular regeneration, working synergistically to accelerate wound recovery.[38] Zixin Zhu *et al.* developed a dynamically adaptive piezoelectric nanocomposite by self-assembling zeolitic imidazolate framework-8 (ZIF-8) on the surface of BTO nanoparticles and loading them with the antibiotic ciprofloxacin (CIP). This design enables a therapeutic mechanism that responds to multiple stimuli (pH and ultrasound) for synergistic wound treatment. In acidic infected microenvironments, ZIF-8 degrades, releasing Zn^{2+} ions and the encapsulated CIP. The combined action of CIP and ROS significantly enhances antibacterial efficacy. Experimental studies confirm that ZIF-8 amplifies the piezocatalytic effect of BTO when stimulated by ultrasound. As ZIF-8 gradually degrades, ROS production diminishes, while the released Zn^{2+} ions promote fibroblast migration and collagen deposition, facilitating tissue regeneration (Fig. 3B).[39] By eliminating excess ROS in local tissues, this strategy reduces inflammatory damage and advances wound healing into the proliferation phase, which is characterized by enhanced ECM deposition, angiogenesis, and granulation tissue formation. Ultimately, this multi-modal approach accelerates diabetic wound closure through the coordinated interplay of antibacterial, anti-inflammatory, and regenerative actions.

3.4.3 Strategies for enhancing antibacterial efficacy against bacterial biofilms. The formation of bacterial biofilms presents a significant challenge in treating bacterial infections. Bacteria within biofilms are encased in an extracellular polymeric substance matrix, creating a natural protective barrier. Conventional antimicrobial agents, including ROS, often exhibited limited efficacy due to their short half-lives and restricted diffusion capabilities. These limitations hindered their ability to penetrate the biofilm rapidly and effectively reach the site of infection. This not only enhances bacterial resistance but also diminishes the effectiveness of existing antimicrobial therapies in clinical settings, leading to the development of chronic infections that are difficult to eradicate. Qingqing Xu *et al.* developed C_3N_4 nanosheets that generate hydrogen gas (H_2) and holes (h^{+}) under ultrasound excitation. The hydrogen gas can penetrate the biofilm's interior, inhibiting bacterial energy metabolism. Concurrently, the holes can act from the outer surface layer, oxidizing polysaccharides and NADH, thereby disrupting the biofilm structure and the electron transport chain. This combined internal and external strategy can efficiently eradicate biofilms in DFUs, promoting wound healing (Fig. 3C).[40]

The integration of inorganic metal nanoparticles, carbon-based nanomaterials, and cationic compounds has emerged as a prevalent antibacterial approach. These elements can effectively work in synergy with piezocatalytic antimicrobial mechanisms to enhance the overall antibacterial efficacy. For instance, Tiantian Liu's team achieved a dual improvement in

Table 4 Dimension and piezoelectric properties of piezoelectric dressings with antibacterial actions

		Piezoelectric properties			
			Electrical output		
Piezoelectric materials	Dimension (μm)	Piezoelectric coefficient (pC N^{-1})	Output voltage (V)/ current (nA)	Experimental conditions	Ref.
$BaTiO_3$	0.15	N/A	N/A	N/A	36
$BaTiO_3$	0.12	N/A	N/A	N/A	37
ZnO/PLA	N/A	N/A	5.0	Ultrasound irradiation intensity: 0.3 W cm^{-2}	38
$BaTiO_3$	0.17	N/A	N/A	N/A	39
C_3N_4	0.01	N/A	N/A	N/A	40
PVDF	0.16	N/A	191.5	N/A	41

piezoelectric performance and antibacterial activity by incorporating silver nanoparticles (AgNPs) into PVDF nanofibers using electrospinning technology. The addition of AgNPs not only significantly increased the β-phase content of PVDF (from 70.7% to 87.4%), amplifying the piezoelectric effect, but also exhibited potent inhibition against *S. aureus*. However, its inhibitory effect on *E. coli* was comparatively weaker, likely due to the lipopolysaccharide layer in the outer membrane of Gram-negative bacteria, which hinders the inward penetration of Ag^+ ions.[41] In the self-powered band-aid developed by Tianyi Lu's team, the amino groups of CS molecules electrostatically bind to negatively charged phospholipids or lipopolysaccharides on bacterial surfaces. This interaction disrupts the integrity of the bacterial membrane, providing an antibacterial action. Additionally, the sharp edges of graphene oxide nanosheets can physically puncture bacterial membranes, while the piezoelectric effect of the PVDF nanofiber layer further enhances antimicrobial efficacy by inducing ROS generation and electroporation[32] (Table 4).

3.5 Drug-loaded piezoelectric dressings

3.5.1 Piezoelectric-controlled release technology. Piezoelectric-controlled release technology represents a significant application of piezoelectric materials in drug delivery. This innovative approach allows for responsive, on-demand drug delivery, overcoming the limitations of traditional drug administration, which typically requires multiple doses to maintain therapeutic drug concentrations in the body, often leading to fluctuations in drug concentration.

In a study by Tanvi Jariwala and colleagues, the feasibility of piezoelectric-controlled drug release was demonstrated by monitoring the release of model drugs. They found that when the electrostatic interaction between the piezoelectric material and the charged drug molecules was stronger than the diffusion force acting along the concentration gradient, the drug molecules could be immobilized on the surface of the piezoelectric material through electrostatic adhesion. In this state, the drug remains trapped without external stimuli. However, when mechanical force is applied, the surface potential of the piezoelectric material alters, changing the strength of the electrostatic binding with the charged drug molecules and disrupting the equilibrium, which results in controlled drug release. Specifically, the researchers developed a mechanically responsive drug delivery system using P(VDF-TrFE) nanofibers. They utilized cationic drug molecules, such as crystal violet and polylysine, for loading experiments. Drug release was triggered by mechanical stimuli, like shock waves, in both *in vitro* and *ex vivo* models. The results showed that the amount of drug released increased with the pressure and duration of the mechanical shock waves, while the non-piezoelectric control group released almost no drug. The study highlights the potential of piezoelectric materials to facilitate on-demand drug release through mechanical stimulation, with the amount of drug released being precisely regulated by factors such as fiber diameter, mechanical stimulation pressure, and dosage (Fig. 4A).[42]

Yani Sun *et al.* developed a self-powered wound dressing loaded with vancomycin. The dressing was prepared using electrospinning with PVDF. Instead of directly loading the drug onto the piezoelectric material, they loaded vancomycin hydrochloride (VAN), which possesses a low positive zeta potential, onto carboxylated multi-walled carbon nanotubes (c-MWCNTs) that have a high negative zeta potential. This process was achieved through electrostatic interactions and van der Waals forces. The introduction of carboxylated carbon nanotubes enhanced the fibers' mechanical strength and toughness and provided a high specific surface area and abundant carboxyl functional groups. These features created numerous adsorption sites for VAN to adhere stably to the surface. Additionally, the high conductivity and specific surface area of c-MWCNTs enhanced the local electric field strength, improving drug release efficiency and forming a stable drug carrier. Experimental results showed that when the dressing was subjected to mechanical stress, the cumulative drug release rate reached 88.57% over seven days. In contrast, without mechanical stress, the cumulative release was 0%. This demonstrated that the dressing could achieve on-demand drug release in response to mechanical stress, effectively releasing vancomycin under such conditions, exhibiting significant antibacterial activity, and reducing inflammatory reactions.[43]

Shibo Fu *et al.* investigated a self-powered hydrogel/nanogenerator system that employs a PTEN inhibitor. Unlike electrospun nanofibers, hydrogels exhibit excellent tissue

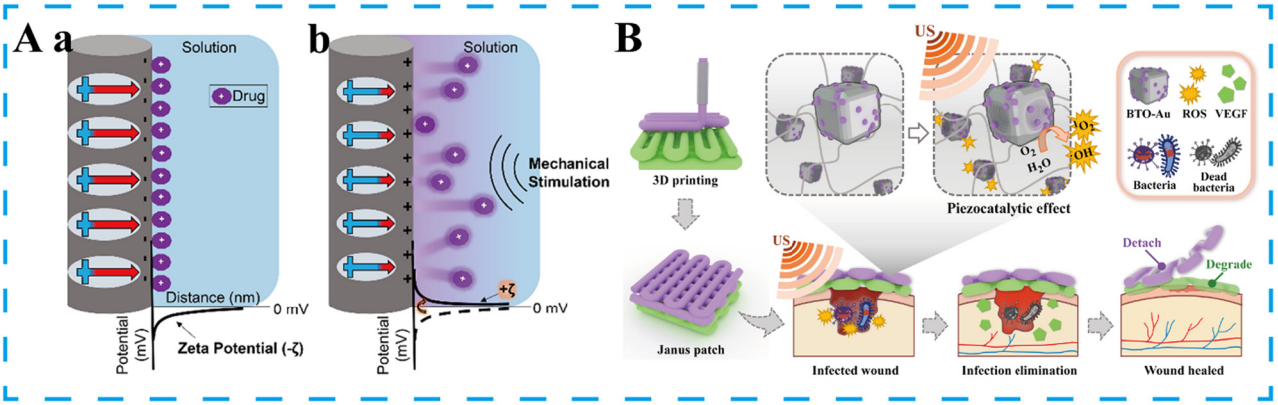

Fig. 4 Drug release of piezoelectric materials. (A) Piezoelectric-controlled release mechanism. Reproduced from ref. 42 with permission from the American Chemical Society Publishing Group, copyright 2021. (B) Degradation-modulated sustained drug release *via* material degradation. Reproduced from ref. 45 with permission from the Creative Commons Attribution License (CC BY 4.0), copyright 2023.

adhesion and mechanical properties, allowing them to adapt to the movement of rats without breaking or detaching. This adaptability ensures the continuity and stability of drug release. The system comprises a piezoelectric nanogenerator made of P(VDF-TrFE) nanofibers, where the electric field strength is dependent on the rats' activity level. The drug-loading component is prepared by polymerizing acrylamide and carboxymethyl CS and incorporating pyrrole monomer nanoparticles to create the hydrogel. The PTEN inhibitor, bpV (HOpic), is integrated into the polypyrrole (PPy) molecular structure as an anion to neutralize its positive charge, facilitating drug loading. When the piezoelectric nanogenerator is mechanically stimulated, the self-powered current flows through the PPy particles. This process allows free electrons to fill the electron holes, restoring the PPy to an electrically neutral state, which in turn releases the anionic drug bpV (HOpic). Notably, the release of the drug is influenced by the rat's activity level. When the rat is active and the electric field strength exceeds 625 mV mm^{-1}, the drug is released rapidly. Conversely, when the rat is at rest or under anesthesia, the electric field strength is lower and insufficient to trigger an adequate release of the PTEN inhibitor. This mechanism helps prevent potential side effects, such as DNA damage, from continuous PTEN inhibition.[44]

3.5.2 Degradation-modulated sustained drug release. In a smart antibacterial system prepared by Zixin Zhu, ZIF-8 was self-assembled on BTO surfaces, followed by the encapsulation of the antibiotic CIP. The pH-responsive degradation of ZIF-8 in acidic infected microenvironments triggered the controlled release of CIP, thereby exerting potent antibacterial effects.[39] Danqing Huang *et al.* engineered a dual-layer therapeutic dressing patch with spatiotemporally programmable functions. The top layer consists of a polyethylene glycol diacrylate hydrogel, which encapsulates gold nanoparticle-decorated tetragonal barium titanate. This layer generates ROS when activated by ultrasound while preventing the leakage of nanomaterials through precise interfacial confinement. The bottom layer is prepared from gelatin methacryloyl (GelMA), which is embedded with bioactive growth factors, such as vascular endothelial growth factor (VEGF), to orchestrate cellular proliferation and tissue regeneration. The release kinetics of VEGF are carefully synchronized with the gradual degradation of the GelMA matrix (Fig. 4B).[45] Table 5 summarizes detailed parameters of drug-loaded piezoelectric dressings.

4. Treatment of DFUs with botanicals

4.1 Botanical compounds promoting wound healing

The application of growth factors in wound repair faces several challenges, including high production costs, short *in vivo* half-life, and potential biosafety risks, which significantly limit their use in clinical settings. Additionally, the overuse of antibiotics has led to a global crisis of antimicrobial resistance. In contrast, plant extracts are emerging as a hotspot in novel wound dressing development and demonstrate immense potential in wound healing applications, such as antibacterial, anti-inflammatory, and pro-angiogenic activities, along with their low cost and natural biosafety profiles. For example, quercetin has been shown to enhance wound healing in diabetic conditions by increasing the expression of heme oxygenase-1 and inhibiting inflammatory signaling pathways, which reduces inflammatory factors such as interleukin-6 and tumor necrosis factor-α. Kaempferol, recognized for its antioxidant and anti-inflammatory properties, boosts the collagen and hydroxyproline content in wounds, accelerates re-epithelialization, and improves wound tensile strength. Similarly, momorcharin increases the TGF-β expression, thereby promoting collagen and protein synthesis. Naringin enhances granulation tissue formation and epithelial regeneration while inhibiting the growth of *S. aureus*. Moreover, baicalein increases the expression of extracellular signal-regulated kinase, phosphorylated extracellular signal-regulated kinase, and heat shock protein 27, which promote angiogenesis and wound

Table 5 Dimension and piezoelectric properties of drug-loaded piezoelectric dressings

		Piezoelectric properties			
			Electrical output		
Piezoelectric materials	Dimension (μm)	Piezoelectric coefficient (pC N^{-1})	Output voltage (V)/ current (nA)	Experimental conditions	Ref.
P(VDF-TrFE)	0.03	N/A	0.39	Pressure: 500 kPa, frequency: 12 Hz	42
PVDF	N/A	N/A	N/A	N/A	43
P(VDF-TrFE)	0.50	N/A	6.28/19.87	Force: 40 N, frequency: 1 Hz	44
$BaTiO_3$	N/A	N/A	N/A	N/A	45

healing. Ginsenoside triggers angiogenesis by regulating microRNA-23a, interferon regulatory factor-1, and inducible nitric oxide synthase levels. In addition, cinnamaldehyde enhances the expression of insulin-like growth factor-1 and glucose transporter 1, which promotes cell proliferation and energy uptake. Oleanolic acid increases fibroblast migration, while plumbagin increases mRNA levels of nuclear factor-erythroid 2-related factor 2 and decreases mRNA levels of Kelch-like ECH-associated protein 1, providing protective effects that accelerate diabetic wound healing.[46] Overall, these bioactive constituents from botanical sources demonstrate significant potential in enhancing the healing process of DFUs.

4.2 Piezoelectric materials combined with botanicals as a future wound dressing

Electroactive biomaterials, including conductive polymers, piezoelectric materials, photovoltaic materials, and electrets, offer multidimensional advantages in drug delivery and tissue regeneration.[47] Among these materials, photovoltaic materials have been successfully combined with natural plant extracts in thermoelectric hydrogel dressings. Minhong Tan and colleagues developed a wireless, biocompatible thermoelectric hydrogel that promotes diabetic ulcer repair by reconstructing directional thermoelectric fields and releasing exosomes derived from ginsenoside.[48] However, this system relies on continuous infrared light irradiation to trigger thermoelectric effects, complicating clinical applications and failing to maintain long-term biomimetic electric fields at the wound site. More critically, prolonged light exposure may induce localized hyperthermia, posing a burn risk for diabetic patients who experience heightened thermal perception thresholds due to peripheral neuropathy. In contrast, combining piezoelectric materials and plant extracts presents a safer and more controllable alternative. While research on integrating piezoelectric dressings with plant extracts remains limited, piezoelectric materials have shown promise in drug delivery and ES of cells and tissues. By incorporating plant extract-loaded wound dressings with piezoelectric materials, the natural advantages of plant extracts, including antibacterial properties, anti-inflammatory effects, and tissue repair capacity, can be significantly enhanced through piezoelectric stimulation. This innovative system enables on-demand and spatially targeted drug release activated by external stimuli such as ultrasound or magnetic fields, allowing for precise drug targeting while minimizing systemic toxicity. By loading plant extracts onto advanced carriers, this electro-biohybrid system offers a promising and highly biocompatible solution for treating diabetic ulcers and other complex, hard-to-heal wounds. It comprehensively optimizes wound healing conditions. The authors believe that advancements in manufacturing technologies for biocompatible piezoelectric scaffolds, precision therapeutic encapsulation, and controlled release technologies could redefine treatment paradigms, positioning piezoelectric-driven wound dressings as the gold standard for wound regeneration.

5. Conclusions and perspectives

DFUs are slow to heal and highly susceptible to infection, while traditional treatment methods often yield limited results. Piezoelectric material dressings offer a promising solution to overcome the limitations of conventional dressings in vascular regeneration, anti-biofilm activity, dynamic response, and metabolic regulation. These dressings utilize the combined effects of electrical, chemical, and multimodal therapies, functioning effectively for active repair and real-time intervention for DFUs. While being recognized as one of the core technologies for the next generation of intelligent DFU dressings, there are still gaps in their clinical translation. Firstly, there is a need to optimize the design of piezoelectric dressings further to enhance their biocompatibility, mechanical properties, electric field parameters, and piezoelectric performance, making them more suitable for clinical use. Secondly, to address the complex situations involved in DFU treatment, it is essential to explore better integrating piezoelectric materials with therapeutic drugs to achieve synergistic therapeutic effects. In particular, combining piezoelectric materials with botanical extracts presents an emerging opportunity to tackle infection, vascularization, and metabolic regulation issues. This approach harnesses the synergistic effects of electrical, chemical, and biological mechanisms, thus overcoming the limitations of single-action therapies and minimizing the risks of drug resistance and toxicity. However, several challenges must be addressed, including ensuring the compatibility of botanicals with piezoelectric materials, maintaining the stability of the components, controlling drug release, standardizing production processes, and translating research find-

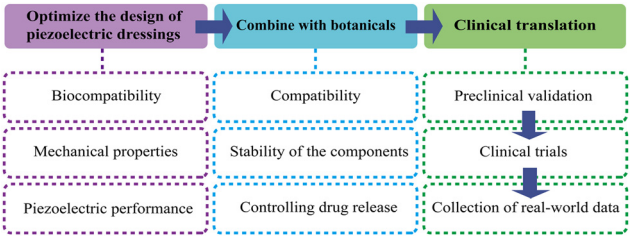

Fig. 5 The development and clinical translation pathway for piezoelectric dressings addressing diabetic foot ulcers.

ings into clinical practices. Lastly, large-scale clinical studies are essential to advance this strategy from laboratory concepts to real-world applications. The safety assessment of wound dressings should encompass the entire "research and development–clinical trial–post-marketing" cycle. *In vitro* human skin models, such as 3D EpiDerm™, aid in preclinical validation by reducing animal testing and accelerating product launches. Clinical trials should utilize multimodal monitoring, which includes clinical evaluation, lab tests, and imaging, to identify risks sensitively. During the post-marketing phase, continuous monitoring and real-world data collection, particularly concerning long-term cumulative toxicity, are crucial. This systematic approach ensures consistent and reliable safety and effectiveness data throughout all stages of testing, maximizing the therapeutic benefits of new dressings while minimizing risks to patient safety. Successful translation of this approach could significantly reshape DFU management strategies, offering more efficient, intelligent, and cost-effective treatment options for diabetic patients worldwide while expanding the boundaries of bioelectronic medicine (Fig. 5).

Author contributions

Ning Li: conceptualization, writing – original draft, writing – review & editing, visualization, supervision, and funding acquisition; Ruodan Xu: conceptualization, writing – review & editing, visualization, supervision, and funding acquisition; Yaqi Yue: writing – original draft, writing – review & editing, and visualization.

Abbreviations

AgNPs	Silver nanoparticles
$BaTiO_3$	Barium titanate
CS	Chitosan
DFUs	Diabetic foot ulcers
ECM	Extracellular matrix
ES	Electrical stimulation
PCM	Piezocatalytic medicine
PI(3)Kγ	Phosphatidylinositol-3OH kinase-γ
PTEN	Phosphatase and tensin homolog
PU	Polyurethane
PVDF	Polyvinylidene fluoride
[P(VDF-TrFE)]	Poly(vinylidene fluoride-trifluoroethylene)
PLA	Polylactic acid
ROS	Reactive oxygen species
TGF-β	Transforming growth factor-β
VAN	Vancomycin hydrochloride
VEGF	Vascular endothelial growth factor
MWCNTs	Multi-walled carbon nanotubes
ZnO	Zinc oxide.

Conflicts of interest

There are no conflicts to declare.

Data availability

No primary research results, software or code have been included and no new data were generated or analysed as part of this review.

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