Advances in Chronic Wound Management: The Role of Antibiofilm-Based Wound Dressings and Theranostic Innovations

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ABSTRACT

Chronic wounds constitute a significant public health burden, with Medicare spending over $30 billion annually on them. For doctors, these wounds provide a problem since they frequently show resistance to conventional therapy. Recent findings about the role of biofilms in the pathogenesis of chronic wounds have led to the consideration of biofilm eradication as a possible therapeutic strategy. Biofilms, which are incredibly resilient and impervious to host defences and antibiotic treatments, are composed of closely packed bacterial clusters coated with extracellular polymeric substances (EPS). Biofilms are believed to be the source of more than 65% of persistent bacterial infections, making wound healing more challenging. Despite the potential of traditional antibiofilm treatments such as silver, iodine, and antimicrobial peptides, problems including low patient compliance, bacterial resistance, and exorbitant prices prevent their widespread use. Nanotechnology breakthroughs have led to dressings based on nanoparticles that are highly effective against biofilms, offering controlled release, targeted medicine administration, and reduced adverse effects. Furthermore, theranostic dressings, which combine therapeutic and diagnostic properties, are becoming a groundbreaking method of wound care that enables accurate drug administration and real-time monitoring. Despite their promise, there are still obstacles to overcome to improve medicinal applications, environmental sustainability, and cost-effectiveness. Future initiatives should focus on developing environmentally friendly materials, expanding access through insurance, and using combination treatments to enhance treatment regimens for chronic wounds. Technologies such as theranostics and nanoparticles can transform the treatment of chronic wounds by offering less invasive, more efficient options.

Keywords: Chronic wounds, Biofilms, Nanoparticle-based dressings, Theranostic wound care, Advanced wound management

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1. Introduction

The skin, being the largest organ of the human body, plays a crucial role in shielding internal tissues from extreme heat, UV radiation, microbial infections, and mechanical injury.[1] This makes it highly susceptible to damage, which can have serious consequences for both patients and the healthcare sector.[1,2] Chronic wounds, in particular, are a significant challenge as they fail to heal properly, causing prolonged suffering for patients and placing a heavy burden on healthcare resources.[3-8] The Wound Healing Society defines healing as "a complex dynamic process that results in the restoration of anatomic continuity and function". In 2024, the U.S. spent more than $50 billion annually on wounds that do not heal, approximately $12-13 billion on surgical wounds that become infected, and over $1 billion on hospital costs related to burns.[9,10] Patients with genetic disorders such as sickle cell disease, diabetes, or advanced age are particularly vulnerable to abnormal wound healing, which may lead to long-term complications. The basic principles for managing a wound are inflammation, proliferation, and remodelling. Inflammation occurs at the injury site as the wound begins to heal. During this phase, inflammatory cells, such as neutrophils and macrophages, are attracted to the wound site. These

cells clean the wound by engulfing bacteria and debris. They interact with keratinocytes, other immune cells, and fibroblasts to prevent bacterial infections.[11-13] Monocytes that circulate arrive within two to three days and differentiate into macrophages. During the early inflammatory phase of wound healing, macrophages and neutrophils work together to debride necrotic tissue and prevent infection. As the inflammatory phase ends and the proliferation stage begins, macrophages adopt a profibrotic, anti-inflammatory role. They produce growth factors such as TGF-β that attract fibroblasts from surrounding healthy tissue.[14] These cells promote endothelial cell migration into the wound by releasing VEGF and other chemicals involved in the formation of new blood vessels and the hyper-vascular nature of granulation tissue.[15] Re-epithelialization occurs due to keratinocytes and stem cells, while fibroblasts and myofibroblasts produce extracellular matrix components and compress the wound. About three weeks after injury, the remodeling process begins, which can take weeks to years. During remodeling, collagen is remodeled from type III to type I, and the wound fully closes. Despite tissue repair, healed skin regains only about 80% of its original strength.[16] Diagrammatically, the phases of wound healing are shown in Figure 1.

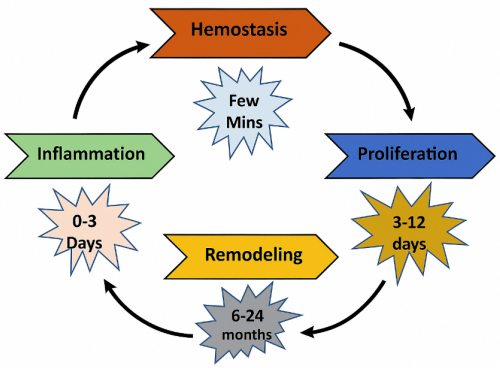

Figure 1: Different phases of wound healing

Biofilms pose a major challenge due to their resistance to antibiotics, adherence to tissue, and immune evasion. These biofilms shield pathogens from host immune responses and antimicrobial agents, promoting chronic inflammation and resistance.[17] Studies have shown that up to 90% of chronic wounds harbor biofilms, which can delay healing and increase the risk of infection-related complications.[18] Microorganisms in wounds can exist in one of two states: the planktonic (free-living) state or the attached, sessile state. Planktonic bacteria are free-floating and typically target research in microbiology. The transition of planktonic bacteria to a biofilm state can be detrimental to the host, as biofilms resist eradication by both host defences and antibiotics. In the sessile form, they aggregate to form structured biofilms that adhere strongly to wound surfaces. These biofilms enhance microbial survival, increase resistance to antibiotics, and significantly delay the wound-healing process.

Wound biofilm formation starts when microbes, whether endogenous or exogenous, attach to the wound surface and multiply. In healthy individuals, the immune system can fight the bacteria in their free-floating state. However, in immunocompromised patients or when bacterial growth is uncontrolled, these bacteria form a complex community protected by a biofilm matrix made of EPS. Thus, the increasing appreciation of biofilm's role in chronic wound pathophysiology underlines the urgency to develop therapies that can effectively target and eliminate these microbial communities, offering new hope for patients suffering from chronic, non-healing wounds.[19-21] Debridement may temporarily reduce biofilm, but it often reforms in deeper tissues.[22] Debridement techniques include:

(i) **Autolytic** – uses the body's enzymes/phagocytes; slow, suited for non-infected wounds.
(ii) **Biological** – uses *Lucilia sericata* larvae secreting proteolytic enzymes.
(iii) **Enzymatic** – applies external enzymes like collagenase for selective necrosis removal.
(iv) **Surgical** – uses sharp tools for fast removal, wound culture, and infection control.
(v) **Mechanical** – non-selective; removes viable and non-viable tissue.[23]

Despite being a common feature of chronic wounds, biofilm cannot be detected or measured using any clinically accessible techniques. Unfortunately, standard wound testing cannot identify biofilm infection or determine how susceptible biofilms are to different substances. Recently, several techniques have been explored to detect and evaluate biofilm formation by microorganisms. Among these, the Congo red agar method, tube method, and tissue culture plate method are widely studied due to their simplicity, reliability, and ability to distinguish biofilm-producing strains. These techniques play a crucial role in understanding microbial pathogenicity and guiding effective therapeutic strategies. The tissue culture plate method appears to be the most effective and reliable for screening biofilm formation compared to the tube and Congo red agar methods.[24] However, these tests are not widely used, and their adoption could benefit clinicians. Additionally, a major challenge in treating biofilm-associated diseases is developing suitable,

standardized biofilm susceptibility testing methods that are clinically useful. The minimum biofilm inhibitory concentration (MBIC), minimum biofilm eradication concentration (MBEC), biofilm bactericidal concentration, and biofilm prevention concentration are new pharmacodynamic parameters recently established to measure antibiotic activity against biofilms.[25] Based on these parameters, many studies have found significant differences in both the quantitative (such as antibiotic tolerance despite susceptibility, altered mechanism of action, phenotypic resistance without genetic resistance) and qualitative (such as higher antibiotic concentration needed and reduced killing effects) effects of most antibiotics on planktonic and biofilm bacteria. Still, some requirements must be met before these methods can be implemented in clinical microbiology labs for routine susceptibility testing, namely, standardized methods and breakpoints are needed.[26,27]

To combat these challenges, recent years have witnessed a surge in the development of advanced wound care strategies that incorporate antimicrobial, regenerative, and diagnostic functionalities. Among these, biofilm-targeted therapies, nanoparticle-based dressings, and theranostic (therapeutic + diagnostic) innovations have gained considerable attention.[28,29] These novel approaches aim not only to eliminate infection but also to modulate the wound environment, promote tissue regeneration, and provide real-time feedback on healing progression.[30]

2. Wound Dressings

A wound dressing is meant to be placed on a wound's surface in a non-invasive manner to encourage healing. In general, wound dressings shield the wound from the outside world to some extent, and many of them also help to maintain an ideal moisture balance and environment for the wound by assisting in the absorption and retention of wound exudates through a variety of mechanisms. Controlling inflammation, preventing microbial colonisation or infection, and encouraging epithelization and tissue remodelling are the three main prerequisites for a wound dressing to be clinically effective. Also, choosing the right wound dressing depends on the wound type, depth, exudate level, and infection status. An ideal dressing (also shown in Figure 2) maintains moisture, protects against microbes, and is affordable, biocompatible, easy to apply, and requires infrequent changes.[31]

Figure 2: The Ideal Properties of Wound Dressings

(a) Moisture Management

For a treatment to be effective, the moisture in the wound bed must be properly managed. First, moist dressings can promote cell proliferation and maintain a clean wound bed. Moist wound dressings create an atmosphere that can shield a wound from bacterial invasion and keep it from drying out. The healing process may be negatively impacted by the presence of biofilms and an excessive amount of exudate. To overcome this, researchers made Moisture-retentive dressings (MRDs) that contain moisture vapor transmission rates (MVTRs) of 35 g/m^2/hr to promote wound healing. In chronic VLU treatment, these dressings are also economical when all costs are taken into account (e.g., cost for materials, nursing, and trip time). Films, foams, hydrocolloids, alginates, and hydrogels are the five fundamental categories of MRDs. Films are thin, transparent, elastic polyurethane sheets that stick to the skin like acrylic but allow gas to pass through. Films can be applied to acute surgical wounds and are the preferred dressing for split-thickness skin graft donor sites. To stop leaks and bacterial contamination, foams are dressings made of hydrophobic polyurethane foam sheets with a hydrophilic surface. If the wound is not extremely exudative, soaking in saline solution could be necessary to remove foam dressings. Cutimed® is an absorbent type of dressing that is used to treat wounds and is composed of seaweed-derived sodium (80%) and calcium (20%) alginate. A chemical reaction between the calcium ions in the dressing and the sodium ions in the exudate causes alginate to change into a moist gel when it comes into contact with it. Because it absorbs exudate and keeps the wound bed clean, this dressing works especially well for wounds that exude a lot.[33]

(b) Antimicrobial Activity

Preventing infection is one of the most crucial elements of good wound care. Wound infection not only slows down the healing process, but it can also make the situation worse and potentially spread. Antimicrobial dressings are therefore necessary to preserve the wound's microbial equilibrium. To stop infections, a lot of work has been done to develop dressing materials with antimicrobial properties. The two antimicrobial substances most frequently found in wound dressing materials are silver and iodine. Iodine's antibacterial activity stems from its ability to enter infections and oxidise essential components of their cells, while silver's antimicrobial properties are dependent on the release of ions when exposed to moist circumstances. Another natural antimicrobial agent is Chitosan, which is non-toxic, biodegradable, and promotes wound healing by killing bacteria. The Manuka honey-containing wound dressing Roosin® was designed to treat pressure ulcers, foot ulcers, and second-degree burns. Mepilex Ag, a commercial dressing containing silver nanoparticles, is another example of a treatment with antibacterial properties. Within 30 minutes, this dressing can inactivate germs associated with wounds, and it can continue to work for up to seven days. Leg and foot ulcers, partial burns, and other low- to moderate exudate wounds are treated with it.[33]

(c) Biocompatibility and non-toxicity

Biocompatibility is considered to be particularly important for any material used on or implanted into the human body. This is particularly true with dressings for wounds. Biocompatibility is defined as the ability of wound dressings to interact with living tissue without causing any adverse reactions and also ensuring the patient's safety and comfort Meanwhile, Toxicology and safety are also important considerations when using developed wound dressings in clinical settings. Evaluating any possible negative effects or allergic reactions that patients may experience from the dressings is essential. To make sure the dressings do not irritate, inflame, or cause any other adverse reactions when they come into contact with the skin, extensive biocompatibility studies should be carried out. It is also critical to monitor the release of any integrated antimicrobial agents or other active chemicals to ensure they do not turn toxic and remain within safe limits. It is necessary to assess any dressing breakdown products' potential impact on the surrounding tissues. The toxicity and biocompatibility of the dressing can be greatly influenced by the polymers, cross-linkers, and additives used in its formulation.[34]

(d) Permeability of Gas

Gas exchange is a crucial feature of wound dressings that permits the interchange of oxygen and carbon dioxide between the wound and the surrounding environment. This exchange is necessary for accelerating wound healing, as oxygen is required for many of the metabolic processes involved in tissue regeneration. Gas exchange-compatible wound dressings usually feature a porous mesh or membrane that permits gas flow. A hydrophilic coating or other surface alterations that help in gas exchange may also be incorporated in these dressings. Dressings that permit gas exchange can not only speed up the healing process but also help to avoid the buildup of extra moisture surrounding the wound, which can cause maceration and slow healing. These dressings can also aid in preventing the accumulation of toxic gases, including carbon dioxide, around the wound by permitting gas exchange.

Electrospun wound dressings filled with pramipexole using cellulose Acetate were developed by Tan et al. (2022. According to the study, the water vapor permeability rate of the wound dressing was approximately 256.18 ± 3.26 mg/cm2/h. Additionally, the researchers observed that wound breathability was made possible by the nanofibers' porous structure. The semi-permeable film dressing DuoDERM® is very flexible and conformable, impermeable to fluids and bacteria, and permits the gas exchange of air and water vapor.[35]

(d) Noncompliance and Comfort and Adaptability

Dressings should not adhere to the wound bed; they might cause damage when removed and impede the healing process. The patient should feel at ease wearing the dressing and be able to move around freely. Lightweight and flexible materials can reduce discomfort, especially for wounds in dynamic areas.

(e) Ease of Application and Removal, and Effectiveness

The dressing should be simple to apply and remove, even in difficult areas (such as joints). Soft, non-adherent dressings are recommended for patients with delicate skin or serious wounds. Cost matters, especially when it comes to wound care over the long term. Advanced dressings may appear more costly at first, but over time, their benefits—such as faster healing, fewer problems, and fewer dressing changes-may make them more cost-effective.[36]

2.1 Types of Wound Dressings

Wound therapy has come a long way in recent years, with modern wound dressings playing a role in current approaches to wound management. Wound dressings can be produced from a variety of materials, including

starch, dextran, chitosan, alginate, polyurethane, cellulose derivatives, hyaluronic acid, polysaccharide derivatives, collagen, and gelatin. Based on the production method and materials used, modern wound dressings can be classified into several categories: films, foams, nonwovens (including electrospun and blow-spun), 3D-printed dressings, and hydrogels. Research is ongoing to develop novel and more advanced wound dressings, like smart polymeric bandages, despite the large variety now available on the market.[37]

2.1.1 Traditional Wound Dressings

Gauze, plaster, and wool dressings are examples of passive/traditional dressings that act as a protective layer to restore the function of the skin underlying. However, by transmitting moisture molecules and gases through the dressings, conventional dressings have the potential to promote infection and slow down the healing process. Although they adhere well to the wound, they can be extremely painful to remove; that is why they are advised for dry wounds. Modern wound dressings, on the other hand, contain more sophisticated formulas that not only cover the wound but also aid in the healing process and avoid dehydration.[38]

2.1.2 Bioactive Wound Dressings

Bioactive wound dressings are made from biopolymers and are intended to improve the healing process by providing encapsulated active ingredients (such as antibiotics, peptides, medications, vitamins, growth factors, *etc*.) to the wound environment. Even though interactive or modern wound dressing materials directly interact with the wound bed to promote the regeneration process. These active substance dressings enhance wound healing activity by creating an active interaction between the dressing and the wound environment. These interactions include removing excess exudate, creating a moist environment in the wound bed, and preventing infection[39]. Because of their biocompatibility, biodegradability, and non-toxic nature, natural materials like hydrocolloids, alginates, collagens, chitosan, chitin, derivatives from chitosan or chitin, and bio-fabrics are frequently utilized in bioactive dressings. Various natural materials have been used for developing bioactive wound dressings.

For example, Singla et al. developed nano bio-composites containing plants, demonstrating that wound dressings made up of biomaterials are ideal for quick restoration, reducing the production of inflammatory cytokines.[40] Tang et al. reported a honey/alginate/PVA nanofibrous membrane by the electrospinning technique, which showed a stronger antibacterial effect.[41] Ionescu et al. developed a nanofiber based on chitosan that showed considerable antioxidant and antimicrobial characteristics, making it suitable for the treatment of chronic wounds.[42]

2.1.3 Composite Wound Dressings

Composite wound dressings consist of multiple layers, each with unique biological properties. These dressings usually consist of three layers and are designed to stick to skin tissues with a tape border made up of transparent film or a non-woven fabric. Composite dressings are frequently used in combination with topical medications and can be used as primary or secondary dressings. While the middle layer of the dressing is often composed of absorbent material, such as graphene-based materials, to maintain a moist environment and encourage autolytic debridement, the top layer protects the wound from infection. To keep the dressing from adhering to freshly granulating tissues, the bottom layer is made of non-adhesive material. Nevertheless, compared to other dressing types, composite dressings may be less flexible and more costly.[43]

2.1.4 Medicated Wound Dressings

By incorporating drug molecules into the dressing itself, medicated wound dressings make an important contribution to the healing process. Antimicrobial chemicals can be used to destroy germs and encourage tissue regeneration after necrotic tissue has been removed. CutisorbTM is an example of an antibacterial dressing product. There are many dressings, such as Silver-impregnated dressings, which come in a variety of forms, such as polyurethane foam film, silicone gels, and fibrous hydrocolloids. Additionally, the widely used antiseptic iodine treatment causes oxidative cell death by interfering with bacterial protein function. Infections can be prevented and treated using antimicrobial dressings, especially when diabetic foot ulcers are present.[44]

2.1.5 Antibiofilm-Based Wound Dressings

Antibiofilm-based wound dressings are essential for managing chronic wounds because they target persistent microbial biofilms, one of the main obstacles to healing. Advanced techniques are required to eliminate these biofilms, as conventional dressings and systemic antimicrobials are often insufficient. To disrupt biofilm structure, reduce microbial load, and restore a favourable wound microenvironment, antibiofilm dressings use techniques such as matrix-degrading enzymes, metal nanoparticles, antimicrobial peptides, chelating agents, quorum-sensing inhibitors, and photodynamic or smart nanomaterial systems. These dressings enhance infection management by

combining antibacterial activity with tissue compatibility, maintaining moisture balance, and modulating inflammation. There are many available products with purported anti-biofilm activity. Here, we discuss the mode of action and clinical significance of available anti-biofilm products, with a focus on levels of evidence for efficacy in destroying biofilms and facilitating positive wound healing outcomes.[46]

Table 1: Marketed anti-biofilm wound dressings: active ingredients and manufacturers

Product Name	Active Ingredient	Manufacturer	References
Silvercel	Silver	Smith & Nephew	46
Acticoat	Silver Nanoparticles	Barret	47
Biopatch	Chlorhexidine	Mann	48
Mepilex	Polyurethane Foam	Santamaria	49
Tegasorb	Honey	Medline Industries	50
Iodosorb	Iodine	Smith & Nephew	51
Aquacel	Hydrofiber	Hurlow	52
Biatain	Hydrocellulose	Xianchao	53
Hydrosorb	Hydrocolloid	Dhivya	54
DermaTech	Collagen	Barnea	55
Prontosan	Betaine/Polyhexanide	Atkin	56
Kerlix	Polyhexamethylene Biguanide	Wibbenmeyer	57

The use of advanced wound dressings, while beneficial, comes with several risks and challenges. One primary concern is the risk of infection, as if dressings are not changed regularly, they can become a source of bacterial growth and infection.[58] Furthermore, frequent dressing changes may lead to the loss of granulation tissue, which is crucial for wound healing.[59] Improper application by inexperienced caregivers can also cause periwound damage, potentially harming the skin surrounding the wound.[60] Additionally, advanced dressings can be more expensive compared to traditional options, adding a financial burden.[61] There is also the risk of allergic reactions, as some patients may be sensitive to the active ingredients in these dressings.[62] Overuse of antimicrobial dressings can contribute to microbial resistance, reducing their long-term effectiveness.[63] Another challenge is the limited efficacy of these dressings, as not all are suitable for every type of wound.[64] Some dressings may fail to manage wound exudate properly, leading to maceration, which can worsen the wound condition.[65] Skin irritation is also a concern, as certain ingredients in the dressings can cause discomfort or adverse reactions for the patient.[66] The environmental impact of the production and disposal of these dressings should not be overlooked, as they can contribute to waste and pollution.[67] Patient compliance is another issue, as some individuals may struggle to adhere to the recommended dressing change schedule, potentially affecting healing.[68]

Additionally, some advanced dressings have specific storage requirements to maintain their efficacy, which may not always be feasible in all healthcare settings.[69] The availability of these specialised dressings can also be limited in certain areas, affecting their accessibility to patients. The proper application technique for these dressings requires adequate training and skill, which may not always be accessible to all healthcare providers.[70] Finally, there is a risk of a false sense of security when relying too heavily on advanced dressings, which could lead to the neglect of other essential aspects of wound care, such as infection control or overall wound management.[71]

High-quality studies regarding the beneficial role of biofilm eradication and the subsequent relationship to wound healing in patients with chronic wounds are lacking and thus represent an unfulfilled need. Many experiments studied biofilm using in *vitro* or animal models, which have inherent limitations in their generalizability and clinical applicability; these need to be addressed. Although *in-vitro* methods have been used extensively to study biofilms, biofilms are different than their *in-vivo* counterparts. In vitro biofilms form large, single 3-D structures and exhibit classic “mushroom-like” multicellular structures. On the other hand, in vivo biofilms lack the mushroom-like structures, are significantly smaller in diameter, and form many small aggregates segregated by host tissue rather than single large structures. Additionally, it is known that biofilm aggregates can form without attachment to a surface, and conventional in vitro biofilm models miss these populations due to their requisite abiotic surfaces. Most importantly, *in-vitro* models fail to accurately recapitulate the complex microenvironment of the human skin wound i.e., the host immune response and metabolic factors which shape the phenotypic and genotypic profiles of the invading bacteria.[72] Animal models provide a more

accurate medium for the study of biofilms but are limited by obvious differences between animal and human physiology, for example, differences in murine and human sensitivity to lipopolysaccharide and murine wound healing occurring primarily via contraction. The fact remains that there is no gold standard *in vivo* model and each may provide answers to different specific questions. Standardized biofilm models that can more accurately replicate the human wound microenvironment are needed so that researchers and clinicians can more easily compare their results and guide therapeutic strategies for patients with wounds.[73] Additionally, the methods used to measure biofilms are not created equal; although there is no gold standard, confocal laser scanning microscopy (CLSM) combined with fluorescence in-situ hybridization (FISH) may be the most powerful tool available. Scanning electron microscopy (SEM) is also often used, but is limited by superficial depth penetration and other factors.[74] Recent consensus guidelines for research on biofilms state that evidence from in vitro and animal models is important to consider when choosing treatments and is helpful in screening for their antibiofilm efficacy. Furthermore, in the absence of RCT-level evidence, the choice of such interventions should be supported by their evidence in promoting beneficial wound healing outcomes.[75,76]

Overcoming the challenges associated with antibiofilm-based wound dressings requires the implementation of several strategies. One effective approach is the use of advanced drug delivery systems, which ensure the targeted and effective application of antimicrobials, thereby reducing potential side effects.[77] Proper training for healthcare providers is also essential, as it can prevent periwound damage and improve overall patient outcomes by ensuring the correct application of the dressings.[78] Additionally, educating patients about the importance of adhering to the dressing change schedule can significantly improve patient compliance and enhance the treatment's efficacy.[79] To address the issue of cost, developing cost-effective dressings and exploring insurance coverage options can make these advanced dressings more accessible to a wider range of patients.[80] Allergy testing before using dressings with potential allergens can also help prevent allergic reactions and improve patient safety.[81] The use of combination therapies, which include mechanical debridement alongside topical antimicrobials, has shown promise in enhancing treatment efficacy by addressing multiple aspects of wound care.[78]

Environmental concerns can be mitigated by developing eco-friendly dressings and promoting proper disposal methods, thereby helping to reduce the overall environmental impact of these products. Regular monitoring of wound progress and dressing performance is crucial, as it allows for early detection of potential issues and facilitates timely interventions.[82] Continued investment in research and development is essential to create new materials and formulations that are more effective and less prone to resistance. Finally, tailoring dressings to the individual needs of patients, based on wound type and severity, can further improve healing outcomes and ensure personalized care.[80]

3. Types of Natural and Synthetic Antibiofilm Agents and their uses in Different Wound Dressings

Over the past few years, there has been a growing interest in exploring a wide range of natural and synthetic molecules that can combat biofilms more effectively than conventional therapies. Many naturally derived substances—such as plant-based phytochemicals (curcumin, flavonoids, tannins), essential oils, honey, proteolytic enzymes, and antimicrobial peptides—have shown impressive ability to interfere with biofilm development while remaining gentle and non-toxic to tissues. On the other hand, laboratory-engineered agents like silver nanoparticles, nitric-oxide–releasing systems, modified chitosan formulations, synthetic peptides, and advanced polymeric antimicrobials offer advantages such as sustained activity, improved stability, and precise targeting of biofilm structures. Together, these diverse agents exhibit multiple mechanisms—including breaking down the extracellular matrix, blocking microbial communication pathways, and improving drug penetration—making them highly promising for next-generation wound-care products. Wound dressings themselves have also undergone a major transformation. Instead of merely covering and protecting the wound surface, modern dressings are designed to act as smart therapeutic systems capable of delivering antibiofilm compounds directly to the infected site. Hydrogels, alginate sheets, hydrocolloids, nanofiber mats, foams, thin polymeric films, and other innovative dressing platforms can be infused with natural or synthetic agents and release them gradually over time. By doing so, these dressings help maintain a moist, healing-friendly environment, keep microbial growth in check, stop biofilms from reforming, and support faster tissue repair and regeneration.[83]

Table: -2 Types of Natural and Synthetic Antibiofilm Agents and their Uses in different Wound Dressings

Type	Agent	Use in Wound Dressings	Ref
Natural	Phytochemicals (e.g., tea tree oil, garlic, aloe vera)	Hydrogel films and Gauze dressings	84,85
	Biosurfactants (e.g., rhamnolipids)	Textile-based dressings	
	Antimicrobial Peptides (e.g., magainins, defensins)	Hydrogel and Foam dressings	
	Microbial Enzymes (e.g., proteases, glycosidases)	Enzymatic debridement dressings	
Synthetic	Synthetic Antimicrobial Peptides	Hydrogel and Alginate dressings	86, 87
	Macromolecular Agents (e.g., polymers, nanomaterials)	Film and Foam dressings	
	Chelating Agents (e.g., EDTA)	Hydrogel and Alginate dressings	
	Quaternary Ammonium Compounds	Gauze and Foam dressings	
	Activated Carbon	Hydrogel films	
	Silver	Foam, Hydrogel, and Alginate dressings	
	Honey	Honey-impregnated dressings	

4. Nanocarrier-mediated wound dressings

Nanoparticles as carriers of therapeutic agents for antibacterial treatment in wound healing. Nanotechnology, particularly the synthesis of NPs, is paving the way for new strategies to improve the wound healing process and to overcome the various challenges related to antifilm wound dressings. Considerable studies have shown that wound dressings containing biocompatible NPs capable of delivering therapeutic agents in a sustained manner have emerged as effective platforms and approaches for the treatment of skin wounds.[88] For example, NPs allow antimicrobial drugs of relatively poor solubility to be delivered and released to the site of injury.[89] This strategy decreases the side effects of drugs because NPs in wound dressings can directly deliver lowered drug doses and release them into the wound with greater efficacy. Until now, numerous kinds of NPs carrying therapeutic agents have been incorporated into wound dressing and proved to have the ability to treat bacterial infections and promote wound healing, mainly including polymeric, liposome, lipid, and inorganic NPs.[90] Recent research conducted with this kind of NPs is listed in Table 3.

Table 3: Recent research reports on nanocarrier-based wound dressings

Type of Carrier	Drug	Method	Research Findings	Ref
Polymeric Nanoparticles	Collagen mimetic peptide tethered vancomycin	Thin film hydration technique	Enhanced antibacterial efficacy in vitro and in vivo through sustained vancomycin release and CMP-based liposomal hybridization within the scaffold	91
Polymeric Nanoparticles	Polyethyleneimine/diazonium diolate	Oil-in-water emulsification solvent evaporation method	Lowered bacterial load and enhanced wound healing in diabetic mice, showing strong potential for treating chronic biofilm-infected wounds	92

Polymeric nanoparticles	Silver sulfadiazine	Double emulsification-sonication method.	Enhanced SSD's antibiofilm activity by disrupting extracellular DNA, achieving markedly greater biofilm eradication with reduced fibroblast toxicity while maintaining prolonged MIC levels	93
Polymeric Nanoparticles	Clindamycin	Oil-in-water (o/w) emulsification solvent evaporation method	Sustained drug release for two days, and the Cly/PPNPs showed superior antibacterial activity and stronger adhesion to negatively charged bacterial cell walls than Cly/PNPs	94
Polymeric Nanoparticles	Gentamicin	Emulsion solvent evaporation method	Promotes tissue regeneration and hastens the healing process.	95
Polymeric Nanoparticles	Insulin	Ionic gelation process	Significantly improved wound healing, outperforming both the PCL/COLL and negative control groups in macroscopic and histological assessments	96
Polymeric Nanoparticles	Azithromycin	Film hydration method	Strong anti-MRSA activity against both planktonic and biofilm forms, along with good biocompatibility and effective skin localization, indicating their suitability for treating superficial infections.	97
Polymeric Nanoparticles	Vancomycin	Emulsion solvent evaporation method	Showed a five-fold stronger antistaphylococcal effect than the standard antibiotic and achieved effective epidermal penetration	98
Polymeric Nanoparticles	Gentamicin	Solvent evaporation	Effectively inhibited *S. aureus, E. coli,* and *P. aeruginosa*, demonstrating strong antimicrobial performance and suitability for use as a wound-dressing delivery system	99
Lipid Nanoparticles	Eucalyptus or rosemary essential oils	High shear homogenization	Showed strong antimicrobial activity, good biocompatibility, enhanced fibroblast proliferation, and improved wound healing. In vivo, the olive–eucalyptus oil combination further accelerated healing and boosted antibacterial performance	100
Lipid Nanoparticles	Antimicrobial peptide and serpin	Water/Oil/Water double emulsion technique	Enhanced antibacterial activity, accelerated wound healing, and provided strong anti-inflammatory effects	101

Inorganic Nanoparticles	Curcumin		Strong antibiofilm activity in inhibition and CFU assays, while demonstrating low cytotoxicity and clear wound-healing potential in the HDF scratch model	102
Inorganic Nanoparticles	AMP esculentin 1a, Esc (1 21)		Advanced nanomedicine for localized treatment of chronic infected wounds	103
Inorganic Nanoparticles	Zn and ciprofloxacin hydrochloride	Sol–gel method	Promoted angiogenesis and skin regeneration through Si-ion release, supported hair follicle growth, and inhibited bacterial activity via zinc-ion release, with Zn ions and CiH showing synergistic antibacterial effects at low concentrations	104
Inorganic Nanoparticles	Gentamicin and rifamycin	Stöber method.	Exhibited sustained, long-lasting antibacterial activity.	105

4. Theranostic-based Wound Dressings

In terms of wound care, theranostic dressings are the next big thing. Theranostic systems combine diagnostic sensors with on-demand therapeutic modules, in opposed to traditional dressings that shield or passively release medications. In addition to providing individualised treatment (such as antibiotic release, phototherapy, or electrical stimulation), this dual functionality enables real-time monitoring of the wound microenvironment (such as pH, temperature, and infection biomarkers)

1. Stretchable dressing integrated with a temperature and pH sensor for wound status monitoring, as well as an electrically controlled drug delivery system for infection treatment.; colourimetric infection-sensing antimicrobial dressings.[106]
2. Multifunctional hydrogels that sense their microenvironment, such as pH, ROS, and bacteria) and release antimicrobials, growth factors, or photothermal agents in response are highlighted in evaluations of theranostic hydrogels and nanohybrids for 2025.[107]
3. Microneedle (MN) platforms for wound theranostics in 2025 describe MN patches that carry genes, antimicrobials, or anti-inflammatory drugs to alter the wound microenvironment in addition to monitoring biomarkers.[108]

The development of a smart theranostic wound dressing that not only allows the visual detection of infection but is also capable of releasing an antibacterial agent in response to wound infections. A move toward intelligent therapeutic techniques facilitates the transition from conventional to precision medicine. This platform's primary goal is to reduce the off-target effects of medications by improving the pharmacokinetics and methodical delivery of therapeutics to the site of action. Modern wound dressings (smart or theranostic) are made to keep an eye on a wound's pH, moisture content, and temperature all of which are critical factors that affect how well a lesion is healing[109]. The dressings that can change their properties in response to the specific microenvironment of the wound are called as smart wound dressings. These can create an alert to medical professionals for the possible presence of an infection without requiring the uncomfortable removal of the dressing. By demonstrating a discernible reaction to biochemical and/or physical indicators expressed during wound infection, several attempts in this area have proven successful.[110]

To examine the possible advantages and drawbacks of smart wound dressings, a new computational model is suggested that incorporates a mechanistic representation of how these wound bed parameters determine the healing rate. This model includes time-varying physiological parameters of the wound bed and edge that are not captured by the current in vitro test methods. Therefore, the extent to which the wound bed temperature distributions can be utilized to optimize dressing design is likely to be limited by gaps in the data. In order to provide real-time monitoring and treatments, smart dressings are made to react

dynamically to the wound environment. To detect changes in wound conditions (such as pH, temperature, or bacterial load), these dressings use sensors, biosensors, or even electronic components. When necessary, they release medications or antimicrobial agents.[111] For example, researchers developed alginate- and polyurethane-based hydrogels with pH-responsive dye as smart dressings for colorimetric wound pH sensing to identify infection.[112] Similarly, the authors revealed a smart cotton swab covalently modified with a pH indicator for monitoring the pH of wounds.[113] Another example of a smart wound dressing is the determination of uric acid content, which serves as a significant and precise indicator of wound status.[114]

These examples illustrate the creation of a smart theranostic dressing capable of visually identifying infections and releasing an antibacterial agent in response to infection. The combination of diagnosis and treatment is referred to as "theranostic". Another benefit of smart wound dressings is that they provide easy-to-use infection-monitoring tools, allowing patients to spend more time at home and minimizing hospital stays and related healthcare costs. As seen during the COVID-19 pandemic, shifting healthcare services from hospitals and clinics to local communities and patients' homes is especially beneficial during a pandemic situation. A simple mechanism of theranostic based wound dressing is shown in Figure 3.

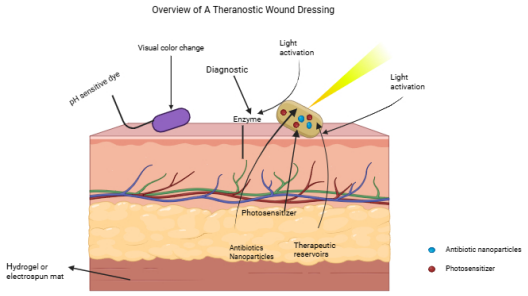

Figure 3: Represents the theranostic wound dressing

Singh et al., (2019) developed a collagen-based theranostic dressing using a prodrug approach that may detect infections visually and persistently. Nowadays, about 10% of medications used in therapy are administered as prodrugs due to the increased interest in this method in the medical profession. This tactic helps regulate the concentration of the active ingredient while also avoiding undesirable aspects of the parent medication. This implies that, in the case of a wound, the active medication will stay a dormant substance and only become active when bacteria are present. For example, a study designed a new theranostic wound dressing using blend electrospinning of polyurethane (PU, primary scaffold) with enzyme-responsive small organic molecules (i.e., prodrug (Pro-Cip) and chromogenic probe (H-Cy). This smart wound dressing responded to bacterial infection by changing color dramatically. This method is simple, non-invasive, and provides ongoing wound environment monitoring without the need for sophisticated equipment.[115] Brooker et al., (2023) describe that by taking advantage of bromothymol blue's (BTB) propensity to change color at infection-associated alkaline pH and the formation of secondary connections between BTB and a wound healing collagen network, a basic wound theranostic dressing prototype was successfully fabricated.[116] Khalid et al. (2020) invented a nanodiamond-silk membrane—a hybrid, multipurpose optical material platform—which is described as a bioinspired dressing with temperature sensing and wound healing capabilities. Electrospinning was used to create the hybrid structure, which resulted in 3D sub-micron fiber membranes with great porosity. By making up for the absence of the extracellular matrix at the wound site, the silk fibers can aid in the healing process. Without removing the dressing physically, the negatively charged nitrogen vacancy (NV-) color centers in nanodiamonds (NDs) function as fluorescent nanoscale thermometers with optically detected magnetic resonance (ODMR) capabilities that can detect temperature changes linked to infection or inflammation in a wound.[117] Punnoy *et al* (2024) developed a silk-based dressing containing levofloxacin, graphene oxide, alginate hydrogel, and a pH indicator dye. The dressing turns green and releases a lot more medication when the pH of the wound increases (for example, to 8), which speeds up the killing of bacteria. In experiments on human skin, graphene oxide improves drug loading and maintains release without causing discomfort.[118] The authors disclosed that a peer-reviewed study from 2023 detailed injectable theranostic hydrogels that combined polydopamine nanoparticles loaded with a porphyrin (TCPP) with polylysine (ePL). Real-time imaging of infected wounds under 410 nm light is made possible by the release of fluorescence induced by acid. After that, photodynamic antibacterial action is triggered by 660 nm illumination, and debris and leftover dressing are later removed by 808 nm light. Experiments conducted in mouse models demonstrated increased angiogenesis, collagen deposition, decreased inflammation, and quicker recovery.[119] NO-loaded copper-based metalorganic frameworks (MOFs)

embedded in electrospun polycaprolactone/gelatin nanofibers were also investigated by researchers. In animal models, wound fluid accelerates diabetic wound healing by breaking down the fibers and releasing copper ions and nitric oxide, which work together to promote angiogenesis, collagen production, and anti-inflammatory effects.[120]

Table 4: Recent Research Reports on Theranostic Wound Dressings

Theranostic Wound Dressings (TWD)	Diagnostic indicator	Therapeutic action	Response trigger	Biocompatibility	Ref
Lipase-responsive PU scaffold	Color change (yellow → red) upon bacterial lipase	Antibiotic release	*P. aeruginosa* lipase hydrolysis	Non-toxic to skin fibroblast	115
Silk-alginate-GO (Graphene Oxide) dressing	Yellow→green at pH ~8	Levofloxacin release	Elevated wound pH	No irritation and allergies	118
Collagen-BTB (Bromothymol blue) hydrogel	Rapid color change within 1 min of contact with simulated wound fluid.	Passive, no drug	pH rise due to infection	≥92 % fibroblast viability by drop casting method)	116
Injectable PLU-PDA hydrogel	Fluorescence under 410 nm	Photodynamic therapy; debris removal	Acid-triggered TCPP release and light	Promotes healing in vivo	121
Nanodiamond-silk membrane	Fluorescent temperature sensing	Passive; supports healing and antimicrobial	Temperature rise (inflammation)	Compatible with mice	122
NO-MOF (Nitric Oxide - metalorganic frameworks fibers	No visual indicator; therapeutic release	NO + Cu (Copper)ions improve healing	Exudate-induced fiber degradation	Effective in the diabetic wound model	120

5. Patents on wound healing

Innovations in this field range from advanced biomaterials and nanotechnology-based dressings to bioactive compounds, microneedle systems, stem-cell therapies, electroceutical dressings, and smart sensors that monitor wound status in real time. Here, in Table 5, there is a compiled report of patents on wound dressings having novel methods, compositions, and devices that are designed to address key challenges such as chronic wounds, biofilm formation, poor vascularization, and antimicrobial resistance.

Table 5: Various Patents on Wound Dressings

Patent No	Title	Findings	Ref
US 11911521	Anti-Bacterial nanofibers	Core–shell nanofibers enabled triggered antibacterial release, where bacterial lipase activity and pH reduction degraded the shell, allowing the antimicrobial agent in the core to be	123

		effectively released	
US 11572578	Reagent kit for detecting biofilm and a method for detecting biofilm	Detecting biofilm in test tissue	124
US 11745001	Therapeutic Bandage with array of Microneedles	The microneedle array is designed to draw foreign agents—modulated by one or both immunomodulatory compounds—from the skin layers into the bandage matrix, where they are absorbed and captured	125
US 20220096706	Electrospun Nanofibers-based dressings	The nanofiber layer can be integrated with multiple microneedles containing an antimicrobial agent and a dissolvable polymer (such as PVP or PVA), enabling effective penetration through the biofilm	126
WO 2021024484 6A1	Biofunctional Hydrogel for Wound Healing	A hydrogel that eradicates biofilm bacteria from wounds and accelerates diabetic wound healing	127
US 20230166101A	Electroceutical dressing for wound care	Electroceutical dressings with three or more electrodes use applied electric currents to prevent and reduce biofilm formation and bacterial infection.	128
US 10874108	Anti-Microbial Compounds Composition	The metal–EDTA complex provides antimicrobial, antibiofilm, and anti-inflammatory effects, increasing biofilm susceptibility to antimicrobial agents and aiding in its removal and sanitization	129
US 105 48948	Methods of treating fungal infections and wound infections	Dressings with Antimicrobial and Antifungal Agents	130

Future perspective & Conclusion

Future advances in chronic wound care will rely on developing sensitive diagnostic tools that can detect key biomarkers—such as exudates—to monitor treatment response and guide personalized therapy. Faster, more accurate methods for identifying early infection and tissue damage are also needed, along with a deeper understanding of how cells and the extracellular matrix interact during healing. Research must also address how wound exudates alter the "biological identity" of modern dressings, especially those containing nanoparticles or nanofibers, since these changes can affect safety and therapeutic performance. Chronic wound management is shifting toward biofilm-targeted therapies, nanoparticle-based

dressings, and theranostic systems that combine treatment and real-time monitoring. Although traditional dressings face limitations like resistance and discomfort, nanotechnology-enabled and smart dressings offer improved healing, targeted delivery, and personalized care. Ensuring affordability, sustainability, and clinical effectiveness remains essential. With rising chronic diseases and antibiotic resistance, the demand for advanced wound technologies will grow, making interdisciplinary collaboration crucial for developing safer, smarter, and more effective wound-care solutions.

Conflict of Interest

The authors declared no conflict of interest

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