Swelling and thermal properties of porous PNIPAM/PEG hydrogels prepared by radiation polymerization (Postprint)

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Abstract

In this study, a series of porous intelligent hydrogels exhibiting lower critical solution temperature (LCST) and rapid response characteristics were synthesized via radiation polymerization, employing N-isopropyl acrylamide as the monomer, polyethylene glycol (PEG) as the pore-forming agent, and N,N-methylene-bis-acrylamide as the crosslinking agent. The hydrogels were characterized by Fourier transform infrared spectroscopy, and the effects of radiation dose on their swelling and thermal behaviors were investigated. Their surface morphologies were examined using scanning electron microscopy. The results demonstrated that PEG molecules functioned solely as a pore-forming agent during the cross-linked polymerization. The swelling ratios of the hydrogels decreased with increasing radiation dose. The LCST was approximately 37°C and showed minimal variation with radiation dose. The frozen water content of the PNIPAM/PEG6000 hydrogel decreased with increasing radiation dose and was higher than that of the PNIPAM hydrogel at 15 kGy. Macropores in the hydrogels were created by the PEG agent, while hydrogels without PEG exhibited a dense surface. The porous hydrogels show promise for applications in the field of artificial intelligence materials.

Full Text

Preamble

Swelling and thermal properties of porous PNIPAM/PEG hydrogels prepared by radiation polymerization

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Abstract

In this study, a series of porous intelligent hydrogels were synthesized by radiation polymerization, exhibiting lower critical solution temperature (LCST) behavior and fast response characteristics. The hydrogels were prepared using N-isopropyl acrylamide as monomer, polyethylene glycol (PEG) as pore-forming agent, and N,N-methylene-bis-acrylamide as crosslinking agent. The hydrogels were characterized by Fourier transform infrared spectroscopy, and the influence of radiation dose on their swelling and thermal behaviors was investigated. Surface morphologies were examined by scanning electron microscopy. The results showed that PEG molecules functioned solely as pore-forming agents in the cross-linked polymerization without participating in the reaction. Swelling ratios decreased with increasing radiation dose. The LCST was approximately 37°C and varied little with radiation dose. The frozen water content of PNIPAM/PEG6000 hydrogel decreased with increasing radiation dose and was greater than that of PNIPAM hydrogel at 15 kGy. Hydrogel macropores were successfully prepared using PEG, while hydrogels without PEG exhibited dense surfaces. These porous hydrogels show promise for applications in artificial intelligence materials.

Key words: PNIPAM, Swelling properties, Thermal properties, Radiation polymerization

Introduction

Hydrogels are hydrophilic polymer networks that can absorb large amounts of water or biological fluids while remaining insoluble due to their three-dimensional cross-linked structure [1]. Stimuli-sensitive hydrogels can alter their swelling behavior, permeability, or mechanical strength in response to external stimuli such as pH changes [2], ionic strength [3], temperature [4], light [5], and electromagnetic radiation [6]. These materials have numerous applications, particularly in medical and pharmaceutical fields [7], including contact lenses [8], burn dressings [9], artificial corneas [10], soft tissue substitutes [11], separation analysis [12], tissue engineering [13], and immobilized enzymes [14].

However, these applications have been limited by low efficiency and slow response rates. Rapid-response PNIPAM hydrogels have been prepared through various methods, including the introduction of dynamic graft chains [15] and interpenetrating network structures [17]. The efficiency and response rate of hydrogels to external stimuli can be controlled by adjusting porosity, which enhances water sorption capability and improves response rate by reducing transport resistance. Therefore, creating porosity in hydrogels has been considered an important processing step.

Several techniques have been developed for preparing porous hydrogels, including phase-separation [18], water-soluble porogen technique [20], surfactant incorporation with subsequent extraction [21], freeze-drying [22], and gas forming [23]. The porous structure facilitates water migration through the large surface area within the pores. PNIPAM hydrogels can be prepared by chemical polymerization, radiation-induced polymerization, and interpenetrating polymer networks. Radiation-induced polymerization offers the advantage of sterilization without requiring initiators or cross-linking agents [24].

In this work, PNIPAM/PEG hydrogels were prepared by radiation polymerization using N-isopropyl acrylamide (NIPAM) as monomer and polyethylene glycol (PEG) as pore-forming agent. The influence of radiation dose on swelling and thermal properties is discussed. These porous PNIPAM/PEG hydrogels are promising candidates for controlled release polymer systems in pharmaceutical formulations.

2.1 Materials

NIPAM (AR, Tokyo Chemical Industry), N,N-methylene-bis-acrylamide (MBA, AR, Tianjin Kermel Chemical Reagent Development Center), PEG (AR, Shanghai Pharmaceutical Group Chemical Reagent Co., Ltd.).

2.2 Preparation of PNIPAM/PEG Hydrogels at Different Radiation Doses

The NIPAM monomer, MBA (2 wt%), and PEG (10 wt%, Mn=6000) were dissolved in water to prepare a pregel solution with total monomer concentration of 5 wt%. Dissolved oxygen was removed by bubbling nitrogen gas for 10 minutes, and the solutions were sealed in tubes before irradiation. Radiation polymerization was carried out using ^{60}Co-γ ray radioactive sources (Institute of Isotopes, Henan Academy of Sciences) with an activity of 7.4$\times$10^{15}$ Bq at doses of 8, 15, and 22 kGy (dose rate: 5 kGy/h). After irradiation, the tubes were stored for two days. The resulting gel samples were cut into thin slices (~3 mm thickness) and soaked in deionized water for 3 days with daily water changes to remove residual monomers and pore-forming agents. Finally, samples were dried to constant weight under vacuum. PNIPAM hydrogels were similarly prepared by homopolymerization of NIPAM monomer with MBA (2 wt%) in deionized water (10 mL).

2.3 Determination of Swelling Kinetics

Swelling properties were studied by measuring equilibrium swelling ratio using the classical gravimetric method. Hydrogels were dried in a 50°C vacuum oven for 24 h to obtain dry weight (m_0). Samples were then immersed in deionized water at 25°C and removed at regular intervals. Excess surface water was quickly wiped with gauze before weighing. After repeated equilibration, constant weight was considered as equilibrium weight (m) at time interval (t). Each sample was measured three times and averaged. The swelling ratio (SR) was defined as

2.4 Determination of Equilibrium Swelling and De-swelling Kinetics

Equilibrium swelling ratio (SR) is defined as where m is the hydrogel weight at equilibrium swelling at a given temperature. The volume phase transition characteristics were tested across temperatures from 25°C to 55°C, covering the lower critical solution temperature (LCST). At each predetermined temperature, dried hydrogels were allowed to swell for over 24 h and weighed after removing excess surface water with gauze. Samples were re-equilibrated three times at each temperature and averaged. The LCST was determined from the temperature at which the swelling ratio curve reached a plateau.

De-swelling behavior was measured beyond the LCST after hydrogels reached swelling equilibrium at 25°C. The gravimetric method was employed to study temperature response kinetics. After weighing m , samples were immersed in a 50°C water bath. At predetermined time intervals, hydrogels were removed and weighed after wiping excess surface water with gauze. The absorbed water at each temperature was calculated, with each sample measured three times and averaged. The water loss rate (LRw) was calculated using Eq.(3), where m_{25} is the water weight absorbed at swelling equilibrium at 25°C and m is the water weight at 50°C.

2.5 Determination of Gel Fraction

Gel fraction was measured by the classical gravimetric method. Hydrogels dried to constant weight (m_0) in a vacuum oven were placed in boiling distilled water for 4 h and repeatedly washed with deionized water to remove sol fractions. The hydrogels were then dried to constant weight (m). Each sample was measured three times. Gel fraction (Gf) was calculated using Eq.(4).

2.6 Fourier Transform Infrared Spectroscopy (FTIR) Analysis

Hydrogel samples were completely dried, ground to fine powder, and pressed into KBr pellets. Infrared absorption spectra were recorded using a Nicolet PROTE/GE/460 spectrometer in the range of 400–4000 cm^{-1}.

2.7 Differential Scanning Calorimetry (DSC) Analysis

The frozen and non-frozen water content of hydrogels was determined by DSC. Hydrogels in equilibrium swelling state at 20°C were cut into ~15 mg samples. Sealed empty sample pans were weighed and quickly frozen to –30°C in the DSC chamber. DSC was conducted using a STA449C integrated thermal analyzer

(NETZSCH, Germany) at a heating rate of 2°C/min under nitrogen atmosphere to test volume phase transition behavior and water evaporation processes.

2.8 Thermal Gravimetric (TG) Analysis

Thermal stability of hydrogels was evaluated by TG analysis. Samples (~20 mg) were dried to constant weight in vacuum, placed in sample pans, and analyzed using a STA449C TG (NETZSCH Co.) from 30–500°C at a heating rate of 10°C/min.

2.9 Scanning Electron Microscopy (SEM) Analysis

Surface morphology of hydrogels was investigated by SEM. Hydrogels were fully swollen in deionized water at 25°C and freeze-dried for 15 h to preserve porous structure. Freeze-dried samples were carefully fractured, mounted on aluminum stubs, and gold-coated. Surface morphologies were examined using a JSM-5610LV SEM (JEOL Corporation, Japan).

3.1 IR Spectra of Hydrogels

Figure 1 [Figure 1: see original paper] shows FTIR spectra of PNIPAM and PNIPAM/PEG hydrogels at 15 kGy radiation dose. Both spectra were similar, with an absorption band at 3200–3600 cm^{-1} attributed to -OH and -NH stretching vibrations. A typical saturated C-H vibration band appeared at 2800–3000 cm^{-1} with similar intensity in both curves. Each spectrum exhibited an amide I band at 1649 cm^{-1} from C=O stretching of PNIPAM and an amide II band at 1546 cm^{-1} from N-H rocking. Absorption bands at 1387 cm^{-1} and 1459 cm^{-1} were assigned to $-CH(CH_3)_2$ groups. No typical C-O-C absorption of PEG molecules was observed at 1050–1150 cm^{-1}, indicating that PEG molecules acted solely as pore-forming agents without participating in the cross-linked polymerization reaction.

3.2 Dependence of Swelling Properties on Radiation Dose

Figure 2 [Figure 2: see original paper] shows swelling kinetics of PNIPAM/PEG6000 hydrogel at different radiation doses at 25°C. Swelling ratio increased with time and approached equilibrium after approximately 30 h, while SR decreased with increasing radiation dose. As shown in Table 1 , gel fraction increased with radiation dose because higher energy intensity during polymerization leads to more complete monomer conversion and increased cross-linking density.

The quantitative relationship between cross-linking degree and absorbed dose is described by Charles [26]:

$$s + s^{0.5} = [p_0/q_0] + 2q_0^{-1}\mu_{2.0}^{-1}R^{-1}$$

where g is gel fraction, s is sol fraction (s = 1 - g), p_0 is the degradation degree, q_0 is the cross-linking degree per unit dose at 1 kGy, $_{2\cdot 0}$ is weight-average molecular weight, and R is radiation dose.

Within a certain radiation dose range, the gel fraction of PNIPAM/PEG6000 hydrogel increased with dose, resulting in greater elastic restoring force of the network and reduced osmotic pressure between the hydrogel interior and exterior. In Eq.(5), q_0 increases with radiation dose. Consequently, the equilibrium swelling ratio of PNIPAM/PEG hydrogels decreased with increasing radiation dose. However, hydrogels prepared at lower doses (e.g., 8 kGy) exhibited low strength despite high SR because water molecules could easily penetrate the network. As q_0 increased with radiation dose, more chemical bonds formed between molecules, creating a more closed system that hindered water penetration and decreased SR. Hydrogels became prone to brittle fracture at doses exceeding 22 kGy due to excessive cross-linking; therefore, 15 kGy was selected as the optimal dose for preparing PNIPAM/PEG porous hydrogels.

The phase transition properties of temperature-sensitive hydrogels are expressed by the water loss rate (LRw) at different temperatures. Higher LRw indicates more pronounced phase transition. Figure 3 shows the de-swelling kinetics of PNIPAM/PEG6000 hydrogels. The average LRw of hydrogels with PEG6000 was approximately 70% within 0.5 h, while PNIPAM hydrogel without PEG showed only ~15% LRw. During shrinking, water in PNIPAM/PEG6000 hydrogel could freely squeeze out. When PNIPAM hydrogel was exposed to 50°C water, phase separation occurred first at the surface, forming a dense layer that prevented water seepage and created numerous tiny bubbles due to increasing internal pressure. In contrast, porous PNIPAM/PEG6000 hydrogel did not form such a dense layer during contraction, and its porous structure facilitated water extrusion with minimal bubble formation.

Figure 4 [Figure 4: see original paper] shows the relationship between equilibrium swelling ratio and temperature for PNIPAM/PEG6000 hydrogel at different radiation doses. SR decreased with increasing temperature below LCST and remained similar above 37°C. Radiation dose had little effect on LCST, which remained around 37°C, demonstrating the temperature-sensitive heat-shrinkable behavior of PNIPAM/PEG6000 hydrogel.

3.3 Thermal Analysis of Hydrogels

The physicochemical properties of hydrogels are determined by interactions between the polymer cross-linked network and water. Three water states are generally recognized in hydrogels: bound water, free water (frozen water), and interstitial water [27]. Bound water forms hydrogen bonds with hydrophilic polymer groups, creating an integral structure with polymer chains. Free water exists in larger network spaces with hydrogen-bonding capability similar to ordinary water. Interstitial water exists in an intermediate state between bound and free water.

During temperature-induced shrinking, water is gradually lost from the network, with free and interstitial water being squeezed out while bound water remains. Consequently, LRw decreases with increasing swelling time until reaching equilibrium. DSC curves of PNIPAM/PEG hydrogels at different radiation doses show an endothermic peak near 0°C, indicating ice phase melting at temperatures lower than in pure water. Assuming the melting enthalpy of frozen water in hydrogels equals that of pure water ($333.7\ \mathrm{J \cdot g^{-1}}$), the frozen water content (Wf) and non-frozen water content (Wnf) can be calculated from the enthalpy (peak area) near 0°C using Eq.(6) (Fig. 5 [Figure 5: see original paper]).

Table 2 shows water content in different hydrogel states. At 0°C, hydrogel enthalpy was less than that of pure water due to different water states, indicating enthalpy changes in frozen water. The frozen water content was greater in PNIPAM/PEG6000 hydrogel than in PNIPAM hydrogel at 15 kGy. The endothermic peak of PNIPAM/PEG6000 hydrogel shifted to lower temperatures and decreased with increasing radiation dose, indicating decreasing frozen water and increasing non-frozen water content. This decrease in frozen water with increasing radiation dose reflects higher network density, lower swelling degree, and reduced frozen water throughout the network, consistent with swelling kinetics results.

Figure 6 [Figure 6: see original paper] shows that both PNIPAM/PEG6000 and PNIPAM hydrogels exhibit a single significant degradation step. The DTG curve indicates minimal reduction in thermal stability, demonstrating that introducing PEG6000 to create porous hydrogels did not alter the thermal degradation mechanism of the PNIPAM matrix.

3.4 SEM Analysis of Hydrogels

When hydrogels are dried under normal conditions, pore structure can collapse due to water loss. After freeze-drying, polymer chains become highly bound and the polymer network-water system exists in a solid state. During water sublimation, the internal polymer network structure is maintained without significant deformation. Therefore, freeze-drying after quenching was employed in this study. After freeze-drying, the cross-sectional morphology could be directly observed by SEM.

Figure 7 [Figure 7: see original paper] shows SEM images of PNIPAM hydrogel and porous PNIPAM/PEG6000 hydrogel cross-sections after quenching in liquid nitrogen. Hydrogels prepared without pore-forming agent showed denser surfaces with only folds formed during freeze-drying. In contrast, PNIPAM/PEG6000 hydrogel exhibited numerous obvious pores, providing channels for water, water-soluble nutrients, and metabolites to transport through the hydrogel.

4 Conclusions

PEG molecules acted solely as pore-forming agents in cross-linked polymerization without participating in the reaction. The equilibrium swelling ratio decreased with increasing radiation dose. The LCST remained around 37°C and was minimally affected by radiation dose. The frozen water content of PNIPAM/PEG6000 hydrogel was greater than that of PNIPAM hydrogel at 15 kGy and decreased with increasing radiation dose. These porous hydrogels show promise as controlled-release polymer systems for pharmaceutical formulations.

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