



Review Paper

pH-Responsive Wound Dressings for Intelligent Wound Monitoring and Targeted Therapeutic Management

Anagha U. V.*, Vimal K. R., Abhirami P. P., Haritha K. K., Priyanka P, Nethaji Ramalingam

Devaki Amma Memorial College of Pharmacy, Kerala 673634, India..

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ABSTRACT

Wound healing is a complex, highly coordinated process that involves haemostasis, inflammation, proliferation, and remodelling. Change in wound pH is known to be an important biomarker indicating wound status, infection and healing progress. Healthy skin and healing wounds possess a slightly acidic environment, while chronic and infected wounds usually show the alkaline pH. Such pH variation has triggered a wide range of research on pH-responsive wound dressings with controlled drug release, antibacterial activity, visual monitoring, and enhanced tissue regeneration. Recent advances in biomaterials, nanotechnology and smart sensing systems enable multifunctional wound dressings such as hydrogels, nanofibers, films, foams, nanoparticle systems and wearable biosensors. These systems can achieve responsive modulation of swelling behavior, degradation rate, morphology and therapeutic release in response to changes in the wound microenvironment. These dressings are increasingly being combined with natural polymers, synthetic polymers, essential oils, nanoparticles, nanozymes and pH-sensitive dyes to improve the healing efficiency and reduce the infection. This review discusses the role of pH in wound healing, classification of pH-responsive dressings, mechanisms of pH-triggered therapeutic release, smart sensing technologies and recent advances in antibacterial and self-healing biomaterials. Current challenges and future prospects towards clinical translation and personalized wound care are discussed as well.


INTRODUCTION

The skin is one human organ that is in direct contact with the outer world. It has important roles in controlling body temperature and sensing

external stimuli to protect the body from injury. [1] Skin injuries are among the most common types of injuries in the human body and can cause pain, discomfort, and even death. [2] Wound healing is a complex and dynamic process that begins after an

*Corresponding Author: Anagha U.V

Address: Devaki Amma Memorial College of Pharmacy, Kerala 673634, India.

Email : anaghadayanidhi@gmail.com

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injury and can be divided into four phases: haemostasis, inflammation, proliferation, and remodelling. [3] Factors such as infection, inflammation, diabetes, pH and temperature can interfere with the healing process at any stage. Chronic wounds are wounds that usually take more than 3 months to heal. They are considered as one of the leading causes of death and also have high treatment costs in bedridden and diabetic patients.[4] The current treatment of chronic wounds is based on the use of custom-made wound dressings for a given healing stage, inflammatory condition, level of moisture, and rate of oozing. However the condition of the wound is generally assessed by visual inspection, and the changing of the dressing is often done unnecessarily, increasing the danger of a second injury or disrupting the healing process. [4,5] The traditional wound dressings such as cotton bandages and gauzes mainly provide the physical protection, but lack the effective prevention of infection, monitoring of the wound conditions and controlled therapeutic release. [6] Consequently, the main focus of current wound care research is on smart wound dressings that can respond to changes in the wound microenvironment.[1] Among the various wound biomarkers, pH has been identified as one of the most significant indicators of wound condition. [2] During the healing process, acute wounds tend to return to an acidic environment, whereas chronic and infected wounds are characterized by alkaline pH ranging from 7 to 9, which is a consequence of bacterial proliferation, inflammatory mediators, and tissue destruction. [1,4] The pH of healthy skin is normally between 4 and 6 which helps to hinder bacterial growth and preserve barrier integrity. [1,2] Increased pH promotes delayed tissue regeneration, biofilm formation, protease activity. [7] Smart biomaterials, such as “pH-responsive wound dressings,” can respond to changes in their local pH by swelling, degrading, changing color, or releasing drugs

under controlled conditions. [1] These dressings can improve healing outcomes, visually display the progression of infection, and deliver therapeutic drugs directly to infected wounds [8].Recent progress in biomaterials, nanotechnology, and wearable biosensors [1,9] has sped up the creation of multifunctional wound dressings such as hydrogels, nanofibers, films, microneedles, and nanoparticle systems that incorporate pH-sensitive materials, antimicrobial agents, antioxidants, and biosensors. These advanced devices offer real-time monitoring, antimicrobial activity, moisture retention, oxygen permeability, and personalized treatment management. [10,11]

This review emphasizes the role of wound pH in wound healing, classification of pH-responsive dressings, mechanism of pH-responsive behavior, intelligent monitoring systems, therapeutic applications, recent advances and future clinical perspectives.

EFFECT OF PH ON WOUND HEALING

Normal pH of Skin

Healthy skin maintains the acid mantle with pH values typically between 4 and 6. [1,12] This acidic environment is also caused by fatty acids, amino acids, perspiration and metabolism of keratinocytes. [12] The acid pH supports the epidermal barrier integrity and inhibits bacterial colonisation. [1,3]

pH Alterations in the Healing Wound

If the skin is injured and the interior tissues and interstitial fluid are exposed, the pH of the wound rises to neutral or alkaline conditions.[2] The chronic wounds are alkaline owing to persistent inflammation and bacterial infection whereas the acute wounds gradually revert to the acidic pH during the healing process. [1,7]

Han et al. reported that infected wounds present significant changes in pH related to bacterial



metabolism and progression of inflammation, whereas chronic wounds generally display pH values in the range 7–9.^[1] The wound pH is also taken into account as a reliable predictor of wound deterioration and propensity to heal.^[4]

Effect of pH on Wound Physiology

The pH of the wound microenvironment is an important regulator of many biological processes associated with tissue regeneration and repair, Proliferation of fibroblasts, Stimulates collagen production, Oxygen release from haemoglobin, Angiogenesis Bacterial growth, Activation of proteases, Biofilm formation, It affects everyone directly. An acidic wound environment promotes fibroblast migration, collagen deposition, increased oxygen availability and angiogenesis that all facilitate healing and promote tissue regeneration. On the other hand, alkaline pH Favors bacterial growth and the activity of matrix metalloproteinases (MMPs) and other proteolytic enzymes, resulting in the breakdown of the extracellular matrix, chronic inflammation, biofilm formation, and slower wound healing. Therefore, maintenance or restoration of an optimal acidic pH is considered as an important approach for good wound healing and prevention of chronic wound development.^[7,13]

Importance of Monitoring pH

Monitoring of wound pH is an important indicator of the healing process and provides insightful information about the physiological state of the wound. pH variation can indicate the presence of bacterial infection, effectiveness of continuation of treatment, biofilm formation, and degree of inflammation in the wound microenvironment. Good healing is associated with a slightly acidic environment, while alkaline pH is characteristic for chronic and infected wounds. Thus, real time monitoring of wound pH can aid in recognizing early pathological change, starting therapeutic

treatments and assessing the treatment efficacy. Therefore, pH-responsive wound dressings serve as theranostic platforms to monitor wound conditions and simultaneously provide customized stimulus-responsive therapeutic administration, thereby enhancing wound management and facilitating tissue regeneration.^[1,9]

pH-RESPONSIVE WOUND DRESSINGS

pH-responsive wound dressings are intelligent biomaterials that can modify their physical, chemical or biological properties according to the change of pH value of the wound.^[1] These systems might respond by: Swollen conduct, Change of colour, Polymer degradation, Controlled drug release, Morphology change, Electrical or optical signal

The development of pH-responsive devices has enabled real-time wound monitoring and targeted therapeutic delivery.^[1,4]

Han et al. reviewed the advanced functions and design strategies of pH-responsive wound dressings, including hydrogels, films, nanofibers, nanoparticle clusters, and microneedles in detail.^[1]

pH-RESPONSIVE DRESSING DESIGN METHODS

pH Responsive Morphology

The morphological transformation realizes the liquid-solid conversion or structural change under particular pH values.^[1,14] Dynamic covalent bonds like Schiff base bonds, imine bonds, and catechol-Fe coordination bonds are commonly used.^[14]

These devices reduce secondary injuries and enable painless removal of dressings.^[15]

pH-Responsive Swelling

Swelling is caused by protonation, deprotonation and electrostatic repulsion of the polymer functional groups.^[16] Increased edema facilitates better pore size and therapeutic release.^[1]



Graphene oxide, polyvinyl alcohol and bacterial cellulose based hydrogels showed improved swelling and curcumin release in alkaline pH.^[17]

Degradation as a Function of pH

Hydrogel degradation is a useful way of controlled medication release.^[1] The hydrolysis of ester bonds in alkaline conditions can lead to the breakdown of hydrogels based on methylcellulose. Expansion of hydrogel network accelerates degradation and therapeutic diffusion in alkaline infected wounds.^[18]

pH Triggered Drug Release

pH-triggered drug release is done by: Hydrogels swelling, Breaking of bonds, Nanoparticles degradation, Ionic bonds, Polymer dissolution. The pH of infected wounds can be either alkaline or acidic, depending on bacterial activity, which increases the release of the drug.^[1,8]

pH-RESPONSIVE WOUND DRESSINGS TYPES

Hydrogels

Hydrogels are three-dimensional networks of hydrophilic polymers which can absorb large quantities of water while maintaining structural integrity.^[1,6] They are suitable for wound healing applications due to their high-water content and extracellular matrix-like structure.^[18]

Advantages

- A humid wound environment
- O₂ permeability
- Controlled drug release
- Biocompatibility
- Enhanced patient comfort

Limitations

- Insufficient mechanical power
- Dehydration possible
- Stability in the long term is poor

Self-healing hydrogels

Self-healing hydrogels recover from structural damage through reversible dynamic interactions such as hydrogen bonding, Schiff base formation and host-guest interaction.^[14] Yang et al. prepared a cellulose nanofibril reinforced hydrogel with excellent mechanical properties, self-healing ability over 90% and pH-responsive release of resveratrol. It is very suitable for acid infected wounds as the cumulative release at pH 5.4 was 2.33 times higher than at pH 7.4.^[10]

Moreover, the hydrogel exhibited excellent antioxidant activity, antibacterial activity and wound healing efficiency.^[10]

Hydrogels Loaded with Essential Oil

Qiu et al. developed a hyaluronic acid-carboxymethyl chitosan hydrogel with essential oils of eugenol and oregano. The hydrogel showed improved pH-responsive degradation and anti-biofilm activity. The release of eugenol increased from 37.6% to 82.1% at acidic pH 5.5 and the degradation was four times higher than at neutral pH.

These methods significantly accelerated the removal of biofilm and the healing of wounds.^[11]

Nanofibrous textiles

Electro spun nanofibers have high porosity and high surface area and their architecture is similar to extracellular matrix.^[19]

Advantages

- Increased cells adherence
- Regulated therapeutic delivery
- Breathability
- High drug load limitations
- Fragile mechanics

Limitation

- Complex manufacturing processes.

pH-responsive nanofibers loaded with curcumin, antibiotics, or silver nanoparticles have exhibited strong antibacterial and wound healing activities.^[17,20]



Membranes and Films

The combination of films and membranes with pH-sensitive indicators enables visual wound monitoring. [1]

Advantages

- Real time visualization
- Light weight construction
- Non-invasive monitoring

Limitations

- Limited absorption of exudate
- Lowered adaptability

Colorimetric wound dressings based on anthocyanins, bromothymol blue, and bromocresol purple are gaining considerable attention because of their ability to show colour change under different wound pH conditions. [4,21]

Bacterial cellulose dressings

Bacterial cellulose has excellent porosity, mechanical strength, moisture retention and biocompatibility. [22]

Shao et al. prepared silver sulfadiazine-loaded bacterial cellulose composites with pH-sensitive release behaviour. The system showed very good antibacterial activity against *Staphylococcus aureus* and *Candida albicans* with good biocompatibility.

This improved infection control as more Ag⁺ and sulfadiazine ions were released in pH-sensitive environments. [22]

Nanoparticle Based Dressings

Nanoparticles have high surface area, controlled drug release and antibacterial properties. [8]

Silica Nanoparticles

Pan et al. prepared chlorhexidine-loaded pH-responsive silica nanoparticles for treatment of chronic wound infections. The nanoparticles showed 4–5 times more release at pH 8–8.5 compared to the physiological pH.

The system demonstrated potent antibacterial activity in ex vivo wound studies. [8]

Nano agents of Copper Peroxide Hydrogels

Zu et al. created a copper peroxide Fenton nano agent hydrogel that can produce hydroxyl radicals in response to pH and hydrogen peroxide independently. [23]

The hydrogel exhibited:

- Potent antibacterial activity through ROS
- Almost 7 logs reduction of bacteria
- Enhanced haemostasis
- Speedier tissue regeneration

This multipurpose solution is a promising next generation antibacterial wound dressing. [23]

pH-RESPONSIVE COMPONENTS

BANDAGE

Natural polymers

Natural polymers are widely used in pH sensitive wound dressings due to their low toxicity, biodegradability, biocompatibility and bioactivity. [1,6]

Natural Polymers:

- Chitosan
- Alginate.
- Hyaluronic acid
- Gelatin
- Collagen
- Celluloses
- Carboxymethyl Chitosan

Benefits

- Toxic-Free
- Biological activity
- Biocompatibility and biodegradability

Alginate and chitosan possess good moisture retention, antibacterial activity and capacity to absorb wound exudates. [24] The addition of collagen promotes tissue regeneration and extracellular matrix formation and hyaluronic acid facilitates angiogenesis and fibroblast proliferation. [25] Cellulose based polymers are known for their high mechanical strength and swelling capabilities, which are suitable for chronic wound therapy. [10]



Synthetic Polymers

Synthetic polymers have tunable responsiveness, flexibility, physicochemical stability and adjustable mechanical strength. [6]

Synthetic polymers:

- Polyvinyl alcohol (PVA)
- PEG (polyethylene glycol)
- Polycaprolactone (PCL)
- Polyacrylic acid
- Methacrylic acid polymers

PVA-based hydrogels are widely used due to their hydrophilicity, film-forming ability and biocompatibility. [17] Polyethylene glycol (PEG) and polyacrylic acid have swelling properties, as well as controlled drug release efficiency. [16]

pH-Sensitive Indicators

Smart wound dressings include synthetic and natural pH indicators for visual monitoring of wound infection and healing. [4]

Common Indicators:

- Anthocyanin
- Bromothymol blue
- Curcumin
- Bromocresol purple
- Phenol red

Anthocyanins are excellent indicators because they change colour dramatically from red in acidic to blue-purple in alkaline conditions. [21] Bromothymol blue and bromocresol purple are also commonly used due to their rapid colorimetric response to pH change in wounds. [4]

Table 1. Common pH Indicators Used in Smart Wound Dressings

Indicator	Acidic Colour	Alkaline Colour	Application
Anthocyanin	Red/Pink	Blue/Purple	Infection monitoring
Bromothymol blue	Yellow	Blue	Smart films and dressings
Bromocresol purple	Yellow	Purple	pH sensing
Phenol red	Yellow	Red	Cell culture and wound sensing
Curcumin	Yellow	Orange-Brown	Antibacterial dressings

MECHANISMS OF pH-RESPONSIVE DRUG RELEASE

pH-responsive therapeutic release based on ambient pH-induced physicochemical changes in polymeric systems. [1]

Polymer swelling

The polymer expansion leads to diffusion of the medicinal agent and to an increase of the pore size. [16]

Bond cleavage

Hydrolysis of ester bonds, Schiff bases and acid labile connections results in the release of medication. [18]

Nanoparticles Decay

The change in pH causes the nanoparticles to degrade and release the medicines they are carrying. [8]

Ionic Bonding

Changes in ionic charge affect polymer interactions and release kinetics. [1]

These procedures raise targeted treatment efficiency, reduce systemic toxicity and improve therapeutic precision. [8]

THERAPEUTIC AGENTS INCORPORATED INTO pH-SENSITIVE DRESSINGS

Antibacterial Agents

- Silver nanoparticles.
- Silver sulfadiazine
- Chlorhexidine



- Ciprofloxacin.
- Tobramycin (Tobrex)
- Polyhexamethylene biguanide (PHMB)

These antimicrobials prevent bacterial colonisation, biofilm formation and chronic wound infection.^[22]

Antioxidants

- Curcumin
- Resveratrol
- Anthocyanins
- Extracts of plants
- Raw honey

Antioxidants decrease oxidative stress, stimulate fibroblast proliferation and accelerate tissue regeneration.^[3]

Essential Oils

- Oregano oil
- Eugenol
- Cinnamaldehyde

Essential oils have strong antibacterial, antioxidant, antifungal and anti-biofilm properties.^[11]

ROS Systems and Nanozymes

Reactive oxygen species generated by Fenton systems and nanozymes can kill antibiotic resistant bacteria and facilitate wound sterilization.^[23]

SMART SOLUTIONS FOR WOUND MONITORING

Current intelligent dressings employ wearable sensor technologies to monitor wounds in real time.^[9]

Colorimetric Monitoring

pH monitors detect the development of infection visually by means of visible colour changes.^[4]

Optical Sensors

Optical sensors detect changes in absorbance or pH-related fluorescence for accurate wound analysis.^[4]

Monitoring with a Smartphone

RGB colour changes and wound condition are analysed digitally using smartphone-assisted devices.^[4]

Wearable Bio Sensors

Dressings with integrated flexible wearable sensors enable continuous monitoring of: pH level, Temperature, Exudate, Glucose, Infection biomarkers.

These technologies support personalized wound care and early detection of infection.^[9,26]

DIABETIC WOUND APPLICATIONS

Diabetic wounds are characterized by:

- Long term inflammation
- Enhanced oxidative stress
- Limited vascularization
- Delays angiogenesis.
- High bacterial burden

pH-responsive dressings improve diabetic wound healing by:

- Control of infections
- Moisture control
- Controlled therapeutic release
- Angiogenesis enhancement
- Oxidative stress reduction

Hydrogels, Janus dressings and nanozyme-loaded systems have shown promising results for the treatment of the diabetic wounds.^[23,27]

BENEFITS OF PH-SENSITIVE DRESSINGS

The pH-responsive wound dressing possesses several advantages over conventional wound dressings for intelligent treatment response and real-time wound monitoring.^[1,4]

The main benefits are:

- Early diagnosis of infection
- Controlled therapeutic release
- Reduced systemic toxicity
- Improved antibacterial activity
- Improved patient compliance
- Monitoring in real time
- Reduced dressing changes



- Rapid tissue regeneration

These smart solutions improve the healing efficacy by dynamically responding to the changes in the wound microenvironment and reducing the unwanted drug exposure. [1,6]

LIMITATIONS AND ISSUES

There are many challenges to the clinical translation of pH-responsive wound dressings despite promising development [1,18]:

- High production cost
- Mechanical instability
- Instability of long-term storage
- Complicated sterilization procedures
- Problems of production scaling
- Regulatory challenges
- No clinical trials
- Potential nanotoxicity

Commercialization requires standardization, biosafety evaluation and broad clinical validation. [18,26]

CONCLUSION

The pH-responsive wound dressing provides a significant advancement in the contemporary wound care, integrating tissue regeneration, controlled drug delivery and wound monitoring in a single platform. Such intelligent dressings are not just like normal dressings which provide only physical protection but they can respond to changes in pH of the wound which is an important indicator of infection, inflammation, biofilm growth and healing process. The responsiveness of these materials is very important for the treatment of acute, chronic and diabetic wounds, allowing the early detection of pathological state and adapting the therapeutic action. Recent advances in biomaterials and nanotechnology have led to the development of many pH responsive systems such as hydrogels, nanofibers, films, bacterial cellulose composites,

nanoparticle-based dressings, microneedles and wearable biosensors. The incorporation of antibacterial agents, antioxidants, essential oils, growth factors and nanozyme-based systems has further improved their ability to fight infection, oxidative stress, biofilm formation and promote tissue generation. Furthermore, the incorporation of wearable electronics, artificial intelligence and digital healthcare technology is transforming pH-responsive dressings into multi-functional theranostic systems for real-time monitoring and personalized therapy, rather than a mere wound dressing. These are promising but still face hurdles in clinical translation, long-term stability, manufacturing scalability, and regulatory approval. Interdisciplinary research and clinical validation is ongoing and is expected to accelerate the development of next generation intelligent wound dressings to improve patient outcomes, reduce healthcare costs and promote precision wound care.

FUTURE PROSPECTS

Future directions of research should be focused on the development of complex pH-responsive wound dressings integrated with wearable biosensors, new biomaterials, artificial intelligence (AI), and smart therapeutic platforms for real-time monitoring of wounds and personalized care. AI-assisted wound assessment combined with smartphone image processing, wireless sensors, and cloud-based healthcare systems has the potential to enable early infection diagnosis, continuous tracking of wound healing progress, and data-driven clinical decision making. [1,26] The use of self-healing biomaterials, multifunctional hydrogels and nanostructured systems is expected to reduce patient discomfort and frequency of dressing replacement and increase dressing longevity, mechanical stability and therapeutic efficacy. [10, 18] Moreover, eco-friendly and biodegradable polymers have gained



great interest as sustainable substitutes for next-generation wound care systems, due to their better regenerative potential, less environmental effect and biocompatibility. [28] The design of multi-stimuli responsive dressings which can respond to pH, temperature, glucose, ROS, enzymes and infection biomarkers simultaneously is expected to facilitate more accurate and flexible therapeutic interventions tailored to the evolving wound microenvironment. [1,4] Advancements in 3D printing and bioprinting technologies and customized manufacturing techniques may allow the development of patient-specific wound dressings with distinct architecture, drug loading and release profiles. [29]

In addition, the synergistic combination of nanozymes, antimicrobial nanoparticles, growth factors, gene delivery systems, and regenerative biomolecules can significantly improve angiogenesis, collagen deposition, antibacterial activity, and tissue remodelling, particularly in diabetic and chronic wounds. [11,23] New theranostic platforms integrating therapy, monitoring and diagnostics into a single device are expected to revolutionize wound care and aid the transition to precision medicine. [18]

However, despite promising results at laboratory level, commercialisation is still hampered by the challenges of large-scale production, regulatory approval, long-term biosafety, product uniformity and translation into clinical use. Future efforts should therefore focus on cost-effective manufacturing strategies, scalable production technology, multicentre clinical trials and rigorous safety assessment. As the global burden and economic impact of chronic wounds continue to increase, it is expected that the incorporation of biosensors, nanotechnology, advanced biomaterials, digital healthcare, and AI-powered analytics will revolutionize the management of chronic wounds and expedite the development of

personalized, intelligent, and highly effective wound care systems in the near future. [30-34]

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