Hydrogels

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INTRODUCTION

A hydrogel is a three-dimensional polymer network made of a hydrophilic polymer or a mixture of polymers. In general, at least 10–20% of the total weight of a hydrogel is water. When a hydrogel is dried, it is called xerogel, or simply a dried hydrogel. When a dried hydrogel is placed in an aqueous environment, it can absorb a large amount of water and swell isotropically to maintain its original shape. Swollen hydrogels maintain their shape without dissolving even in abundant water because of the presence of chemical or physical cross-linking of polymer chains. The extent of swelling depends inversely on the cross-linking density. When more than 95% of the total weight is water, the hydrogel is also called superabsorbent. It is not unusual to see hydrogels with more than 99% of water.

Because of the presence of high water content and the rubbery property, hydrogels have been frequently compared with the natural tissues. The similarity to natural tissues renders hydrogels useful in biomedical and pharmaceutical applications. Further, depending on the chemical structures of the constituting polymers, hydrogels can be tailored to respond to external stimuli, such as temperature, pH, solvent composition, electric field, light, and specific biomolecules. Those hydrogels can undergo change in swelling/deswelling, shape change, and sol–gel transformation upon stimulation by external factors, and they are often called “smart hydrogels.” Such an interesting nature of the smart hydrogels has allowed their use in controlled drug delivery, biomechanical devices, and separation systems.

The advent of nanotechnology has provided new avenues for engineering materials in nano- and micro-scales. In recent years, there have been extensive studies on potential applications of hydrogels in nanotechnology. Most of the studies have tried to exploit the unique properties of hydrogels, such as the hydrophilic nature of the surface, soft physical properties, and environmental sensitivity. Of particular interest has been nanoscale fabrication and manipulation of hydrogel-based materials that may lead to scientific and technological advances. Here, we review the current technologies on the preparation and potential applications of hydrogel-based nanomaterials, including hydrogel nanoparticles, hydrogel-coated nano/micro devices, inorganic (or organic) nanoparticle-entrapped hydrogels, and molecularly imprinted hydrogels.

HYDROGELS IN NANOTECHNOLOGY

The hydrophilic polymer molecules of a hydrogel are interconnected by cross-linking, and this structure prevents dissolution of the polymer chains in an aqueous solution despite absorption of a large amount of water by the hydrogel. Hydrogels are generally classified into chemical and physical gels, according to the type of cross-links. Chemical gels are produced by cross-linking of hydrophilic polymers via covalent bonding. In an aqueous solution, they absorb water until they reach equilibrium swelling, which depends on the cross-linking density. On the other hand, physical gels are generated by noncovalent bonding, such as molecular entanglements, electrostatic interactions, hydrogen bonding, and hydrophobic interactions. These interactions, in contrast to covalent bonding, are reversible and can be disrupted by changes in physical conditions, such as temperature, pH, ionic strength, and stress.

Fig. 1 illustrates representative mechanisms of hydrogel formation. There are a number of different
macromolecular structures that form physical or chemical hydrogels. Hydrogels can be designed to undergo biodegradation in a physiological solution,\textsuperscript{[1–3]} exhibit rapid response to physical stimuli,\textsuperscript{[4–6]} or reach the equilibrium swelling level within a few minutes.\textsuperscript{[7–9]}

Furthermore, there are differences in preparation methods and properties between chemical and physical gels, and each gel type has its own advantages and disadvantages for the design of specific materials or devices involving nanotechnology. Physical gels have been primarily used for biomedical applications, especially in the form of polymer micelles or self-aggregates for controlled drug delivery to the specific sites of action. They are spherical in shape and have the mean diameter ranging from nanometers to micrometers. Because nanoparticles are frequently administrated via the systemic route, it is desirable to construct them with biodegradable polymers so that they can degrade.

Fig. 1 Representative methods of hydrogel formation. (A) Chemically cross-linked hydrogels are prepared from monomers, oligomers, or polymers in the presence of cross-linking agents. The chemical cross-linking proceeds via radical polymerization or polycondensation reaction. (B) Physically cross-linked hydrogels can be formed by ionic interactions, hydrophobic interaction, or hydrogen bonding.
into low molecular weight entities eligible for renal excretion. Chemical gels that are covalently cross-linked provide a variety of potential applications because of their high stability in harsh environments, such as high temperature, acidic/basic solutions, and high stresses. In addition to drug delivery, chemical hydrogels have been considered as the constituents of diagnostic, electronic, and photonic devices.[10–12]

**Nanoparticle-Bearing Hydrogels**

Incorporation of functional nanoparticles into a hydrogel matrix produces unique properties, which cannot be found in other conventional organic/inorganic materials. Nanoparticles can be entrapped into a hydrogel matrix by chemical bonding or physical interactions with the polymer backbone of the hydrogel that have rubber elasticity and the stimuli-sensitive swelling/shrinking behavior. The entrapment of polymer nanoparticles, forming a crystalline colloidal array (CCA), into a hydrogel matrix has displayed different colors without adding coloring agents, responding to external stimuli.[10,13] By incorporating 10–12 nm magnetite (Fe$_3$O$_4$) or maghemite ($\gamma$-Fe$_2$O$_3$) into a hydrogel matrix, the shape of hydrogels can be modulated by applying magnetic field.[14,15]

Monodispersed colloidal particles are reported to form CCAs via slow particle sedimentation, centrifugation, and spin coating.[10,13,16] The CCA diffracts visible and near-infrared light at wavelengths dependent on the lattice spacing, which produces an intense color. By combining the characteristic of the CCA with stimuli-sensitive hydrogels, novel functional hydrogels have recently been prepared. Of various hydrophilic polymers, poly(N-isopropylacrylamide) (PNIPAM) and its copolymers have been widely used to prepare chemical gels containing CCAs, because they show fast stimuli-sensitive volume phase transition and are readily prepared by the free radical polymerization of monomers in the presence of a difunctional cross-linking agent.[10–12,14] Weissman et al.[10] prepared PNIPAM hydrogels by photopolymerization in the presence of polystyrene nanoparticles (99 nm in diameter) as a CCA component and $N,N$-methylen-bis-acrylamide as a cross-linking agent. This chemically cross-linked CCA hydrogels exhibited various colors according to the temperature that changes the hydrogel volume affecting the array lattice constant. Polyacrylamide-based hydrogels have also been investigated to entrap the CCA lattice.[13] Although polyacrylamide does not provide thermo-sensitive volume transition like PNIPAM, it allows incorporating molecular-recognition groups (e.g., crown ethers for metal ions and glucose oxidase for glucose) during its polymerization or by simple chemical modification. The recognition events may make the gel swell because of changes in environments within the hydrogel matrix, such as an osmotic pressure and pH, which increases the mean separation between the colloidal spheres, and thus changes the diffracted light to longer wavelengths. More recently, the use of monodispersed nanoparticles as a hydrogel matrix has been developed[11,16,17] This technique involves preparation of monodispersed hydrogel nanoparticles by radial polymerization in the presence of the cross-linker and surfactant, and formation of nanoparticle networks (colloidal crystal gels) by centrifugation[16] or chemical cross-linking.[11,17] The resultant hydrogel matrices displayed a bright iridescence in the visible region of the spectrum and underwent a reversible color change in response to changes in the temperature or pH. For chemically cross-linked nanoparticle networks, the color was changed depending on the concentration and size of the nanoparticles.

Nanoparticles have also been incorporated into a hydrogel matrix to develop novel materials sensitive to stimuli, such as light[18] and magnetic fields.[14] The gold nanoshell, composed of a thin layer of gold surrounding a dielectric core (e.g., gold sulfide), is one of the representative nanoparticles that have been incorporated into chemical gels, resulting in unique optical properties.[19–21] The diameters of both the core and shell are known to be responsible for the optical properties of nanoshells.[19,20] As the core size and shell thickness can be readily manipulated during the fabrication process, the optical extinction profiles of the nanoshells can be adjusted to observe light at desired wavelengths. Recently, by using nanoshells which absorb near-infrared light, hydrogel/nanoshell composites have been prepared for photothermally modulated drug delivery.[22] Embedding the nanoshells in PNIPAM hydrogel produced unique properties by which the composite hydrogel exhibited volume transition upon the irradiation of near-infrared light, i.e., the nanoshells in the hydrogel matrix converted light to heat, raising the temperature of the composite above the low critical solution temperature of PNIPAM. Because near-infrared light is capable of being transmitted through tissue, such hydrogels bearing gold nanoshells may have promising potential as an injectable drug delivery system for low molecular weight drugs, peptides, proteins, and genes.[18,19,21,22]

**Molecularly Imprinted Hydrogels**

Design of a precise macromolecular architecture that can selectively recognize target molecules has gained significant attention because of its potential applications for separation processes, immunoassays,
biosensors, and catalysis. Molecular imprinting technology has been developed as a response to the need to create such architectures. In general, molecular imprinting within polymers involves formation of prepolymerization complex between the template molecule and functional monomers, polymerization in the presence of a cross-linking agent and an appropriate solvent, and removal of the template. Once the template is removed, the polymer network may have specific recognition elements for the target (or template) molecules. This nanoimprinting process is of great importance because it can create three-dimensional binding cavities for specific target molecules.

Because most recognition processes are associated with three-dimensional structure of the recognition site, it is preferable to limit the movement of the polymer chain that may affect affinity or selectivity to target molecules. Therefore, conventional methods to prepare molecularly imprinted polymers have used high ratios of the cross-linking agent to functional monomers, which leads to formation of rigid polymer matrix with low average molecular mass between cross-links. On the contrary, imprinting within hydrogels requires different methods because they undergo changes in three-dimensional structure upon coming in contact with water. To maintain imprinting structure in an aqueous environment, hydrogels have been prepared by spatially varying cross-linking density. As density fluctuations in the polymer network include microregions of localized higher cross-linking, hydrogels could retain an effective imprinting structure as well as proper rigidity to produce adequate specificity. Another promising strategy for imprinting within hydrogels is to match polymerization and rebinding solvents in terms of dielectric constant, polarity, and protic nature. This may reduce differences in swelling behavior, resulting in high binding affinity to target molecules. Also, in designing the network architecture for hydrogels, it is important to choose the length of the functional monomer and the molecular mass of the cross-linking monomer to endow with specificity to target molecules.

Molecular imprinting provides shape-specific cavities (or nanovacuoles) that match the template molecule or chemical groups capable of specifically interacting with the template molecule. Of various polymers, ethylene glycol dimethacrylate and methacrylic acid have been most widely used for the formation of imprinted polymers, where template molecules can be antibiotics, carbohydrates, peptides, enzymes, and enzymes. Alvarez-Lorenzo et al. and Hiratani et al. have developed molecularly imprinted hydrogels by polymerizing in the presence of template molecule, functional monomer, and thermo-sensitive monomer. These hydrogels showed high affinity to target molecules as well as stimuli-sensitive recognition, by which the imprinted sites disappeared upon gel swelling and reformed upon shrinking.

The imprinted hydrogels, sensitive to analyte, have been the focus of many investigations for controlled drug release. A few examples are shown in Fig. 2. Fig. 2A shows that enzymes may be included in the hydrogel to invoke local pH changes by binding to analyte, and thus initiate the hydrogel swelling, modulating the drug release rate; in Fig. 2B, cross-links can lose their function by free analytes and this leads to hydrogel swelling to change the drug release rate; and in Fig. 2C, binding of analytes to specific sites or functional groups on the polymer backbone may change hydrophilicity (or hydrophobicity) of hydrogels, inducing swelling (or shrinking) in an aqueous environment. It should be emphasized, however, that the currently available imprinting techniques involve nonspecific binding sites that decrease the specificity to target molecules. The precise control of the network structure of hydrogels via nanotechnology will contribute to a number of applications, including microfluidic devices, biomimetic sensors, drug delivery system, and membrane separation technology.

**Hydrogel Nanoparticles**

Because of their biocompatibility and soft rubbery nature, hydrogels have been extensively studied in biomedical and pharmaceutical fields. Macroscopic hydrogels have been studied for sustained drug delivery owing to their slow swelling kinetics. Microparticulate hydrogels for drug delivery have been examined more widely because of their unique properties resulting from small size. Initially, hydrophobic nano- and microparticles have been used extensively for systemic drug delivery, but it was soon found out that they were readily taken up by the reticuloendothelial system, and this exhibited short residence time in blood. Thus, in an attempt to improve hydrophilicity for prolonged circulation time, the surfaces of the hydrophobic nanoparticles have been modified by conjugating, blending, and coating with hydrophilic polymers, such as polyethylene glycol (PEG) and PEG-containing block copolymers.

Hydrogel nanoparticles have a special role in drug delivery in the sense that they have all the advantages of both nanoparticles and hydrogels with regard to the particle size and hydrophilicity. Hydrogel nanoparticles can swell rapidly because of large surface area and short diffusion path length for water. They can be modified to have reactive groups on the surface and are useful to introduce functional moieties, such as targeting and other bioactive moieties. Hydrogel nanoparticles consisting of stimuli-responsive polymers may exhibit corresponding responsive properties, which
are often found to become much faster than bulk hydrogels. Studies of hydrogel nanoparticle have intensified during the past decade because of enormous potentials in the development and implementation of new stimuli-responsive or smart materials, biomimetics, biosensors, artificial muscles, drug delivery systems, and chemical separation systems.

Chemically cross-linked hydrogel nanoparticles have been prepared in the presence of hydrophilic monomers, cross-linking agents, and emulsifiers. Advances in technology have enabled precise control of the core–shell structure of hydrogel nanoparticles. The core–shell nanoparticles have been synthesized to modify surface properties of core particles or to provide stimuli-sensitivity for nonresponsive particles. Recently, multiresponsive core–shell hydrogel nanoparticles have also been developed by Jones and Lyon and Gan and Lyon. They synthesized temperature- and pH-responsive hydrogel nanoparticles with core–shell morphologies, where core particles composed of PNIPAM were prepared via aqueous free radical polymerization, and then used as nuclei for subsequent polymerization of acrylic acid copolymers. Their swelling/deswelling thermodynamics were easily controlled by chemical manipulation of the core and shell structures, thus displaying both temperature and pH dependence. Without chemical cross-linking, core–shell hydrogel nanoparticles can also be prepared on the basis of the electrostatic interaction between water-soluble polymers. Prokop et al. have demonstrated that by atomizing the aqueous solution containing core polymer with negative charge, the nanosize droplets are encapsulated with cationic polymer solution by the electrostatic interaction (Fig. 3). This methodology showed promising potential as a protein delivery system.

Self-assembled hydrogel nanoparticles based on hydrophobically modified polysaccharides have been extensively studied as a drug carrier because of their excellent biocompatibility and ease of preparation. It is well known that polymeric amphiphiles, upon contact with an aqueous environment, spontaneously form micelles or micelle-like self-aggregates via undergoing intra- or intermolecular associations between hydrophobic moieties, primarily to minimize interfacial free energy. Hydrophobically modified polysaccharides are also known to self-assemble in aqueous media to form a unique core–shell structure that consists of hydrophobic segments and hydrophilic segments, respectively (Fig. 4). This type of hydrogels have multiple inner cores, which physically crosslink the hydrophilic polymer chains. A number of polysaccharides have been investigated to create self-assembling systems, including dextran, glycol chitosan, ...
pullulan, curdlan, and curdlan, These polysaccharides are natural water-soluble polymers that are inherently biocompatible and biodegradable. The core–shell structure of self-assembled hydrogels can be employed as a potential delivery system that can effectively deliver hydrophobic drugs. It has been recently demonstrated that hydrophobically modified polysaccharides capable of forming nano-sized self-aggregates can imbibe hydrophobic drugs and release them in a sustained manner.

Hydrogel Coating on the Surfaces

Surfaces of hydrophobic substrates have been frequently modified with hydrophilic polymers to achieve desirable properties for in vivo applications. Surface modification with hydrophilic polymers is known to minimize nonspecific interactions with blood proteins, cells, and tissues. The hydrophilic polymers commonly used for surface coating include PEG, polysaccharides, and poly(vinyl alcohol). To physically coat hydrophilic polymers on the nanoparticles, the solvent extraction/evaporation method has been used. After the oil-in-water emulsion is prepared by adding the organic solution containing a hydrophobic polymer into the aqueous solution of a hydrophilic homopolymer or a block copolymer, the organic solvent is removed by evaporation or extraction, thus forming the hydrogel layer on the formed nanoparticles. The outer layer of a hydrophilic polymer in the nanoparticle is anchored by various interactions with the core polymer chains, such as physical entanglement, hydrophobic interaction, and hydrogen bonding. This approach has been frequently used for surface modification of biodegradable nanoparticles, such as poly(D,L-lactide) (PLA), poly(lactide-co-glycolide), and polyphosphazene.

The hydrogel coating on the nanoparticles has also been achieved by radical polymerization. For poly(isobutyl cyanoacrylate) (PIBCA), the monomer was emulsified in an aqueous solution containing PEG that acts as a nucleophile initiator of polymerization through its hydroxyl terminal groups. Once the aqueous pH is adjusted to 1, polymerization is initiated, thus forming PEG-coated PIBCA nanoparticles. PNIPAM has been coated on the nanoparticles by radical polymerization in the presence of hydrophobic
nanoparticles to be coated, \( N,N'-\text{methylenebisacrylamide} \) (cross-linker), ammonium persulfate (initiator), and sodium dodecyl sulfate (emulsifier). The thickness of the outer hydrogel layer on the nanoparticles was readily controlled by varying the concentrations of the monomer and emulsifier.\(^{[64]}\)

Hydrogels that coat metal and semiconductor nanoparticles are of considerable interest because of their unique size-dependent physicochemical properties.\(^{[65–67]}\) Precise control of the structure and surface properties of nanoparticle would make them more attractive for use in biomedical applications. Inorganic nanoparticles have been conjugated to biomolecules such as sugars, peptides, proteins, and DNA. Such conjugates showed many advantages as fluorescent biological labels,\(^{[66–68]}\) primarily appearing from inorganic nanoparticles, including high quantum efficiencies, optical activity over biocompatible wavelengths, and chemical or photochemical stability. It should be emphasized that in spite of numerous potential applications, inorganic nanoparticles to be coated, \( N,N'-\text{methylenebisacrylamide} \) (cross-linker), ammonium persulfate (initiator), and sodium dodecyl sulfate (emulsifier). The thickness of the outer hydrogel layer on the nanoparticles was readily controlled by varying the concentrations of the monomer and emulsifier.\(^{[64]}\)

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nanoparticles have suffered from their aggregation and lack of biocompatibility. Hydrogel coating on such nanoparticles may not only prevent their aggregation by changing the surface hydrophilicity, but also improve their biocompatibility. Furthermore, use of stimuli-responsive hydrogels may provide unique properties for nanoparticles. Recent efforts have led to the development of hydrogel-coated inorganic nanoparticles that exhibit structural changes responsive to stimuli such as light. For example, hydrogel-coated gold nanoparticles have been prepared using surfactant-stimuli such as light. For example, hydrogel-coated particles that exhibit structural changes responsive to stimuli-responsive hydrogels may provide unique methods to improve their biocompatibility. Furthermore, use of stimuli-responsive hydrogels will improve the surface characteristics. These technologies will accelerate the development of various drug delivery and biomedical devices, as well as other electronic and photonic devices.

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REFERENCES


