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ADVANCES IN SELF-HEALING HYDROGEL SYNTHESIS AND ITS BIOMEDICAL POTENTIAL

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ABSTRACT

Hydrogels capable of self-healing have emerged as a significant category of materials with diverse applications in biomedicine. This paper explores the latest advancements in the fusion of self-healing hydrogels, highlighting novel designs and applications. It delves into the underlying mechanisms enabling these hydrogels to repair themselves and their pivotal role in biomedical procedures. The research showcases how self-healing hydrogels can be utilized across various biomedical procedures such as wound healing, tissue engineering, and drug delivery. Researchers, engineers, and healthcare professionals seeking to leverage the full potential of self-healing hydrogels for enhancing healthcare and addressing medical challenges will find this paper a valuable resource.

KEYWORDS: Hydrogels, Self-Healing, Biomedical, Tissue Engineering.

INTRODUCTION

Polymer networks form the foundation of hydrogels, extensively employed in the realm of biomaterials. Diverging from metallic or ceramic counterparts, hydrogels offer the advantage of customization to replicate the properties of soft tissues. The versatility and innovative design approaches associated with hydrogels have invigorated the field of biomaterials science. However, their susceptibility to damage or wear during regular use poses a challenge

in biological systems. Consequently, materials scientists and bioengineers have concentrated efforts on developing hydrogels capable of self-healing at the point of damage in recent years.[1]

For millennia, people have sought suitable biomaterials to address tissue damage resulting from trauma or illness. The progress in biomaterials science has enabled the development of tissue engineering techniques and reconstructive strategies capable of generating living constructs and delivering various therapeutic agents such as cells, medications, cytokines, and polynucleotides for therapeutic, diagnostic, or theragnostic purposes. Hydrogels, a class of biomaterials, are gaining prominence for their utility as fillers and carriers for diverse medications, biomolecules, and cells. Several types of hydrogels have been effectively employed, distinguished by their structural resemblance to the native extracellular matrix in terms of swellability, porosity, and biocompatibility.[2]

The ability of living tissues to self-heal is fundamental to their resilience against repeated damage. Within biological systems, vascular networks play a crucial role in this process by releasing Factor VIII, forming reversible self-healing polymer-colloid aggregates, delivering biochemical components such as Von Willebrand factor (VWF) to the injury site, and promoting clotting through the conversion of fibrinogen to fibrin fibers. Drawing inspiration from this natural mechanism, White and colleagues have devised microcapsule-based systems that release healing agents in response to environmental stimuli at the site of damage. However, several issues need addressing before these materials can be utilized as human implants, including limitations in self-healing cycles and potential alterations to material properties due to the incorporation of fillers.[3]

SELF-HEALING MECHANISMS

The ability of hydrogels to self-heal is based on a common principle that involves a mobile phase. This phase facilitates the closure of cracks through mass transfer and the reconnection of broken links within the hydrogel matrix. The reconnection process is usually facilitated by covalent or noncovalent bonds, and it can be achieved through dynamic covalent bonds and metal coordination bonds in the case of chemical bonds. Weak sacrificial links like ionic, hydrogen, or hydrophobic bonds underpin noncovalent interactions. Recently, researchers have been able to create double-network hydrogels that are mechanically robust, elastic, and have quick self-healing properties by combining the aforementioned covalent and noncovalent bonds. In this section, we will discuss the main mechanisms that underlie the

self-healing capabilities of these hydrogels. We have divided this section into three separate subsections, with the first two dealing with self-healing mechanisms based on either noncovalent or covalent bonds. The final subsection covers the principle of operation for double-network hydrogels.[9]

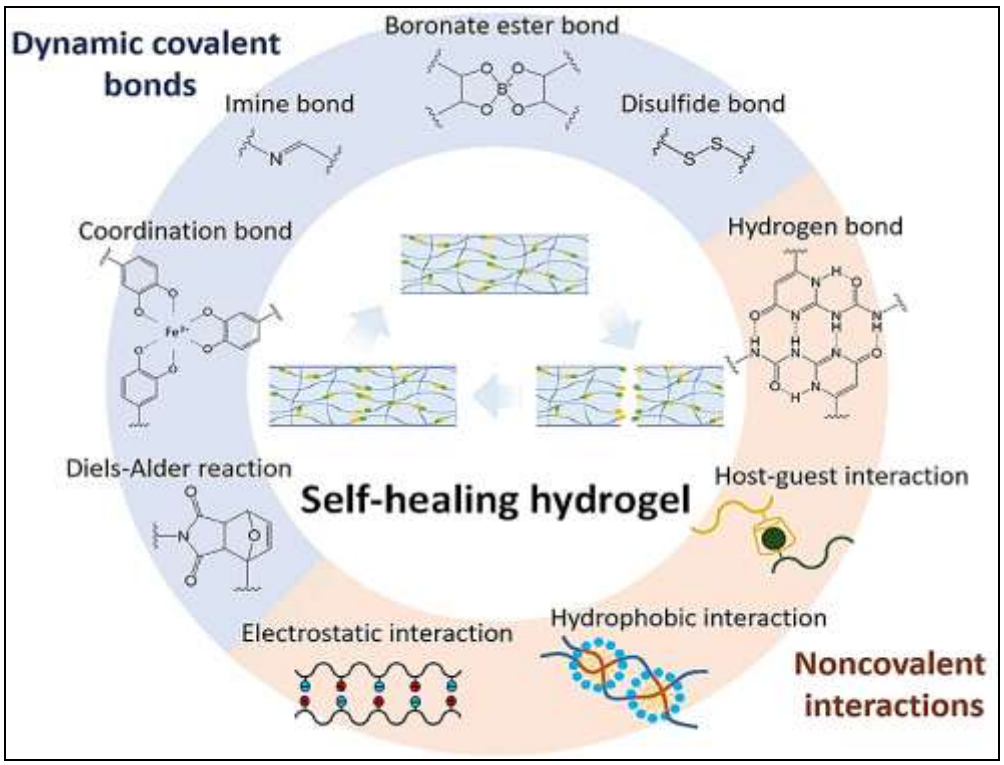

Figure 1.1: Self-healing Mechanism.[9]

Non-covalent interaction

This section discusses self-healing hydrogels resulting from noncovalent crosslinks, particularly hydrogen bonds,[1,4] host-guest interactions,[1,7,8] and hydrophobic interactions.[1,5,6,7] To create hydrogels with fast healing times and strong self-healing properties, various types of interactions are utilized. However, these interactions often result in hydrogels that are weak and inflexible. In the upcoming subsections, we will analyze the mechanical advantages and disadvantages of each interaction scheme. Additionally, we will suggest potential solutions in case any issues arise.[9]

1. Hydrogen Bonding

Crosslinked hydrogels based on hydrogen bonds are formed by reversible cross-linking of polymeric networks. In these networks, hydrogen atoms interact with highly electronegative atoms like nitrogen, oxygen, and fluorine. These hydrogels have stronger bonds and better self-healing capabilities. Hydrogels formed through hydrogen bonding are relatively less

stable than self-healing hydrogels made with ionic and covalent interactions. They developed a self-healing hydrogel containing guanosine, cytosine, and modified hyaluronic acid that doesn't require the application of healing agents.

To facilitate the reorganization of tissue and closure of wounds, researchers developed a conductive hydrogel by combining acidic poly(3,4-ethylenedioxythiophene) and poly(styrenesulfonate) with guar gum, a water-soluble galactomannan. Moreover, a self-healing polyvinyl alcohol (PVA) hydrogel that forms hydrogen bonds at the fracture site can be produced using the freeze-thawing technique, due to sufficient free hydroxyl groups in the PVA chain.[4]

2. Hydrophobic Interactions

Hydrophobic interactions play a significant role in the assembly of hydrogels. These interactions are important in various physical associations like guest-host complexes and biorecognition motifs, which have been discussed earlier. In addition, hydrophobicity can be utilized to form hydrogels through less specific interactions. This is achieved by incorporating hydrophobic domains into polymers to facilitate network assembly. The self-assembly of peptide amphiphiles largely depends on hydrophobic interactions, which have been reviewed extensively.[5,7] In aqueous situations, nonpolar molecules or hydrophobic chain segments often form groups to decrease their contact with water. Generally thixotropic and reversible, the network of these hydrophobically linked structures is robust against disturbances.[6]

3. Ionic Interactions

Hydrogels, which can form reversible electrostatic interactions between oppositely charged ions to physically cross-link, demonstrate rapid self-healing abilities. Additionally, environmental changes such as pH shifts, achieved through the deprotonation of charged components, can modify the mechanical characteristics of these hydrogels.[1] Hydrogels can repair themselves by forming coordination bonds between Fe3+ and carboxylic groups in AA and alginate molecules. This allows hydrogels to regenerate, restoring both their mechanical strength and electrical conductivity. Another way to create self-repairing hydrogels is by using ionic bonds, which enable reversible electrostatic interactions between oppositely charged components. These interactions can occur through ionic bridges connecting polymers with similar charges, influenced by ions with opposing charges, or between polymers with different charges. For example, alginate hydrogels, made from negatively charged alginate

pre-polymers and crosslinked with divalent ions like calcium, illustrate the latter scenario. Another promising method involves using electrostatic interactions between charged nanomaterials and the hydrogel matrix. Although less common, this strategy leverages the versatile properties of nanomaterials to enhance the hydrogel system with various additional characteristics.[7]

Nanomaterials can significantly enhance the toughness and durability of hydrogels due to their well-established ability to dissipate energy within these materials. Although ionically bonded hydrogels can be easily prepared through simple mixing procedures, they suffer from brittleness and lack of elasticity as major drawbacks. However, these limitations can be overcome by combining ionically crosslinked hydrogels with a covalently cross-linkable polymer, resulting in a double-network hydrogel composed of flexible and interpenetrating polymeric networks. Moreover, the noncovalent cross-linking interaction's electrostatic force imparts self-healing properties to the hydrogels. During a specific period, a hydrogel that has been artificially divided into two pieces through electrostatic attraction can automatically repair itself, a process referred to as "zwitterionic fusion".[7]

4. Host–guest interactions

Supramolecular materials with host-guest relationships have a unique advantage in biomaterials applications due to their selective, complementary interactions. Some guest groups, such as adantane, ferrocene, azobenzene, cholic acid, and cholesterol, are currently in use in biomedical research and show promise. The hydrogel's redox-responsive characteristics are due to ferrocene, and the step strain rheology measurement test demonstrated its self-healing ability. Even after the hydrogel's polymeric network distorted at 200% strain, it was able to recover up to 90% of its initial G' value, likely due to the host-guest affinity between βCD and Fc. B-cyclodextrin-based hydrogels also have good self-healing qualities, and adamantine (Ad), a molecule that resembles Fc and forms an inclusion complex with βCD, demonstrated quick self-healing and shear-thinning characteristics in a supramolecular hyaluronic acid grafted with βCD and Ad hydrogel. This hydrogel has the potential to be used in 3D printing as support matrices and inks due to its rapid structural restoration properties. To create a hydrogel with dual crosslinking properties, CD-MeHA and Ad-MeHA, CD-Ad was used to synthesize it. This hydrogel exhibits the ability to form a host-guest complex, resulting in accelerated self-healing within approximately one second. Furthermore, the layer-by-layer assembly of CD-MeHA and Ad-MeHA hydrogels

demonstrated a shear-thinning ability, making them suitable for ink applications in the creation of layer-by-layer hydrogels. To boost the resilience and stability of the cationic CD oligomer for wound treatment, it underwent enhancement by crosslinking with glycidyl trimethylammonium chloride and allyl glycidyl ether, utilizing epichlorohydrin. The hydrophobic cyclodextrin and aromatic components within gelatin interacted, resulting in the formation of a shear-thinning hydrogel. This gel, crafted from cyclodextrin-modified alginate and methacrylated gelatin, exhibits considerable promise for tissue engineering applications.[12, 13]

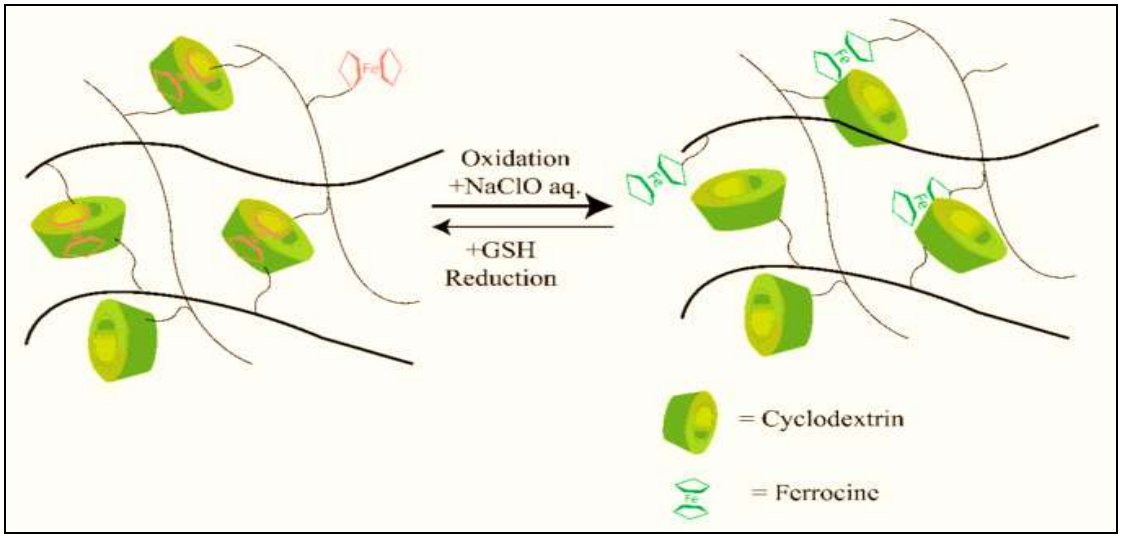

Figure 1.2: Illustration of the mechanism of host-guest interaction-based redox-active SHH.[3]

Covalent Interactions

In this section, we'll delve into the chemical composition of self-repairing hydrogels, highlighting the creation of dynamic covalent bonds through various reactions such as Diels-Alder, boronate ester, imine, and disulfide reactions. These covalent bonding methods, along with the noncovalent self-repairing mechanisms mentioned earlier, are pivotal in the progression of self-repairing hydrogels.[9]

1. Dynamic covalent bond

Unlike traditional covalent bonds, dynamic covalent bonds possess a unique capability to reconnect spontaneously without external stimuli. This exceptional trait distinguishes them, granting them an extraordinary capacity. Consequently, dynamic covalent bonds produce a robust self-repair mechanism that functions independently, blending the reversibility of non-covalent interactions with the stability of covalent bonds. These dynamic bonds form based

on the fundamental principle that various reactions within the same process attain an equilibrium state. Under specific conditions, one outcome may emerge as more stable, taking precedence over others. Nonetheless, it's crucial to acknowledge that these reactions remain highly dynamic, retaining the ability to revert to alternative outcomes and restore the original compounds.[9]

Dynamic covalent bonds are highly prized in the realm of chemistry for their rarity compared to traditional covalent reactions. In recent years, dynamic covalent crosslinks have been harnessed to produce a variety of self-healing hydrogels, with imine bonds being particularly prevalent. Consequently, our initial emphasis will be on exploring the chemistry of these bonds and their potential role in facilitating self-healing processes. Unlike conventional chemical gels, which feature irreversible covalent bonds and tend to be too brittle for biomedical applications due to susceptibility to fatigue, chemical self-healing hydrogels leverage reversible dynamic covalent chemistry. This encompasses various bond types such as acryl hydrazone bonds, disulfide bonds, imine bonds, Diels-Alder (DA) reactions, and phenylboronate complexations. In comparison to physical gels, self-healing hydrogels formed via dynamic covalent bonds typically exhibit superior mechanical properties. The synthesis of self-healing hydrogels often relies on dynamic covalent chemistry, encompassing processes like imine formation, boronate ester complexation, catechol-iron coordination, Diels-Alder reactions, and disulfide exchange. While dynamic covalent bonds exhibit a slower dynamic equilibrium compared to non-covalent interactions, they tend to be stronger.[10]

2. Chelation

Chelation is defined as the formation of multiple coordinate bonds between one positively charged transition metal ion and ligands, which are organic molecules.[14] Notably, the ligands surround the transition metal ion to produce incredibly intricate lattice structures. Every ligand can contribute electrons to the metal ion; usually, the metal receives two or more electrons from each ligand. As opposed to the usual situation in standard covalent bonds, where one electron is involved in each atom, the bonding is effectively a covalent bond involving two electrons from the same atom. However, the binding energy of these metal complexes is usually stronger than that of covalent bonds because of their lattice structure and the large number of donor atoms they contain.[16, 15] However, chelation differs from covalent bonds in that it can exhibit high reversibility, elasticity, and adhesivity simultaneously. Chelation can therefore produce materials that are extremely elastic,

adhesive, and self-healing. The sticky feet of mussels, which have recently been connected to chelation between Fe+3 and catechol ligands, are a prime example of this in nature.[17] Catechol can bind Fe+3 with a strength of up to 33 kcal mol−1, and it can form reversible bonds with titanium interfaces at a bond strength of up to 800 pN, which is nearly 40% stronger than the bond between silicon and carbon.[18] This provides insight into some of the amazing properties of chelation complexes and explains why they have become a crucial part of numerous hydrogels that can heal themselves.[20, 19]

SELF-HEALING PROCESS

As was previously noted, some materials are capable of self-healing in the absence of external stimuli, while others need external stimuli such as pressure, pH, light, and temperature to complete the process.[21,22] Therefore, based on whether the self-healing process has happened spontaneously, we divide the self-healing materials into nonautonomic and autonomic groups.[6]

Nonautonomic self-healing

Because the environments in which non-self-healing materials form three-dimensional networks differ from typical room temperature and atmospheric conditions, they cannot repair cracks or other damage alone. These materials are usually in the form of certain polymers that lack active groups that spontaneously form covalent bonds or induce non-covalent interactions. Therefore, in order for materials to acquire the additional energy necessary to reveal close groups and the ability to heal themselves, external stimuli are necessary during the healing process. A common example is pH-responsive hydrogels. According to the results, the hydrogel did not self-heal at pH 7, but was able to recover its original intact shape under both alkaline (pH 9) and acidic (pH 3 and 6) conditions (Figure 1). 5a). G1 (3-branched polyethylene oxide) and G2 (dithiodipropionic acid hydrazide) were used in the creation of the gel, and G3 (hexanedipropionic hydrazide) containing amino groups only at the end of the chain was prepared for comparison. The hydrogel, known as HG1G2, contained acrihydrazone and disulfide bonds, which allowed damage to be repaired in both acidic and alkaline environments through disulfide exchange and acylhydrazone bond reconstruction. Although neither underwent a neutral rearrangement, both bonds locked kinetically based on chemical bond dynamics. However, the acylhydrazone exchange reaction was facilitated by the addition of catalytic aniline during the preparation, leading to

the observation of self-healing behavior. This indicates that the hydrogel at pH 7 was able to self-heal after the activation of the catalytic aniline.[2,3,6]

Autonomic self-healing

Materials with autonomous self-healing properties have the ability to repair themselves without external stimuli or healing agents. This self-healing behavior is often observed in specific supramolecular hydrogels, such as supramolecular PVA hydrogels. There are many hydrogen bonds between the available hydroxyl groups of the PVA chains, which allows the hydrogel to be maintained due to its covalent balance, allowing the PVA hydrogels to repair themselves. In particular, a recent study demonstrated the autonomous self-healing behavior of PVA/GO hydrogel even after freezing and thawing without the need for further manipulations. This finding highlighted the potential of hydrogen bond reconstruction as a strong non-covalent interaction under mild conditions. In addition, the hydrogel had many reversible ester bonds between PVA chains and GO in addition to hydrogen bonds that bind PVA molecules together, especially under acidic conditions. As seen in Fig. 5b, a self-healing property was observed when the two sliced samples were reconnected to the original sample without additional triggers. However, certain hydrogels have autonomous self-healing properties only under certain conditions. As previously mentioned, the hydrogel of acryloyl-6-aminocaproic acid (A6ACA) was hydrogen-bonded cross-linked and showed self-healing properties only at low pH levels (pH < 3) because the carboxyl groups at the end of the chains could only. completely protonate in acidic medium. The autonomous self-healing ability of a material depends mainly on its ability to exhibit cross-linking groups, whether chemical or physical, without external stimulation.[6]

BIOMEDICAL APPLICATIONS OF SELF-HEALING HYDROGELS

Self-healing hydrogels are becoming increasingly popular in the biomedical field. For example, self-healing hydrogels containing biomacromolecules (liposomes, peptides, nucleic acids and polysaccharides) have shown encouraging applications in drug delivery, tissue engineering and cell culture.[1–5, 23]

1. Drug Delivery

One potential application of self-healing hydrogels is their use as delivery systems that can be achieved through host-guest interactions. A group of researchers, including Burdick and colleagues, successfully developed shear-thin and self-healing hydrogels using supramolecular self-assembly facilitated by Ad or CD-edited hyaluronic acid (HA) guest-host

interactions. To allow proteases to degrade the assembly at a later stage, Ad was attached to HA via a cleavable peptide bond. When b-CD and Ad peptide-modified HA were mixed, a supramolecular hydrogel was formed with shear thinning and almost instantaneous self-healing properties. After subcutaneous injection, the hydrogels degraded when proteases, especially MMP-2 and collagenase, hydrolyzed the peptide. In addition, by adjusting the amino acid residues of peptides, it is possible to further modify the degradation kinetics of hydrogels. The simple material formation, ease of injection and bioreactive material degradation of this material system offer unique opportunities for therapeutic delivery (eg growth factors, cells). Injectable externally assembled polyethylene imine hydrogels have also been used as an siRNA delivery method. Feng and colleagues created a multifunctional and bioadhesive polycaprolactone-b-CD (PCL-CD) polymer to deliver hydrophilic and hydrophobic drug molecules locally and continuously. PCL-CD polymer can form a supramolecular hydrogel partly through host-guest interactions with PEG linker molecules Ad-PEG-Ad and b-CD-grafted hyaluronic acid. Delivery of chondrogenic agents (transforming growth factor b1 and ketogenic) by PCL-CD polymerases facilitates chondrogenic differentiation of hydrogel-encapsulated human mesenchymal stem cells (hMSCs).[23]

A self-healing hydrogel based on host-guest interactions between β-cyclodextrin-modified PEI and adamantane-modified PEG was designed for local siRNA release. The modified polymers are combined with siRNA to create polyplexes that can increase cell viability and transfection efficiency. A GFP-expressing rat was intramyocardially injected with siRNA-encapsulated hydrogel, which increased Cy5.5 siRNA uptake and maintained GFP silencing for 1 week. Xing et al. reported an injectable self-healing collagen-gold hybrid hydrogel with tunable mechanical properties. The hydrogel was created using non-covalent interactions between collagen and then biomineralized gold nanoparticles and electrostatic interactions between positively charged collagen chains and negatively charged tetrachloroaurate ([AuCl4]−) ions. The hydrogel was designed for local delivery and gradual release of a light-sensitive drug, which led to a significant increase in the efficiency of combined photothermal and photodynamic therapy in an in vivo antitumor assay using a subcutaneous mouse model. In vivo intratumor therapy was made possible by the development of self-healing hydrogels based on glycol-chitosan and DFPEG (GC-DP), which enabled the sustained release of an antitumor drug injected into the diseased area using the GC-DP hydrogel. In addition, the ionic GC-DP hydrogel was found to be sensitized to microwaves, which facilitated high-

temperature hyperthermia for tumor ablation. A multi-tumor system was created by combining doxorubicin/docetaxel-loaded poly(lactic-co-glycolic acid) (PLGA) nanoparticles and iron oxide with GC-DP hydrogel under chemotherapy and magnetic hyperthermia. The in vivo antitumor efficacy of the system was found to be higher when exposed to an alternating field compared to the hydrogel containing PLGA nanoparticles loaded with doxorubicin and docetaxel.[9]

2. Tissue engineering

Tissue engineering is a widely accepted treatment for patients with severe trauma and non-regenerative tissues or organs. Tissue engineering was created to repair damaged tissue, as organ transplantation is a limited option, and xenografts carry the risk of immune rejection. As a newly developed type of scaffold materials, injectable self-healing hydrogels have been investigated to repair cartilage tissue, nervous systems, and skull bones. The self-healing property of the gel allows it to maintain some mechanical strength for tissue growth upon injection and in situ gelation.[9]

Gel materials intended for use as matrices in wound repair must be nontoxic, biodegradable, and controlled by drugs, growth factors, and proteins. They should also be chemically and physically similar to the microenvironment surrounding the damaged tissue. Due to the reversible sol-gel transition property, injectable self-healing hydrogels can repair irregular lesions more effectively than traditional scaffold materials. A robust hydrogel called dextran-graft-Ureido-pyrimidinone (DEX-UPy) has been shown to be a suitable scaffolding material for cartilage-bone repair.[9] The hydrogel was used to encapsulate bone morphogenetic protein 2 (BMP-2)-expressing chondrocytes and bone marrow stem cells (BMSCs). Both chondrocytes and BMSC/BMP-2 can stimulate bone and cartilage regeneration. After loading the syringe, the gel containing cells and BMSCs/BMP-2 was injected into the syringe. The liquid gel was quickly adjusted after injection and then integrated due to its internal shear thinning, simulating the physiological condition of cartilage growth in bone. Hydrogel complex was administered subcutaneously to a nude mouse; gels containing only chondrocytes or BMSC/BMP-2 were used as controls. The results of the quantitative analysis showed that cartilage consumed more space than bone, which was consistent with the results of another study. Therefore, this injectable self-healing DEX-UPy hydrogel should be a good choice for cartilage and bone tissue repair. When used as a temporary model, the scaffold gel must degrade in the body at a rate corresponding to tissue regeneration. DEX-Upy gel can be

ingested by physical contact but cannot be chemically degraded in vivo. The degradation rate of DEX-Upy gel correlates with the growth of different tissue types, according to the results. In addition, controlled release of growth factors and encapsulated drugs is possible. In summary, this scaffold contained three important components of tissue engineering: growth factors, cells and bioactive material. The special self-healing and injectable properties of the scaffold gel are important properties, as they allow long-term growth of this tissue, correcting mechanical wear and extending service life.[1–9, 23]

3. 3D Printing

Such complex multidimensional structures can be created using additive manufacturing techniques such as 3D printing, computer-aided design, and hardware that can store materials, including bioprinted cells. Printed materials have a big impact on the limitations of 3D printing. Hydrogel inks are particularly useful in biomedical applications, where they can be used to create structures that can be used to replace, repair or model tissues and mimic or reproduce properties of the cellular environment. Burdick and colleagues report the use of supramolecular hydrogels in multi-material and high-resolution 3D printing of structures. The ink can be continuously and directly written into the structures as support gels during the extrusion process three-dimensionally through host-guest interactions. Hydrogels used in host-guest crosslinking processes use HA modification. It was chosen because it is compatible with living organisms and is chemically modifiable. To make the printing platform more flexible, we added inks that can still be chemically cross-linked, so hydrogels do not need to be stabilized.[23] 3D printing can create three-dimensional tissue-like structures composed of bioplastic and cells for tissue engineering applications in a single manufacturing process. 3D bioplastics are typically cell-based hydrogels and are called bioinks because they can reproduce properties in a cellular environment. 3D bioprinting, which allows materials to be printed at any point in 3D space with high resolution, multiple length scales, etc., is not yet widely available. Burdick and colleagues recently published a series of works on directly 3D bioprinted shear-thin hydrogels (biopaints) to support hydrogels (support gels) constructed from supramolecular assembly using the host-host complex Adamantine (Ad), β-cyclodextrin and HU (HA).) has changed. These hydrogels recovered rapidly due to non-molecular and reversible bonds. These bonds allow both the "ink" and the "support gel" to degrade under physical stimulation (eg, shear stress), but still allow the material to be placed in any position in 3D space (on the support gel) after that 3D. printing method. used to engineer mesenchymal stem cells (MSCs) into a support gel 3T3 fibroblasts (3T3).[1]

4. Interfacial adhesion

Dynamic adhesion of wet and soft materials such as biological tissues is an important but very difficult subject. In the clinic, covalent bond-based adhesives (cyanoacrylate) and PEG-based adhesives (DURASEAL, Confluent Surgical) for wound repair and wound dressings have limited tolerance to local tissue contraction, movement, or body fluid flow. Thus, a hard tissue interface adhesive made from ultramolecular building blocks is highly desirable. Scherman and co-workers used a highly branched PRx with a CB[n] chain to form dynamically linked hydrogels through CB[n]-mediated molecular recognition. Sophisticated placement (or selectivity) of the second guest moiety effectively adds flexibility and versatility to these systems, allowing adhesion to be controlled by photoexcitation with azo-specific materials and interfaces when needed. These superpolymer adhesives have the added benefit of being controllable in room temperature and soft water conditions, allowing the adhesive to self-heal and cure without additional hardeners. They also investigated the use of superhydrogel networks based on CB[8] for dynamic bonding of a variety of porous substrates, including wood, bone, titanium, and glass. The development of this macroscopic, dynamic host-host molecular recognition adhesion is an innovative way to create the next generation of tissue adhesives and wound dressings.[23]

CHALLENGES AND FUTURE OUTLOOK

Self-healing hydrogels face several challenges, including biocompatibility, mechanical properties, controlled release, scalability, and long-term stability. However, these hydrogels have great potential in many fields such as 3D bioprinting, wound healing, drug delivery, tissue engineering and disease monitoring. Biocompatibility ensures a minimal negative reaction, while the mechanical properties of the hydrogels balance their self-healing capacity. Precise gel design is required to achieve controlled release. In addition, scalability is very important for cost-effective production. In addition, hydrogels can be used in biosensors for real-time disease monitoring and 3D bioprinting of tissue architectures.

CONCLUSION

Self-healing hydrogels are widely used in biomedical applications with great potential in medicine and healthcare. These hydrogels have shown promise in wound healing, regenerative medicine, drug delivery, and tissue engineering. They are an important tool in the development of new treatments and medical devices because they can repair themselves, mimic the extracellular matrix found in nature and provide a supportive environment for

cells. Although research is still ongoing, it seems that self-healing hydrogels have a bright future for changing the way we treat various biomedical problems.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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