

## A Comprehensive Review on Wound Dressings Focus on Hydrogel-Based Materials

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**Abstract.** Bio-based aerogel is a lightweight, porous and high specific surface area nanomaterial prepared from natural biomacromolecules, which has shown great potential for application in the food field in recent years. Bio-based aerogels exhibit excellent adsorption, sustained release, and biocompatibility. In this paper, the preparation methods of bio-based aerogels, including the types of raw materials, the mechanism of the sol-gel method and the drying process were systematically reviewed. The physical and functional properties of bio-based aerogels were discussed. The applications of bio-based aerogels in food preservation mats, food freshness indication labels, nutrient delivery carriers, and fat in artificial meat substitutes were summarized. In addition, the challenges of bio-based aerogels in terms of large-scale production, food safety and consumer acceptance were discussed, and the future development of bio-based aerogels in functional food and industrial production were prospected.

**Keywords:** *Bio-based aerogel; sol-gel method; water absorption and water stability; freshness pads; artificial meat fat substitutes*

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### 1 Introduction

A wound is any breach in human tissue or organs triggered by physical, chemical or other assaults; its closure is a four-act play—clot, inflammation, proliferation and remodelling—whose tempo is set by wound class, systemic disease and the dressing chosen. As a temporary skin substitute, dressings serve to protect the wound, stop bleeding, prevent infection, and may also provide fixation. With in-depth research on wound healing, it is recognized that wound dressings should not only cover the wound but, more importantly, possess functions that promote wound healing [4-6]. Dressings fall into three tribes—classic gauzes, bio-derived membranes and engineered synthetics—each obeying different rules of moisture, oxygen and bio-activity; the review ahead maps their logic, lineup and clinical track record.

Traditional or “inert” dressings—gauze, cotton pads, bandage rolls—cost pennies, run off simple looms and still account for the lion’s share of clinic use. However, traditional dressings have many disadvantages and limitations in application, such as the inability to maintain a moist wound environment, the tendency for granulation tissue to grow into the mesh of the gauze, and the risk of exogenous infection when the dressing becomes saturated [7]. Currently, some manufacturers use impregnation or coating methods to improve the auxiliary performance of dressings. For example, petrolatum or triacylglycerol-based oil gauze can address the problem of adhesion between the dressing and wound granulation tissue. Furthermore, incorporating 3% tribromophenol bismuth into petrolatum gauze creates Xeroform dressing, which has good therapeutic effects on hypoosmotic wounds

[3, 8]. Additionally, incorporating antibiotics into the dressing can effectively provide local anti-infection effects, avoiding the side effects associated with systemic antibiotic use; it is a simple and effective bacteriostatic method. Although methods like impregnation and coating significantly improve the adhesion and antibacterial properties of traditional dressings, these dressings only provide physical protection and do not promote wound healing, which has led to the emergence of biological dressings.

## 2. Biological Dressings

Biological dressings are new types of wound repair and protection dressings developed based on the "moist healing" theory for trauma repair proposed by Winter in the early 1960s [9]. Compared to traditional dressings, they are closer to the ideal requirements, possessing good biocompatibility, degradability, moisturizing properties, and cause less adhesion to wound tissue, reducing damage to new tissue. They promote wound healing primarily by maintaining a moist healing environment, reducing pain, creating a hypoxic or anoxic, slightly acidic environment, and providing enzymatic debridement [10-11]. Based on the source of the dressing material, they can be classified into natural biological dressings and synthetic biological dressings.

### 2.1 Natural Biological Dressings

Natural biological dressings are processed and extracted from natural materials, mainly including animal skin-based biological dressings (autologous skin, allogeneic skin, xenogeneic skin) and non-skin animal-based biological dressings (alginate dressings, collagen dressings, chitosan dressings). The research progress on several common natural biological dressings is summarized below.

#### 2.1.1 Animal Skin Dressings

Skin grafts come in three flavours—your own (autologous), someone else's (allogeneic) or animal (xenogeneic). Autografts heal best but carve a second wound; allografts mimic native skin yet rely on cadaveric donors, bumping into religious taboos and scarce supply, so they serve mainly as experimental controls rather than front-line dressings [12]. The source of autologous and allogeneic skin is extremely limited, making it unable to meet needs in cases of large-area trauma. Therefore, xenogeneic skin, which has a structural composition similar to human skin, has become a relatively ideal trauma dressing. Porcine-derived biological dressings, as representatives of xenogeneic skin dressings, have high homology with humans, are widely available, inexpensive, and relatively simple to store and use. Thus, wound dressings made from pigs are widely used. Zhu Lei et al. [13] used porcine visceral membrane to create a new biological dressing that can accelerate the epithelialization process of skin wounds, advance wound healing time, improve the quality of skin wound healing, and promote collagen production. Porcine-derived biological dressings possess almost all the biological characteristics of allogeneic skin but struggle to address issues like rejection, revascularization, and poor antibacterial properties, making them unable to resist bacterial infections.

#### 2.1.2 Collagen Dressings

Collagen dressings are typically made from animal-derived type I collagen or type I collagen. During wound healing, they can promote fibroblast proliferation and accelerate the migration of endothelial cells within the wound. They have weak antigenicity, good biodegradability, and good biocompatibility. After appropriate cross-linking, they can have hemostatic and coagulant effects [12, 14-15]. Pure collagen dressings have poor stability and limited exudate absorption capacity. Therefore, to compensate for the deficiencies of collagen dressings, collagen is often combined with substances like chitosan, polyvinyl alcohol, and hyaluronic acid to improve their properties. For example, compounding silver carp fish scale collagen protein with chitosan in a 1.00:0.25 ratio creates a composite film dressing with good mechanical strength and anti-infective properties, while also extending the degradation time of collagen [16]. Ye Chunting et al. [17] used type I collagen protein and polyvinyl alcohol as the main raw materials. Leveraging the good flexibility and tensile strength of polyvinyl alcohol film to overcome the insufficient mechanical strength of pure collagen film, they prepared a collagen dressing with good cell compatibility, sufficient pore size and porosity, and good mechanical strength. Due to the poor exudate absorption capacity of collagen dressings, they are not suitable for exudative and infected wounds.

### 2.1.3 Alginate Dressings

Alginate dressings are adherent films made from an insoluble polysaccharide alginate. These dressings have extremely strong hygroscopicity, capable of absorbing exudate nearly 20 times their own weight, making them suitable for highly exuding chronic wounds. Sodium ions in the wound exudate can exchange with metal ions like calcium ions in the dressing, converting insoluble calcium alginate into soluble sodium alginate, thereby forming a stable sodium alginate network gel on the wound surface. This maintains a moist environment on the wound, conducive to wound healing and skin regeneration, and accelerates wound healing [18]. The sodium alginate network gel formed on the wound surface has good sealing properties, preventing bacteria from entering the wound. Thomas et al. [19] found that alginate can activate macrophages to resist the invasion of pathogenic microorganisms. Furthermore, alginic acid can serve as a carrier for metal ions, binding with various metal ions to form salts, such as silver, copper, and zinc, which have excellent antibacterial effects. Alginate dressings also have good hemostatic function. Zinc alginate fibers have a coagulation effect and can enhance platelet activity. Insoluble zinc alginate can be processed into functional fibers that slowly release zinc ions [20]. Due to the strong water absorption and swelling properties of alginate dressings, auxiliary fixation is needed, and they are not suitable for dry wounds or those with hard scabs. Representative products include Sorbsan, Kaltostat, and Algoderm.

## 2.2 Synthetic Biological Dressings

As biology and polymer chemistry accelerate, the shelf keeps filling with synthetic membranes spun from petro- or bio-monomers, each engineered for a specific moisture, gas or drug-delivery profile. Compared to natural materials, synthetic materials allow better control over the synthesis process, adjustment of molecular weight, and improvement of forming technology. Therefore, dressings made from synthetic materials have obvious advantages over natural biological dressings, such as ease of observation and being good drug carriers. By build method they sort into four tribes—thin films, porous foams, water-swollen hydrogels and self-adhesive hydrocolloids—each tuned to a different wound micro-climate.

### 2.2.1 Film Dressings

Films are see-through skins of polyurethane or PTFE that seal in moisture, let clinicians eyeball progress and bathe nerve endings in fluid, cutting the “air-hit” sting. Their downside is thirst: too little absorption lets exudate pool underneath, risking maceration and infection in heavily leaking wounds. They are often combined with other materials to prevent infection [7, 18]. Lee et al. [21] used electrostatic spinning technology to prepare a dressing from polyurethane, chitosan, and silver sulfadiazine, which could effectively inhibit the proliferation of bacteria such as *Pseudomonas aeruginosa* and Gram-negative bacteria, thus providing an anti-infection effect during wound healing. Films therefore suit shallow scrapes, suture lines or low-weep grazes; familiar faces are Opsite, Tegaderm and Bioocclusive.

### 2.2.2 Foam Dressings

The raw materials for foam dressings are usually polyurethane, polyvinyl alcohol, etc. These dressings have a porous structure, which is conducive to absorbing exudate. Gases like oxygen and carbon dioxide can almost completely pass through. Foam dressings are highly malleable, can serve as drug carriers, provide good protection for the wound, and create a warm, moist microenvironment conducive to wound healing. Moreover, these dressings are light and comfortable for patients. However, due to the porous structure of foam dressings, granulation tissue can easily grow into them, causing secondary damage upon removal, and they are prone to infection. These dressings lack pressure-sensitive adhesive and require auxiliary materials for fixation. The dressings are opaque, making it difficult to observe the wound healing process [22]. Foam dressings have good advantages for large wounds and highly exuding wounds, such as lower limb venous ulcers and diabetic foot. Representative products include Lyofoam, Allevyn, and Tielle [3].

### 2.2.3 Hydrogel Dressings

Hydrogel dressings are created by placing hydrophilic polymer materials like polyacrylamide and epoxy polymers on a permeable polymer liner film. These dressings can prevent wound tissue dehydration, maintain a moist wound environment, and simultaneously, when the hydrogel comes into contact with wound tissue, it can undergo repeated hydration, continuously absorbing wound exudate. Relying on collagen-degrading enzymes in the wound exudate, they degrade necrotic tissue, thereby aiding granulation tissue growth and accelerating wound healing. Additionally, hydrogels have a mild cooling effect, which can significantly reduce the incidence of inflammation and soothe patient pain. However, these dressings are prone to swelling, causing separation from the wound, lack a bacterial barrier function, can lead to maceration of the surrounding skin, and lack adhesion, requiring an outer dressing for fixation [23-24]. Currently, hydrogels are often used in combination with antibacterial drugs in clinical practice to complement each other's strengths. For example, silver ions have bacteriostatic and sterilizing effects and can create an antibacterial environment. Fan Xiaoli et al. [25] accelerated the wound healing process by combining hydrogel with silver ions. Hydrogel dressings are mainly suitable for dry, refractory wounds, pressure ulcers, and chemical injuries. Representative products include Intrasite, Span Gelgelipem, Nu-gel, and Aquaform.

#### 2.2.4 Hydrocolloid Dressings

Hydrocolloids sandwich a tacky inner gel (gelatin, pectin, carboxymethyl-cellulose) between a waterproof polyurethane lid and a thin rim of rubber/paraffin adhesive that keeps the whole patch in place [18]. Because the gel layer never bonds to raw tissue, the dressing lifts off pain-free while still sealing the defect; its thickness sets the soak-up budget. Native enzymes in the colloid liquefy slough, wake up macrophages and quietly autolyse necrosis, speeding the trip from debris to granulation [26]. The trade-off is opacity—clinicians must peel the patch to see underneath—and near-zero breathability, which can trap malodorous volatiles under the film. The colloid swells after absorbing exudate, increasing the risk of infection. Hydrocolloid dressings are suitable for chronic ulcers and bedsores. Representative products include Granuflex, Comfeel, and Tegaserb.

### 3 Functionalized Hydrogel Dressings

Once skin is breached, four overlapping acts—hemostasis, inflammation, proliferation and remodelling—must run in sequence; small defects close in 1–2 weeks, but full-thickness or large-area wounds can stall at any stage: bleeding that will not quit, inflammation that smoulders, or tissue that simply forgets to rebuild. We survey how today's engineered hydrogels tackle the key roadblocks at every phase of skin repair: instant clotting, microbe/ROS quenching, and orderly tissue rebuilding, capped by recent dressings that stay functional from sub-zero battlefields to scorching industrial burns.

#### 3.1 Rapid Hemostatic Hydrogel Dressings

Stopping the bleed is step one: lose 30 % of total blood volume in minutes and survival plummets, yet clamping flow within half an hour could avert roughly 40 % of trauma deaths. Thanks to seamless conformity, built-in tack and cell-friendly chemistry, hydrogels now front the race for fast, pressure-free bleeding control. Once smeared or sprayed, the gel grabs the defect like a second skin, staunching blood and serum while blocking bacterial entry in the same stroke.

Early hemostatic hydrogel materials had simple structures and single functions. For example, the earliest used alginate material was widely used as a hemostatic material due to its absorption capacity ten times its own volume, but it had no other effective functions for wound healing. Later, cytokines were added to collagen extracted from animals, giving it not only hemostatic function but also a certain effect on promoting wound healing. Nowadays, with in-depth research on various materials, it has been found that many raw materials can serve as carriers for certain groups in reactions due to their easily modifiable group structures.

Liang blended hyaluronic-dopamine with rGO@PDA to craft HA-DA/rGO@PDA—a black, tacky gel that clots fast, scavenges ROS, and carries current for future sensing. PDA's catechol grid donates electrons, killing microbes, quenching radicals, conducting electrons and letting torn gel re-knit without external triggers. Catechol/quinone motifs on DA and PDA couple with tissue proteins through amino–thiol Michael addition and Schiff-base links, anchoring the gel firmly to the wound bed and staunching bleeding in a mouse-liver trauma model.

In addition to improving material functions, the formation of new materials under different conditions and the improvement of material structures are also research hotspots. Hong et al. used gelatin methacrylate (GelMA) and ortho-nitrobenzyl-based photo-trigger molecule (NB)-modified hyaluronic acid (HA-NB) as raw materials to prepare Matrix Gel hydrogel with excellent mechanical properties, wet tissue adhesion performance, and rapid hemostasis. The synthesis of Matrix Gel utilizes an ultraviolet light-triggered gelation mechanism: light causes the double bonds on GelMA to self-crosslink, while the photo-generated aldehyde groups on HA-NB can further crosslink with the amino groups on GelMA, jointly constructing a double-network structure of Matrix Gel, significantly enhancing the mechanical properties of the hydrogel, and simultaneously achieving rapid sealing and long-term resistance to fluid impact. In addition, the Schiff base reaction between the photo-generated aldehyde groups and the tissue interface can give Matrix Gel good wet tissue adhesion performance, capable of resisting a burst pressure of 290 mmHg, far exceeding conventional systolic blood pressure (120 mmHg). Therefore, Matrix Gel can quickly adhere to the wound under arterial pressure and stop bleeding rapidly. For wounds with 4–5 mm damage in the pig carotid artery, Matrix Gel can completely seal the wound within 20 seconds, with no bleeding after surgery.

### 3.2 Antibacterial Hydrogel Dressings

Once bacteria colonise a wound the site can suppurate, healing stalls and, at worst, sepsis threatens life—so potent, durable antimicrobial action is now a baseline demand for any advanced dressing.

According to different antibacterial mechanisms, polysaccharide antibacterial agents represented by chitosan and its derivatives, inorganic nanoparticle antibacterial agents represented by nano-silver and nano-ZnO, and other antibacterial agents with multiple functions are systematically introduced.

#### 3.2.1 Chitosan and Its Derivative Antibacterial Hydrogel Dressings

Chitosan, also called chitin or polyglucosamine, chemical name polyglucosamine [1-4]-2-amino- $\beta$ -D glucose, is the deacetylated product of chitin, derived from plant cell walls, fungal cell walls, and arthropod exoskeletons. It is the only alkaline polysaccharide found in nature in large quantities so far, appearing as white powder or flaky solid. The antibacterial mechanisms of chitosan are: ① The amino group with positive charge in chitosan interacts electrostatically with the protein or phospholipid with negative charge on the bacterial surface, thereby destroying the bacterial surface structure; ② Chitosan penetrates the cell wall and cell membrane into the bacteria, binding to DNA to prevent bacterial DNA transcription; ③ Chitosan chelates with metal ions, preventing the uptake of trace elements and combining with nutrients necessary for bacterial growth.

With in-depth research, scientists have found that the metabolic activities and enzymatic biochemical reactions of microorganisms often occur in water. The slight solubility of chitosan in water greatly reduces its contact with microorganisms in water, thus limiting its antibacterial activity. Water-soluble chitosan derivatives can be prepared by chemical modification. After modification, the intramolecular hydrogen bonding in chitosan is inhibited, the interaction between molecular chains and water molecules is enhanced, and water solubility is improved, thereby significantly increasing the contact between chitosan and bacteria and enhancing antibacterial activity. Commonly used modification strategies include: ① Using the amino and hydroxyl groups in chitosan molecules to undergo nucleophilic reactions with haloalkanes to prepare alkylated derivatives; ② Reacting with haloalkanoic acids or glyoxylic acid to prepare carboxylated derivatives; ③ Introducing quaternary ammonium salts to obtain quaternized derivatives.

Wahid spun a chitosan/bacterial-cellulose semi-IPN, locking the two biopolymers with glutaraldehyde bridges to create a nanofibrillar mesh that stops microbes while staying transparent and flexible. The hybrid network tolerates higher temperatures than either parent polymer and clears both Gram-positive and Gram-negative panels in zone-inhibition tests. The kill rate rises or falls with the BC/chitosan mix, since higher chitosan loads pack the film with extra positive charges that puncture bacterial envelopes. When the ratio is 1:5, the inhibition rate can be as high as 88%.

Gan et al. prepared an antibacterial hydrogel with contact enhancement based on the mussel adhesion chemical mechanism. A diene-modified dopamine (MADA) tethers the gel to microbial walls, dragging germs into intimate

contact with bactericidal moieties—quaternised chitosan (QCS) and DMAEMA—so the kill step happens at point-blank range. In vivo, the same patch doubles as a regenerative scaffold and an infection shield—spurring granulation while keeping bacteria out—making it a one-step dressing for fast, sterile repair. Zhao grafted an aniline tail onto quaternised chitosan (QCSP) and blended it with benzaldehyde-tipped PEGs; the two chains click via dynamic imine bonds, yielding a self-healing, conductive and cytocompatible gel that kills microbes while relaying bio-signals. QCSP in the hydrogel has electrical activity, antibacterial activity, antioxidant activity, and hemostatic performance. The hydrogel composed of QCSP and 1.5% by volume PEGs-FA has excellent coagulation performance. Leveraging chitosan's innate repair cues plus the antioxidant and mild electrical stimuli of the polyaniline block, the gel closes full-thickness skin gaps markedly faster than either polymer alone. Huang introduced sulfonate arms onto chitosan via nucleophilic substitution (Fig. 1); the resulting SCS outperforms native chitosan chloride, slashing exopolysaccharide output and metabolic activity in *E. coli* and *S. aureus* biofilms and thus halting their build-up.

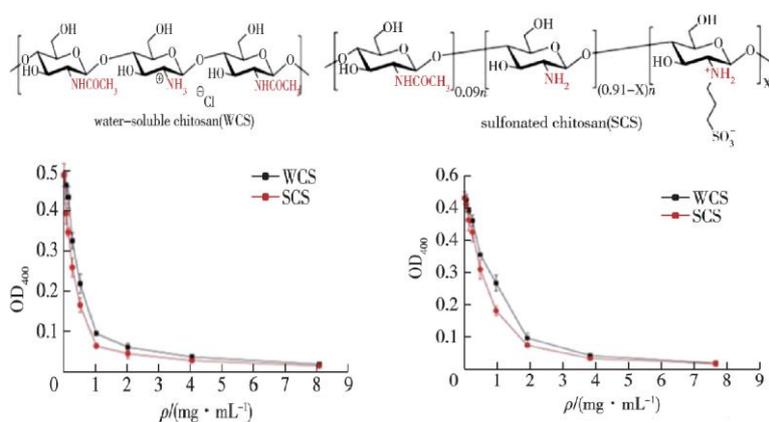


Figure 1 Sulfonated chitosan SCS prepared by nucleophilic substitution reaction [13]

### 3.2.2 Nanomaterial-Based Antibacterial Hydrogel Dressings

#### 1) Nano-Silver Hydrogel Dressings

The application of silver as an antibacterial material can be traced back to the 1960s, when scientists developed devices for purifying water systems based on the ionization of silver and copper. Subsequently, in the 1980s, Japan developed silver-loaded zeolite antibacterial agents in response to the outbreak of *E. coli*. Entering the 21st century, with continuous in-depth research on silver antibacterial, nano-silver antibacterial agents with different particle sizes have been developed and widely used in different fields.

Nano-silver's broad-spectrum punch comes from a triple hit: pitting the cell membrane, stalling DNA transcription and flooding the cytoplasm with lethal ROS. The synthesis of nano-silver hydrogels mainly includes two methods: ① In situ reduction of compounds such as  $\text{AgNO}_3$  or  $\text{C}_2\text{H}_3\text{AgO}_2$  in the hydrogel matrix to obtain nano-silver; ② Adsorption of nano-silver suspension by the hydrogel. The good combination of nano-silver and hydrogel allows the dressing to continuously release Ag after contact with the wound, thus achieving long-term antibacterial effects.

Niu et al. used in situ synthesized nano-silver and polyethylene glycol-modified methyl methacrylate as raw materials to prepare an injectable nano-silver hybrid hydrogel. This hydrogel has good anti-*Staphylococcus aureus* and *Escherichia coli* properties. Kim et al. prepared an injectable methylcellulose hydrogel containing nano- $\text{Ag}_2\text{O}$ , in which the Ag provided by the silver acetate precursor can be in situ synthesized into nano- $\text{Ag}_2\text{O}$  in the hydrogel matrix, while the remaining  $\text{CH}_3\text{COO}^-$  can reduce the gelation temperature of the hydrogel through the salting-out effect. Burn wound experiment results show that the methylcellulose hydrogel containing nano-silver has good antibacterial properties and accelerates wound healing ability. Li et al. in situ synthesized nano-silver in a hydrogel matrix cross-linked by sodium lignosulfonate and polyvinyl alcohol to prepare an antibacterial hydrogel containing nano-silver. The antibacterial effects of lignin and nano-silver

complement each other, significantly enhancing the antibacterial performance of the hydrogel. Liu co-dispersed aminated silver nanoparticles (Ag-NH<sub>2</sub> NPs) and gelatin inside carboxylated cellulose nanofibres, anchoring both phases to the anionic scaffold for a metal-laden, yet cell-friendly, antimicrobial gel. With only 0.5 mg mL<sup>-1</sup> nano-silver, the gel keeps 100 % viability of surrounding cells yet sterilises the defect, staunching bleed and self-repairing after strain; in infected full-thickness models it closes 90 % of the gap within the test window, marrying potency with cytocompatibility.

## 2) Nano-Zinc Oxide (ZnO) Hydrogel Dressings

ZnO's high surface area and surface positive charge let it dock on bacterial walls, punch holes and leak out cytoplasmic contents. The Zn<sup>2+</sup> released by nano-ZnO in water can enter the bacteria and destroy their protease structure. The reactive oxygen species generated by ultraviolet irradiation of nano-ZnO can oxidize organic matter in the bacteria. Compared with other nano-oxides, ZnO has the advantages of stable physicochemical properties, safety, non-toxicity, and good biocompatibility, thus having broad application prospects.

Namazi et al. added nano-ZnO to a swollen oxidized starch hydrogel to prepare a nanocomposite hydrogel. ZnO fillers also tune gel swelling across pH and ionic strength while keeping lethal activity against both \*S. aureus\* and \*E. coli\*. Physical entrapment is easy but caps the dose and leaks it quickly; Rakhshaei therefore grew ZnO in situ inside a chitosan-gelatin scaffold, locking nanorods uniformly throughout the matrix for a slow, sustained ion release. In-situ ZnO outperforms physically blended powder: smaller, better-anchored crystals kill faster yet leach fewer free ions, cutting cytotoxicity. Abdeen pushed the same idea into a glutaraldehyde-cured chitosan/PVA lattice, achieving comparable microbe clearance with even less ZnO load. The antibacterial performance of this scaffold is better than that of erythromycin and metronidazole, and the bacteriostatic activity of the hydrogel significantly increases with the increase of ZnO content. With in-depth research, to maximize the function of materials, many researchers have discovered the synergistic effect of nano-ZnO and other antibacterial particles. Mao et al. assembled Ag/Ag@AgCl in the hydrogel by ultraviolet photochemical reduction, and then incorporated nano-ZnO by precipitation to prepare an Ag/Ag@AgCl/ZnO composite hydrogel. Ag/Ag@AgCl can use visible light to enhance the reactive oxygen species of ZnO, thereby improving the photocatalytic and antibacterial activity of ZnO. After 20 minutes of simulated visible light irradiation, the inhibition rates of the hydrogel against *Escherichia coli* and *Staphylococcus aureus* reached 95.95% and 98.49%, respectively, and it can be used for rapid wound disinfection. In vivo experiment results show that the Ag<sup>+</sup> and Zn<sup>2+</sup> released from the composite hydrogel can cause an immune response, producing a large number of white blood cells and neutrophils. Immune cells and nanomaterials play a synergistic antibacterial role, thereby significantly promoting wound healing.

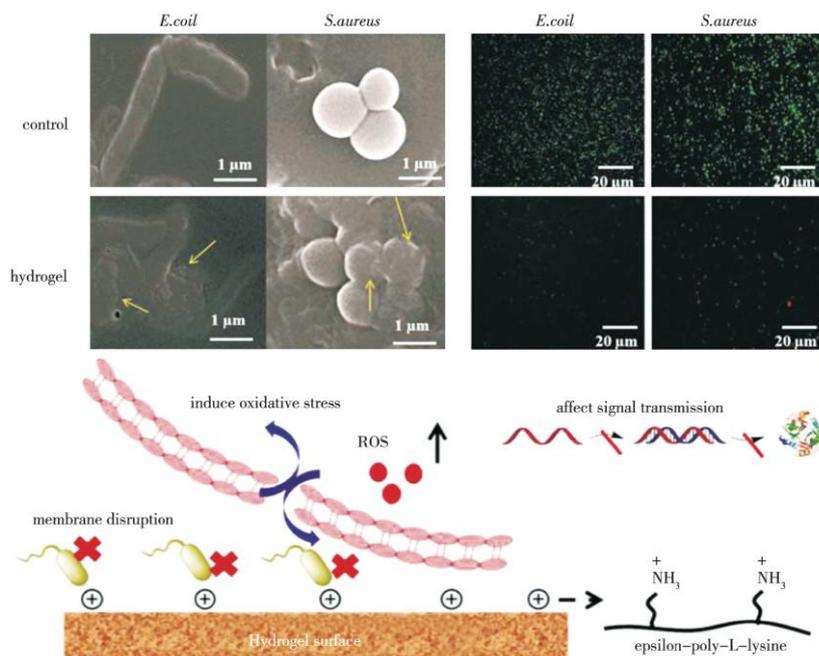
## 3) Nano-Calcium Fluoride (CaF<sub>2</sub>) Hydrogel Dressings

CaF<sub>2</sub> is a calcium-based inorganic material with good biocompatibility and antibacterial activity. F<sup>-</sup> blocks the glycolytic enzyme enolase, starving bacteria of ATP by shutting down sugar uptake and the entire glycolytic pathway. Shin precipitated nano-CaF<sub>2</sub> inside an injectable alginate, creating a shear-thinning gel that releases trace F<sup>-</sup>; colony counts drop for both \*E. coli\* and \*S. aureus\*, proving fluoride's metabolic choke-hold works inside a hydrogel depot. F<sup>-</sup> release scales with CaF<sub>2</sub> load, stays below cytotoxic thresholds yet boosts fibroblast division; in full-thickness mice wounds the same gel speeds extracellular-matrix deposition and cuts closure time. Jeong et al. uniformly embedded nano-CaF<sub>2</sub> in hyaluronic acid (HA) hydrogel by in situ precipitation to prepare a hydrogel dressing with antibacterial activity. By adjusting the concentration of CaCl<sub>2</sub> and NH<sub>4</sub>F and the precipitation time, it was found that the shorter the precipitation time, the faster the release rate of F<sup>-</sup>. The F<sup>-</sup> release rate of the sample precipitated for 10 minutes is greater than that of samples precipitated for 30 minutes and 1 hour. Colony tests show that the hydrogel has antibacterial effects against both *Escherichia coli* and *Staphylococcus aureus*. In addition, when observing the full-thickness wound healing in rats, it was found that the CaF<sub>2</sub> hydrogel is more conducive to accelerating wound healing than the pure hydrogel.

### 3.2.3 Other Antibacterial Hydrogel Dressings

Wang stitched dopamine into ε-polylysine to create a mussel-foot-silk-like protein derivative (PPD), then let horseradish peroxidase (HRP) trigger in situ cross-linking, gelling the mix within seconds under the skin. EPL's

cationic backbone acts as an in-built antibiotic, killing both Gram-negative (\*E. coli\*) and Gram-positive (\*S. aureus\*) cells without any external drug (Fig. 2). Thanks to the catechol–lysine synergy, the gel also sticks under blood, seals wounds in seconds and later orchestrates skin repair—three jobs in one injection. Xi blended the natural antibiotic aloe emodin with photothermal carbon dots; a brief NIR pulse heats the dots, flooding the wound with ROS for instant sterilisation, then sustained emodin release keeps bacteria at bay after the light goes off. In a murine \*S. aureus\* wound, the light-on/light-off tandem cut bacterial counts by 99 % while letting host cells proliferate unhindered.



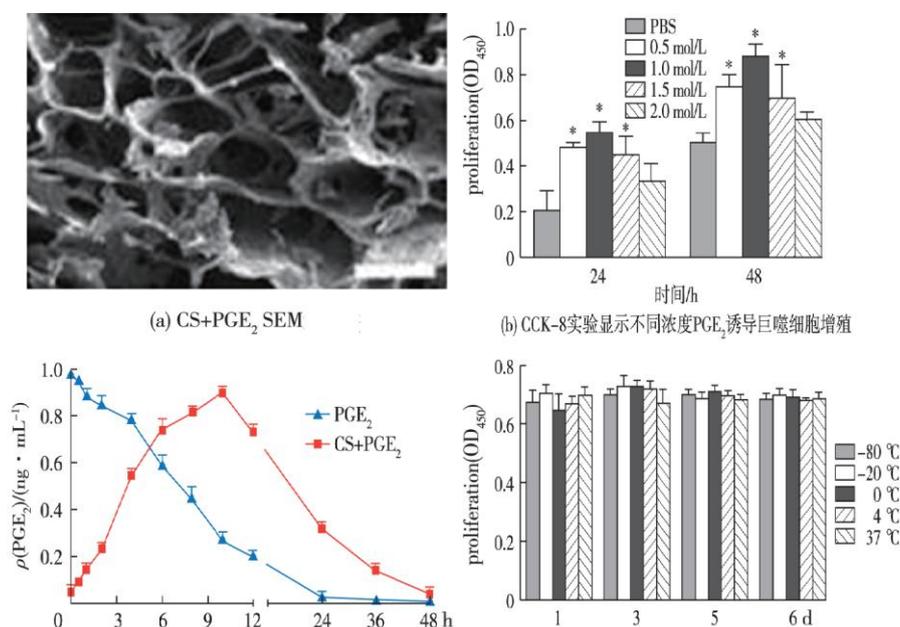
**Figure 2** An injectable hydrogel with antimicrobial properties [26]

Han free-radical-co-polymerised styrene, polycaprolactone-HEMA and guanidine-bearing methacrylate into core–shell nanogels whose cationic surface both kills planktonic bacteria and stops them sticking to the gel, giving a long-lived anti-adhesion shield. The guanidine segments punch holes through membranes while the hydrophobic polycaprolactone blocks form a low-energy surface that microbes cannot anchor to, combining kill and repellent tactics. Cotton grafted with these nanogels stays strongly water-repellent and retains 86 % kill activity against \*S. aureus\* and \*E. coli\* even after fifty laundry cycles, turning ordinary cloth into a durable, wash-proof infection barrier.

### 3.3 Anti-Inflammatory Hydrogel Dressings

In the early stage of wound healing, local wounds will experience varying degrees of tissue necrosis and vascular rupture, making them susceptible to external microbial infection. Inflammatory reactions occur within hours, manifested as congestion, serous exudation, and leukocyte migration. In the early stage of skin damage, leukocytes are mainly neutrophils. Their phagocytic ability and secreted proteases can kill local bacteria and help clean up necrotic tissue. Three days after skin injury, leukocytes are mainly macrophages. Macrophages are the main inflammatory cells and play a series of key roles in the inflammatory response: ① In the inflammatory phase, macrophages can identify and remove necrotic tissue, cell debris, and pathogens, cleaning the wound surface; ② In the transition stage from the inflammatory phase to the proliferative phase, the macrophage phenotype transforms into the M2 type. M2 cells can promote fibroblast proliferation and angiogenesis by secreting growth factors such as PDGF, EGF, TGF- $\alpha$ , TGF- $\beta$ , and IL-1, thereby promoting granulation tissue formation. Persistent bugs or any lingering foreign body switch macrophages to “angry” mode, flooding the wound with IL-1, IL-6 and TNF- $\alpha$  that can tip healing into a chronic, inflammatory stalemate. A constant cytokine storm amplifies collateral tissue damage and stalls closure; current anti-inflammatory hydrogel design therefore follows two main tracks: ① Use polypeptide substances in the hydrogel network structure to promote the

polarization of M1 macrophages to the M2 phenotype, transitioning from pro-inflammatory to anti-inflammatory, reducing inflammation while promoting tissue repair; ② Alleviate inflammatory responses by loading and sustained release of anti-inflammatory drugs.



**Figure 3** Composite CS+PEG2 hydrogel with anti-inflammatory, remodeling and tissue regeneration properties [30]

Chen et al. used laminin as a raw material to prepare a polypeptide composite hydrogel of chitosan and SIKVAV [amino acid sequence: serine-isoleucine-lysine-valine-alanine-valine]. Chen et al. used CD86 to label M1 macrophages and CD163 to label M2 macrophages. The experimental results on skin inflammation showed that chitosan modified with polypeptides indeed has significant anti-inflammatory effects.

Zhang's chitosan depot trickles PGE<sub>2</sub> for days; bioluminescence images show this slow feed nudges macrophages toward the reparative M2 state, quieting inflammation while new vessels sprout (Fig. 3). Reinke et al. [31] prepared the host macromolecule  $\beta$ -cyclodextrin chitosan (CS-CD) and the guest macromolecule dextran ibuprofen (Dex Ibu) respectively. By threading ibuprofen into  $\beta$ -cyclodextrin cavities, a supramolecular gel delivers two waves of relief—burst release for immediate pain and sustained diffusion for days-long inflammation suppression. First, wound esterases snap the  $\beta$ -CD/ibuprofen link, dumping free drug to block TNF- $\alpha$  secretion and blunt the early inflammatory spike. Second, the chitosan backbone itself kills \*E. coli\* and \*S. aureus\*, so the same gel that douses cytokines also starves the infection that would otherwise keep them coming.

### 3.4 Tissue-Regenerative Hydrogel Dressings

Regenerative hydrogels act as programmable pharmacies—clicking antibiotics, anti-inflammatories or growth factors into their mesh and dropping them exactly when and where the wound signals for help. Their protein cargo is dominated by cytokines—VEGF for vessels, FGF7 for fibroblasts, tissue factor F3 for rapid clotting—each released in sync with the healing clock. Gels grafted with cytokine cocktails or ECM peptides can also flip key molecular switches—MAPK, PI3K, integrin clusters—that accelerate every downstream repair step.

Moore spun a peptide nanofibre (MDP) carrying K<sub>2</sub>(SL)<sub>6</sub>K<sub>2</sub> repeats; once injected under rat skin it is rapidly colonised by host cells, sparks a brief, helpful inflammatory burst and floods the site with cytokines that summon vessels, nerves and fibroblasts before the gel itself vanishes and healthy tissue fills the void [32]. The MDP hydrogel, based on structurally and chemically simple peptides, provides an important route for the development of peptide-based hydrogel dressings for wound healing and shows promise in healing diabetic

ulcers. Xi et al. [33] created a nanocellulose composite hydrogel using bacterial nanocellulose and acrylic acid as raw materials and studied its effect on fibroblasts at the cellular and molecular levels. At the cellular level, fibroblasts rapidly adhered to the hydrogel, maintained a certain morphology and viability, had restricted migration, and proliferated continuously on the hydrogel matrix. Gene screening shows the gel simultaneously up-regulates eight repair drivers—IL-6, IL-10, MMP-2, cathepsin K, FGF7, GM-CSF, TGF- $\beta$ 1 and COX-2—while throttling pro-coagulant F3, tipping the molecular balance toward rapid, orderly healing.

Huang et al. [34] used carboxymethyl chitosan (CMC) and aldehyde-modified nanocellulose (DACNC) as raw materials to prepare an injectable self-healing composite hydrogel (CMC/DACNC). The abundant active cross-linking points in the hydrogel network are prone to breakage and remodeling, enabling the hydrogel to self-heal within a short time. Cell experiments confirmed the good biocompatibility of this hydrogel, indicating it can serve as an extracellular matrix to support 3D cell culture and accelerate wound healing. More importantly, the hydrogel degrades rapidly in amino acid solutions, facilitating painless removal of the wound dressing (Fig. 4).

Mao et al. utilized the dynamic coordination between PEG and mangiferin liposomes to create an injectable, anti-hypoxic, wound-healing multifunctional hydrogel (MF-Lip@PEG). By modulating the Bax/Bcl-2/caspase-3 axis, the same gel also suppresses hypoxia-driven apoptosis, rescuing cells at the wound edge from oxygen-starved death. In a random-pattern skin-flap model, the injectable MF-Lip@PEG gel cut necrosis from  $\sim 45\%$  to  $<15\%$ , proving its triple punch—damp inflammation, block infection and seed new vessels—translates directly into salvaged tissue. Park loaded chitosan microparticles with Substance P and TGF- $\beta$ 1, then suspended them in thermo-responsive Pluronic F127; once gelled, SP bursts free during early inflammation while TGF- $\beta$ 1 trickles out later, keeping each signal at the dose and moment the wound needs it. Notably, the CSMP-PF hydrogel can repair skin damage caused by local ionizing radiation. SP promotes tissue regeneration by increasing the number of myofibroblasts, promoting angiogenesis, and enhancing extracellular matrix deposition, while TGF- $\beta$ 1 accelerates wound healing by regulating cell proliferation, migration, and differentiation.

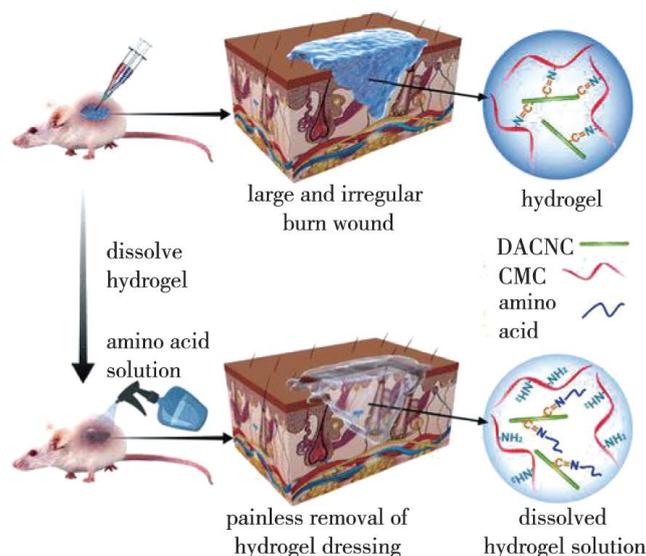
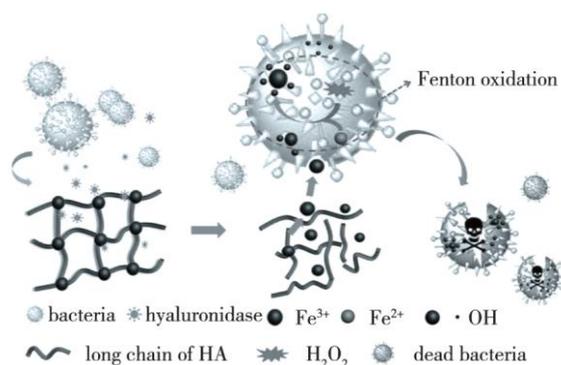


Figure 4 Injectable self-healing composite hydrogel (CMC/DACNC) [34]

### 3.5 Multifunctional Hydrogel Dressings

With ongoing research, the requirements for hydrogel dressings have increased, as different wounds may have different needs. Among them, hydrogels with both antibacterial and wound-healing promotion functions are a major focus. Therefore, this section focuses on the application of hydrogel dressings in two main aspects: Wound Treatment: Utilizing the antibacterial activity of hydrogel dressings to prevent bacterial infection, the anti-inflammatory activity to alleviate inflammation at the wound site, and the mechanical elasticity to provide protection. Wound Healing: Promoting epithelialization, collagen formation, angiogenesis, and skin regeneration.



**Figure 5** Schematic diagram of the antibacterial mechanism of HA-Fe-EDTA hydrogel [38]

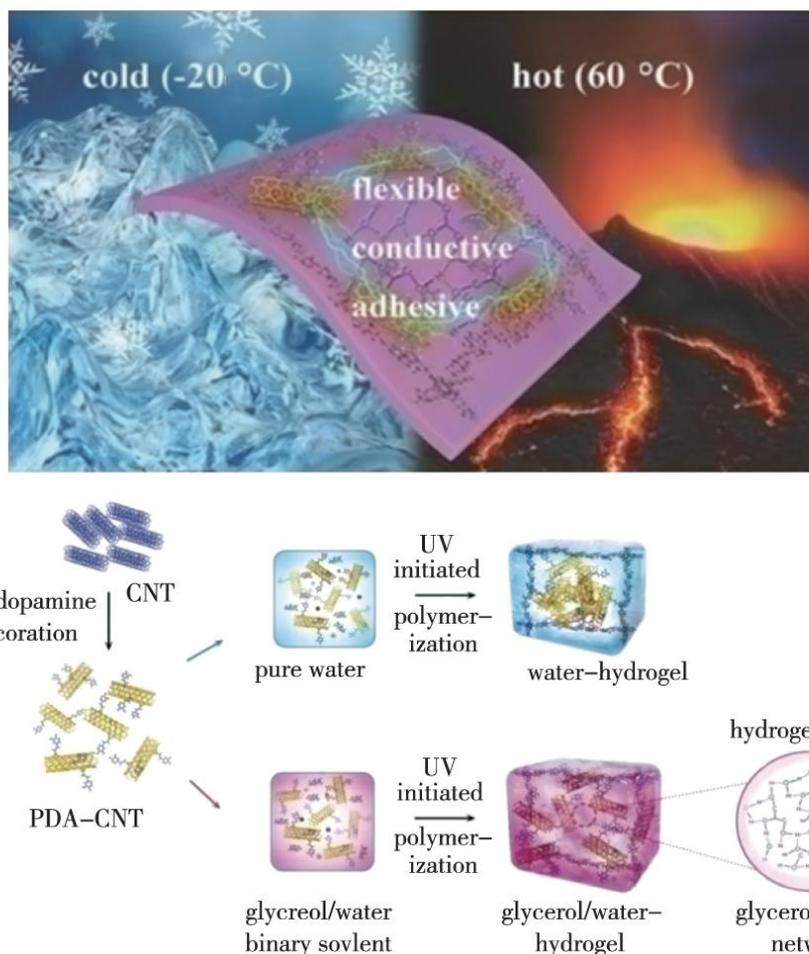
Wang photo-copolymerised N-acryloyl glycinamide with 1-vinyl-1,2,4-triazole to give PNAGA-PVZT—a single network that is antibacterial, anti-inflammatory, self-healing and thermoplastic, so it can be moulded like putty before curing yet reheat after strain. Dense, reversible hydrogen bonds knit and re-knit the chains, granting the gel repeated self-repair, re-moulding and full recyclability, while the triazole rings supply both bacterial kill and cytokine-dampening power. The hydrogel significantly inhibits the growth of *E. coli* and *S. aureus* and also markedly reduces the inflammatory response caused by subcutaneous implantation, indicating good tissue compatibility.

## 4. Advanced Functional Dressings

### 4.1 Antifreeze and Heat-Resistant Hydrogels

The practicality of hydrogel dressings is closely related to their solid-like mechanical behavior and water-like transport properties. Ordinary hydrogels, rich in hydrophilic groups and with high water absorption, freeze easily below the freezing point, becoming brittle, hard, and less conductive. At high temperatures, water molecules cannot be stably fixed in the polymer network, causing the hydrogel to dehydrate and dry out. Antifreeze and heat-resistant hydrogels can function normally under low and high temperatures, broadening their application range.

Han et al. [40] polymerized acrylamide and acrylic acid monomers in a glycerol-water mixed solution via UV polymerization to create an alcohol/water hybrid gel. Finally, polydopamine-wrapped carbon nanotubes were woven through the mesh, turning the already smart gel into a frost-proof, heat-stable, current-carrying and tissue-gluing patch (Fig. 6). As a stretchy, self-adhesive electrode it keeps reading crisp ECG traces even after a full day at  $-20\text{ }^{\circ}\text{C}$ , proving its worth for field trauma monitoring from arctic rescues to desert evacuations.



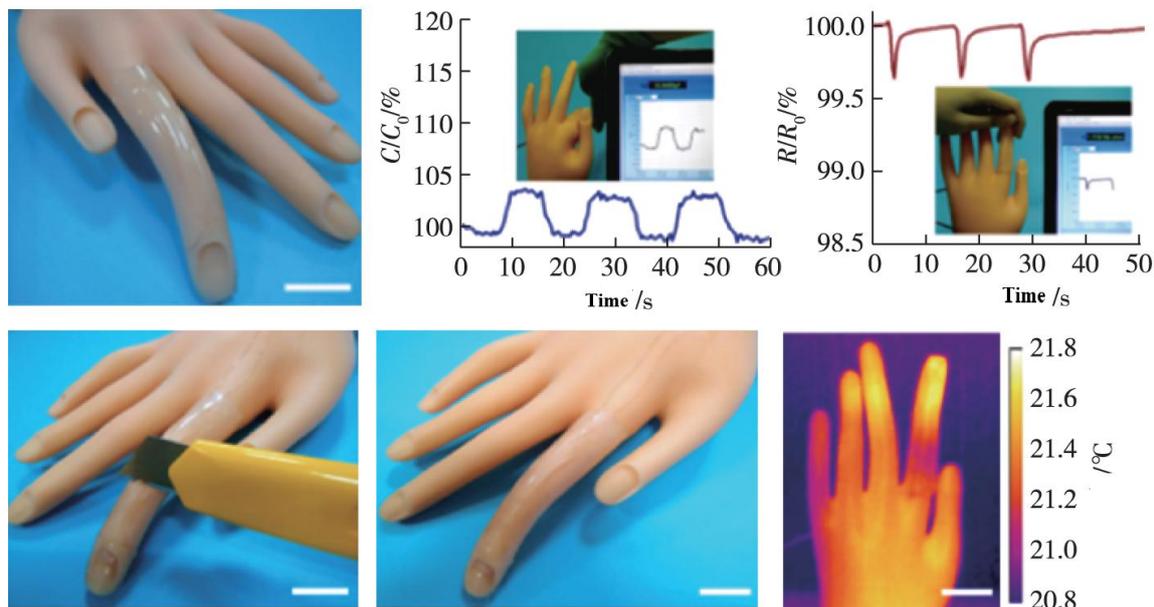
**Figure 6** Antifreeze, heat-resistant, conductive, and self-adhesive hydrogel (PDA-CNT) [40]

Morelle et al. added  $\text{CaCl}_2$  to a polyacrylamide-sodium alginate double-network hydrogel, creating a composite hydrogel with good antifreeze properties, high mechanical strength, and conductivity even at  $-57^\circ\text{C}$ . The fracture toughness of this hydrogel is higher at low temperatures than in a warm aqueous state, with toughening mechanisms including crack pinning, crack deflection, and micro-void formation. It can also be used as an ionic conductor combined with a dielectric elastomer for stretchable ionic touch sensors at low temperatures. Zhang et al. dissolved cotton linter cellulose in an inorganic salt ( $\text{ZnCl}_2/\text{CaCl}_2$ ) system and utilized the coordination between cellulose and metal ions ( $\text{Zn}^{2+}$ ,  $\text{Ca}^{2+}$ ) to prepare a cellulose hydrogel that is reversible at high temperatures and antifreeze. When the temperature exceeds  $60^\circ\text{C}$ , the sol-state hydrogel can transform into a solid state upon cooling. This thermal reversibility allows the sol to be injected into different molds to form hydrogels of various shapes. The cellulose hydrogel containing salt hydrates remains pliable without brittle fracture when knotted at room temperature ( $25^\circ\text{C}$ ) and sub-zero conditions ( $-10^\circ\text{C}$ ), demonstrating its antifreeze property and plasticity. Importantly, the resulting cellulose hydrogel maintains good ductility, flexibility, and conductivity even at temperatures as low as  $-70^\circ\text{C}$ , broadening its application as an antifreeze material.

#### 4.2 Electronic Skin (E-skin) Hydrogels

Electronic skin is a paper-thin, rubber-soft tactile sensor that can be cut, wrapped or printed like plastic film; its pixel pitch shrinks to sub-millimetre scales, letting it feel hardness, warmth, texture and weight almost as delicately as human fingertips. Laminated on the wrist or chest, the same film turns into a round-the-clock pulse, heartbeat and thermometer, streaming subtle health shifts to phones or clinics for early-warning diagnostics. Conductive hydrogels—wet, elastic and threaded with electron highways—mimic the softness and watery micro-environment of living tissue, giving e-skin the stretch, safety and signal fidelity it needs. Load the same gel

with drugs and it becomes a medicated second skin, dribbling antibiotics or anti-inflammatories exactly where strain or heat sensors detect trouble, speeding repair while it monitors.



**Figure 7** Applications of bionic skin in strain, temperature sensing, and self-healing [45]

Gan UV-cured a polyacrylamide/chitosan matrix, then used the cationic chitosan strands as a template to anchor and oxidatively grow polypyrrole (PPy) throughout the network, yielding a triple-threat gel: wire-like conductivity, leather toughness and full cytocompatibility. The PPy mesh doubles as a wired pharmacy: a small voltage swing oxidises or reduces the chains, shrinking or expanding the pores to throttle drug release on demand. While PPy oxidises it traps anionic drugs (e.g., dexamethasone phosphate) as dopant counter-ions; flip the potential negative and the backbone turns neutral, ejecting the drug in step with the applied current. Experiments on a rat full-thickness skin defect model showed that this hydrogel promotes wound healing and repair. Moreover, it can function as e-skin to monitor human motion in real-time and as a stress sensor to detect load.

Lei engineered a supramolecular polyelectrolyte hydrogel whose chains are zipped by tunable, non-covalent cross-links; the result squeezes like rubber, re-stitches when cut and can be moulded by hand at room temperature. Crystal-clear and skin-soft, the gel feels warmth, stretch and touch, acting as an all-in-one bionic dermis that feeds temperature maps, strain curves and pressure fingerprints to external circuits. Glued to a plastic prosthetic finger, the same film turns dummy digits into sensors: bending alters capacitance (strain), warming changes resistance (temperature), so the artificial finger “feels” every squeeze, twist or heat pulse just as real skin would (Fig. 7).

Zhang et al. [46], mimicking skin’s layered architecture, carried out in-situ polymerization atop a hydrophobically cross-linked conductive hydrogel, fabricating a stretchable, ultra-durable bilayer hydrogel strain sensor ideal for wearable electronics. The bilayer gel works as a sensitive strain gauge that tracks both large limb motions and faint pulses; its sticky outer coat locks to skin while insulating the current-carrying core, shielding tissue from any electrical tingle.

## 5. Summary and Outlook

Hydrogels, as a new type of medical dressing, complement and enhance the functions of existing dressing types. They combine rubber-band elasticity, air- and moisture-permeability, high fluid uptake, biocompatibility and tailorable chemistry—qualities that let them manage infected, non-healing lesions from arctic deployments to desert burn units.

This review maps how functional hydrogels shepherd a wound from insult to closure, then spotlights next-gen variants—frost-proof, heat-proof and electronic skins—that keep working when ordinary dressings fail. Current hydrogel dressings have evolved from single raw materials to multiple interacting components, their structures have progressed from single to double networks, and their functions have expanded from single to multiple purposes. However, the efficacy of current hydrogel dressings remains somewhat limited. Enhancing functional properties through improved material structure to effectively treat various wound types remains a key research focus. For instance, injectability is a significant advantage of hydrogels. Utilizing temperature-dependent sol-gel transitions allows liquid hydrogel to be injected into irregularly shaped or internal wounds, where it solidifies in situ due to body temperature, enabling localized treatment.

Future research directions should focus on "intelligentization" and "functionalization." This includes developing environmentally responsive (e.g., pH, temperature, light) "smart" hydrogels for controlled drug release and real-time monitoring. Combining hydrogel sensors with microelectronics could lead to closed-loop "sense-process-act" systems for personalized medicine. Furthermore, creating multifunctional dressings with combined abilities (e.g., antibacterial-conductive, adhesive-antibiotic releasing) for complex wounds like diabetic ulcers is a promising avenue. Embracing green chemistry principles by using sustainable materials (e.g., cellulose from waste) and designing easily degradable hydrogels will also be crucial for future development.

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