

Thermosensitive Behavior of Poly (*N*-isopropylacrylamide) Hydrogel Particles Prepared by Various Conditions

Hidenobu Shimizu, Takafumi Koshina, Risei Wada and Masaru Okabe
Department of Applied Chemistry, Faculty of Engineering, Kanagawa Institute of Technology,
1030 Shimo-ogino, Atsugi, Kanagawa, 243-0292, Japan
Fax: +81-46-242-8760, e-mail: shimizu@chem.kanagawa-it.ac.jp

Thermosensitive poly (*N*-isopropylacrylamide) (PNIPAM) hydrogel particles were prepared by precipitation polymerization in the aqueous medium at 70°C with varying an initiator concentration and characterization of the resulting particles was extensively investigated. Potassium persulfate was used as an initiator. Thermosensitive behavior of PNIPAM particles was evaluated by measuring the temperature dependence of the hydrodynamic size with dynamic light scattering. Below the lower critical solution temperature (LCST), the hydrogel particles were highly swollen with water and had average diameters in the range of 800-2200 nm. Above the LCST, the size decreased to 400-700 nm. In addition, the swelling ratio was found to increase drastically with increasing the initiator concentration, likely due to the presence of a hairy polymer on the particle surface. According to the particle size analysis by transmission electron microscopy, the particle size increased with increasing the initiator concentration. From these results, the polymerization mechanism of PNIPAM hydrogel particles was discussed.

Key words: hydrogel particles, thermosensitive polymer, poly (*N*-isopropylacrylamide), lower critical solution temperature, precipitation polymerization

1. INTRODUCTION

Submicron-sized hydrogel particles with thermosensitivity were first prepared from *N*-isopropylacrylamide (NIPAM) and *N*, *N*'-methylenebisacrylamide (MBAAm) by Pelton and Chibante in 1986 [1]. Since then many studies have been made on the colloidal properties of thermosensitive PNIPAM particles (particle size, electrophoretic mobility, affinity for proteins, etc.) [2-4].

Monodisperse PNIPAM particles can be generally produced by precipitation polymerization above their lower critical solution temperature (LCST) in water, and the sizes of the resultant particles are in the range of 350-550 nm in diameter. Smaller particles have been synthesized by using microemulsion polymerization [5] and emulsion polymerization [6, 7]. To date, however, little attention has been paid to the preparation of PNIPAM hydrogel particles in the 1-10 μ m size range. Particles in this size range have been of great interest in biomedical field, information industry, microelectronics, etc.

Dowding et al. reported the synthesis of PNIPAM hydrogel particles in the diameter of 2.0 μ m at 25°C by using inverse suspension polymerization [8]. In this method, however, some residual emulsifier or stabilizer remains adsorbed or grafted on the particle surface. We present here the preparation of larger PNIPAM particles with clean surfaces by the change in polymerization conditions. The effect of initiator concentration during polymerization on particle size and thermosensitive behavior has been investigated and discussed.

2. EXPERIMENTAL

2.1 Materials

N-isopropylacrylamide (NIPAM, Acros Organic) was recrystallized from a 1:1 (v/v) mixture of hexane and toluene before use. Potassium persulfate (KPS) (Kanto Chemical Co., Inc.) as an initiator was recrystallized from the distilled water. *N*, *N*'-methylenebisacrylamide (MBAAm) was purchased from Kanto Chemical Co., Inc. and used as received.

2.2 Preparation of thermosensitive hydrogel particles

A mixture of 2.5 g NIPAM, 0.025 g MBAAm, and 45 g distilled water was put into a 100 ml round-bottom flask equipped with a stirrer, a nitrogen-inducing tube, and a condenser. Nitrogen gas was blown into the flask to purge oxygen. The system was kept at 70°C in a water bath. Polymerization was initiated via addition of a given amount of KPS dissolved in 2.5 g water. The reaction was allowed to proceed at 70°C for 1 h to reach almost 100% conversion. The resulting PNIPAM particles were centrifuged to separate them from the medium. They were redispersed in distilled water. This purification process was repeated three times.

2.3 Characterization of hydrogel particles

The size and morphology of PNIPAM particles were observed by means of transmission electron microscopy (TEM) (JEOL EX-2000). Small amounts of the particle dispersion were infinitely diluted with distilled water. The diluted samples were applied on collodion-coated Cu grids.

The hydrodynamic diameters of PNIPAM particles were measured by using a homemade light scattering apparatus equipped with a multi- τ digital time correlator (ALV-5000) and a He-Ne laser ($\lambda=632.8$ nm). The

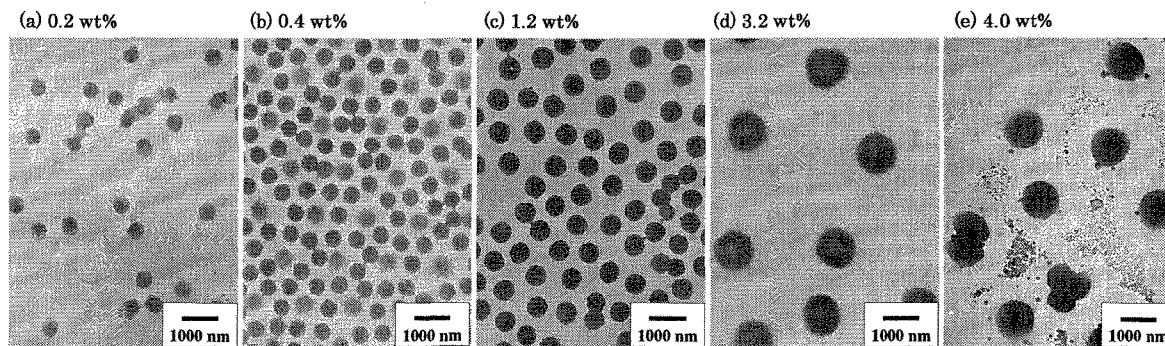


Fig. 1. Transmission electron micrographs of PNIPAM hydrogel particles prepared by precipitation polymerization with varying initiator concentration.

measurement angle was fixed at 90° .

3. RESULTS AND DISCUSSION

3.1 Particle size and morphology

PNIPAM hydrogel particles were prepared by precipitation polymerization at 70°C in aqueous medium with varying an initiator concentration from 0.04 wt % to 4.8 wt % (based on NIPAM monomer weight). The TEM micrographs of several of these particles are shown in Fig. 1. All particles were almost spherical and the size distribution was narrow. However, a large number of tiny particles were observed for the particles prepared by higher initiator concentration (especially above 4.0 wt %). In addition, the interface of these particles gave fuzzy images, likely due to the presence of a hairy polymer on the particle surface.

As evidenced from TEM images, an average particle size was around 350 nm at lower initiator concentration, whereas the size increased to *ca.* 1200 nm when the initiator concentration increased above 3.0 wt %. The effect of initiator concentration on particle size is summarized in Fig. 2. It can be found from Fig. 2 that the particle size increased with increasing the initiator concentration.

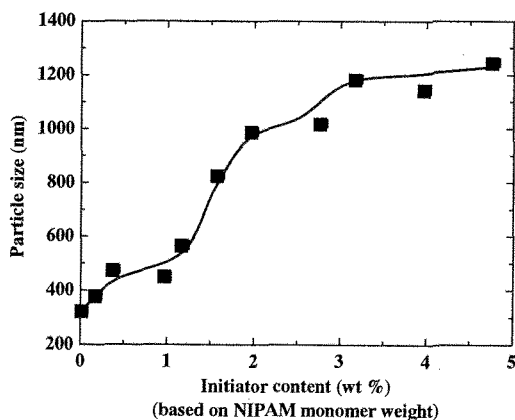


Fig. 2. Effect of initiator content on particle size as determined by TEM.

3.2 Temperature-effect on hydrodynamic diameter

Hydrodynamic diameters of PNIPAM hydrogel particles were measured with dynamic light scattering in diluted dispersions. Fig. 3 shows the variation of the

hydrodynamic diameter as a function of temperature. All samples exhibited a narrowly single peak at any temperature. As expected, the hydrodynamic diameters were dependent on the dispersion temperature. But, the thermosensitive behavior showed a different trend for the initiator concentration. Below 1.2 wt % of initiator concentration, a remarkable change of the diameter was observed around 32°C , which corresponds to the LCST of PNIPAM chains [9]. On the other hand, a clear transition temperature was not observed above 1.6 wt %. The diameter decreased continuously and then kept constant with increasing temperature.

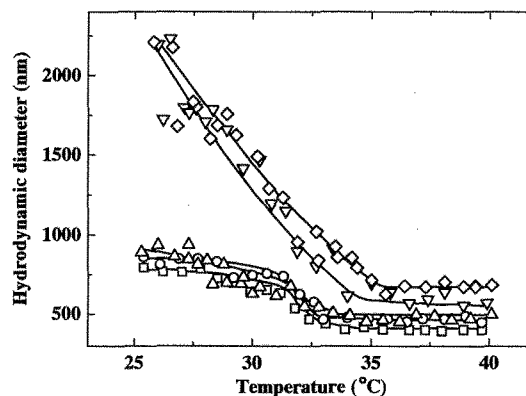


Fig. 3. Temperature dependence of hydrodynamic diameter of PNIPAM particles prepared with initiator concentration of (□) 0.2 wt %, (○) 0.4 wt %, (△) 1.2 wt %, (▽) 3.2 wt %, and (◇) 4.0 wt %.

The hydrodynamic diameters of hydrogel particles also depended on the initiator concentration. PNIPAM particles produced by an initiator concentration of 4.0 wt % had an average hydrodynamic diameter of 2200 nm at 25°C . The diameter decreased to 700 nm at 40°C . On the other hand, the diameters of PNIPAM particles prepared with an initiator concentration of 0.2 wt % varied from 800 nm at 25°C to 400 nm at 40°C . The dependence of the diameters on the initiator concentration was basically in agreement with the TEM results. However, the hydrodynamic size at a temperature above the LCST was relatively smaller than the size of dried particles measured by TEM. This trend seems to be remarkable for PNIPAM particles prepared with higher initiator concentration. That is because hydrogel particles may have a tendency to flatten and spread on the TEM grid during the sample preparation.

3.3 Swelling/Deswelling

The swelling-deswelling process can be described quantitatively in terms of the amount of solvent filled in hydrogel particles. The ratio of swelling is defined as $(d/d_0)^3$, where d is the hydrodynamic diameter and d_0 is that at 40°C. We calculated the swelling ratio from Fig. 3. The results are shown in Fig. 4. The data illustrated in Fig. 4 indicate that the swelling ratio of these hydrogel particles increased as the temperature dropped. This would reflect the hydration of the amide moieties in PNIPAM chains. Further, it is interesting to note that the swelling ratio of these particles is strongly affected by the concentration of the initiator employed and the ratio ranged from 7 to 35 as the concentration increased from 0.2 wt % to 4.0 wt %. However, the swelling ratio did not change in proportion to the initiator content and it exhibited the almost same change as the particle size did (see Fig. 2). Several researchers have reported that the swelling ratio depended on the concentration of cross-linker, with a decrease in cross-linker concentration resulting in an increased degree of swelling [6, 10]. But, in the present study, an amount of cross-linker in the feed was constant, and thus the dependence on the initiator concentration may be due to the difference in particle formation process. We will discuss the mechanism of this process in the next section.

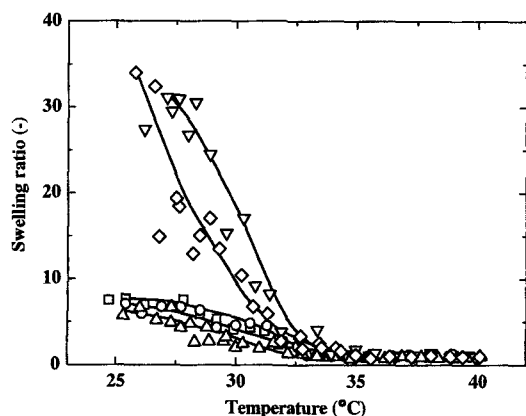


Fig. 4. Temperature dependence of swelling ratio of PNIPAM particles prepared with initiator concentration of (□) 0.2 wt %, (○) 0.4 wt %, (△) 1.2 wt %, (▽) 3.2 wt %, and (◇) 4.0 wt %.

3.4 Mechanism of particle formation

In the present study, precipitation polymerization was used to produce PNIPAM hydrogel particles because this is a simple and useful method. In precipitation polymerization [11], the monomer and the initiator are both soluble in the polymerization medium, but the medium is a poor solvent for the resulting polymer. PNIPAM chains are insoluble in the aqueous medium above LCST and thus precipitation polymerization can be applied for the production of colloiddally stable thermosensitive PNIPAM particles.

Let us now consider the mechanism of precipitation polymerization of NIPAM with MBAAm. At the start of the process, NIPAM and MBAAm are present in a

homogeneous solution. Adding KPS as an initiator to the polymerization medium, KPS decomposes and the free radicals react with water-soluble NIPAM monomer to form oligomeric radicals. The growing PNIPAM chains, which undergo a phase separation into dense globules, precipitate to form precursor particles. At this stage, the solution turns translucent. These precursors coagulate with each other until mature particles reach efficient stabilization through the ionic surface charges provided by the anionic initiator.

According to the above-mentioned mechanism, an increase in an initiator concentration could provide a large number of colloiddally stable precursor particles, resulting in the formation of smaller particles. The TEM results shown in Fig. 1 indicate that some smaller particles can be observed at higher initiator concentration. But, the effect of initiator content on diameter of PNIPMA particles showed unexpected results; the higher the concentration of the initiator was, the larger the diameter of the final particles was. This may be related to the extent of aggregation of precursor particles. An increase in the initiator concentration led to a large number of precursors. This would facilitate aggregation reaction between the precursor particles, resulting in the formation of larger particles. In addition, each final particle would consist of many precursor particles, which probably not chemically but physically interact with each other. As a result, a greater degree of swelling would take place for particles prepared with higher concentration of initiator as shown in Fig. 4. These particles with high swelling ratio might decompose to smaller ones by strong mechanical forces. Detailed investigations will be described elsewhere.

4. CONCLUSIONS

Precipitation polymerization of NIPAM in the aqueous medium at 70°C with varying the initiator concentration leads to the following conclusions:

1. PNIPAM hydrogel particles have a narrow size distribution irrespective of the initiator concentration.
2. Particle size increases with increasing the initiator concentration from 350 nm at 0.04 wt % to 1200 nm at 4.8 wt %.
3. A greater degree of swelling is observed for particles prepared with higher initiator concentration. This has been ascribed to the presence of hairy structure on the surface.

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