Abstract: Hydrogels have attracted extensive attention due to their excellent swellability, permeability, and biocompatibility. In recent years, the demand for multifunctional hydrogels has been on the increase; there is also an increased need to utilise hydrogels in more varied and extreme applications, such as low temperature, anoxic environment, ultraviolet damage, burns, and the marine environment. Furthermore, traditional hydrogel materials cannot meet the requirements of the application in extreme environments. Therefore, it is necessary to design and develop hydrogels that are adaptable to certain extreme conditions. This review summarises recent advances in hydrogels that meet application requirements under extreme conditions, particularly in the biomedical field and prospects for their future development.

1 Introduction

Hydrogels are polymer materials with a three-dimensional network structure formed by non-covalent or covalent bonds, such as the electrostatic interaction, hydrogen bond and covalent chemical cross-linking. The polymer network of hydrogels contains a large amount of water and can maintain the shape of a special semi-solid material [1–3]. Owing to these many excellent properties, hydrogels can be used in many fields, such as tissue engineering [4–7], drug release [8–10], and soft electronics [11–13]. However, current hydrogels applications are generally restricted under certain extreme conditions, such as polar exploration, mountain climbing, and skiing. Under these extreme environments, the hydrogels might encounter low temperatures, anoxic environment, ultraviolet (UV) exposure, and burns. For example, traditional conductive hydrogels tend to freeze below 0°C and lose their elasticity and electrical conductivity, which limits their use at low temperatures [14–16]. In addition, several studies have considered the difficulty of applying hydrogels to treat burns [17] and against UV damage effectively [18], and hydrogels that have special performance requirements in terms of fatigue resistance [19, 20] and oxidation resistance [21, 22]. In the design of hydrogels, it is also necessary to develop hydrogels that are suited to the anoxic environment to promote wound healing. Therefore, designing hydrogels with specific functions for certain extreme environments at the molecular level is of significant importance.

At present, research on hydrogels is mainly aimed at improving the mechanical properties and functionality of materials, ignoring the drawback in the practical application environment of hydrogels, especially their specific material properties under extreme conditions. In this study, the research progress in hydrogels for extreme conditions is reviewed from the aspects of preparation methods and material design, and the application in biomedicine is highlighted. It is hoped that this review will provide new research inspiration and directions for the development of hydrogels applied in extreme conditions.

2 Hydrogel application in a low-temperature environment

Stretchable conductive hydrogels are indispensable for future applications in various fields, such as stretchable sheets [23], flexible energy storage devices [24], electrodes [25], sensors [26], and wearable devices [27]. To achieve these goals, the key issue is the simultaneous introduction of mechanical strength and electrical conductivity. Conductive hydrogels have been extensively studied among researchers in various fields to date; e.g. conductive polymer hydrogels are used in flexible supercapacitors and sensors. However, conventional conductive hydrogels composed of pure water systems inevitably freeze at low temperatures and lose electrical conductivity and flexibility, which severely limits their practical application at low temperatures. The most widely used strategy to prepare hydrogels with resistance to low temperatures is to introduce organic solvent or ions to reduce the freezing point of water in the hydrogel network.

2.1 Binary (organic/water) solvent method

A binary solvent hydrogel is obtained by introducing two miscible solvents (organic and water) into the polymer network prior to gelation. Liu and co-workers [28] used a freeze-resistant binary solvent system to obtain a high-strength conductive oil-based hydrogel with frost resistance (Fig. 1). In the antifreeze conductive organic hydrogel, the binary solvent can effectively prevent oil-based hydrogels from freezing at low temperatures. Owing to its cold resistance, this conductive oil hydrogel exhibits stable flexibility and strain sensitivity even as low as −40°C. Combining freeze tolerance, conductivity, and self-healing capabilities, this new oil hydrogel is expected to motivate researchers to design flexible and wearable devices for applications at sub-zero temperatures.

Our research team prepared a freeze-resistant, heat-resistant, conductive, super-strong, self-adhesive hydrogel (Fig. 2) by replacing the single aqueous solvent in traditional hydrogels with glycerol–water binary mixed solvent [29]. Unlike traditional hydrogels, the strong hydrogen bonding between glycerol and water in the alcohol/water hybrid gel network allows water molecules to be firmly anchored in the polymer network, thereby allowing the alcohol and water to mix. The researchers also demonstrated that the hydrogel can be used as a flexible self-adhesive electrode for biosignal detection in low temperature (−20°C), high temperature (60°C), and can maintain long-term effectiveness in a normal temperature environment (greater than one month). In the field of wound dressing, the animal burn and
frostbite model proves that the hydrogel has good antifreeze and heat resistance. Such a hydrogel with antifreeze, heat resistance, and long-term stability has broad application prospects in extreme conditions.

2.2 Solvent displacement-method

Solvent displacement-method is a fast, facile and one-pot method for preparation of organohydrogels, which replaces water in the hydrogel with organic molecules through soaking water-based hydrogel into organic solvent. Zhou and co-workers [30] developed a solvent replacement method to successfully transform ductile hydrogel into a low-evaporation and anti-icing water-controllable tough organic hydrogel (Fig. 3). In this method, the tough hydrogel is subjected to simple soaking, and the moisture contained therein can be replaced by a mixed solvent such as glycerine, hexanediol, and sorbitol, to form a tough organic hydrogel. Under the influence of the mixed solvent and the polymer network structure, the icing behaviour of the solvent molecules is effectively suppressed. On the other hand, the obtained tough organic hydrogel exhibits excellent resistance because the solvent does not evaporate easily. Hydrogel freezing is not observed at \(-70°C\), good mechanical flexibility is also obtained, the gel retains its good moisturising properties in air or even under vacuum-drying conditions. In addition, the antifreeze and dry properties of the ductile organic hydrogel can be effectively regulated by the varied replacement of different solvents.

2.3 Ionogels

Ionogels can be formed by introducing an ionic liquid (IL) or ionic salt into a physically or chemically cross-linked network of polymer matrices. Ionogels are widely used in flexible energy storage devices, actuators, and sensors, due to their unique physicochemical properties such as high ionic conductivity, non-flammability, transparency, and thermal and electrochemical stability [31, 32]. Feng and co-workers [33] made IL-based click-ionogels using thiol–ene click chemistry under mild conditions (Fig. 4). The ionic interaction between poly(1-butyl-3-vinylimidazolium fluoroborate) and pyromellitic acid (BTCA) forms a sacrificial network. Thiol–ene click chemistry forms a covalent network. The ionic cross-linking networks and thiol–ene click-through networks are synthesised by a one-pot reaction. After 10,000 fatigue cycles, the click-ionogels continues to exhibit excellent mechanical properties and resilience. In addition, due to the unique properties of ILs, these click-ionogels exhibit high ionic conductivity, transparency, and non-combustibility over a wide temperature range (\(-75\) to \(340°C\)). These enticing features make the click-ionogels great potential to be a safe and stretchable conductive material.

Simply adding ionic salt is another way to prepare antifreezing hydrogels. Suo and co-workers [34] developed a new type of antifreeze hydrogel (Fig. 5). The hydrogel maintains high stretchability, toughness, and electrical conductivity at temperatures as low as \(-57°C\). The researchers reduced the liquid phase freezing point by adding an ionic compound [calcium chloride (CaCl₂)] to the flexible polyacrylamide-alginate double-network hydrogel. The freezing point of the hydrochloride is changed from 0 to \(-57°C\) by soaking it in different concentrations of CaCl₂ solution. At \(-15°C\), the gel that was not

![Fig. 1 Schematic illustration of the preparation and structural characterisation of the anti-freezing conductive organohydrogels [28]](image1)

![Fig. 2 Design idea of antifreeze, heat resistant, conductive, super strong, self-adhesive hydrogel based on glycerol–water binary solvent [29]](image2)

![Fig. 3 Illustration of the fabrication of tough organohydrogels from tough hydrogels by in situ displacement with cryoprotectants [30]](image3)
reported for the first time the mechanical properties of hydrogels at low temperatures, and revealed additional toughening mechanisms such as crack pinning, crack deflection, and micro-cavitation due to the solid–liquid phase separation at low temperatures. Finally, the researchers demonstrated new possibilities for hydrogel applications at low temperatures, including stretchable ion touch sensors operating at freezing points, and the stretchability and load capacity of tough hydrogels under freezing conditions.

3 Hydrogel application in treating burns

Burns are one of the most serious skin injuries, it causes greater physical stress than other traumas [35]. High altitude environments, as one of the typical extreme conditions, often cause UV burns. In special working environments, certain chemicals can also cause burns due to high temperature and high pressure. When tissue burns, fluid exudation in the blood vessels causes tissue oedema. Delayed closure of burn wounds increases the risk of infection and even leads to serious medical complications [36, 37]. Therefore, effective burn dressings are needed to control wound infection and promote wound healing [38].

Hydrogel materials have high water absorption capacity and good biocompatibility and can be removed automatically without damaging granulation tissue or epithelial cells [39]. Hydrogels also have a significant cooling and soothing effect on the skin and are very helpful in easing pain from wounds [40]. Therefore, hydrogels are ideal burn dressings, and it is of great significance to design and develop hydrogels that can be used to cure burn wounds.

3.1 Humidity self-regulation hydrogel as a burn dressing

Burn dressings present different challenges in the different stages of healing of the wound. There is a large amount of liquid exudate around the wound early during wound healing, and therefore the dressing is required to exhibit strong hygroscopicity to absorb exudate in the early stage of wound healing. The evaporation of water in the late stage of wound healing leads to dryness of the wound, and it is easy to damage the newly formed granulation tissue to cause secondary damage when the dressing is changed. It is, therefore, important to require the dressing to adapt to and adjust for changes in the moisture content present in the wound environment during wound healing.

Chen and co-workers [40] prepared a water-soluble hydrogel as a burn dressing. A solvent-soluble medium is prepared by dissolving sodium carboxymethylcellulose and sodium alginate in water and then adding chitosan to stabilise it by high-speed stirring. This is followed by suspension in a water-soluble matrix, using a thermal-bonding technique to obtain a self-adjusting anti-adhesion hydrogel burn dressing. The self-adjustment performance of the prepared dressings was studied. It was found that the SR-AA dressing extract demonstrated significant growth in the early growth of L-929 and human skin fibroblasts, while excessive growth in the later stage was inhibited, and the cytotoxicity rating was proved. Thus, the hydrogel demonstrates good cell compatibility. The SR-AA dressing extract has three important characteristics: self-adjusting, anti-adhesive, and healing. It has a broad prospect for deep burn wounds in the human body and is expected to provide relief to burn patients and be efficient for post-burn management.

3.2 Cell-laden hydrogel

Cell-laden hydrogels promote closure, re-epithelialisation, granulation tissue formation, and vascularisation of burn wounds. It should be admitted that heretofore pristine hydrogels are not as effective for severe burns. Cell-laden hydrogels have their advantages in severe burn applications, and their applications have the potential to aid skin grafting. Alapure et al. [41] provide a feasible solution for the treatment of burns using mesenchymal
stem cells (MSCs) combined with biological materials. They inoculated MSCs into a biodegradable mixed hydrogel, ACgel, which was synthesised from unsaturated arginine-based poly(esteramide) and CS derivatives. The MSC adhered to the surface of the ACgels. ACgels ensured the high survival rates of the MSCs within six days of culture. The hydrogel was coated on the burn surface eight days after the full thickness of the burn wound was removed, and the hydrogel performed well in the burn wound.

3.3 Bacterial cellulose-based hydrogel

Hydrogels based on bacterial cellulose are increasingly popular due to their biocompatibility. Previous studies have demonstrated that bacterial cellulose/acrylic acid (BC/AA) hydrogels promote burn wound healing. Mohamad et al. [42] extended the use of BC/AA hydrogels by adding human epidermal keratinocytes and human dermal fibroblasts to BC/AA hydrogels. The results show that BC/AA hydrogel has a significantly higher advantage in promoting healing time and effect than other hydrogels; thus, it is very suitable for use as a burn biomaterial. Therefore, BC/AA hydrogel has broad application prospects as wound dressings and cell carriers.

4 Application of special-function hydrogel in anoxic environments

Oxygen plays an important role in wound healing and there is growing evidence that tissue oxygenation levels may be an important rate-limiting factor in skin healing responses [43, 44]. The level of wound oxygenation measured by oxygen partial pressure is a key determinant of healing rates [44]. Clinical observations strongly supported by the experimental evidence indicate that wound healing is delayed under hypoxic conditions. Poor wound healing delays the re-epithelialisation of dermal fibroblasts due to insufficient oxygen levels [45]. Thus, customisable polymer treatments that accurately supply oxygen directly to wounds can circumvent low oxygen levels with the goal of accelerating the basic mechanisms of wound healing.

Asahkka et al. [46] developed a novel biocompatible hydrogel by conjugating various perfluorocarbon (PFC) chains with fluorinated methacrylamide CS (MACF) able to repeatedly take up and deliver oxygen at beneficial levels. Such new fluorinated and bio-derivatised CS materials can form injectable or mouldable photo-cross-linked hydrogels. The amount of oxygen in the hydrogel can be controlled by changing the type of PFC substitution in the hydrogel network, thereby enabling control of the volume and rate of oxygen delivery, providing a beneficial oxygen level for up to five days. Since these systems are capable of reloading oxygen multiple times, they can be used for long periods of time (as long as weeks). Fibroblasts respond well to the enhanced oxygen environment produced by MACF and can aid accelerated wound healing in anoxic environments.

5 Anti-UV hydrogel

UV rays pose a great threat to the skin and eyes, furthermore, there is a strong correlation between UV skin damage and skin cancer [47]. Therefore, the use of functional materials, such as hydrogels, to resist UV damage has received increasing attention.

Our research team proposed a design concept for the in-situ formation of conductive polymer nanofibres in a hydrogel network, which has a good anti-UV effect [48]. Hydrophilic polydopamine (PDA)-hybridised polyppyrrole (PPy) was used to form hydrophilic conductive nanocomposites. The high-conductivity composite is copolymerised with acrylamide to form nanofibres in situ in the hydrogel network; thus, a new hydrogel material with transparent and UV-blocking, conductive, and self-adhesive properties has been successfully developed.
Reactive oxygen species (ROS) play an important role in the tissue structure of Ag-Lignin NPs; the inset is high-resolution lattice electron microscopy (HRTEM) micrograph shows the core-shell structure of Ag-Lignin NPs; the inset is Ag element mapping. Generation of radicals by the redox reaction between Ag-Lignin NPs and ammonium persulfate (APS), triggering the gelation of the hydrogel under an ambient environment. Our research team has also explored antioxidant hydrogels and developed a plant-inspired catechol chemistry-based hydrogel that forms a long-lasting reduction–oxidation environment within the hydrogel network. This redox system continuously produces catechol groups, imparting long-term and reproducible adhesion to the hydrogel and good oxidation resistance. Skin repair experiments demonstrate that hydrogel has a good ability to promote wound healing and accelerate tissue regeneration.

7 Conclusions and future perspectives

In summary, we reviewed some of the advances in hydrogels that have been applied in some extreme conditions or fulfilled specific application requirements in recent years. Although these works provide some materials with certain application prospects and solutions to different extreme conditions, there are still enormous challenges in the clinical application. First of all, clinical application has higher requirements regarding the safety of materials. Thus, it is necessary to design and develop multifunctional hydrogel materials that not only meet the performance requirements of extreme applications but also satisfies the requirements of clinical material safety. Furthermore, the actual application environment of hydrogel materials is more complicated and varied; it is not only necessary to meet the requirements of a single extreme condition, but that of multiple extreme conditions. Nowadays, attention is paid to only individual extreme conditions or special performance studies, ignoring the complexity of the material application environment. Hence, it is desirable to design a smart hydrogel with multiple complex environmental adaptabilities at the molecular level. Although hydrogels that satisfy a variety of specific requirements for clinical applications are still a long-standing challenge in medical development, fortunately, scientists have made significant progress and it is expected that greater advances for clinical applications will be realised.

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