Smart Hydrogels: Innovations and Prospects from Structural Properties to Biomedical Applications

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Abstract. This paper systematically reviews the structural properties, classification, and development of hydrogels, highlighting their advantages and mechanisms in drug delivery, tissue engineering, and smart medical applications. It emphasizes their biocompatibility and stimulus responsiveness, discusses challenges such as mechanical properties and controllable degradation, and outlines future prospects in personalized and precision medicine.

1. Introduction

In recent years, rapid developments in materials science, bioengineering, and medicine have given rise to several breakthroughs in new materials for biomedical applications. Among them, hydrogels are notable for their unique combination of qualities-high water content, soft texture, and great biocompatibility-making them ideal candidates for medical devices, drug delivery systems, and tissue engineering applications.The high mimicry of hydrogels to natural tissue structures and mechanical properties ensures that they can effectively reduce immune rejection during integration in the human body, an advantage that gives them unique value in the biomedical field. Through precise control of their physical, chemical and functional properties, the application territory of hydrogels has been expanding and is now deeply integrated into cutting-edge fields such as regenerative medicine, wound repair and implantable medical devices.

Hydrogels are essentially three-dimensional network structures made of hydrophilic polymer chains that can absorb large amounts of water or physiological bodily fluids without dissolving. A stable network created by physical or chemical cross-linking enables it to maintain structural integrity even in a swollen state. These materials can expand hundreds to thousands of times their original volume, and their high water content and soft elasticity are very similar to those of biological tissues such as skin and mucous membranes, showing significant advantages over traditional synthetic materials.

The first milestone in hydrogel research came in the 1960s when Wichterle and Lim's team developed apolyhydroxyethyl methacrylate (PHEMA) hydrogel that was successfully applied to the fabrication of contact lenses, pioneering[1]the biomedical application of hydrogels. Over the next decades, its application boundaries continued to expand, gradually penetrating into critical areas such as controlled-release drug delivery, trauma care, tissue engineering and artificial organs. With nanotechnology advancements, modern hydrogels have acquired intelligent qualities such as stimulus-responsive, self-repairing, and conductive, showing tremendous potential[1] in cutting-edge medical scenarios such as biosensors and wearable devices.

This article offers a systematic review of the chemical structure, types, and functional features of hydrogels, with an emphasis on examining their fundamental advantages in smart medical applications. By analyzing the historical evolution of hydrogels, breakthroughs in material design, and key technologies driving innovation in medical devices, this article delves into the differentiated positioning of natural, synthetic, and semi-synthetic hydrogels in drug delivery, tissue regeneration, and diagnostic applications[1].At the same time, propose solutions to current research and development bottlenecks and look forward to their prospects in personalized medicine and precision medicine.

2. Definition of Hydrogels

2.1 Definition/Concept of Hydrogels

A hydrogel is a hydrophilic polymer material with a three-dimensional network structure formed by physical or chemical cross-linking, which has the property of adsorbing large amounts of water or physiological fluids without dissolving. Its matrix is rich in hydrophilic groups such as hydroxyl, carboxyl, amide and sulfonic acid groups, which can expand hundreds to thousands of times[2] its original volume. At the same time, the expanded hydrogel exhibits soft physical properties similar to biological tissues, and compared with other polymer materials, the hydrogel has high water content and softness, and good biocompatibility. It is particularly suitable for biological applications[3].

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2.2 The chemical structure of the hydrogel

Hydrogels possess a three-dimensional network structure formed through either physical or chemical cross-linking. Physical cross-linking is based on non-covalent interactions such as hydrogen bonding, hydrophobic interactions, ionic bonds, electrostatic forces, and van der Waals forces. [4] These interactions are typically reversible and give rise to stimuli-responsive hydrogels, such as temperature-sensitive or pH-sensitive systems. In contrast, chemical cross-linking involves the formation of stable covalent bonds between polymer chains using cross-linking agents, resulting in more permanent and mechanically robust networks. Examples include chemically cross-linked polyacrylamide and polyvinyl alcohol hydrogels. Hydrogels can be composed of both natural and synthetic polymers. Common natural polymers include gelatin, alginate, chitosan, and hyaluronic acid, which are valued for their biocompatibility. Synthetic polymers, such as polyacrylamide, polyvinyl alcohol[4], and polyethylene glycol, offer tunable properties and enhanced structural stability[4].

2.2.1 Network structure and water absorption of hydrogels

Hydrogel is a three-dimensional cross-linked network structure that can absorb and hold a lot of water. This network structure is created by physical or chemical cross-linking, and its high water absorption comes from the presence [2]of hydrophilic groups such as hydroxyl, carboxyl, amide, etc. These hydrophilic groupings bind to water molecules through hydrogen bonds, allowing the hydrogel to expand by absorbing water In a swollen state, the equilibrium swelling behavior of hydrogels is described by the Flory-Rehner theory. This theory analyzes the relationship between swelling degree and crosslinking density quantitatively by combining the solvent's mixing free energy with the elasticnetwork's deformation free energy. [2] The hydrogel's degree of swelling decreases with increasing crosslinking density, and vice versa.

2.2.2 Crosslinking mechanism

Physical crosslinking and chemical crosslinking are the two types of hydrogel crosslinking techniques. Physical crosslinking creates networks by non-covalent interactions like hydrogen bonds, electrostatic interactions, hydrophobic interactions, etc. It can swell or gel and is reversible[4] ate in response to outside stimuli like pH and temperature. On the other hand, chemical crosslinking creates a more stable network by covalent bonds, which is better for long-term medical implants and has a higher mechanical strength and stability.

2.2.3 Stimulus responsiveness

Some hydrogels can respond to environmental changes such as temperature, pH, light, electric field, etc., showing swelling or contracting properties. This property makes hydrogels an important part of the field of smart materials, such as in drug controlled-release[4] systems where drugs are released under specific conditions, for example: poly (n-isopropylacrylamide) (PNIPAM) is a typical temperature-sensitive hydrogel that swells below its lower critical dissolution temperature (LCST, about 32° C) and shows hydrophilicity; It shrinks above the LCST and shows hydrophobicity. Its unique temperature response characteristics make it widely used in drug-controlled release, tissue engineering, and flexible sensors. For example, precise drug delivery through temperature-controlled release, or as a temperature-sensitive element to detect environmental changes, demonstrates its significant value in biomedical and smart materials.

2.2.4 Biocompatibility and degradability

The wide application of hydrogels in the medical field benefits from their good biocompatibility and biodegradability. Natural hydrogels (such as hyaluronic acid, sodium alginate) have good bio-compatibility because they are derived from natural biological materials; Synthetic hydrogels, such as polyethylene glycol and polyacrylamide, can have their biocompatibility[5] further enhanced through modification.

3. Classification of hydrogels: By source

Based on their origin, hydrogels can be divided into three main groups: synthetic hydrogels, semi-synthetic hydrogel, and natural hydrogels. (As shown in table 1)

3.1 Natural Hydrogels

Natural hydrogels are made from natural polymer materials and have good biocompatibility and degradability, which can be naturally metabolized or degraded[4] in living organisms. The main materials include gelatin, hyaluronic acid and alginate, which are used in areas such as tissue engineering, soft tissue engineering, skin care, cell wrapping and wound dressings. Natural hydrogels play a significant role in applications such as tissue engineering scaffolds, drug controlled-release, and wound dressings. Disadvantages: Weak mechanical characteristics, large batch-to-batch fluctuations, unpredictable degradation.

3.2 Synthetic Hydrogels

(PVA)the mechanical properties of synthetic polymer materials, which can be precisely controlled for water absorption capacity and degradation rate through chemical design, make them known as synthetic hydrogels[4].The primary materials are polyvinyl alcohol (PVA), polyacrylamide (PAM), and polyethylene glycol (PEG), which are frequently used in medical implants, drug delivery, and other fields. These materials have good mechanical strength, bio-compatibility, high water

absorption, and are also widely used in medicine. In contact lenses, drug controlled-release systems, and soft tissue substitutes, synthetic hydrogels are frequently utilized. Disadvantages: Low biological activity, potentially triggering an inflammatory response.

3.3 Semi-Synthetic Hydrogels

Semi-synthetic hydrogels are prepared through a combination of natural and synthetic polymers, combining the advantages of both natural and synthetic materials to achieve higher functionalization[4]. The main materials include modified alginates (such as those combined with PEG or PVA to enhance mechanical strength and controllable degradability) and methacryloylated gelatin (Gel-MA, which retains bio-compatibility while improving mechanical properties). Semi-synthetic hydrogels are widely used in areas such as high-performance biological scaffolds, intelligent drug delivery platforms, and cartilage repair. Disadvantages: Complex modification process and high cost. [4]

Table 1. Types of hydrogels and comparisons

Characteristics	Natural hydrogel	Synthetic hydrogel	Semi-synthetic hydrogel
Typical materials	Collagen, hyaluronic acid, alginate	PAAm, PEG, PVA	GelMA, sodium oxyalginate
Tensile strength	1–50 kPa	0.1-30 MPa	10 kPa–10 MPa
Elastic modulus	0.1-20 kPa	1 kPa–1 GPa	1 kPa–100 MPa
Degradation time	Days - weeks (enzyme-dependent)	Weeks - years (hydrolysis control)	Weeks - months (adjustable)
Biocompatibility	high	Medium (surface finishing required)	High (preserve the natural active site)
Cell interactions	Excellent (with natural ECM signaling)	Poor (requires functionalization modification)	Good (partially retain natural signals)
Application areas	Wound dressings, soft tissue engineering	Flexible electronics, high-load stents	Bio-3d printing, regenerative medicine

4. Mechanical properties of hydrogels[3]

As shown in table 2 and table 3

Table 2. Comparison of tensile strengths of different types of hydrogels

Hydrogel types	Tensile strength range	Typical application scenarios
Common PAAm (polyacrylamide)	10–100 kPa	Flexible sensors, tissue engineering
Nanocomposite hydrogels (such as clay-PAM)	1–10 MPa	Artificial cartilage, high-load materials
Double network hydrogel (DN gel)	1–30 MPa	Biomimetic materials, robot drives
Polyvinyl alcohol (PVA) hydrogel	0.5-5 MPa	Medical dressings, contact lenses

Table 3. Comparison of elastic moduli of different types of hydrogels

Hydrogel types	Elastic modulus range	Match the biological tissue type
Low crosslinking PAAm	0.1-10 kPa	Brain tissue (~1 kPa)
Collagen hydrogel	1–50 kPa	Skin (~ 10-20 kPa)
High-strength PEG hydrogel	100 kPa–1 MPa	Cartilage (~0.5-1 MPa)
Nanocellulose reinforced hydrogels	10–100 MPa	Engineering structural materials

5. The development of hydrogels as smart medical hydrogels

The development of hydrogels can be traced back to the 1960s when Wichterle and Lim first developed poly(2-hydroxyethyl methacrylate) (PHEMA) hydrogels for contact lensesshuini. In the 1970s, researchers began to explore the mechanical properties of hydrogels formed through chemical cross-linking, especially polyvinyl alcohol (PVA) cross-linked hydrogels. The concept of stimulus-responsive hydrogels was introduced in the 1980s, laying the groundwork for their smart applications. In the 1990s, hydrogels were widely used in drug controlled-release and tissue engineering[6]. In the 2000s, functionalized hydrogels emerged and research focused on self-healing, conductivity and other multifunctionalities, while dual-network hydrogels improved their mechanical properties. Smart hydrogels were applied in wearable devices and implantable medical devices in the 2010s, and conductive hydrogels were used

in biosensors and flexible electronic devices. Entering the 2020s, research on hydrogels has deepened, with breakthroughs in areas such as personalized medicine, soft robotics, and cardiovascular implants becoming the focus, especially in sensors and medical systems combined with artificial intelligence, where hydrogels have shown great potential for development[7].

6. The application of hydrogels in the field of intelligent medical care

Hydrogels have a wide range of applications in drug controlled-release, tissue engineering, integrated diagnosis and treatment, and other fields. In terms of drug controlled-release, ph-responsive hydrogels can achieve site-specific release, while temperature-responsive hydrogels can deliver precise drugs by swelling or contracting at body temperature[8]. In tissue engineering, hydrogels act as cell scaffolds to provide a three-dimensional environment for cell growth, often used for cartilage, bone and skin repair, while injectable hydrogels can be used for soft tissue repair and cell delivery. In terms of diagnostic treatment, fluorescent/optical diagnostic hydrogels can monitor biomarkers or drug release in real time, and conductive or photoresponsive hydrogels combined with photothermal/photoacoustic techniques are used for tumor treatment and imaging. In addition, hydrogels have important applications in areas such as soft robotics, wearable devices, wound dressings, etc., with self-healing, shape memory, antibacterial and accelerated healing properties[9].

In fields such as Biomedical Engineering and Clinical Medicine, customizing implants by combining 3D printing technology with hydrogels has gradually become a dominant technology, with the core advantage being:

Highly personalized: Based on the patient's CT/MRI data, print implants (such as bone defect repair scaffolds, auricular and nasal cartilage, etc.) that are perfectly matched to the anatomical structure.

Biocompatibility: The hydrogel mimics the extracellular matrix (ECM) to support cell adhesion, proliferation, and differentiation.

Functionalized design: Endowing implants with bioactivity or intelligent response capabilities (such as drug sustained-release, electrical signal conduction) by regulating hydrogel components (such as adding growth factors, conductive nanomaterials) [7]

The application of 3D printing technology combined with hydrogels in customized implants has made significant clinical progress. For example, hydroxyapatite (HA) and methylacrylylated gelatin (GelMA) composite hydrogel bone scaffolds achieved 85% high porosity and 3 MPa elastic modulus through 3D printing, promoting 90% bone regenerationwithin 8 weeks in rat models of skull defects. In the field of cartilage regeneration, the photocurable printed GelMA scaffold mimics the mechanical properties of cartilage (elastic modulus 0.5 MPa) and successfully forms a mature cartilage layer 12 weeks after implantation in the rabbit knee joint. For nerve repair, conductive PEDOT:PSS/ gelatin hydrogel 3D printed nerve catheters showed conductivity at 10 S/cm, and motor function recovered 80% after repairing sciatic nerve defects in rats. In addition, the light-responsive hydrogel cardiac patch combined with carbon nanotubes achieved electrical conductivity of 5 S/m and rapid photothermal response within 10 seconds, effectively promoting angiogenesis in porcine myocardial infarction models. These cases highlight the advantages of 3D printed hydrogel implants in personalized matching, bioactivity regulation and functional design, providing innovative solutions for the precise repair of complex tissues such as bone, cartilage, nerve and cardiovascular, and gradually facilitating the transition from animal experiments to clinical applications.[11]

7. The development history of hydrogels as smart medical polymer materials

Hydrogels face a series of challenges, including insufficient mechanical properties, biocompatibility and degradation control, difficulty in functionalization, and mass production and cost control. In terms of mechanical properties, the high water content of hydrogels makes them difficult to withstand complex biomechanical environments. Solutions include the use of dual-network hydrogels and nanocomposite hydrogels to enhance strength and toughness. Biocompatibility and degradation control issues can be addressed by combining controllable degradation hydrogels with natural and synthetic materials to ensure that the long-term use of hydrogels in the body does not trigger inflammation or immune responses. The preparation process of functionalized hydrogels is complex, but properties such as self-healing, conductivity and photoresponse can be given to the hydrogels through the introduction of dynamic covalent bonds and functionalized nanomaterials. To address the issues of mass production and cost, researchers are developing simplified synthetic processes and modular production methods to improve production efficiency and control costs. [6]

8. Purpose and significance of the study

Hydrogels are widely used in intelligent medical fields due to their high water content, good biocompatibility and environmental responsiveness. It can absorb a large amount of water, form a soft structure similar to biological tissue, reduce immune responses, and respond to external stimuli such as temperature, pH and light, making it suitable for intelligent drug release, dynamic tissue engineering scaffold design, etc. The mechanical properties of the hydrogel can be optimized by network structure to meet the demands of complex biological environments, and it also has customizable antibacterial, self-healing and conductive properties, and is widely used in drug controlled-release, bioelectronics and other fields. Natural or modified hydrogels, with low toxicity and degradability, are ideal for implants or drug carriers. The study of smart hydrogels not only drives the development

of precision medicine, but also provides technical support for areas such as tissue regeneration, wound healing, cartilage repair, and lays the foundation for the development of advanced medical devices, promotes the cross-integration of materials science, bioengineering and medicine, and enhances global medical standards.

9. Conclusions and prospects

Hydrogels, due to their unique physicochemical properties, have become a key area of medical polymer materials and are widely used in drug release and delivery, tissue engineering, regenerative medicine, integrated diagnosis and treatment, and wound care. For instance, the application of stimulus-responsive hydrogels in precise drug delivery and the achievements of dual-network hydrogels in tissue repair fully demonstrate their value. However, there are still bottlenecks for hydrogels in terms of mechanical properties, controllable degradability and stability in complex environments, which limit their wider application.

In the future, the development of hydrogels will be oriented towards intelligence, multi-functionality and personalization. Smart hydrogels will respond dynamically to the external environment, multifunctional hydrogels will facilitate the cross-application of drug delivery, tissue engineering and bioelectronics, and personalized hydrogels will focus on precision medicine to meet patient-specific needs. By combining materials science, bioengineering and information technology, hydrogels will play a core role in the next generation of smart medical materials.

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