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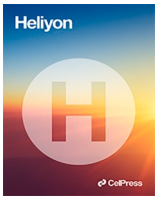

Review article

Multi-functional dressings for recovery and screenable treatment of wounds: A review

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ABSTRACT

Considerable research has focused on advanced wound dressing technology over the past decade. The increasing emphasis on health and medical treatment is crucial to the modern healthcare system. Consequently, high-quality wound dressings with advanced standards are essential for superior medical care. Next-generation multifunctional wound dressings feature antibacterial properties, pain relief, biocompatibility, drug delivery, flexibility, and exudate absorption. Today, biomimetic models, tissue engineering, and synthetic skin are integrated with emerging wound healing technologies, offering a new perspective on wound management. Based on the classification model of multifunctional and advanced wound dressings, various AI-assisted wound management technologies are also highly efficient. The primary goals of advanced wound dressing technologies include faster wound healing, prevention of microbial contamination, preservation of skin aesthetics, reduction of treatment costs, and increased patient comfort. The latest technologies in this field not only promote faster healing and the treatment of deep wounds but also emphasize continuous control and monitoring of the healing process. These screenable wound dressings can be smart sensors to detect wound status based on parameters such as pH, moisture, temperature, and oxygen levels. This enables wound status monitoring and appropriate treatment responses. These technologies facilitate wound observation and monitoring, as well as the evaluation and control of the healing process through various models and strategies, such as the fabrication of functional nanomaterials, computer algorithms, and artificial intelligence. This review presents an overview of the most prominent new technologies in wound dressings, along with their innovative approaches.

1. Introduction

The skin, as the body's largest organ, plays a crucial role in maintaining overall health by regulating temperature, providing sensation, and acting as a barrier against pathogens. When the skin's integrity is compromised by trauma, burns, or other injuries, effective wound treatment becomes essential [1,2]. Wound treatment encompasses a spectrum of methodologies, ranging from surgical interventions to wound dressings, with the latter being particularly advantageous due to its non-invasive nature. However, the

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management of wounds is not always straightforward; chronic wounds, such as diabetic foot ulcers, pressure ulcers, and venous leg ulcers, necessitate more sophisticated approaches. Since wound healing has different stages (Fig. 1), it is possible to speed up the healing process by intervening in each stage. Consequently, the field of wound dressing is evolving rapidly to address these challenges and is advancing day by day [3,4].

Since the earliest human civilizations, wound dressings have been widely used to protect the wound bed and promote healing by preventing potential infections. Ancient Egyptians, for instance, used honey to prevent and treat disease and suturing wounds to stop bleeding. [5], while Greeks and Romans employed vinegar and wine-soaked dressings [6]. Over time, the materials and methods used in wound dressings have evolved significantly. In the 19th century, the introduction of antiseptic dressings marked a significant milestone, reducing infection rates and improving healing outcomes [7,8]. The progress has been progressed with a new dressing called moist modern wound dressing that uses new polymers including polyurethane, alginates, hydrocolloids, hydrogels, collagen, chitosan, pectin and hyaluronic acid to transfer medicine to all types of acute and chronic wounds. Also, biological polymers are used as scaffolds for tissue engineering and skin grafting, and medicinal agents such as antibiotics, vitamins, minerals, growth factors, and other wound healing accelerators that play an active role in the healing process can be placed in these cases. Controlled release of these drugs, a specific goal generally involves prolonging the effect of the active drug over time by allowing sustained release from a polymeric dosage form [9]. Oxygen therapy is also one of the methods that leads to wound healing, stimulating healing and stopping wound infection [10]. Today, the development of advanced wound dressings continues to build on this rich history, incorporating cutting-edge technologies and materials.

In recent years, many innovative preparations of wound dressings have been introduced, including nano-formulations and other novel dosage forms (Fig. 2). Nano-formulations, for example, utilize nanoparticles to deliver drugs directly to the wound site, enhancing therapeutic efficacy and reducing side effects [11,12]. These newer preparations maintain the physical properties of conventional dressings and offer added benefits, such as faster healing and anti-inflammatory effects. The integration of these technologies into wound dressings represents a significant advancement in wound care [13].

Developing such novel drug delivery systems demands extensive and advanced scientific knowledge in pharmacology, pharmaceutics, and nanotechnology. Pharmacology provides insights into the mechanisms of drug action and interactions, while pharmaceutics focuses on the formulation and delivery of medications. Nanotechnology, with its ability to manipulate materials at the molecular level, offers new possibilities for enhancing the performance of wound dressings [14]. By utilizing these scientific disciplines, researchers can create more effective and efficient wound dressings that meet the needs of patients and healthcare providers. However, more extensive and advanced scientific knowledge in pharmacology, pharmaceutics, and nanoscience/nanotechnology is demanding for the development of such novel drug delivery systems manufactured to produce better products more efficiently, at higher drug loading and at a lower cost to patients for the treatment of wound diseases, in fulfillment of the tenet of the pharmaceutical profession to improve the health of the public [15,16].

One of the most significant advancements in recent years is the development of multi-layer and multi-functional wound dressings. These advanced dressings are designed to address multiple aspects of wound care simultaneously. Multi-layer dressings combine different materials to offer a range of benefits, such as enhanced moisture retention, improved breathability, and increased structural support [17,18]. Multi-functional dressings integrate various functionalities, including antimicrobial protection, tissue regeneration promotion, and exudate management. By incorporating these features, multi-layer, and multi-functional wound dressings provide a comprehensive approach to wound care, improving healing outcomes and patient comfort [19].

Until now, many review articles have been published on various aspects of wound dressings in terms of infection management [10], wound healing improvement [20], sensor-assisted wound monitoring [21], and theranostic dressings [22]. However, this review is focused on advanced and multifunctional wound dressings for emergency wounds. First, multifunctional wound dressings and the various subcategories within this field are studied. Subsequently, screenable wound dressings are reviewed and interpreted based on responsive and controllable management, monitoring, and feedback on wound dressings. Furthermore, advanced skin repair materials in wound dressings and cell-based and tissue-engineered materials, alongside biomimetic and fish skin dressings, are described, and their advantages and challenges are discussed. New and advanced technologies in wound management, including FREMS 3D printing [23], electrospinning [24,25], and hydrogels [26] are then expanded upon. Finally, the future outlook for wound dressings and wound dressing innovation is reviewed, and fish skin wound dressings are considered a natural alternative in this field compared to synthetic artificial skin [27].

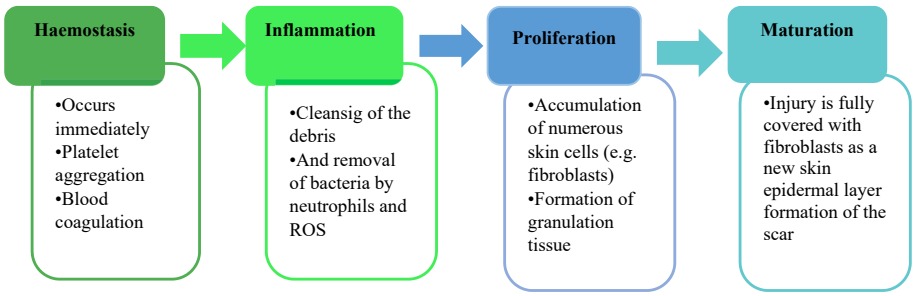

Fig. 1. Stages of wound healing.

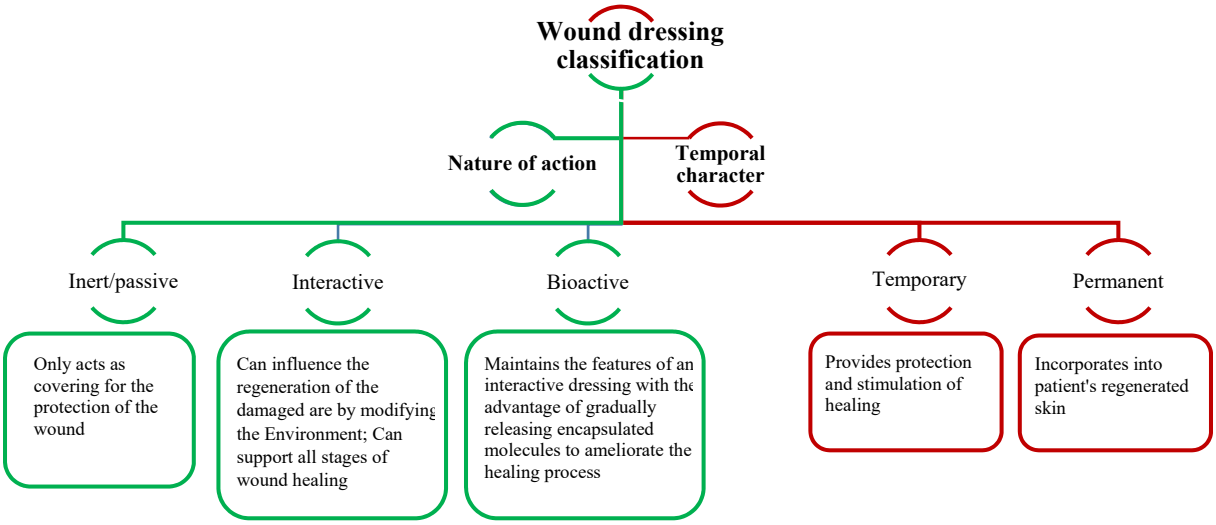

Fig. 2. Wound dressing classification.

2. Multi-functional wound dressings

Multifunctional wound dressings address various aspects of wound healing, including managing wound exudate, aiding tissue regeneration, and preventing bacterial infection. These dressings typically contain multiple modules that work together to create an optimal environment for wound recovery [28]. The specific components and their function can vary depending on the type of wound and the patient's needs. Some standard components of a multifunctional wound dressing with various antibacterial, temperature, homeostatic, analgesic, and growth factor-enhanced capabilities are listed in Fig. 3. Multifunctional wound dressings can also utilize biocompatible nanomaterials, stem cells, and keratinocyte growth factor stimulators that accelerate the wound regeneration and healing process. These materials can provide scaffolding for new tissue growth, activate growth factors and other signaling molecules, and modulate the immune response [20,29–32]. For instance, skin tissue engineering utilizing nanotechnology can incorporate biomaterials and nanomaterials to enhance tissue regeneration, deliver growth factors, provide scaffolding, and modulate the immune

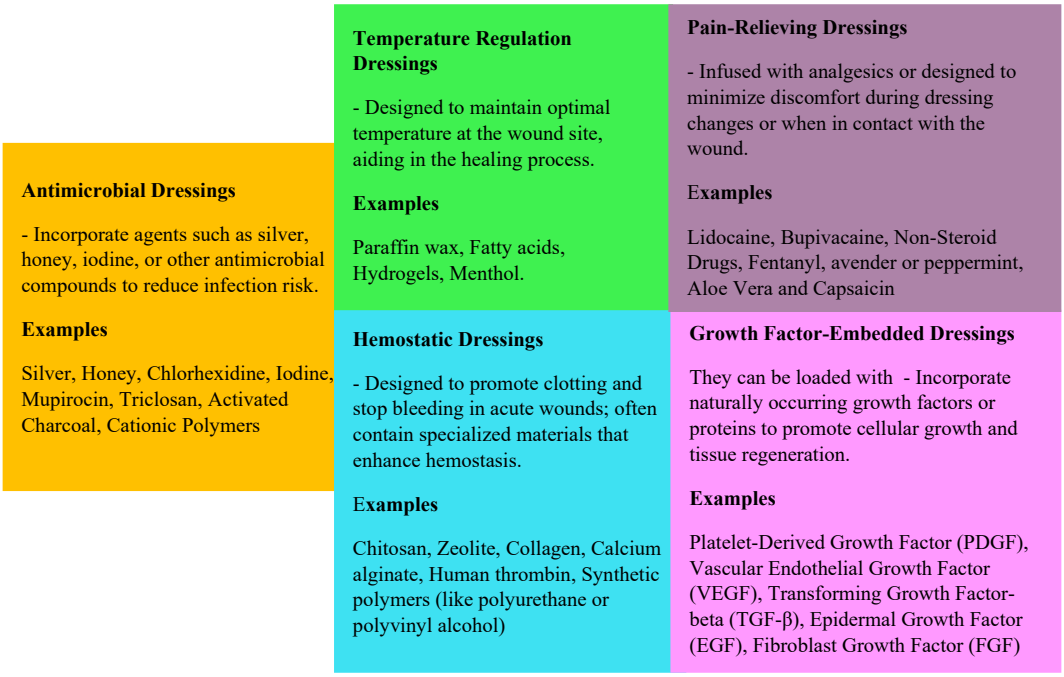

Fig. 3. Classification of wound dressing based on functionality.

response for effective wound management [33]. Biomaterial dressings can modulate the immune response, deliver signaling molecules, and enhance skin regeneration, showcasing significant potential in tissue engineering for promoting tissue repair and regeneration [34].Since biomaterials interact with immune cells to improve the skin repair process, they can induce complete skin regeneration through immune cell mechanisms. As a result, nanomaterials strengthen the fields of tissue engineering and provide better compatibility, response, and controllability in treatments.

In a study conducted in 2021, a multifunctional dressing of electrospun composite membranes of PCL/Chitosan/Curcumin was fabricated by a simple hybrid electrospinning technique. Curcumin-loaded chitosan tripolyphosphate nanoparticles were prepared and loaded to improve the sustained release of curcumin at the wound site. Curcumin with antioxidant, anti-inflammatory and wound healing activities sprayed on the surface of PCL/CS/CUR nanofibers leads to cell proliferation of human dermal fibroblasts and enhances the antioxidant, antibacterial effect at the wound site. Chitosan tripolyphosphate resulted in a gradual release profile and controlled delivery pattern of nanoencapsulated curcumin. Electrospraying of CURCSNP with the fabricated electrospun nanofibers had no adverse effect on the average diameter of the dressing nanofibers. In addition, the hydrophilic properties of curcumin and chitosan nanoparticles increased the degradation rate of the electrospun PCL/CS/CUR scaffold. In fact, functionalization of PCL/CS/CUR with CURCSNP significantly improved the antibacterial effect against MRSA (methicillin-resistant staphylococcus aureus) by 99.3 % and the antioxidant activity by 89 %. The results showed that at day 15 of wound closure, PCL/CS/CUR electrosprayed with CURCSNP resulted in 98.5 % and 96.4 % wound healing rates in non-infected and Staphylococcus aureus-infected wounds, respectively, with the novel multifunctional wound dressing with antibacterial activity of nanofibers [35].

A thermosensitive smart hydrogel loaded with therapeutic agents was developed by Zhiwei Wu et al. The formulation contained self-assembled nanoparticles called CIZ, which consisted of chlorogenic acid (CA), indocyanine green (ICG), and zinc ions (Zn^{2+}). These nanoparticles were loaded into a chitosan-β-glycerophosphate hydrogel called CIZ@G, which enabled rapid gel formation under photothermal effects. The designed hydrogel showed good biocompatibility for drug release in diabetic foot ulcers (DFU). This multifunctional hydrogel dressing, taking advantage of the dual function of CA and zinc ions, had strong antioxidant and anti-inflammatory effects. The hydrogel also contained a chitosan-based thermosensitive drug, which, when heated with ICG irradiation with an 808 nm laser, could increase the expression of vascular endothelial growth factor (VEGF) and platelet endothelial cell adhesion molecule-1 (CD31) and promote angiogenesis. Both in vitro and in vivo experiments confirmed that CIZ@G could effectively inhibit the growth of *Staphylococcus aureus* after laser irradiation and accelerate wound regeneration within 14 days. CIZ@G could rapidly gelatinize at the wound site after laser irradiation and slowly release drugs to combat bacterial infections. This integrated approach, which includes antibacterial, anti-inflammatory, antioxidant, and angiogenesis-promoting properties, enabled the multifunctional dressing to effectively address key challenges of diabetic wounds and demonstrate its significant potential for broad clinical applications [36].

2.1. *Moisture management*

Among the range of wound dressings available for wound healing, moist dressings have gained considerable popularity due to their

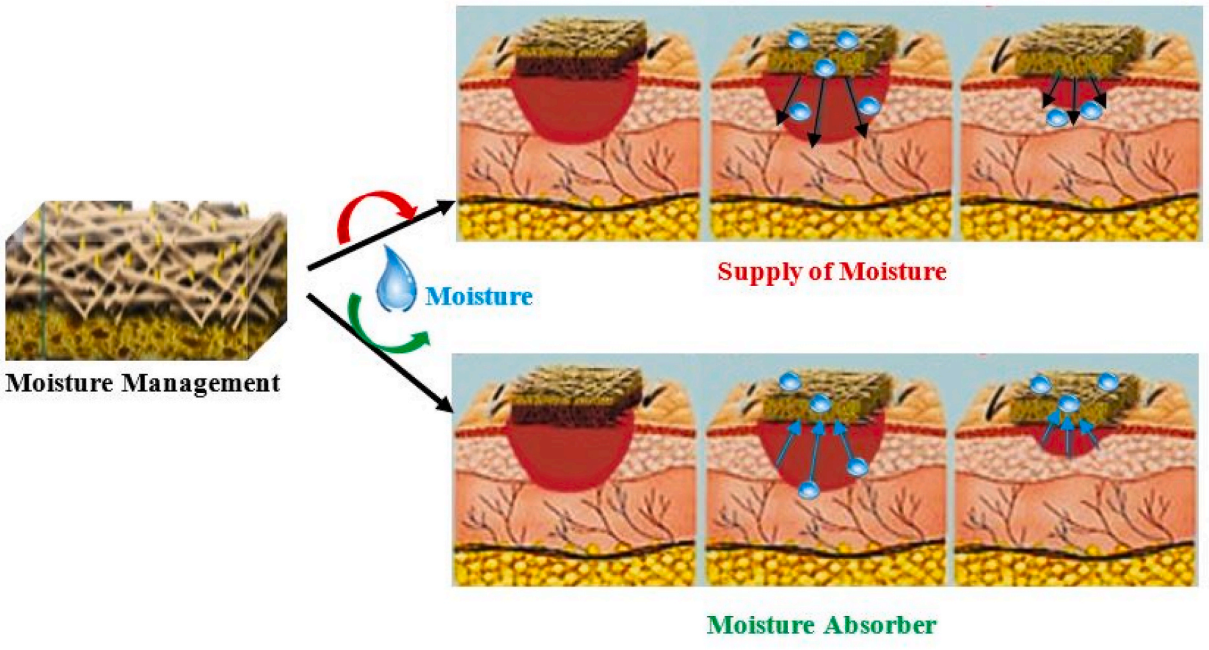

Fig. 4. Different mechanisms of moisture management.

ability to create an optimal environment for wound healing. These dressings can absorb and manage wound exudate and maintain a moist environment that promotes healing (Fig. 4) [9]. One of the essential benefits of using moist dressings is the importance of maintaining and producing the necessary moisture for chronic wounds where the wound bed may be dry and lack the moisture needed for healing and wounds with heavy exudates. These moisture-absorbing dressings can promote rapid wound healing, reduce infection rates, reduce the frequency of dressing changes, and reduce overall treatment costs [37]. Below two examples of different applications of such dressings are examined.

In 2024, a three-layer temperature-dependent fibrous wound dressing was developed. The dressing consisted of a hydrophilic cotton layer, a thermosensitive layer (TPPU), and a hydrophobic layer of polyurethane (PU) nanofibers. The TPPU layer comprises nanofibers designed from polymers, PU, and silver nanoparticles with an upper critical solution temperature (UCST) via free radical polymerization. The TPPU middle layer showed changes in its wettability upon heating, adjusting the thickness of the hydrophobic layer and ultimately creating the appropriate structure to guide spontaneous fluid transport. The polymer showed hydrophobicity at low temperatures and hydrophilicity at high temperatures. This was observed by a change in the turbidity of the solution from opaque to transparent. The polymer swelled at room temperature due to the formation of hydrogen bonds in its chains, resulting in an opaque solution. Intramolecular hydrogen bonds weakened as the temperature increased, and intermolecular hydrogen bonds with water molecules formed. The positive effect of the newly fabricated dressing was tested on diabetic wounds, as it induced collagen synthesis and increased epithelialization while reducing inflammation and ultimately accelerating the wound-healing process [38].

In another research work conducted by Zhan Xu et al., a multifunctional diabetic wound monitoring dressing with real-time rapid moisture drainage was designed via a smartphone integrated with Python-RGB applications. Since hyperglycemic tissue exudates and bacterial infections often accompany diabetic wounds, the healing of such wounds has become a significant challenge, which seriously delays the healing of diabetic wounds. Non-adherent, pH-responsive (5–9) dressings with antibacterial properties were proposed for exudate management and wound monitoring. In this synthesis, cellulose was used, and then a pale pink fabric was combined with antioxidants by soaking the nonwoven cellulose in a red cabbage anthocyanin/ethanol solution and air drying. The reason for using red cabbage anthocyanin was its responsiveness to pH changes. Finally, the Janus dressing was prepared by directly electrospinning PCL (polycaprolactone, hydrophobic) and antibacterial chlorhexidine (hydrophilic) on the top layer. With its antioxidant, pH-sensitive, hydrophilic cellulose coating and antibacterial hydrophobic polycaprolactone backing layer that directly contacts wounds, Janus dressing can unilaterally and irreversibly drain wound exudates and weaken moist adhesion to the wound. In this design, the healing

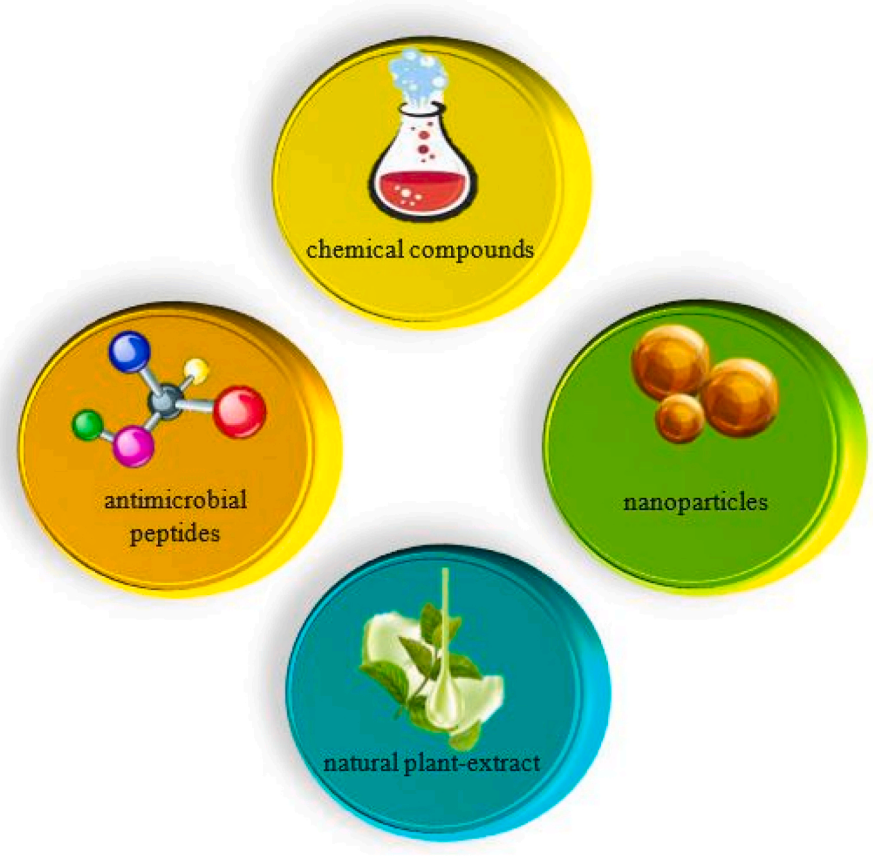

Fig. 5. Classification of antimicrobial agents.

process can be monitored in situ based on the distinct pH-responsive colors of the Janus dressing at different stages of healing. In vivo assays and histopathological studies demonstrate superior healing speed, collagen deposition, epithelialization, and angiogenesis of this moisture-absorbing dressing [39].

2.2. Antimicrobial activities

Many multi-functional wound dressings incorporate use antimicrobial agents to prevent the growth and spread of bacterial infection into the bloodstream and cause inflammatory shock. These agents can be in the form of antibiotics, antifungals, or other antimicrobial nanomaterials [40–42]. Antimicrobial agents can be categorized into several types: chemical-based compounds, plant-derived natural compounds, antimicrobial peptides, and nanoparticles The latter can be further divided into metallic and non-metallic nanoparticles (Fig. 5) [43]. Some agents from each category have been successfully patented and have entered the market (Table 1) [44].

2.2.1. Classification of nanomaterial antimicrobial activity

The classification of nanomaterial antimicrobial activity encompasses several dimensions, including nanomaterial properties, mechanisms of action, types of microorganisms, and current policies aimed at developing a standardized approach for distinguishing nanomaterial antimicrobial activity (Fig. 6). The primary types of nanomaterials used for antimicrobial purposes can be categorized as follows:

Metal-based nanomaterials: Some metal-based nanoparticles, such as Silver nanoparticles (AgNPs), gold nanoparticles (AuNPs), copper nanoparticles (CuNPs), and iron nanoparticles (FeNPs), which release metal ions can disrupt bacterial function [45]. AgNPs are the most extensively studied and utilized antimicrobial nanomaterials due to their broad-spectrum activity against bacteria, viruses, and fungi [46]. AgNPs can damage the microbial cell membrane, generate reactive oxygen species (ROS), and inhibit microbial DNA. They have also been shown to phosphorylate key bacterial proteins and inactivate their regulatory mechanisms for cellular processes such as exopolysaccharide biosynthesis and transport [47]. Although AuNPs are less commonly used than AgNPs, their antimicrobial properties have been consistently investigated. Generally, AuNPs are often combined with other antimicrobial agents to enhance efficacy and can be functionalized to target specific pathogens [46].

Metal oxide nanoparticles: The photocatalytic properties of TiO2 nanoparticles are effective in destroying microorganisms through light-induced ROS production, making them suitable for antimicrobial coatings and surfaces [46]. In some studies, zinc oxide nanoparticles have been shown to have an effect against a wide range of bacteria. Zinc oxide nanoparticles can disrupt cell membranes capable of producing ROS and bind to microbial proteins and DNA [48].

Carbon-Based Nanomaterials: Fullerenes, carbon nanotubes, and graphene oxide possess unique structural properties that contribute to their antimicrobial activity. These materials can physically disrupt microbial membranes, leading to their antimicrobial effects [49].

Biopolymer nanoparticles: Biopolymer nanoparticles are significant in biomedical applications due to their engineered properties and biocompatibility. These nanoparticles offer advantages such as the controlled release of antimicrobial agents [50,51].

Composite nanomaterials: Composite nanomaterials involve the hybridization of different types of nanoparticles to enhance antimicrobial efficiency. For example, composites containing silver nanoparticles have been found to be more effective against certain bacteria than silver-chitosan composites [52].

Various studies have highlighted the importance of incorporating antimicrobial agents into wound dressings to enhance their effectiveness. For instance, a survey by Meredith and Forbes demonstrated the rapid antimicrobial activity of ionic silver, EDTA, and benzethonium chloride-containing surgical cover dressing compared to other silver-containing dressings [38]. Additionally, research by Liang and Pierce involved the preparation of chitosan hydrogels incorporating a natural antimicrobial peptide, epsilon-poly-L-lysine. The hydrogels were tested for antimicrobial efficacy in vitro and ex vivo. First, the hydrogels were evaluated against planktonic cultures of *Pseudomonas aeruginosa*, *Staphylococcus aureus*, and Candida albicans. The results significantly reduced *Pseudomonas aeruginosa* and *Staphylococcus aureus* populations but were less effective against Candida albicans. Then, the hydrogels were applied to a reproducible porcine ex vivo skin wound model infected with a polymicrobial biofilm consisting of multidrug-resistant *Pseudomonas aeruginosa*, methicillin-resistant *Staphylococcus aureus*, and Candida albicans. The results showed that dressings such as alginate/CMC/Ag, cadexomer iodine, and HOCl exhibited promising antibiofilm activity. Specifically, the reduction of *Pseudomonas aeruginosa* was significant both in vitro and ex vivo, while the results were ineffective against Candida albicans [53]. These studies demonstrated the importance of antimicrobial activities in various applications including wound recovery, which mainly

Table 1
Examples of patents related to antimicrobial agents.

Granted patent number	Definition
US10836872	Visible light-curable water-soluble chitosan derivative, chitosan hydrogel, and preparation method therefor
EP3253424B1	Honey can deodorize wounds, has anti-inflammatory properties, stimulates tissue growth, manages pain, and minimizes scarring.
CN102327161A	The polyurethane wound dressing has two layers, top and bottom, and a hydrogel coating in the middle layer. This maintains the wound healing environment, shortens healing time, resists bacteria, and reduces infection.
WO2007045931A2	The wound dressing is a combination of Manuka honey and Manuka plant extract, which is a natural plant extract with antibacterial properties.

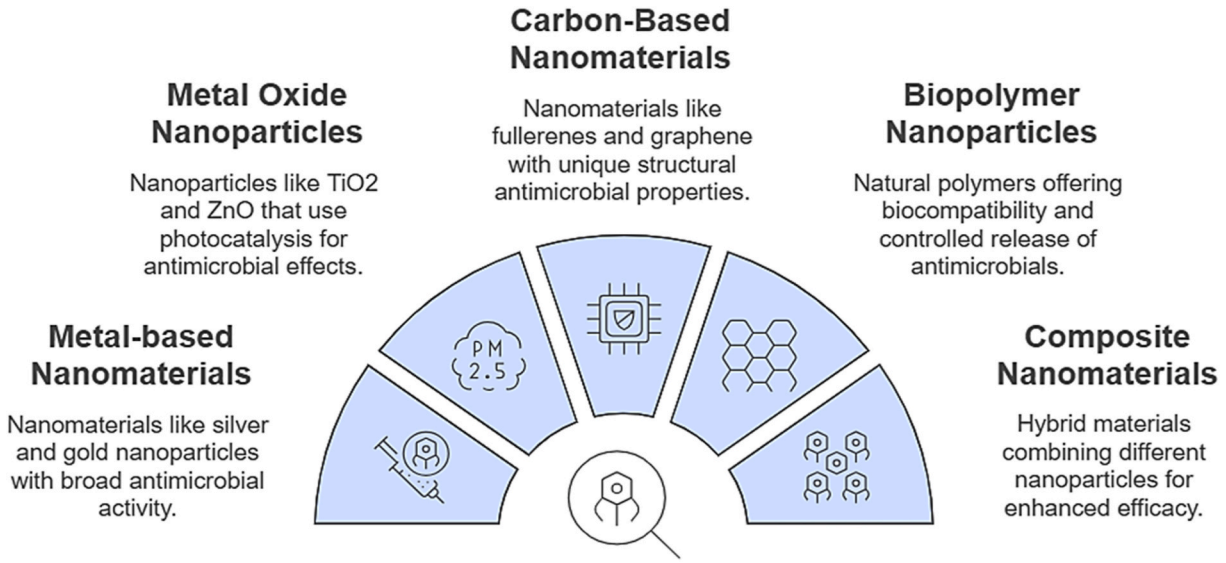

Fig. 6. Nanomaterial antimicrobial activity.

focuses on multifunctional wound dressings incorporating other antimicrobial agents to reduce the growth of various bacteria and prevent disseminated infections.

3. Screenable wound dressings

Screenable wound dressings are advanced medical products designed to assess and manage wounds effectively. They offer a range of functions, including moisture management, temperature regulation, infection control and pH control, while allowing for real-time monitoring of wound status. Advanced wound dressings can simultaneously incorporate monitoring technologies in addition to medications that track the wound healing process and provide feedback to healthcare professionals. This can help optimize treatment and improve patient outcomes [54].

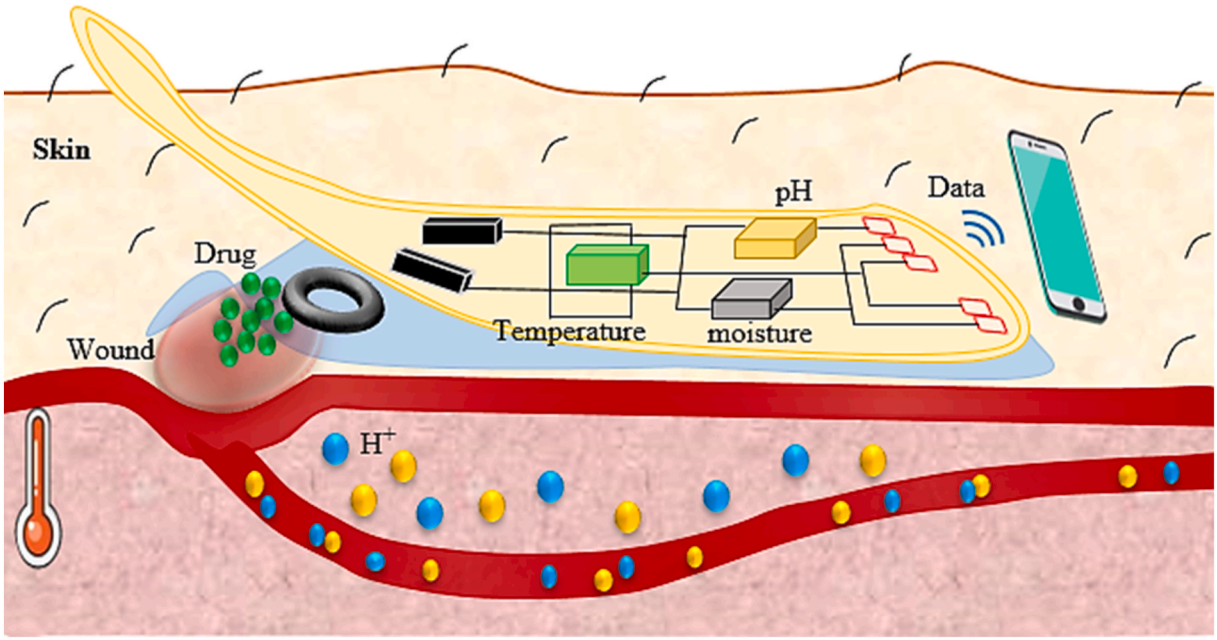

Fig. 7. Theranostics wound dressing with temperature, humidity, and pH sensing modules.

3.1. Monitoring and feedback

Wound monitoring dressings represent a significant advancement in wound care, integrating diagnostic capabilities with therapeutic functions. These innovative dressings use various technologies to monitor vital parameters such as pH, temperature, glucose levels, and reactive oxygen species (ROS), thereby improving the management of wound healing processes. In addition to wound monitoring being particularly important, developing dressings with unique properties for wound recovery and healing is vital. Therefore, creating systems that, in addition to wound monitoring, can also be useful by timely release of a specific dose of wound-healing compounds is known as theranostic smart dressings. Recently, innovative theranostic smart wound dressings have been introduced to facilitate the timely administration of optimal therapeutic doses directly to wound sites and simultaneously enable real-time biomarker monitoring to assess wound conditions. The main advantages of these theranostic materials include improved pharmacokinetics of therapeutic agents, reduced cytotoxicity, and reduced off-target drug effects. However, reports on theranostic wound dressings are limited due to the emerging technology (Fig. 7).

For example, Chen et al. in 2017. designed a smart theranostic wound dressing consisting of ciprofloxacin-enhanced luminous porous silicone (LuPSi) designed to detect and combat infected wounds. In vivo studies demonstrated its ability to accurately monitor infected wounds by detecting color changes caused by reactive oxygen species (ROS) and pH changes in the wound area. In addition, the rapid oxidation of LuPSi facilitated the immediate release of ciprofloxacin and effectively inhibited and controlled wound infection [55].

Zhou et al. developed a two-layer theranostic wound dressing made of UV-curable GelMA that incorporated antimicrobial vesicles and fluorescent carboxyfluorescein. The dressing released gentamicin sulfate and silver nitrate as antimicrobial agents and showed color changes in response to bacterial toxins or enzymes secreted by *Pseudomonas aeruginosa* and *Staphylococcus aureus*. In vitro and in vivo test results confirmed the efficacy and effective and timely response of the dressing for colorimetric detection and inhibition of pathogenic bacteria [56].

Singh et al. designed a smart theranostic wound dressing using an enzyme-responsive polyurethane scaffold with a prodrug and probe, which allows for simultaneous monitoring and treatment of wound infection. Activation of both prodrug and probe was initiated by an extracellular enzyme secreted by bacteria, lipase. In vitro studies demonstrated that this theranostic wound dressing provides accurate colorimetric detection of wound infection while exhibiting high antibacterial efficacy with minimal cytotoxicity. Theranostic hydrogels composed of L-arginine-modified chitosan and oxidized dextran modified with phenylboronic acid have been targeted for treating infected wounds. These pH-responsive and bacteria-responsive hydrogels demonstrated antibacterial properties against methicillin-resistant *Staphylococcus aureus*. Furthermore, their capacity to induce angiogenesis and collagen remodeling was

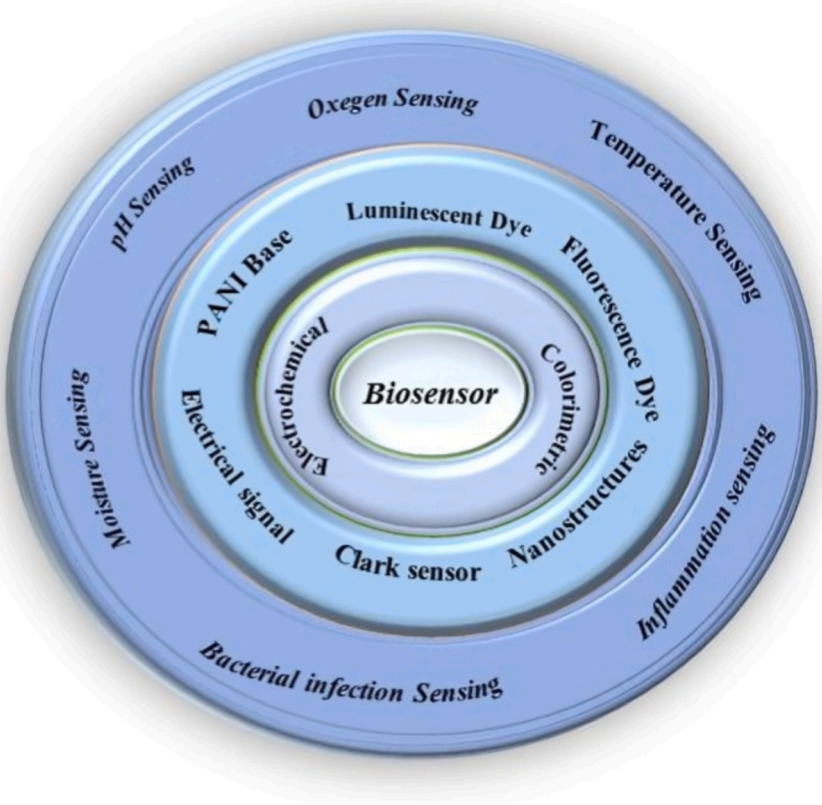

Fig. 8. Multi-functional wound dressings for analysis at the moment of the wound.

confirmed through an infectious motor wound-healing model [57]. Zheng et al. developed flexible two-color hydrogels made of polyacrylamide, chitosan, carbon quantum dots, and phenol red to monitor wound pH levels, reduce bacterial infections, and improve wound healing. These hydrogels exhibit remarkable hemostatic and adhesive properties that facilitate wound healing through potent antibacterial effects and skin repair capabilities. Furthermore, they were integrated with a digital data management system to provide real-time assessments of wound status [58].

In a study by Cui et al., an H2O2-responsive theranostic wound dressing was formulated using graphene quantum dots on luminescent porous silicon, which was injected with epidermal growth factor (EGF) and insulin and embedded in a chitosan film. Fluorescence imaging of the smart dressing was recorded under a UV flashlight (377 nm) to track free radicals during the healing process. In vitro and in vivo studies demonstrated that the smart dressing effectively controlled H2O2 levels in the wound microenvironment and enhanced cell proliferation and migration while significantly enhancing the healing of diabetic wounds [59]. Duan et al. developed a thermal signal-based theranostic approach to diagnose and manage chronic wounds. They used a NIR-active dye, IR820, encapsulated in porous silicon carriers sealed with calcium ions, allowing for the monitoring of photothermal activity generated by reactive oxygen species (ROS) as well as photothermal and photodynamic antibacterial therapy [60]. This innovative theranostic platform exhibited remarkable therapeutic effectiveness and ease of detection in models of diabetic wound infections.

Mirani et al. developed a multifunctional dressing capable of detecting pH changes to indicate bacterial infections and delivering the antibiotic gentamicin. The dressing demonstrated antibacterial therapeutic effects without harming primary human keratinocytes and fibroblasts, making it a suitable option for treating skin wounds. In addition, a smartphone recording system was implemented to provide quantitative data for patients and healthcare professionals to monitor wound conditions [61]. Although real-time diagnostic sensors [62,63] can provide rapid and real-time monitoring through sophisticated electronic sensors that collect and display data every second or every minute, such advantages are unnecessary for monitoring wound healing, as the healing process takes much longer. In many cases, rapid and real-time monitoring is not helpful (Fig. 8).

3.2. Responsive and controllable management

Responsive and controllable wound dressings significantly advance wound care, offering tailored treatment based on specific conditions. Interestingly, controllable wound dressings are often characterized by being responsive to stimuli and capable of intelligent responses to changes in the wound microenvironment (such as temperature, pH, moisture, etc.) (Fig. 9).

In a study by Yutong Yang et al. in 2023, a self-adjusting wound dressing with response to multiple stimuli and control of antibacterial activity was proposed. Specifically, MoS2 was designed as a nitric oxide (NO)-responsive oxygen species (ROS) L-arginine (MSPA) and encapsulated in carboxymethyl chitosan/poly (N-isopropyl acrylamide) (CMCS/PNIPAM) based cryogel was encapsulated by the multiple reaction.) was included. In response to the slightly acidic environment of bacterial infection, cryogels contribute to the absorption capacity of bacteria through acidic protonation behavior and effectively increase the antibacterial effect of photodynamics. Controllable delivery of ROS, NO, and remote wound management with NIR light was developed as a responsive and controllable system. Nanozyme-based cryogels with multiple stimuli effectively remove bacterial biofilm through NO-assisted photodynamic and photothermal treatment. Multiple enzyme activities such as cryogels effectively eliminate oxidative damage and accelerate collagen deposition and angiogenesis in infected wounds [64].

In a research work reported in 2018, aqueous solutions of polyvinyl alcohol, combined with magnetic Fe3O4 nanoparticles (MNPs) coated with citric acid, were used to produce composite fibers with a 100–300 nm diameter and controllable MNP loading. The fibers are stable in polar solvents such as ethanol and show no MNP precipitation for over 4 weeks. The ability to remotely trigger this release system in the dressing and its biocompatibility and lightweight feature have great potential for using these fibers as a smart drug

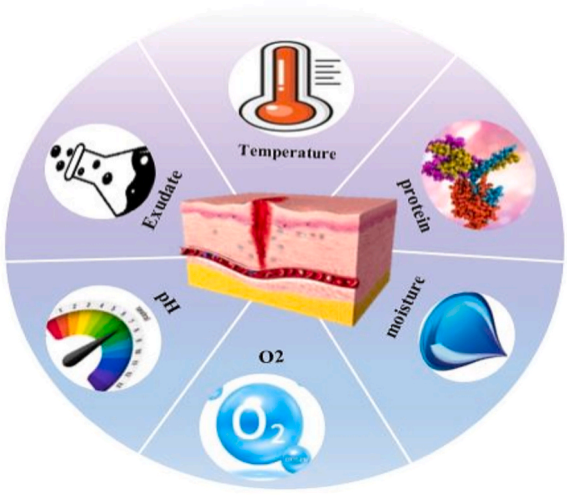

Fig. 9. Wound markers monitoring.

release agent for acetaminophen (a model drug). This designed system can accommodate various drugs such as antibacterial, anti-inflammatory, or skin-repairing drugs and can be used as a smart and controllable wound dressing [65].

In another report by Zi-Yuan L et al., a completely lightweight hydrogel dressing that can rapidly and remotely control dressing changes for chronic wounds was proposed. In this hydrogel dressing, a two-component hydrogel was synthesized: methacrylated hyaluronan (MeHA) and a photosensitive cross-linked ortho-nitrobenzyl derivative (o-NB). Hyaluronan (HA) was designed as the dressing skeleton for its anti-cell adhesion property and promotion of several biological processes, including cell migration, proliferation, angiogenesis, and wound healing. Finally, hyaluronan was functionalized with methacrylate to achieve in situ photogelation to seal the wound surface and promote angiogenesis. The photosensitive molecule o-NB was also used as a cross-linker to enable contactless dressing changes. The dressing system could be activated within 30 s by visible light irradiation ($\lambda > 500$ nm) and transformed into a quasi-liquid upon UV irradiation. ($\lambda = 254$ nm, 4 min). This wound-free and rapidly removable hydrogel dressing is applicable for treating diabetic wounds. The hydrogel system could gel the wound bed in situ under visible light within 30 s and dissolve by UV light irradiation within 4 min, if necessary. In addition, the possible mechanism, including cell proliferation and inflammatory regulation, of improving wound healing was further investigated. In a diabetic mouse model, significant wound healing was observed within 2–3 weeks due to the reduction of secondary damage during frequent dressing changes. Since this dressing plays a role in the healing processes of epithelialization, collagen deposition, cell proliferation, and inflammation regulation, it indicates a synergistic effect of the responsive hydrogel dressing for therapeutic efficacy. These results suggest that the MeHA-NB hydrogel can promote wound healing by accelerating re-epithelialization and ECM synthesis. Dressing changes with light stimulation have a clear advantage in promoting chronic wound healing, as secondary damage to the newly formed epithelium was minimized [66]. In summary, Responsive and controllable wound dressings represent a more advanced approach to wound care, focusing on dynamic management of the wound environment. In contrast, traditional dressings usually provide static support and protection.

4. Advanced skin repair materials

Human skin is an anisotropic, nonlinear, and viscoelastic material, and its mechanical properties are affected by age, position, hydration, etc. It is essential to measure its frictional interaction with wound dressings by in vivo testing. Therefore, an artificial, measurable skin model for human skin is critical. Nowadays, many artificial skin models (ASM) are commercially available for specific wound-healing purposes. Silicone elastomers and polyurethanes are the most common materials used to prepare ASM [67]. These technological advancements have enabled the creation of innovative wound dressings that enhance the healing process. For example, bioelectric dressings mimic the body's natural electrical signals to promote wound healing and epithelialization [68].

Among these advanced materials, hydrogels, which are hydrophilic polymer-based materials, can maintain a moist environment and aid wound healing. They have good biocompatibility and biodegradability. On the other hand, hydrocolloids are adhesive dressings that absorb wound exudate and create a moist healing environment, making them suitable for various wound types [69]. Alginates, derived from seaweed, are particularly effective for moderately to heavily exuding wounds as they can absorb large amounts of exudate [69]. Foam dressings are highly absorbent and maintain a moist wound environment, often used for partial and full-thickness wounds [69]. Transparent film dressings provide a barrier to bacteria while allowing gas exchange, making them useful for superficial wounds and skin tears [69].

4.1. Artificial skin wound dressings

Artificial skin can be used in various clinical applications, including treating burns, chronic wounds, surgical incisions, and skin graft sites. It is often applied to promote wound healing, reduce scarring, and improve overall outcomes for patients with compromised skin integrity. Artificial skin products continually evolve with advances in biomaterials, tissue engineering, and regenerative medicine. Healthcare providers consider the specific needs of each patient and wound type when selecting the most appropriate artificial skin product for optimal wound care and healing [32]. Artificial skin, also known as skin substitutes or bioengineered skin (Table 2), is a synthetic material designed to mimic the structure and function of human skin. It is used in wound care to promote healing, provide a barrier to infection, and support tissue regeneration [70,71]. In manufacturing artificial skin, cell therapy methods, 3D printing skin, factors influential in skin synthesis signaling pathways, and functional biomaterials are used, among which 3D bioprinting skin

Table 2
Skin substitutes based on definition and application in wound healing.

Skin Substitutes	Definition	materials	Ref
Synthetic	These skin substitutes are made from synthetic materials. They provide a protective barrier over the wound, promote moisture retention, and help facilitate healing.	silicone, polyurethane, or bioengineered polymers	[73]
Biological	These skin substitutes are derived from biological sources, such as human or animal tissue.	collagen, fibrin, dextran, chitosan, alginate, cellulose, …	[74, 75]
Composite	These skin substitutes combine both synthetic and biological materials to provide a more comprehensive approach to wound healing.	scaffold, growth factors, and protective barrier (e.g., Leukoplast barrier)	[76]
Temporary	These skin substitutes are designed for short-term use to provide immediate coverage and wound protection. The body may absorb them over time as new tissue forms underneath.	human cadaveric skin, tilapia fish, Porcine, banana tree leaves and potato peel	[77]

technology is considered an innovative and effective method of manufacturing artificial skin (Fig. 10) [72].

5. Cellular and biological components in wound management

5.1. Cellular components in wound management

Tissue-engineered skin substitutes, categorized into cell-containing matrices and acellular matrices, offer temporary or permanent wound coverage with a minimal risk of infection. Despite their clinical efficacy, these advanced dressings present a cost barrier when compared to commercially available wound dressings [23]. In wound management, a multifaceted approach often incorporates biological molecules and various cells to orchestrate chronic wound control, mitigate scarring, and promote immunomodulation, angiogenesis, and protection. These cellular components maintain moisture balance, remodel the extracellular matrix (ECM), and expedite wound closure. Key cellular players include epithelial cells, which facilitate re-epithelialization; fibroblasts, responsible for synthesizing vital ECM constituents such as collagen; keratinocytes, pivotal in epidermal regeneration and wound sealing; and stem cells, like mesenchymal stem cells. Additionally, anti-inflammatory cells, notably macrophages, play a crucial role in dampening inflammatory responses, while melanocytes and adipocytes also contribute to the wound healing milieu [78,79].

A notable investigation by M. Lashkari et al. led to the development of a mesenchymal stem cell-imbued bilayered scaffold. This innovative construct integrates a freshly prepared collagen/alginate hydrogel with polycaprolactone/gelatin fibers, which are electrospun directly onto the hydrogel base. Adipose-derived stem cells are then introduced to this composite structure. Empirical evidence from this study highlights a decrease in inflammation, bolstered angiogenesis, enhanced re-epithelialization, and collagen restructuring in full-thickness wounds of rats treated with the stem cell-enriched bilayered scaffold. Prospective research endeavors are encouraged to explore the integration of antioxidant agents to potentiate mitochondrial donation or to elevate antioxidant enzyme function, thus intensifying the therapeutic antioxidant properties of mesenchymal stem cell-based treatments [79].

In parallel, specific investigations have leveraged cellular factors within wound dressings to amplify biological compatibility and efficacy. For instance, L. Zhang et al. engineered a dynamic hydrogel bioadhesive tailored to diabetic ulcers. This hydrogel, a collagen and aldehyde-functionalized polyethylene glycol concoction, encapsulates umbilical cord stem cell factors. The resultant bioadhesive demonstrates heightened adhesion capabilities and biocompatibility alongside accelerated cellular engagement, neovascularization, and robust collagen deposition. The researchers posit that diabetic foot ulcers exhibit near-complete healing when treated with this advanced dressing [80].

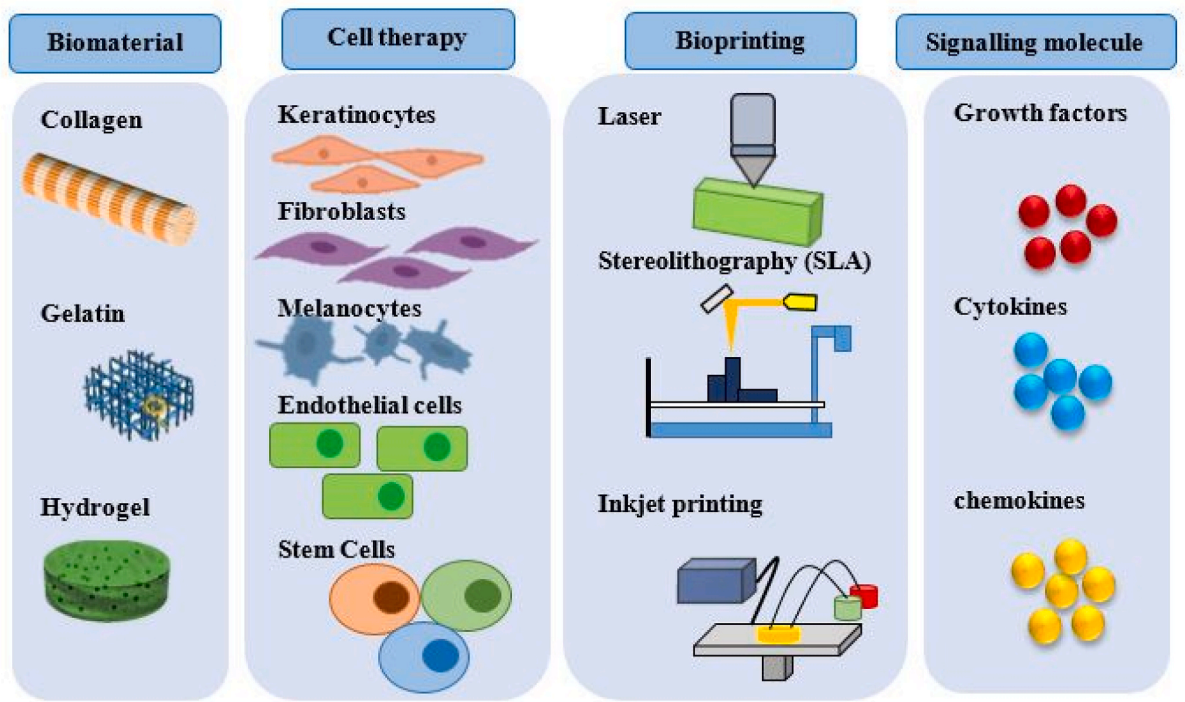

Fig. 10. Key requirements for the fabrication of artificial skin for wound healing.

5.2. Biomimetic wound dressings

Biomimetic wound dressings are advanced wound care products designed to mimic the natural healing environment of the body and promote tissue regeneration. These dressings are typically composed of biocompatible materials that closely resemble the extracellular matrix (ECM) of human tissues [81]. One of the critical features of biomimetic approaches is their structural resemblance to native tissues. By mimicking the architecture and composition of the natural extracellular matrix, these dressings provide a conducive environment for cell attachment and proliferation (Fig. 11) [82]. Additionally, the incorporation of bioactive molecules in biomimetic materials facilitates biological signaling, guiding cellular response and promoting tissue regeneration [83]. Despite their therapeutic potential, biomimetic wound dressings face cost, scalability, and long-term stability challenges. Manufacturing these advanced materials at scale while ensuring economic feasibility remains a hurdle. Additionally, ensuring the long-term stability of biomimetic materials for sustained performance poses a challenge. Rigorous clinical validation is also essential to demonstrate the safety and efficacy of these novel wound dressings [84,85].

5.3. Fish skin wound dressings

Using fish skin to treat wounds is an old and natural approach to wound management that has gained attention in recent years. Derived from fish skin, typically tilapia or salmon, these dressings have unique benefits in wound healing and tissue regeneration [27, 86]. In a paper published in 2022 (Fig. 12), using methacryloyl gelatin extracted from fish skin (FMA) by grafting optical cross-linking groups onto fish gelatin, synthesized pH-responsive IOFs with structurally vibrant colors using FMA mixt. Chitosan (CS) and poly-acrylic acid (PAA) were used to propagate colloidal crystals. The reasons for using fish skin in wound healing are its brilliant biocompatibility and low immunogenicity, as well as its functions to promote tissue growth and accelerate wound healing. In addition, creating interconnected nanopores, composite IOFs with high specific surface area can be combined with vascular endothelial growth factor (VEGF) to achieve antibacterial and angiogenic capabilities in accelerating wound healing, as well as PAA incorporated into the hydrogel system. It acts as a pH-responsive unit and can provide wound monitoring [87].

Fish skin wound dressings have several key features that make them ideal for wound dressing. They are rich in type 1 collagen, similar to human collagen, and promote cell adhesion and proliferation. The structure of the fish skin allows gas exchange and moisture retention, creating a favorable environment for healing. In addition, fish skin contains bioactive compounds that have antimicrobial properties and reduce the risk of infection in wounds [88]. One of the other main advantages of using fish skin as a wound dressing is its biocompatibility. Since fish skin is biodegradable and mimics human tissue, it reduces the risk of adverse reactions and inflammation. The collagen in fish skin regenerates tissue and accelerates wound closure. Fish skin dressings are also affordable and readily available, making them a good option for both acute and chronic wounds [89,90]. Clinical studies have shown the effectiveness of fish skin wound dressings in wound healing, especially in chronic wounds such as diabetic wounds and burns. The antimicrobial properties of fish skin help prevent infection, while the collagen content stimulates new tissue formation. Fish skin dressings are also effective in reducing pain and inflammation caused by wounds and help the patient's comfort during the healing process [91]. While fish skin wound dressings offer several advantages, challenges such as resource availability, standardization, and cultural acceptance must be addressed. Ensuring consistent quality and safety of fish skin products is critical to widespread adoption. Cultural considerations and ethical sourcing practices should also be considered when using fish skin dressings in different populations [92].

6. New advanced and emergent technologies in wound dressing

Nowadays, according to the studies conducted on the different classifications of wound dressings (Fig. 15), it can be seen that wound dressings with natural material origin can be effective in treatment and therapy. Rapid healing of wounds and the combination of these types of dressings with real-time wound analysis can revolutionize the field of wound dressings and improve patient outcomes;

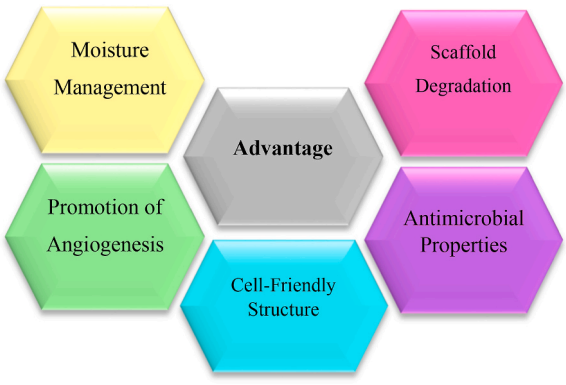

Fig. 11. Advantages of biomimetic dressings.

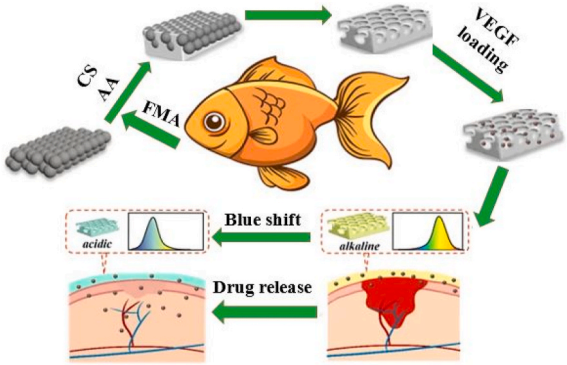

Fig. 12. The preparation cycle of composite IOF and fish skin and its application in dynamic pH measurement and wound healing.

however, more research is needed to understand their effectiveness and safety in different clinical settings fully. Fig. 13 shows the effective technologies in smart wound dressings for advanced management of various types of wounds. Several examples of biopolymers applied in the synthesis of smart wound dressings due to their significant advantages are listed in Table 3. Dressings have a great diversity because the rapid healing of wounds and the multifunctionality of dressings can make the emergence of nanotechnology-integrated dressings essential, so a consensus on their classification is necessary to understand the importance of the field of consumption, industry [93–99], and technology with innovation. Therefore, the most extensive classifications in wound dressings were reached using the SCOPUS, ScienceDirect, and Web of Science databases. With this information, it was found that wound dressings can be classified based on the type of wound and purpose of use, technology, and manufacturing industry (Table 4) to ensure an appropriate and accurate approach to therapeutic goals and the correct selection of dressings (Fig. 14).

6.1. FREMS technology

"FRAMES" (Frequency Rhythmic Electrical Modulation System) is a technology that sends biocompatible rhythmic electrical impulses that stimulate cellular activity in the wound area. The treatment method is also known as Lorenz therapy. The operator adjusts the impulse amplitude using a remote control according to the patient's sensitivity threshold and the stimulated tissue. The system modulates maximum amplitude according to the ion balance of the tissue underneath the electrodes to keep it constantly balanced (Biofeedback). Impulses have an active and recovery phase, guaranteeing ion balance in the tissue involved in the process. It has a significant application in accelerating the healing of chronic wounds, including diabetic and venous wounds, chronic wounds, severe burns, and bedsores in older people. This system shows its effectiveness in reducing pain and accelerating wound closure by increasing the stimulation of blood flow to the tissue (enhanced blood circulation helps to deliver nutrients and immune cells that are vital for the healing process), strengthening the formation of granulation tissue, Reducing the intensity of pain with effective electrical

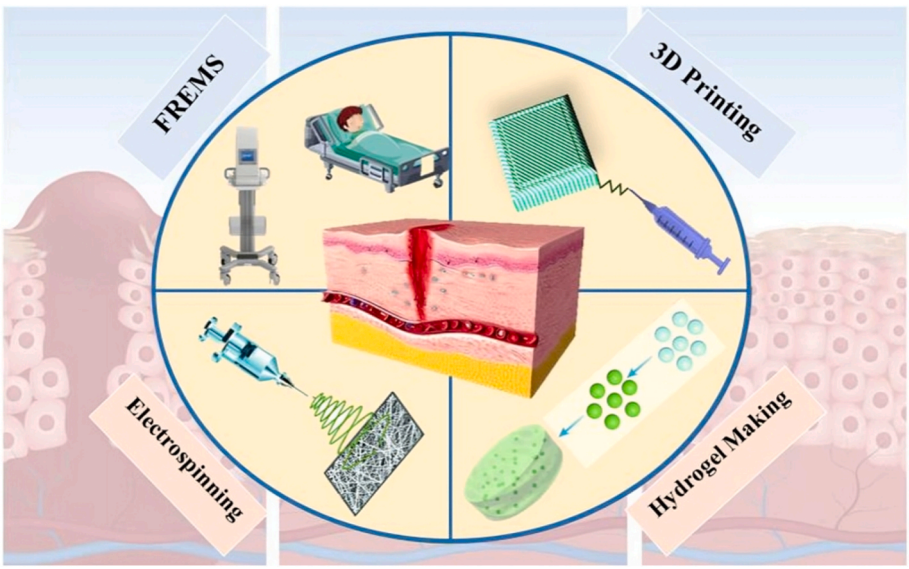

Fig. 13. Effective technologies in smart wound dressings.

Table 3
Names of functional biopolymers and their advantages.

Bio-polymeric materials	Advantage	Ref
Hydrogel	Biodegradable, strong moisture absorption, biocompatible	[100]
Polylactic acid (PLA)	can degrade and be absorbed by the body over time	[101]
Silk Fibroin	biocompatibility, biodegradability, and ability to be designed flexibly	[102]
Platelet-Derived Extracellular Vesicles (PEVs)	enhancing neovascularization and cell migration and reducing inflammation and scarring	[103]

stimulation on pain receptors (fiber C) [104] and increasing endorphin (a non-invasive approach that targets the endorphinergic structures of the brain and increases the secretion of beta-endorphins) [105] secretes and accelerates epithelialization, which is very important for wound healing [106].

In the research project conducted in 2024 by Marco Contardi and his group in order to investigate films based on Alg-PVPI in combination with FREMS in diabetic mouse models, Alg-alginic acid sodium salt, glycerol was used to make Alg-PVPI was used. Alg-PVPI films caused the agglutination of red blood cells and the attachment of platelets to the surface of the Alg-PVPI film, thus facilitating the hemostatic process. In general, it can be said that Alg-PVPI films have a high level of blood and biocompatibility, coagulation effect, and capacity to enhance cell proliferation. To evaluate wound closure with a diameter of 6 mm, diabetic rats were divided into different groups and treated with Alg-PVPI films, treated with FREMS, and simultaneously treated with FREMS and Alg-PVPI films. A photo of the wound was taken immediately after the biopsy (day 1). A two-layer dressing was applied, images were collected on days 1, 3, 5, 7, 9, and 12, and the degree of wound closure was checked. FREMS technology showed gradual wound closure and resulted in recovery of 70 % of the original damaged area of the wound. Mice treated with PVPI-based films showed a slight difference in the progress of the wound-healing process. In addition, the levels of inflammatory mediators, such as IL-6, IL-1β, and TNF-α, were decreased in mice treated with FREMS and Alg-PVPI. The overall results show how the simultaneous application of FREMS technology and bioactive wound dressing can increase the capacity of both devices to treat hard-healed wounds in diabetic patients [106].

Santamato et al. applied either antiseptic topical alone or with FREMS to venous leg wounds for 3 weeks. They found FREMS led to a decrease in wound surface area by 90 % at 30 days from treatment cessation, which was significantly superior to that seen in the control arm [107]. Eduard Kurz's FREMS was used in a clinical trial involving patients with lumbar spinal stenosis (LSS) suffering from narrowing of the neuroforamina and spinal canal. It is still not completely clear whether post-surgery LSS patients are treated with FREMS technique early after surgery or whether delayed recovery would be more beneficial [108].

RCTs) randomized controlled trials (to date) have assessed the effect of FREMS on lower extremity wound healing. Unfortunately, all did not clarify whether the participant or investigator was blinded. Also, most studies support the beneficial effects of pulsed current on the protective management of skin wounds. Although waveforms and other methods look promising, there is not yet much experimental data to recommend a definitive conclusion with many healed patients regarding using FREMS in skin wound recovery.

6.2. 3D printing technology in wound management

Three-dimensional (3D) printing has established its role among the various methods for making wound dressings due to its layer-by-layer approach and the combination of cellular bio-inks. The type of polymer (biological, synthetic, or combined) can be selected according to the kind of wound. In the field of wound healing, these materials may be enriched with functional biological agents such as antibiotic agents, growth factors, and other drugs to accelerate wound healing and create multiobjective wound dressings (Fig. 16) [23,112,121].

Schadte et al. developed a printable 3D bioink comprising tetrapodal zinc oxide (t-ZnO) nanostructures as the antibacterial agent, combined with a sodium alginate hydrogel to create open porous and closed cell structures with orifices below 500 μm. To examine the antimicrobial activity of the printed wound dressings, the researchers used *Staphylococcus aureus*, a common wound pathogen known for its multi-drug resistance. The study yielded two significant findings. First, while a 5 % concentration of t-ZnO significantly inhibited bacterial growth, increasing the concentration to 15 % further reduced the survival rate of *S. aureus*, with a more pronounced effect in open lattice wound dressings compared to closed ones. Second, bacterial growth was higher on the closed lattice wound dressings than on the open ones, even in the absence of t-ZnO. This finding is crucial for the design of printed wound dressings. The researchers suggested that the antimicrobial effects of t-ZnO are due to its ability to release zinc ions and produce reactive oxygen species (ROS), which are better supported by the open lattice structure. The not fully crosslinked alginate can also retain Zn^{2+} ions, enhancing the antimicrobial properties. Therefore, the most favorable design for a wound dressing would be one with open lattices and fully crosslinked alginate [122,123].

In another study, Siebert et al. developed a 3D-printed hydrogel patch that encapsulates vascular endothelial growth factor (VEGF) and incorporates photoactive and antibacterial tetrapodal zinc oxide (t-ZnO) microparticles. This multifunctional scaffold is designed to be light-triggered. To achieve this, they utilized the antimicrobial and semiconductor properties of t-ZnO, which has a bandgap in the UV range, to act as a photoactive agent. This allowed the incorporation of VEGF in the presence of UV–visible light without releasing it during the synthesis process, which involved UV cross-linking. This interdisciplinary work resulted in a controlled release of VEGF, promoting blood vessel formation and providing antimicrobial properties. The in vivo experiments suggest this smart wound dressing platform is highly effective [123].

Moreover, 3D printing wound dressings can be personalized based on the shape and size of the dressings, profile of reales, does, and

Table 4
Classification of wound dressings based on types, definition and available samples

		Types and definition	Available samples	Ref.
Wound dressing classification	Composition & purpose	Primary: These dressings are directly applied to the wound bed to protect it and promote healing.	gauze, non-adhesive dressings, hydrocolloids, hydrogels, and foam dressings	[66, 109]
		Secondary: These dressings are used to secure the primary dressing in place and provide additional protection and absorption	adhesive tapes, bandages, and packaging	[109]
		Interactive: These dressings are made from biological materials such as human or animal tissue.	alginate dressing, collagen dressing, and silver dressing	[110]
		Biological: These dressings are made from biological materials such as human or animal tissue.	skin grafting, amniotic membranes, and growth factor dressings	[111]
		Advanced: These dressings incorporate advanced technologies to provide optimal wound healing conditions.	NPWT dressings, bioengineered skin substitutes, and 3D-printed dressings	[23, 112, 113]
		Antimicrobial: These dressings contain agents that help prevent or manage wound infections.	silver dressings, iodine dressings, and honey-based dressings	[92, 114]
		Compression: These dressings apply pressure to the wound site to manage edema and promote circulation.	pressure bandages and covers	[109, 115]
	Technology & field of use	Traditional: provide a simple barrier to protect the wound and absorb exudate.	gauze, cotton, and non-adherent pads	[109]
		Advanced: These dressings are designed to create a moist wound environment, promote healing, and manage exudate.	Hydrocolloids, hydrogels, foams, alginates, and collagen dressings.	[110]
		Antimicrobial: They are beneficial for wounds at risk of infection or infected wounds.	silver, iodine, or honey	[100, 114]
		Biological & Bioengineered: They provide a scaffold for cell growth and can help promote tissue regeneration in chronic or complex wounds.	human or animal tissue	[92, 111]
		Negative Pressure Wound Therapy (NPWT): NPWT dressings use negative pressure to promote wound healing by removing excess exudate.	VAC Freedom from KCI, Foam Dressing, silver, Smith & Nephew.	[113, 116]
		Compression: They are commonly used for venous ulcers, lymphedema, and other conditions that require compression therapy.	Intermittent Pneumatic Compression (IPC) devices & Foam dressings	[115]
		Silicone: Silicone dressings are designed to create a gentle, adherent interface with the wound bed while minimizing trauma during dressing changes.	Silicone Foam dressing, Silicone Gel Sheets, Silicone Adhesive dressing, Silicone Hydrogel dressing	[117]
		Foam Dressing: They are suitable for wounds with moderate to heavy exudate and can help maintain a moist wound environment for optimal healing.	Foam dressing, Foam Gel Sheets, Foam Adhesive dressing, Foam Hydrogel dressing	[115]
	industry and market segment	General: These dressings are widely used in various healthcare settings, including hospitals, clinics, and home care.	gauze dressings, non-adherent pads, and primary adhesive dressings	[109]
		Acute: These dressings are designed in acute care settings, such as emergency departments, operating rooms, and intensive care units. They are often sterile and provide a barrier to protect wounds from infection.	sterile gauze dressings, transparent film dressings, and surgical dressings	[109]
		Chronic: These dressings are formulated explicitly for chronic wounds that require long-term management, such as diabetic ulcers, venous ulcers, and pressure ulcers.	Hydrocolloid dressings, hydrogels, alginates, and collagen dressings	[66, 110]
		Pediatric: These dressings are designed for pediatric patients, considering their unique skin characteristics and needs. They are gentle and non-irritating and often come in colorful designs, making them more appealing to children.	NPWT, bioengineered skin substitutes and growth factor dressings, Smith & Nephew	[113, 116]
		Geriatric: These dressings are tailored to meet the needs of elderly patients, who may have fragile skin, reduced mobility, and comorbidities that affect wound healing. They focus on gentle adhesion, ease of application, and effective management of wound exudate [	Hydrocolloid dressings, Alginate dressings, Foam dressings, honey	[118]
		Sports Medicine: These dressings are designed for athletes and active individuals who may experience wounds, abrasions, or blisters during sports activities. They are durable, flexible, and water-resistant, able to withstand movement and sweat.	Transparent Film dressings, Foam dressing, Hydrocolloid dressings	[119]
		Veterinary: These dressings are specifically formulated for use on animals, such as pets, livestock, and horses. They address the unique challenges of wound management in veterinary medicine and may come in different sizes and shapes to accommodate various animal species.	Sterile Gauze Pads, Adhesive Bandages, fish skin	[109, 120]

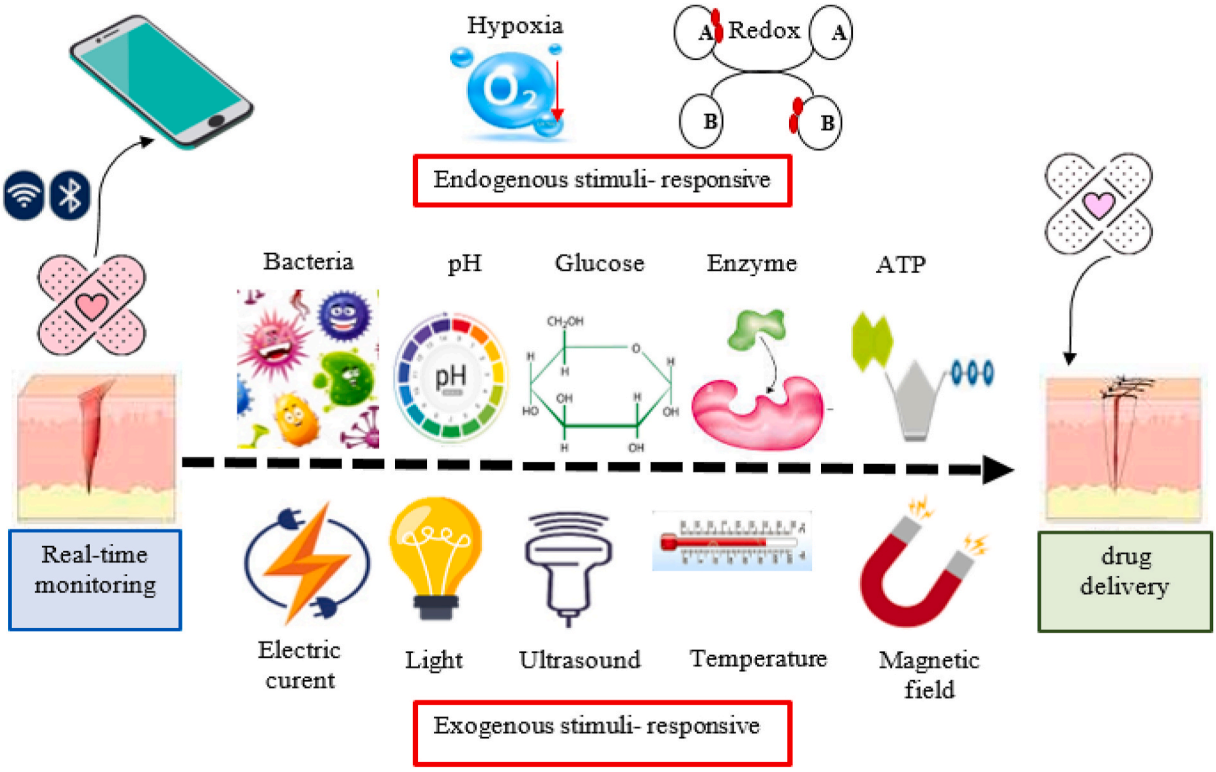

Fig. 14. Smart wound dressing for advanced wound management.

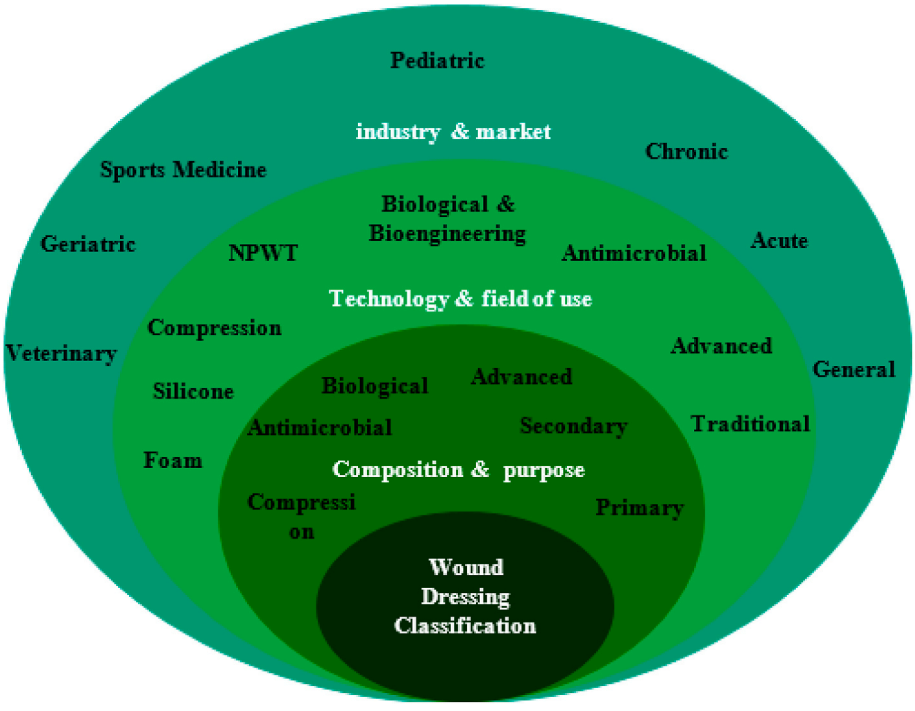

Fig. 15. Classification of wound dressing.

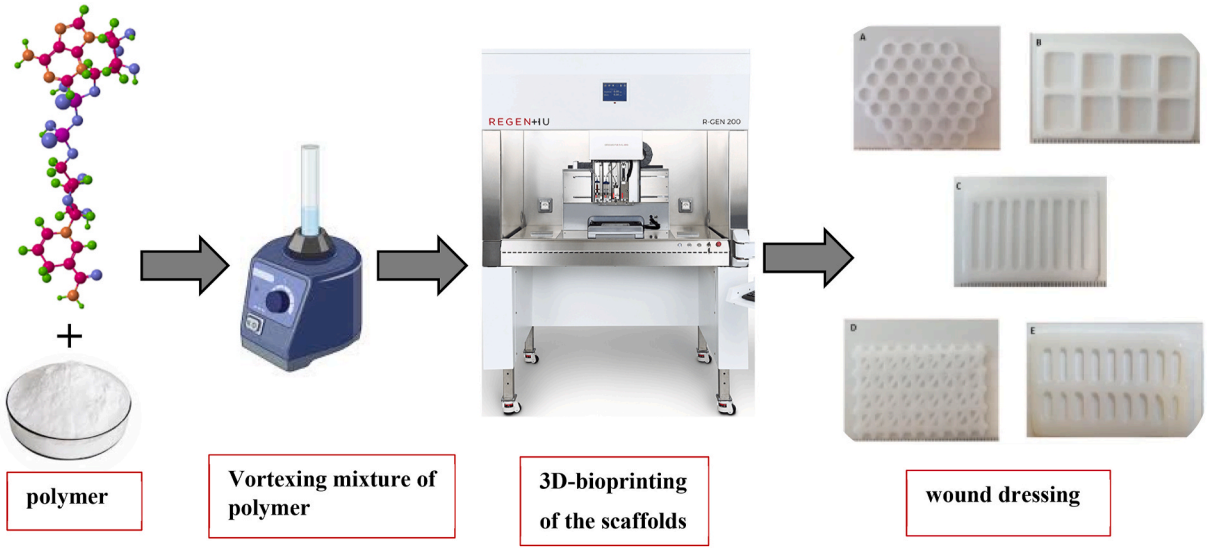

Fig. 16. Steps of wound dressing synthesis with 3D bio-printing method.

types of active ingredients of drugs incorporated in it, porosity, swelling, and degradation rate [124]. In their research, Philipp Schadte et al. developed a zinc-oxide-tetrapod (t-ZnO) infused sodium alginate wound dressing platform tailored for patient-specific protein delivery. Utilizing a custom-made setup, they achieved the application of nozzles with orifices smaller than 500 μm. They fabricated structures with varying infill densities, both closed and open, and post-printing, treated them with 1M calcium chloride for 60 s for cross-linking. The t-ZnO-laden alginate platform exhibited optimal antibacterial properties at a 5 % concentration against *S. aureus* while proving non-detrimental to human skin cells. Furthermore, t-ZnO, the platform's primary component, demonstrated antibacterial prowess and a propensity for binding surface proteins (active pharmaceutical ingredients) with an isoelectric point above 7. The tetrapodal structure of ZnO rendered it significantly less toxic than conventional ZnO. The biocompatible alginate showcased easy gelation, derivatization potential, and excellent printability. The study concluded that the open structures offered superior antibacterial activity without compromising skin integrity [122].

6.3. *Hydrogel-making technology in wound management*

In a study by Kyung Lee and Seungsin Lee, palmarosa essential oil, recognized for its anti-inflammatory and antimicrobial properties, was integrated as a bioactive agent into the core of polyvinyl alcohol (PVA) nanofibers. This incorporation was facilitated through emulsion electrospinning using a single nozzle, which was succeeded by a heat treatment to augment the aqueous stability of PVA. The resultant core/sheath PVA-based composite, particularly those with a web area density of 3 g/m^2, demonstrated satisfactory gas and moisture vapor permeability, critical for effective wound care. Moreover, it showed a notable capacity for absorbing wound exudates. The inherent antibacterial properties of the essential oil, in synergy with the composite's engineered attributes, make this PVA-based material a promising candidate for bioactive wound-dressing applications [125].

In a notable study by X. Zhang et al., a multifunctional dressing comprising a hydrogel base, magnetothermally responsive microfibers, a drug delivery system, and mesenchymal stem cell-laden microfibers was engineered. The magnetothermally responsive component, consisting of a Fe3O4@SiO2-interpenetrating polymer network (IPN), enables magnetothermal heating via magnetic nanoparticles and exhibits thermoresponsive behavior attributable to the IPN. This design allows for targeted antibiotic release at the desired site. Additionally, including stem cell-laden microfibers promotes enhanced re-epithelialization, tissue remodeling, collagen synthesis, and granulation tissue formation. The hydrogel's structural properties, including its ability to provide a moist environment, absorb exudates, sustain therapeutic cells, and facilitate controlled drug delivery, collectively contribute to accelerated wound healing [126]. Hydrogels may undergo cross-linking via chemical or physical means. Physical cross-linking, which relies on reversible intermolecular interactions, is preferred due to the absence of chemical cross-linking agents, although it may compromise stability and mechanical strength. In contrast, chemical cross-linking involves permanent, robust covalent bonds formed by chemical agents, with the degree of cross-linking influencing the hydrogel's swelling behavior [127].

To circumvent the issues of toxic photoinitiator residues and slow in-situ curing associated with injectable photo-cross-linked hydrogels, J. Zhang et al. developed an injectable, in-situ photo-cross-linked hydrogel dressing devoid of photoinitiators featuring rapid in-situ curing and robust antibacterial properties. The polymerization is initiated through the photodimerization of the dipole-dipole interactions within the quaternary ammonium heterocyclic rings of polyvinyl alcohol-bearing styrylpyridinium groups (PVA-SBQ) under UV light, rendering the hydrogel biocompatible, free of photoinitiators, water-soluble, and mechanically sound. The hydrogel's antibacterial efficacy also originates from the polymer's positively charged groups. Incorporating a natural macromolecule, oxidized sodium alginate (OSA), enhances biocompatibility and provides ample reactive sites. The inclusion of polydopamine particles

endows the hydrogel with photothermal therapeutic capabilities. Ultimately, the study demonstrated that this hydrogel accelerates the repair of infected wounds, supported by its sensitive and stable sensing properties [128]. The future of wound dressing is evolving rapidly with advancements in materials science, biotechnology, and digital health [129]. New international trends in wound dressing are shaping the landscape of wound care and driving innovation in the field. Some key areas and developments in the future of wound dressing are shown in Fig. 17.

These trends reflect the ongoing evolution of wound dressing technologies and practices on an international scale, focusing on improving patient outcomes, enhancing wound care efficiency, and advancing the field of wound healing. Healthcare providers, researchers, and industry stakeholders are working together to leverage these trends and innovations to address the complex challenges associated with wound management and promote better quality of life for patients.

6.4. *Electrospinning technology in wound management*

An alternative method for producing wound dressings is electrospinning, which fabricates micro-to nanoscale ultra-fine fibers from both natural and synthetic polymers, provided they are amenable to electrospinning (Fig. 18). Key parameters influencing the suitability of a polymer for electrospinning include polymer concentration, which must be balanced to mitigate surface tension effects or excessive viscosity; solvent characteristics, such as boiling point, evaporation rate, and vapor pressure; electrical conductivity; molecular weight; and viscosity [130]. The electrospinning process, based on electrohydrodynamics, garners interest due to its ability to produce fibers with small pore sizes, high specific surface area, high porosity, flexibility, low roughness, and mechanical properties akin to human skin, such as ductility and tensile strength. Nanofibrous structures derived from this technique act as breathable barriers that prevent contamination penetration [131], maintain high porosity, exhibit a random mesh arrangement, and preserve a moist environment around the wound by minimizing water loss [125,132–135]. Both natural polymers, predominantly sourced from animals and plants, and synthetic polymers are employable in this technique, each offering distinct advantages and limitations. Synthetic polymers excel in mechanical properties, thermal stability, and processing versatility but often lack biodegradability and cell-binding sites. Conversely, natural polymers are noted for their excellent biocompatibility, low cytotoxicity, and presence of bio-binding sites, albeit with less favorable physical properties. Consequently, blends of both polymer types are frequently utilized in electrospinning to balance desired mechanical characteristics and bio-functionality [24,136,137].

A conventional electrospinning apparatus can produce diverse fibers by modulating parameters such as needle type, polymer concentration, collector and spinneret configuration, voltage, flow rate (solution feed ratio), and the distance between spinneret and collector. This device generates an electric field from the spinneret and sends it to the fiber collector by applying high voltage. The predetermined flow rate ensures consistent injection of the syringe contents. At the needle tip, droplets form, and upon the electrostatic force surpassing the solution's surface tension, a 'Taylor cone' emerges. Consequently, a charged polymer jet is expelled from the Taylor cone's apex. The solvent rapidly evaporates during its trajectory, leaving a solid fiber that follows a helical path. Ultimately, the fibers are randomly deposited onto the collector [24,132,138].

In a study by Kyung Lee and Seungsin Lee, palmarosa essential oil, recognized for its anti-inflammatory and antimicrobial properties, was integrated as a bioactive agent into the core of polyvinyl alcohol (PVA) nanofibers. This incorporation was facilitated through emulsion electrospinning using a single nozzle, which was succeeded by a heat treatment to augment the aqueous stability of PVA. The resultant core/sheath PVA-based composite, particularly those with a web area density of 3 g/m^2, demonstrated satisfactory gas and moisture vapor permeability, critical for effective wound care. Moreover, it showed a notable capacity for absorbing wound exudates. The inherent antibacterial properties of the essential oil, in synergy with the composite's engineered attributes, make this PVA-based material a promising candidate for bioactive wound-dressing applications [125].

A study conducted in 2022 aimed to prepare electrospun chitosan/gelatin nanofiber scaffolds reinforced with different amounts of

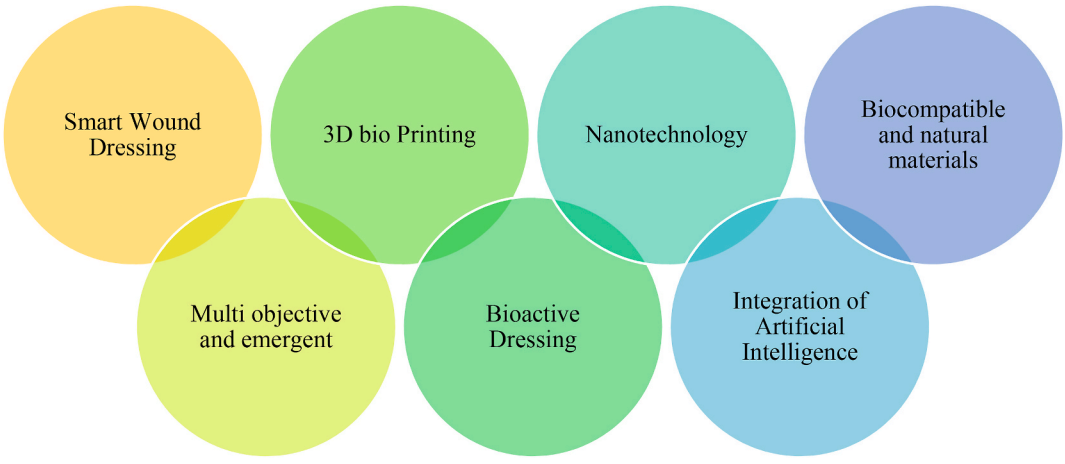

Fig. 17. Areas that can bring the emergence of scar wearers with innovation in the future.

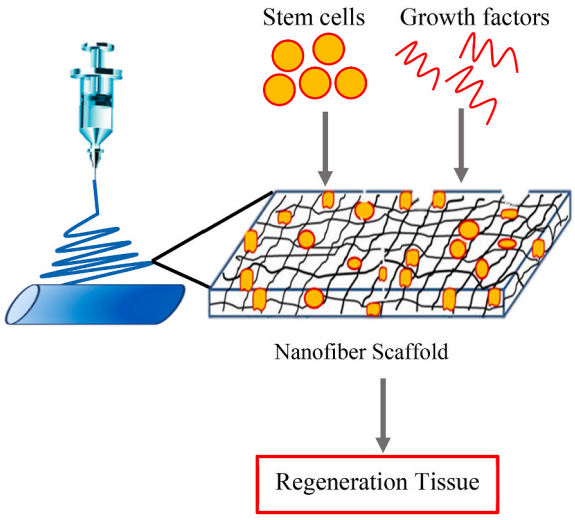

Fig. 18. Schematic diagram showing the fabrication process of nanofibrous scaffolds.

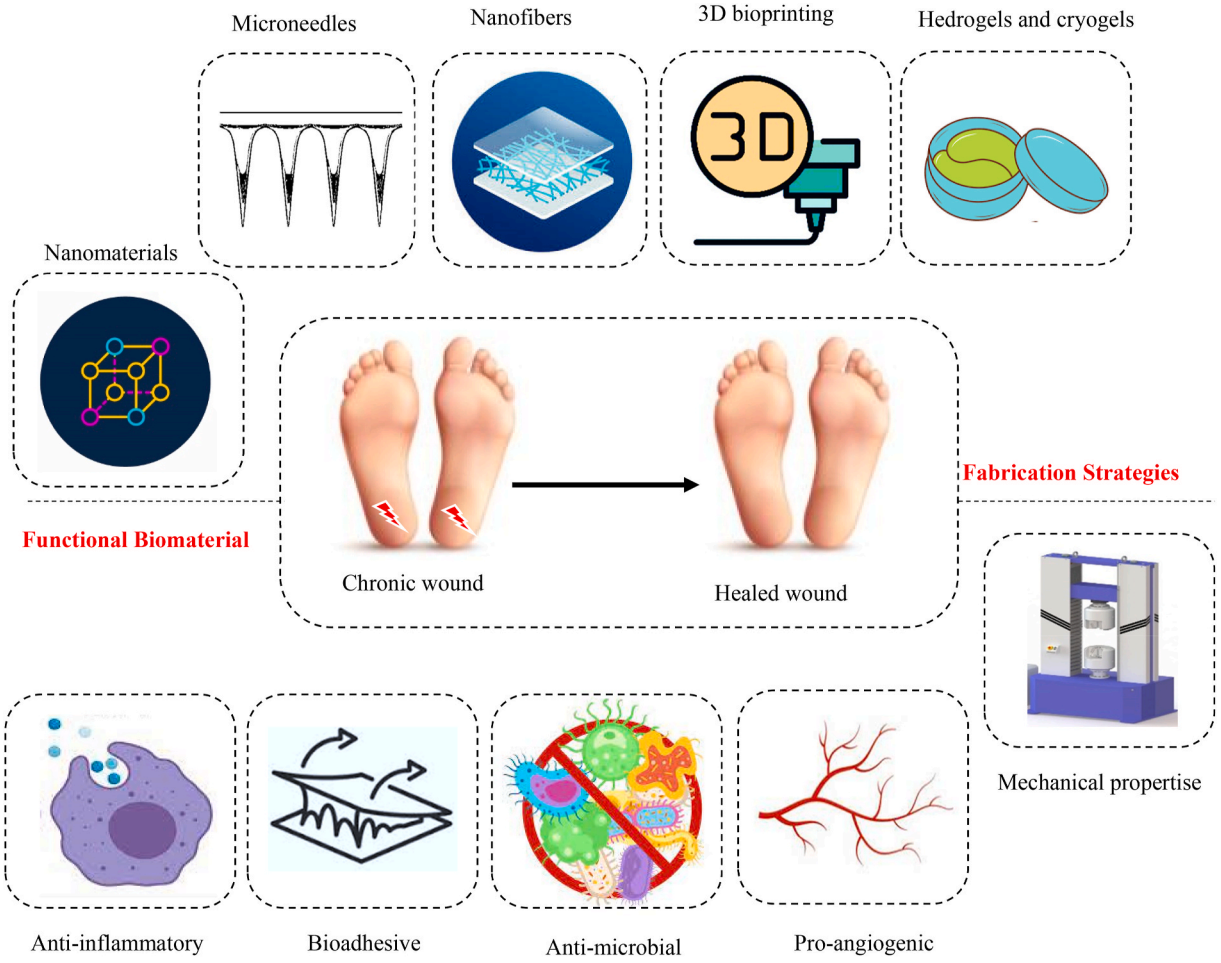

Fig. 19. Fabrication strategy and applied biomaterial in wound dressing.

graphene nanosheets for use as antibacterial and wound healing scaffolds. Nanofibers reinforced with 0.15 % graphene nanosheets produced the smallest diameter (106 ± 30 nm) and the highest porosity (90 %), showing good biodegradability and swelling. It is interesting to note that the reinforced nanofibers With 0.15 % of graphene nanosheets, the growth inhibition percentage of *E. coli* and *S. aureus* was 50 % and 80 %, respectively. During culture with nanofibers, cell viability assay did not show any cytotoxicity on human fibroblasts, and graphene nanosheets showed a positive effect on cell migration ability [139].

7. Future perspective on wound dressing

Scaffolds made from natural materials (proteins such as collagen, gelatin, plasma-derived fibrin, keratin, chitosan, and dextran) have become increasingly popular because they exhibit better cell adhesion, compatibility, and in vivo degradability [4]. Scaffolds are fabricated for wound dressings using various techniques (Fig. 19). Nanocomposite scaffolds also incorporate nanomaterials into the scaffold structure, resulting in biological benefits such as enhanced angiogenesis and improved mechanical properties [111,140]. Decellularized matrix scaffolds involve the complete removal of tissue cells, allowing for recellularization with alternative cell types, such as stem cells, while maintaining the native, non-immunogenic 3D structure, as well as complex protein complexes [141,142]. Biodegradable polymer scaffolds [143], bioprinted wound dressings, electrospun wound dressings, and hydrogel-based wound dressings are also used. These can be loaded with therapeutic agents [144] to act as drug delivery systems or integrated with sensors for real-time wound monitoring, demonstrating “smart” capabilities.

Stem cells from various anatomical sources are used in applications that repair damaged tissue and have shown varying success in preclinical settings. Given that cultured epithelial autografts have been successfully used to regenerate burn scars, future research will focus on epidermal stem cells. This cell type is significant for skin wound healing because it can maintain epithelial homeostasis and requires an available microenvironment to support its pluripotency. These stem cells can control skin morphogenesis, homeostasis, and repair. The loss of epidermal stem cells at the wound margin may be responsible for non-healing wounds. Given the importance and ability of these cells to form intact epithelium, there is a tremendous opportunity for the clinical use of these stem cells and bioengineering technologies in the near future for the treatment of deep wounds [145].

Although dermal equivalents or multifunctional dressings have been introduced to the market and some are used by healthcare providers, the healing and cosmetic outcomes are still poor, perhaps reflecting the importance of focusing skin regeneration research intensively on wound healing and closely examining the cellular behavior, molecular pathways, and factors involved in wound maintenance [146]. However, with the continued development of manufacturing techniques, artificial intelligence technologies, and simulations of the wound recovery process, the creation of scaffolds suitable for various types of wounds may be facilitated in the near future.

7.1. Innovative approaches

Innovative approaches to wound dressing have evolved significantly in recent years, integrating advances in nanomaterials science, biotechnology, and medicine. These innovations aim to improve wound healing quickly, reduce infection rates, attempt to reduce extensive scarring and achieve healing at the lowest cost. These advances in wound dressing technology demonstrate the potential of responsive and controllable dressings to revolutionize wound care by providing targeted therapy and promoting faster healing processes. Such innovative approaches with smart designs are practical for various wounds [147]. Innovations in smart dressing design include gels such as cryogels and hydrogels, the extensive use of nanoparticles and nanozymes, sensors monitoring wound emergents, and the use of bioactive and biocompatible materials.

Cryogels based on nanozymes responsive cryogels with MoS2 were designed by L. Wang in 2023, which contain a nitric oxide (NO) releasing precursor that responds to various stimuli such as pH, near infrared (NIR), and temperature. They adapt to different stages of wound healing and help to attract bacteria and enhance antibacterial efficacy through the release of ROS and NO-induced by NIR light [148]. Injectable hydrogels can respond to matrix metalloproteinases (MMPs) and release therapeutic agents such as curcumin to enhance wound healing efficiency. This injectable hydrogel dressing is adhesive and self-healing. Hydrogel dressings are made from a combination of materials that form a gel-like environment upon contact with moisture. This helps to create a moist healing environment while facilitating autolytic debridement, or in other words, the removal of dead tissue through the body’s natural processes. Hydrocolloid dressings are often used for superficial to moderate wounds [149]. Another example of a responsive hydrogel-based microneedle dressing was developed by Z. Guo in 2022 using a glucose-responsive insulin-releasing hydrogel. This microneedle dressing accelerates diabetic wound healing by releasing insulin in response to glucose levels, leading to improved wound healing outcomes and better blood glucose control [150].

These advancements in wound dressing technology demonstrate the potential for responsive and controllable dressings to revolutionize wound care by providing targeted treatment and promoting faster healing processes.

7.2. AI-assisted management

Artificial Intelligence (AI) offers transformative potential in increasing diagnostic accuracy, refining and managing wound conditions, personalizing treatment plans, optimizing resource allocation, and improving patient outcomes in wound care. Numerous opportunities for AI in burn wound management can be envisioned, including increasing diagnostic accuracy through machine learning algorithms, early detection of complications through continuous monitoring, optimal allocation of resources, and improving surgical outcomes with AI-assisted planning and personalized recovery programs.

Early detection of the complications of infection-prone wounds can significantly affect the patient's recovery. Artificial intelligence systems in this field can continuously monitor patients and analyze data from wearable devices and sensors to detect early signs of infection or other complications. This real-time monitoring allows for rapid intervention, potentially preventing severe complications and improving wound healing [151].

Caring for all types of wounds and planning and performing reconstructive surgeries for patients often requires significant resources, including specialized equipment and trained personnel. AI can optimize resource allocation by predicting patient needs based on burn severity and expected recovery time. Hospitals can use artificial intelligence for recovery and tracking the progress of wound healing through wearable devices [21]. AI can also facilitate remote monitoring, allowing healthcare providers to adjust the release of the required dose of medication for wound healing based on real-time data and patient feedback. In addition, AI-enabled robotic systems can help surgeons Assist during plastic procedures, increase accuracy, and reduce the risk of error, ultimately leading to more efficient and effective care [152].

In a study conducted in 2022, Surachate Kalasin et al. developed an integrated wound dressing from poly (vinyl acrylic) gel@PANI/Cu2O NPs to stimulate pH-responsive flow during the wound healing process. Effectively, a chip-free bandage tag with a Mxene/PTFE capacitive electrode and acrylic adhesive inductance was fabricated to match the resonant frequency the smart wearable antenna generated. Applying a higher activation voltage to the wound dressing electrodes placed more copper ions in the PVA/PANI gel hybrid shell, increasing the flexible artificial intelligence (FLEX-AI) conductive response. This non-contact smart wearable technology provided a healthcare solution to monitor hard-healed wounds and maximize clinicians' efficiency by minimizing the risk of disease infection. This integrated wound dressing worked with a deep artificial neural network (ANN) algorithm for chronic wound monitoring through short-range communication to an integrated radio frequency with 94.6 % accuracy [32].

In a work done in 2023 by Xin Tingzheng and colleagues for wound management and repair. A paper-like battery-free multiplex sensor (PETAL) is designed for comprehensive wound assessment using deep learning algorithms. This sensor is made using design software and with the help of a computer with suitable dimensions and channel width for temperature, pH, trimethylamine, uric acid, and humidity from a two-dimensional printed cellulosic paper sheet with wax and five colorimetric sensors. Different wounds became. Sensor images captured by a mobile phone were analyzed with neural network-based machine learning algorithms to determine the healing status. In this design, polyvinyl alcohol (used due to its biocompatibility, low propensity for protein adhesion and low toxicity), uricase, phenol red, sodium 3,5-dichloro-2-hydroxybenzenesulfonate (DHBS) and HRP were used. The design is designed so that the transparent surface layer allows the skin's natural function of oxygen and moisture exchange while allowing the image to be displayed for accurate image capture and analysis. The bottom wound contact layer protects the wound bed from direct contact with the sensor panel to minimize wound tissue disturbances. This pad is also designed to stick the sensor to the skin gently. A blood filtration membrane was placed between the cellulose paper sensor panel and the lower adhesive contact layer to facilitate the complete removal of red blood cells from the wound exudate. When the assembled PETAL patch was placed on the wound, the wound exudate first contacted the blood filtration membrane. It caused a color change according to the concentration of the relevant analyte. For off-site diagnosis through secretions collected from scratches and burn wounds, the PETAL sensor could determine the healing status with the help of accurate analysis of wound images by artificial intelligence with 97 % accuracy. The PETAL sensor enables early warning of adverse events, which can necessitate clinical intervention to facilitate wound care management [153].

However, challenges such as data quality and standardization, bias in AI models, ethical and privacy concerns, and integration with existing healthcare systems were also highlighted. The "black box" nature of AI, regulatory hurdles, and the need for physician training create additional barriers to implementation. Artificial intelligence has the potential to revolutionize burn wound management by providing more accurate and efficient care. Addressing challenges related to data quality, bias, ethical issues, and technical integrity is critical to realizing these benefits. Standardized data protocols, robust governance frameworks, ongoing training of practitioners, and transparent regulatory guidelines are essential for effective AI integration. Continued research and collaboration between technologists, clinicians, and policymakers are critical to fully exploiting the potential of AI in precision burns, ultimately improving patient outcomes and advancing the field.

8. Conclusion

Considering the emerging dressings and new technologies such as smart dressings, 3D printing, hydrogel, and nanotechnology for quick wound healing, it can be concluded that today, multi-functional wound dressing can be essential because the importance of treatment and increased effectiveness of the health of damaged tissue and wounds caused by burns, traffic accidents, and diabetes will be possible only with proper care and wound care and careful and immediate monitoring of the wound. Since multi-purpose wound dressings contain various subunits for tissue regeneration and repair, prevention of wound infection, wound surveillance, and immune response modulators, they are excellent in managing wound healing. These subunits, which are named modules, work separately and independently but have a complex relationship with each other to provide wound monitoring.

Today, it can be understood that telemonitoring with advanced wound care can reduce treatment costs and clinic visits and supports the effectiveness of monitoring technologies in optimizing wound care and patient recovery outcomes. Overall, this innovative approach has great potential to revolutionize wound management, provide personalized care, and improve the quality of life for individuals. The development of multipurpose emergency wound dressings represents a significant leap in medical technology. Integrating nanomaterials, such as silver nanoparticles, graphene, and nanofibers, offers unique advantages over traditional wound dressings. Their increased surface area and reactivity improve biocompatibility and enhance the efficacy of therapeutic agents. As it has been seen in various studies, these advanced dressings can not only facilitate rapid hemostasis but also actively respond to the wound environment, thus promoting optimal healing conditions. These innovative dressings leverage nanoscale materials and

structures to enhance healing, reduce infection risk, and provide multifunctional capabilities, including hemostatic properties, antimicrobial action, and controlled drug release. Future research should focus on the scalability of production methods and the thorough evaluation of biocompatibility and long-term effects in clinical settings. Additionally, incorporating smart technologies, such as sensors and drug-delivery systems, could further refine the functionality of these dressings, catering to individual patient needs and dynamically responding to changes in the wound environment.

Declaration of generative AI and AI-assisted technologies in the writing process

We solely used Grammarly and other AI-assisted technologies to improve the English language and overall clarity of this article. No AI tools were used to write the content itself.

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CRediT authorship contribution statement

F. Moradifar: Conceptualization, Validation, Writing – original draft, Writing – review & editing. **N. Sepahdoost:** Conceptualization, Writing – original draft. **P. Tavakoli:** Writing – original draft. **A. Mirzapoor:** Conceptualization, Data curation, Formal analysis, Validation, Writing – original draft, Writing – review & editing.

Declaration of competing interest

Enclosed herewith please find a manuscript entitled "**Multi-functional Dressings for Recovery and Screenable Treatment of Wounds: A review**" don't have any conflict interest. We hope this We emphasize that the contents have neither been published nor submitted elsewhere. I should also state that all authors are aware of this submission. There is no conflict of interest (financial or others) upon data presented.

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