

Review Article on Biomedical Lubricant Hydrogels as Cartilage Substitutes

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Abstract

This article underscores the increasing popularity of hydrogel lubricants in the biomedical domain and presents a comprehensive exploration of their potential as substitutes for cartilage. This understanding forms the foundation for the development of hydrogel-based lubricants that are designed to emulate these natural functionalities. Providing detailed insights, this article navigates through cutting-edge bio-inspired architecture techniques tailored to create hydrogels for cartilage. The emphasis is on achieving superior strength through diverse network architectures, substantiated by case studies and experimental results. To address tribological properties, novel surface modification techniques have been introduced to augment the strength of hydrogel lubricants, thereby enhancing their performance in biomedical applications. Practical applications of synthetic joint materials and natural bone tissues are discussed, offering a tangible perspective, further detailing the application of hydrogels to surfaces, and exploring methods for their incorporation into synthetic joint materials or natural bone tissues. A comprehensive overview of the techniques and considerations is presented, focusing on the effective applications across various biomedical settings. Reviewing the current challenges from diverse viewpoints, this article outlines potential research directions for hydrogel lubricants inspired by cartilage. Insightful guidance is provided to guide future studies on the development of novel materials for biomechanics and technology. In conclusion, this study emphasizes the pivotal role of hydrogel lubricants in biomedical applications. It underscores the ongoing need for exploration and innovation, drawing inspiration from the remarkable properties of natural articular cartilage to propel advancements in this evolving field. For instance, during the mixing or gelation process of hydrogel precursors, fluid flow can influence factors such as the distribution of crosslinking agents, polymerization kinetics, and overall homogeneity of the hydrogel structure. Achieving a controlled and uniform structure within the hydrogel is crucial for optimizing its mechanical properties, including its strength. In summary, the Reynolds number may be more relevant in the processing steps affecting hydrogel formation rather than directly analyzing the internal structure of the hydrogel itself. Techniques such as microscopy and spectroscopy are often employed for detailed structural analysis of hydrogels. Fluid dynamics plays a role in the analysis of the hydrogel structure by influencing the processing conditions during hydrogel formation. Fluid dynamics can impact the structural analysis of hydrogels in several ways.

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INTRODUCTION

Articular cartilage joints possess properties such as wear resistance and super lubricity [1]. Joints experience low friction coefficients because of these articular cartilage properties despite most of the load on the human body [1, 2]. These low friction coefficients occur owing to the specific structure and chemical composition of articular

cartilage [3–5]. Unlike most tissues, the articular cartilage structure is 2–4 mm thick. Analysis of whether the artificial cartilage of a hydrogel can be considered as a solid lubricant in tribology can reduce friction between surfaces without the need for liquid or semi-solid lubricants. These materials are typically in the solid state and can be directly applied to the surfaces of artificial joints. The function of solid lubricants and hydrogels is to form a protective layer on the surface, reduce direct metal-to-metal contact in artificial joints, and improve the efficiency of mechanical systems in artificial joints. Hydrogen is a thin film composed of a single solid or a combination of solids introduced between two rubbing surfaces of artificial joints to modify the friction and wear. Bounded solid lubricants are classified as solid lubricants (SLs). Tribology refers to solid lubricants that are intentionally herded or bound to the material surfaces. They are intended to lubricate that this pounding can occur through various mechanisms, and the goal is to create a stable and durable lubricating layer with the help of hydrogen to reduce the friction between the interacting surfaces.

Owing to aging, cartilage may be damaged [6–9]. Damaged articular cartilage cannot be repaired owing to the absence of blood vessels in the cartilage. Damaged articular cartilage can be repaired by transplantation [10, 11], joint fusion [12], and chondrocyte transplantation [13, 14]. The major drawback of all transplantation treatments is that they do not meet the minimum mechanical properties, which includes problems such as donor site lesions [15, 16]. This can be resolved by a process called total joint replacement surgery, which includes biomaterials and lubricants that together provide better mechanical properties such as load-bearing capacity and lubricant properties. These materials adhere to the surfaces, providing a protective layer that minimizes direct metal-to-metal contact in artificial joints to improve the mechanical efficiency of artificial cartilage using hydrogels as biolubricants.

Significant efforts have been made to improve the quality of the biomaterials used in artificial joints. [17–20]. UHMWPE and Ti6Al4V are artificial biomaterials that can be used to create artificial joints. The wear debris particles produced under natural lubrication differ [21]. This results in a rise in temperature, which causes the water content of the lubricant to evaporate [22–24]. Osteolysis can be induced by high fluid pressure (19629), which is proportional to the friction force, and therefore increases the friction force.

The cartilage in joints is composed of collagen fibers with multiple orientations [25, 26]. Viscoelastic collagen fibers and proteoglycans form a solid phase, whereas synovial fluid creates a fluid phase. Cartilage exhibits exceptional lubrication qualities owing to its soft and wet compositional structure. Hydrogels contain a large amount of water, which makes them delicate substances with interconnected three-dimensional structures. Hydrogels have been shown to have numerous benefits such as hydrophilicity, biocompatibility, and tunable physicochemical properties [27–30]. However, most hydrogels are mechanically weak and require reinforcement to improve their load-bearing capacities. The results of this hydrogel for patients with tissue injuries can be improved by developing strong biocompatible hydrogels with suitable structures [31–36]. After briefly addressing parts of the articular cartilage, various lubrication mechanisms for the joints were examined. The design principles and fabrication methods used to obtain improved tribological properties are briefly explained. Strategies for attaching hydrogels to artificial joint components and bone tissues were also discussed. Finally, the difficulties and potential outcomes of using hydrogels in clinical applications were discussed. It is important to know that the effectiveness of bounded solid lubricant hydrogels depends on factors such as the application method, which subtracts the material, and proper surface preparation and application techniques, which are critical for achieving optimal performance. This can be achieved by plasma coating, which is a relatively new commercially available sterilization method that has only recently been applied to UHMWPE used in total joint replacements.

EFFECT OF HYDROGEL UNDER PROTEOGLYCANS

Natural articular cartilage is mainly consisting of chondrocytes, extracellular matrix, proteoglycans, and water [37, 38]. Proteoglycans are large molecules composed of a core protein and long chains of

carbohydrates called glycosaminoglycans (GAGs), which are crucial components of the extracellular matrix in various connective tissues such as cartilage, tendons, and skin. The core protein of a proteoglycan is attached to GAG chains, which are composed of repeating disaccharide units that give proteoglycans their unique structure and properties. Negatively charged GAGs attract water molecules, contributing to the gel-like consistency of the extracellular matrix and providing tissues with resilience, lubrication, and the ability to withstand compressive forces. Proteoglycan hydrogels can be used to create biomaterials for various biomedical applications. Hydrogels are water-absorbing polymers that mimic the properties of natural tissue. Proteoglycans are often incorporated into hydrogel formulations to enhance the biomimetic nature of the material. The hydrophilic nature of proteoglycans, with their glycosaminoglycan (GAG) chains attracting water, complements the water-retaining properties of hydrogels. This combination creates a hydrated environment conducive to cell growth and tissue engineering. Proteoglycans contribute to the structural and biochemical components necessary for mimicking the natural extracellular matrix conditions.

In summary, the compatibility of proteoglycans with hydrogels lies in their ability to work together to create biomaterials that closely resemble the native microenvironment of certain tissues, thus making them suitable for applications, such as tissue engineering and drug delivery. In tissues, such as cartilage, proteoglycans, and collagen fibers help maintain the structure and function of the tissue. They play a vital role in regulating the water content, joint lubrication, and overall tissue integrity. As the name implies, elastic cartilage is flexible and can withstand repeated bending inside the extracellular matrix (ECM). Because the fibrillar component is predominant, the fibrocartilage should be viewed as a transition tissue between hyaline cartilage and typical connective tissue. The articular cartilage knee joint is approximately 0.03 cm thick, depending on where it is in the joints, and the cartilage thickness varies. The four unique segments comprise natural articular cartilage along the depth direction (Figure 1a). The compressive moduli of all layers were close to 79, 2100, and 320000 kPa, respectively [39]. The distinctive cartilage structure can reduce the contact stress and increase the joint contact area [40, 41].

The energy generated during impact and torsion can be released by the internal and external water flows of the joint. Additionally, synovial fluid in the joint space provides nutrients to cartilage cells [42, 43]. The components of synovial fluid also help reduce friction (Figure 1b) [44, 45]. Klein et al. were inspired by this unusual structure and were able to achieve a COF (0.001) between sliding surfaces at contact pressures of approximately 10.1325 bar [45]. Since then, several different types of polymer brushes have been used to create brush structures on various substrates, and their lubrication mechanisms in aqueous media can be categorized as hydration lubrication [46–51].

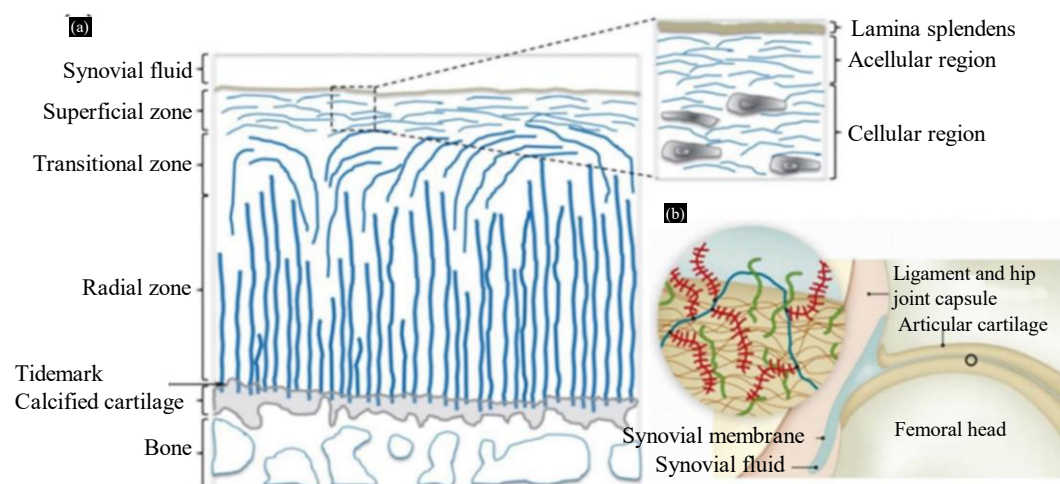


Figure 1. (a) Illustration of the collagen orientation [52]. (b) Functional biomacromolecules HA, aggrecan, and lubricin [53].

APPLICATION OF HYDROGELS

The tissue is intricate, with numerous layers and scales, and is covered with biological macromolecules and biological macromolecules. According to the various motion patterns, the lubricating properties of cartilage undergo dynamic modifications that are both configurable and adaptable.

Scientists have developed numerous models of lubrication mechanisms since the nineteenth century through experimentation and simplification of theoretical formulae. On the basis of experiments, Reynolds derived the mathematical formulas under the assumption of Newtonian fluid and incompressible and so on... in 1886, which laid the groundwork for hydro dynamic lubrication [54] hydrodynamic lubrication comes under the region 3 after the boundary lubrication region 1 and mixed film lubrication region 2 in region 3 stribeck's effects applicable, it refers to the phenomenon in tribology, the study of friction, where the friction coefficient between two surfaces decreases initially and then reaches a steady state, this effect is often observed when two surfaces are in relative motion and is influenced by factors such as lubrication and surface roughness, the steady state is also the assumption of Reynolds equation. The Striebeck effect is relevant to the Reynolds equation in the context of lubrication theory. The Reynolds equation describes the flow of a thin lubricating film between two surfaces in relative motion. Lubrication is crucial for reducing friction and wear in machinery, and The Striebeck effect is significant for understanding the frictional behavior between surfaces. As the surfaces enter relative motion and lubrication is introduced, the initial reduction in friction, a characteristic of the Striebeck effect, plays a role in the formation of the lubricating film. This reduction in friction was due to the adaptation of the lubricant to the surface, which changed the interactions between the surfaces.

In the context of the Reynolds equation, the Striebeck effect contributes to the establishment of a stable lubricating film, as shown in Figure 2(b). The initial decrease in friction allowed the lubricant to form a sufficient film and, as the relative motion continued, the friction stabilized at a lower level. This stabilized frictional state is crucial for the proper functioning of lubricated components in machinery, preventing excessive wear and ensuring efficient operation. According to Reynolds, the articular cartilage surface is partitioned to transfer loads via hydrodynamic pressure between the opposing surfaces. MacConaill ascribed the lubrication mechanism of a joint to lubrication [55]. Jones concluded from his research that friction resistance is correlated with fluid film lubricant mechanics and is the most suitable lubrication state for joint surfaces [56]. Fein discovered through further research that hydrodynamic pressure could be developed to overcome the friction of synovial fluid when two bearing surfaces come into contact without sliding [57]. Mow et al. proposed a biphasic lubrication mode to describe the compressive deformation behavior of articular cartilage after considering the effect of the resistance produced by the reactive motion between the fluid and solid phases in articular cartilage [58]. This theory describes articular cartilage as a soft, porous, and permeable substance composed of synovial fluid and an incompressible elastic solid matrix. Articular cartilage has a very low permeability of 10^{15} – 10^{16} m⁴/Ns. The collagen network structure in cartilage restricts interstitial fluid flow when the cartilage is compressed, and the contact mode changes to the solid mode.

Elastic-hydrodynamic lubrication (EHL) is a term used to describe the elastic deformation of bearing surfaces along with the viscosity effects of lubricants [59–61]. A type of fluid-film lubrication, known as elastic-hydrodynamic lubrication, results from the pressure created in the event of nonconformal contact, which causes elastic deformation of the two opposing surfaces [62]. Low sliding-speed contacts with high loads typically result in boundary lubrication [63, 64]. The asperities of the tribopairs are in contact with each other, and a molecular-level boundary film is formed to primarily support the load. According to Dowson, relying solely on a particular lubrication mode during routine activities does not result in the lubricating properties of the articular cartilage. Instead, different lubrication modes were spontaneously adjusted and worked synergistically to create a mixed lubrication mechanism.

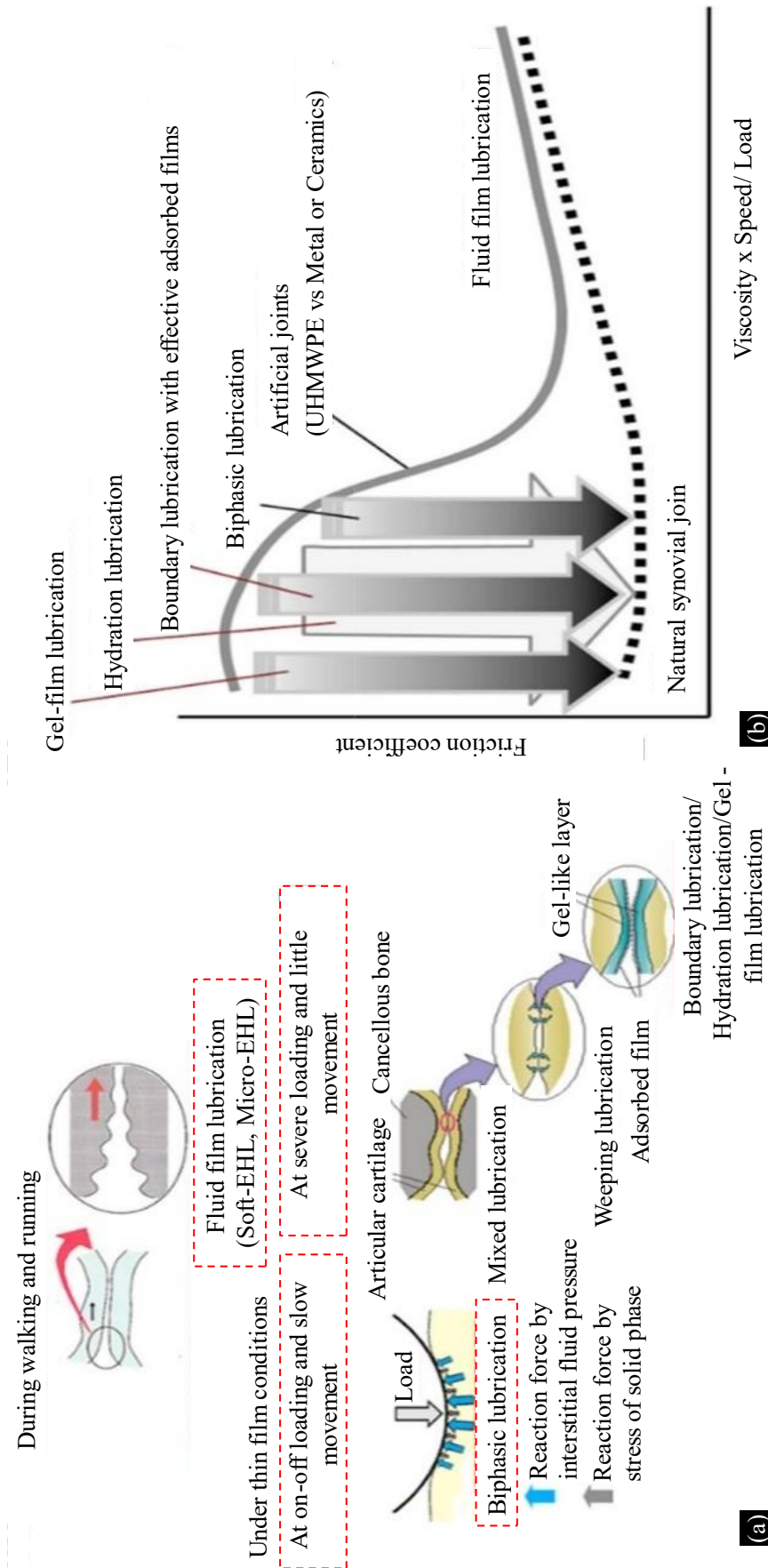


Figure 2. Adaptive multimode lubrication mechanisms (a). (b) A multimode adaptive lubrication Steinbeck curve [65-66].

Murakami et al. [65] recently proposed an adaptive multimode lubrication mechanism for natural synovial joints. Each lubrication mode appears to be completely controlled by adjusting the duty parameter (lubricant viscosity and sliding speed) or the load (Figure 2). Gong et al. proposed a repulsion–adsorption model to explain the lubrication mechanism of hydrogels [66, 67]. According to Figure 3, from the viewpoint of the interfacial interaction between the polymer and solid materials, the polymer chains on the gel surface are either attracted to or adsorbed onto the solid surface depending on the properties of the surface, and the friction is caused by the elastic deformation and lubrication of the hydrated state of the polymer chains. In the repulsive case, friction is primarily caused by the hydration film between the polymer and the solid, and the fluid tends to be drawn into the interfaces as a result of repulsion. In the attractive case, the hydrogel chains that have been adsorbed on the substrate and the hydrogel layer between the two surfaces deform elastically to produce friction. The results of the friction tests can be predicted using this model as follows: the friction force in the repulsive state is lower than that in the adsorption state, and increases with increasing adsorption strength. Additionally, friction is significantly influenced by the physicochemical characteristics of hydrogels, including cross-linking density, water content, mechanical characteristics, and surface roughness, as well as the measurement conditions (applied load, sliding frequency, and counterparts). Using a four-factor, two-level designed experiment, Furey et al. thoroughly investigated the tribological behavior of poly (2-hydroxyethyl methacrylate) (poly HEMA) hydrogels [68]. The applied load, lubrication, hydrogel crosslinking density, and hydrogel hydration level were used as the experimental variables. One of the results showed that the COF increased as the density of the hydrogel crosslinks increased, because the capacity for lubricant absorption decreased. Additionally, high loads and high hydration levels produced higher wear, whereas high crosslink densities produced lower wear in the hydrogels. These factors, load, and hydration, also had significant effects on hydrogel wear.

FABRICATION TECHNIQUES OF HIGH-STRENGTH HYDROGEL

For long periods, the replacement materials should have the ability to withstand impact loads. The hydrogel water content is high because of its poor mechanical properties, and the dissipation of energy in a single structure hydrogel is poor, indicating that the practical applications of single-structure hydrogels are limited. This indicated that the mechanical properties depended on the hydrogel structure. Hence, high-strength hydrogel articular cartilage has been developed by designing a hydrogel structure.

A double network hydrogel was produced by a two-step polymerization process (Figure 4a) [69, 70]. The mechanical properties gain by double network hydrogel is brittle and rigid. Next, a neutral monomer was used for the rigid network. Finally, the double rigid network becomes softer. This soft double network hydrogel has better mechanical properties [71], similar to the suppression of laughter. Gong et al. presented a series of DN hydrogels as potential materials for synthetic cartilage (Figure 4b) [72–75].

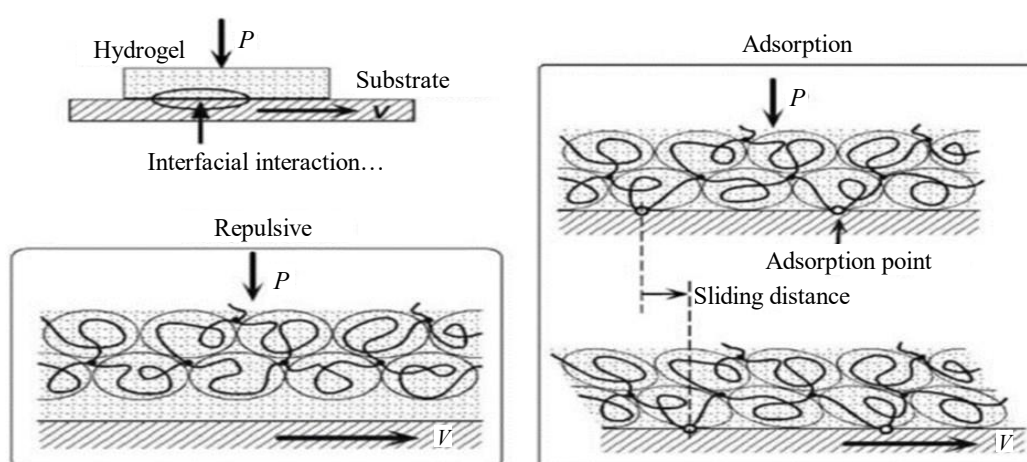


Figure 3. The adsorption-repulsion concept of hydrogel friction is depicted.

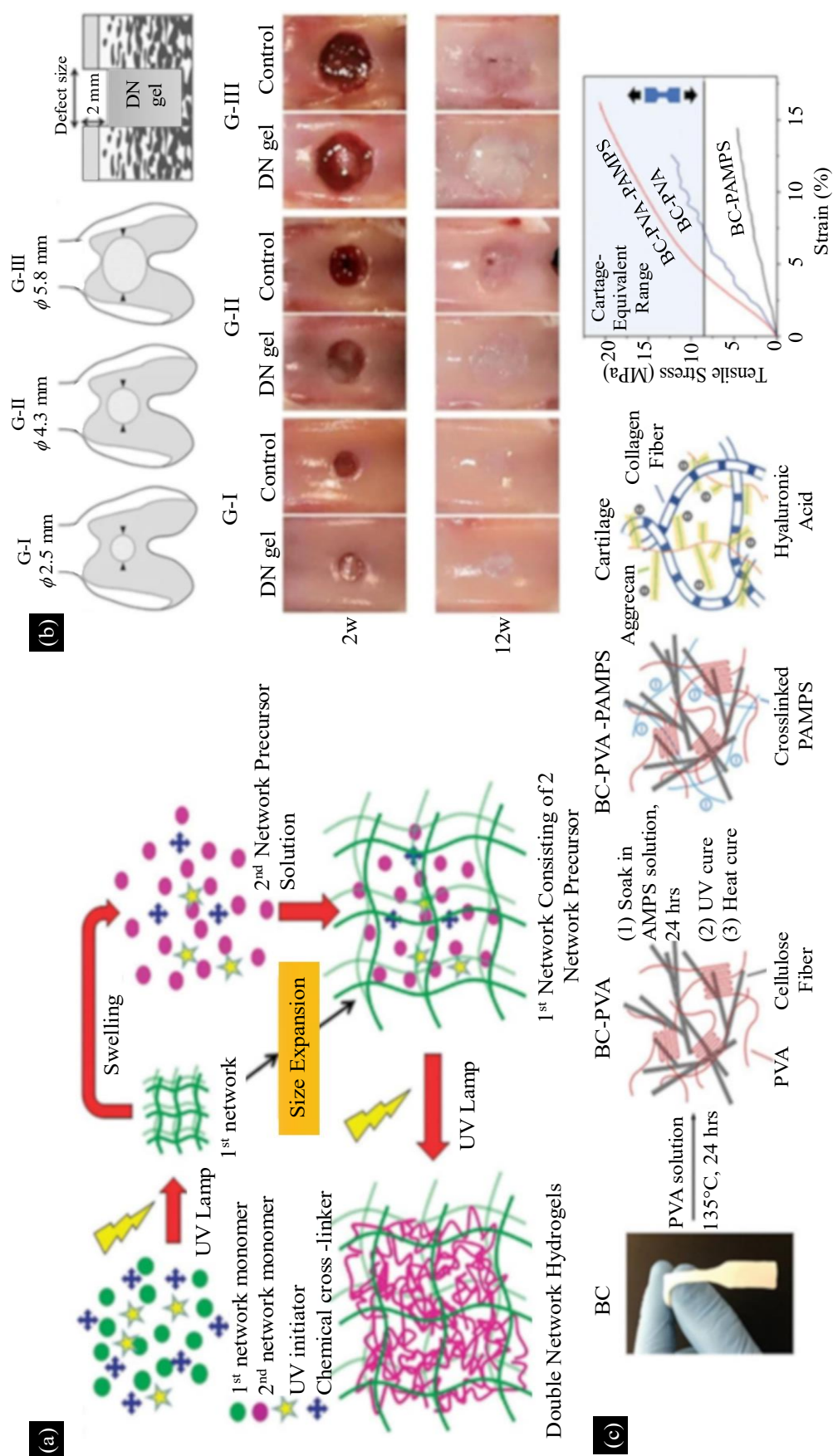


Figure 4. Chemically connected double network (DN) hydrogels may be created using a two-step polymerization process (a) [84]. (b) The use of DN hydrogel to stimulate cartilage regeneration and the overall appearance of the treated joint surface at 2 and 12 weeks [75]. (c) Tensile stress-strain curves and an illustration of the BC-PVA-PAMPS hydrogel production method [82].

In 2009, they created an implantation plug from a polyDN hydrogel and PAMPS [76]. The high creep resistance of Mouratoglou polymerized acrylamide [77]. Consequently, the superlubricity and water content decreased. The capacity of the gels to absorb water was increased by Mouratoglou's polymerized acrylamide, and because the squeezed water formed a boundary film, the COF decreased. The disadvantage of traditional covalent DN hydrogels is that they cannot recover the sacrificial bonds under significant mechanical deformation. Recently, various novel DN hydrogels that are cross-linked by hydrogen bonds [78, 79], hydrophobic interactions, and ionic interactions have been created [80, 81]. A synthetic hydrogel composite with durability and mechanical behavior resembling that of cartilage was reported by Wiley et al. (Figure 4c) [82]. This double network hydrogel has a viscoelastic effect and high tensile strength. Without the use of a cross-linking agent, Wang et al. created a BC and silk fibroin (SF) DN hydrogel by soaking BC in an aqueous SF solution [83, 84].

The network of the dual-crosslinked hydrogels was more uniform than that of the DN hydrogel. This hydrogel is created from a network of polymers that further crosslinks as a result of other interactions. One type of hydrogel was created by Gong et al. using cation and anion monomers [85]. To dissipate energy and improve toughness, the electrostatic attraction between them may function as a reversible cross-linking bond in the original network. Acrylamide and acrylic acid were copolymerized by Zhou's group as monomers to create a chemically cross-linked P(AAmcoAAc) hydrogel. This hydrogel was then soaked in an aqueous solution containing Fe³⁺ ions to create a P(AAmcoAAc)Fe³⁺ hydrogel (Figure 5a) [86]. From 0.4 MJ/m³ for P(AAm coAAc) to 27.8 MJ/m³ for P(AAm P(AAm coAAc) Fe³⁺ hydrogel, the toughness increases dramatically. In the P(AAmcoAAc) network, Fe³⁺ induced tridentate metal coordination with the COOH group and functioned as a second network to improve the mechanical properties. Gao et al. created a biomimetic bilayer coating on the surface of polydimethylsiloxane using this technique (Figure 5b). It consisted of a sturdy P(AAmcoAAc)Fe³⁺ hydrogel substrate and an entangled polyzwitterionic polyelectrolyte brush layer on top. Excellent anti-wear properties were demonstrated by the ability of the coating to maintain a low friction coefficient (COF 0.05) over 50,000 sliding cycles under a 10 N load. The mechanical properties of the hydrogel can be further enhanced by adding more physical interactions to the initial dual physical cross-linking networks [88, 89]. Jiang et al. created a PVA- and chitosan-based multiphysical cross-linked hydrogel [90]. The polymer chains were entangled and crystallized to form the hydrogel, and immersion in a sodium citrate solution increased the mechanical strength of the hydrogel. After electrostatic cross-linking with chitosan and citrate, the mechanical performance of the gel was significantly enhanced by numerous physical interactions.

AIM OF REVIEW ARTICLE ON HYDROGEL

Investigations into the biostructure and lubrication mechanism of articular cartilage will aid in the design and construction of cutting-edge hydrogel lubrication materials. Hydrogels have tremendous potential for cartilage treatment and replacement. Double-network hydrogels and DC-linked hydrogels are only a few recent advancements in hydrogel materials that are inspired by cartilage and have good mechanical strength, which we have comprehensively summarized in this study. In addition, a number of innovative bonding techniques involving bone tissues, prosthetic joint substrates, and hydrogel lubricating materials have been developed [88]. High-performance hydrogel lubricating materials have undergone substantial advancements in research; however, there are still many obstacles to overcome before they can be used in clinical settings. The following points can be taken into consideration for future research studies: (1) Although numerous studies have concentrated on creating low-friction hydrogels inspired by bio-articular cartilage, the inherent mechanical capabilities of these materials for load bearing and fatigue resistance are still subpar when compared to actual cartilage. Therefore, it is necessary to evaluate material properties under properly simulated conditions. (2) Hydrogel materials for cartilage with excellent durability should also be assessed for potential future applications in terms of biostability, degradation characteristics, and bioabsorbability. (3) The majority of synthetic high-strength cartilage hydrogels are mechanically improved, which is detrimental to tribological characteristics [89]. To create a dynamic equilibrium between mechanical strength and hydration, new

techniques need to be devised. In summary, we believe that the development of the hydrogel lubricating materials discussed here, as well as upcoming innovations in the field, will significantly advance the study of innovative cartilage hydrogel materials for clinical use. The Reynolds number is typically used to characterize the flow of fluids, and it may not be directly related to the strength of hydrogels [90]. However, if hydrogel strength is explored in the context of fluid dynamics, the Reynolds number could indirectly influence hydrogel performance by affecting factors such as mass transport or shear forces within the gel. The hydrodynamic region, which is often characterized by certain Reynolds numbers, is more strongly associated with the fluid flow behavior than directly influencing the strength of the hydrogels. However, understanding the fluid dynamics is crucial for the fabrication and application of hydrogels. In the context of hydrogels, factors such as the mixing efficiency, shear forces, and mass transport during gelation or polymerization can affect the final properties of the hydrogel, including its strength. Efficient mixing and proper mass transport can lead to more uniform crosslinking, potentially contributing to the higher strength of the resulting hydrogel. Therefore, while the hydrodynamic region itself may not directly enhance hydrogel strength, optimizing the processing conditions within this region could indirectly contribute to the development of high-strength hydrogels. The Reynolds number is primarily used to analyze the flow patterns and transitions between laminar and turbulent flows in fluid dynamics. Although it may not directly help in analyzing the internal structure of hydrogels, understanding the fluid dynamics during the fabrication or application of hydrogels can indirectly provide insights.

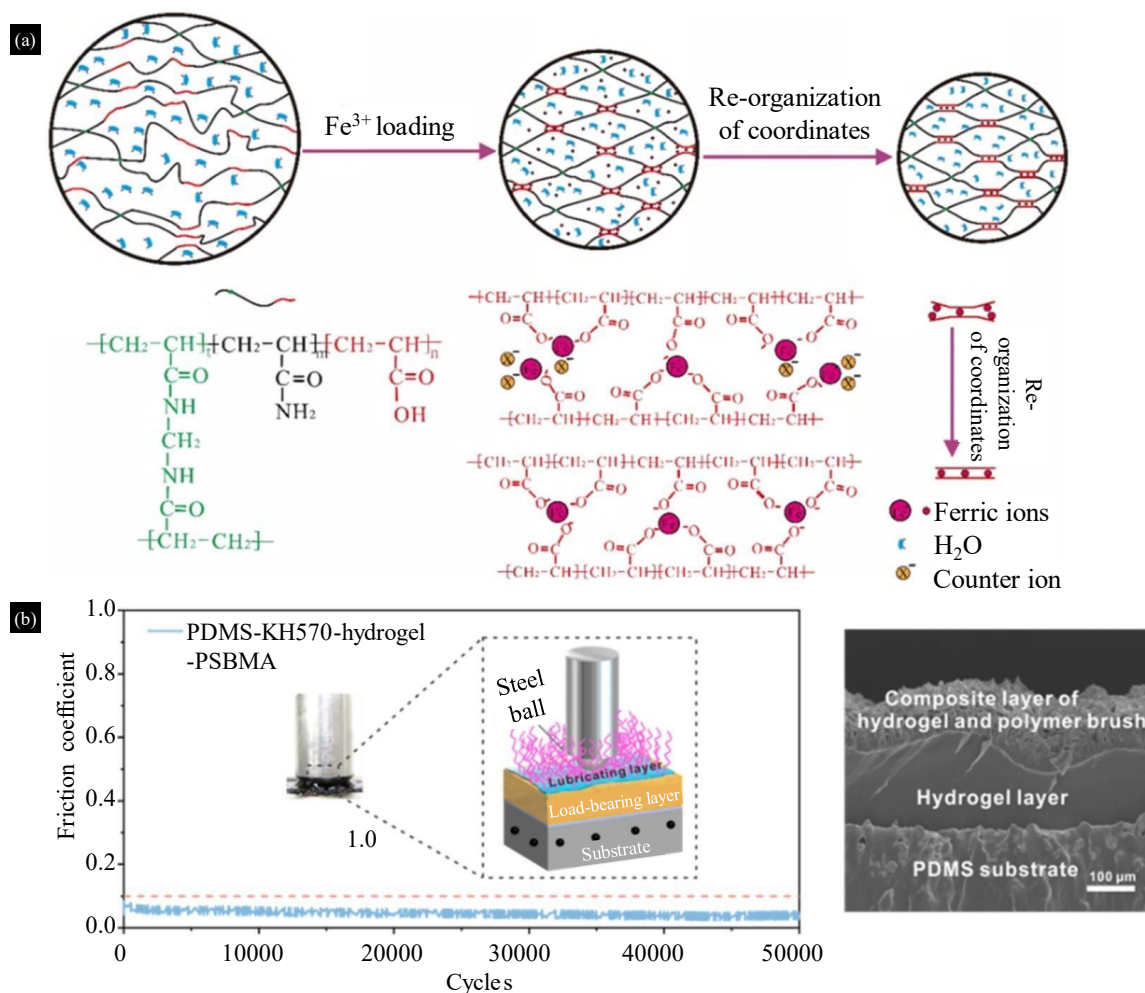


Figure 5. (a) P(AAmcoAAc) Fe^{3+} dual-crosslinked hydrogel preparation [86]. (b) Left: COF-cycles curve of a bilayer coating at an applied load of 10 N for 50,000 friction cycles. Right: cross-sectional SEM image of polydimethylsiloxane (PDMS) with bilayer covering [87].

CONCLUSION

In summary, the article highlights the considerable promise of hydrogel lubricants as alternatives to natural cartilage in biomedical applications. The development of hydrogels inspired by biological systems, combined with cutting-edge surface modification techniques, presents encouraging solutions to the challenges faced in joint replacement and cartilage repair. These hydrogels, with their capacity to mimic the natural lubrication of cartilage, as well as their flexibility and biocompatibility, are positioned as essential materials for future advancements in medical science.

The ongoing research and experimentation discussed in the article stress the crucial need for continuous innovation to improve the mechanical properties and tribological performance of these materials. By tackling current challenges and exploring new possibilities for hydrogel applications, the field can progress towards achieving effective and long-lasting solutions for patients with cartilage-related conditions. The article also highlights the importance of a multidisciplinary approach, integrating knowledge from biology, chemistry, and engineering, to fully unlock the potential of hydrogels in biomedical applications.

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