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SHORT COMMUNICATION

A new strategy to prepare temperature-sensitive poly(*N*-isopropylacrylamide) microgels

Jian-Tao Zhang · Xiang-Li Liu ·
Alfred Fahr · Klaus D. Jandt

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Abstract In this study, a new method was developed to prepare temperature-sensitive poly(*N*-isopropylacrylamide) microgels by free radical precipitation polymerization using siloxane coupling agent as the new crosslinker. Ammonium persulfate acted as the initiator for the radical copolymerization as well as the catalyst for the hydrolysis/condensation of the siloxane groups. The particle diameter and polydispersity of the microgels were measured by photon correlation spectroscopy and the results display that the microgels are monodisperse. The microgels exhibit temperature sensitivity and the phase transition temperature is approximately 31 °C. Furthermore, the diameter of the microgels changes upon heating and cooling processes. These were observed to be reversible. The novel crosslinking method described herein is the condensation of siloxane groups, which is totally different from the traditional double-vinyl crosslinkers. This innovative approach offers an alternative path to prepare functional core–shell particles and inorganic/organic hybrid materials.

Keywords Microgel · Temperature sensitive · Poly(*N*-isopropylacrylamide) · Siloxane coupling agent

J.-T. Zhang · K. D. Jandt (✉)
Institute of Materials Science and Technology (IMT),
Friedrich-Schiller-University Jena,
Löbdergraben 32,
07743 Jena, Germany
e-mail: k.jandt@uni-jena.de

X.-L. Liu · A. Fahr
Department of Pharmaceutical Technology,
Friedrich-Schiller-University Jena,
Lessingstr. 8,
07743 Jena, Germany

Introduction

Temperature change is a widely observed phenomenon in nature, such as in physiological systems. Temperature-sensitive materials have, therefore, attracted significant interest of many researchers due to their ability of intelligent response to external temperature changes. Perhaps the most extensively investigated class of responsive polymers are temperature-sensitive poly(*N*-isopropylacrylamide) (PNIPAAm), which exhibit a phase transition, named lower critical solution temperature (LCST) around 32–34 °C, which could be adjusted to 37 °C by copolymerization with a more hydrophilic monomer [1, 2]. PNIPAAm undergoes a reversible phase transition caused by the coil-to-globule transition close to its LCST. Due to this unique property, PNIPAAm has been designed into versatile forms in the field of material sciences, such as bulk hydrogels, microgels, brushes, spheres, micelles, etc. [2–4]. Colloidal microgel particles composed of stimuli-responsive polymers have attracted considerable attention due to their importance from both academic and application viewpoints [5–11].

PNIPAAm-related microgels have been utilized to design sensors, drug delivery systems and so on [7, 9, 11]. For example, Serpe et al. have studied the loading and release of the anti-cancer drug, doxorubicin, from the PNIPAAm microgel films and they found the materials exhibited temperature-dependent release properties [9].

Pelton and Chibante [8] first reported PNIPAAm microgels and, in due course, they have been thoroughly investigated theoretically and experimentally. For example, Hellweg et al. [10] found that concentrated PNIPAAm microgels can form colloidal crystallization and the crosslinker content and the internal structure of the particles do not have a great influence on the final colloidal crystals. Huang and Hu [11] also synthesized bulk hydrogels by covalently bonding self-assembled microgels. The covalent bonding contributes to structural stability and self-assembly provides the gel with the crystal structures that diffract light, resulting in colors [11]. pH sensitivity could be introduced by copolymerization with ionic monomers during the preparation process. Microgels with core–shell or core–shell–shell structures have been developed through seeded polymerization technique: the core was firstly synthesized by precipitation polymerization and then acted as nuclei at a higher temperature for the coating of the shell parts [12, 13]. For example, Hellweg et al. have prepared polystyrene (PS) core/PNIPAAm shell hybrid particles and investigated the swelling properties. The core–shell structure of the particles was revealed by means of small angle neutron scattering [13]. PNIPAAm composite microgels have also been prepared by introducing functional groups into the particles, which could act as reactors for the synthesis of inorganic nanoparticles [14].

So far, PNIPAAm microgels were prepared by the precipitation polymerizations, where persulfates and sodium dodecyl sulfate (SDS) were used as the initiator and stabilizer, respectively. Double vinyl monomers, such as *N*,*N*′-methylenbisacrylamide (MBAAm) or ethylene glycol dimethacrylate (EGDMA), were used as crosslinkers to prevent the microgels from dissolving in water at low temperature [5]. Diacrylated polyethylene glycol was also employed to prepare PNIPAAm microgels [15]. Kuckling et al. have developed a novel method to prepare thermosensitive nanogels from photo-crosslinkable copolymers of NIPAAm and dimethyl maleinimido acrylamide. The particles were formed by UV irradiation of the polymer solution in water at 45 °C [16, 17]. In these reaction systems, no other reactive functional groups could react with inorganic monomers, which makes it difficult to prepare inorganic/organic composite materials, such as core–shell particles through simple reactions.

In this communication, temperature-sensitive microgels were prepared by precipitation polymerization method using 3-methacryloxypropyl trimethoxysilane (MPTMS) as the co-monomer as well as the new crosslinker to generate the PNIPAAm microgel networks. MPTMS is a bifunctional molecule capable of reacting with vinyl monomers via its methacryloxyl group and with hydroxyl group through hydrolysis/condensation of methoxysilane groups, which has been extensively utilized to modify many inorganic materials [18–20]. Herein, copolymerization of NIPAAm with MPTMS was carried out at 70 °C in water using ammonium persulfate (APS) as an initiator. Due to the acid environment caused by APS, the hydrolysis/condensation of methoxysilane groups resulted in the formation of crosslinked microgels. This crosslinking method is, to the knowledge of the authors, reported for the first time to prepare temperature-sensitive PNIPAAm microgels. It provides a new way to prepare responsive, hybrid organic/inorganic nanoparticles with core–shell structures because of the different reaction types of the polymerization and crosslinking. Moreover, due to the degradability of Si–O–Si bonds in hydrofluoric acid, these microgels crosslinked by siloxane coupling agent have potential applications as the templates to prepare highly ordered, porous polymeric materials with well-defined structures and pore sizes, which could be simply adjusted by changing the environmental temperature.

Experimental

Materials

N-isopropylacrylamide (NIPAAm) was purchased from Sigma-Aldrich Logistik GmbH (Schnelldorf, Germany) and purified by recrystallization in hexane. 3-methacryloxypropyl trimethoxysilane (MPTMS, Acros) was purchased from KMF Laborchemie Handels GmbH, Leipzig, Germany and used without purification. Ammonium persulfate (APS) and sodium dodecyl sulfate (SDS) were used as supplied by Sigma-Aldrich.

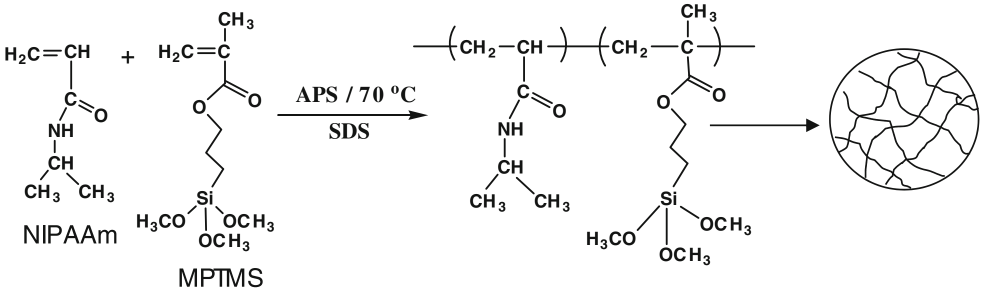
Preparation of PNIPAAm–MPTMS microgels

PNIPAAm–MPTMS microgels were prepared by precipitation polymerization. Briefly, 20 μl MPTMS and 1 ml SDS (10 mg/ml) were added into 10 ml NIPAAm (20 mg/ml) solution and nitrogen was bubbled for 30 min to remove oxygen. After being stabilized for 30 min at 70 °C, the solution was initiated by addition of 1 ml APS (8 mg/ml), which was degassed by nitrogen. The reactions were carried out at 70 °C for 6 h. Then the particles were purified via dialysis (dialysis membrane, MWCO 10,000, Sigma) against water for 2 weeks. A control sample was prepared for comparison as described above without adding SDS.

Characterization of PNIPAAm–MPTMS microgels

Microgel particle sizes and polydispersities were determined via photon correlation spectroscopy (PCS, Nano-ZS, Malvern Instruments). Dialysis dispersions were diluted and the samples were allowed to equilibrate at each temperature point for 5 min before data collection. Each data presented in this paper represents the average value of five measurements with a 60-s integration time for each measurement. The measurement angle was 173°. Data were analyzed with Dispersion Technology Software 4.20. To study the reaction kinetics, 50 μl reaction solution was taken out at given time points and was diluted with 20 folds water. Then the diameter and the scattering intensity

Scheme 1 The formation scheme of the temperature-sensitive PNIPAAm–MPTMS microgels initiated/catalyzed by APS at 70 °C



(derived count rate) were immediately measured by PCS. Morphologies of the microgel particles were observed via scanning electron microscopy (SEM, Leica 440i). The diluted dispersions were dropped onto mica substrate and dried at room temperature in air. The samples were coated with gold vapor before observation.

Results and discussion

Monodispersed PNIPAAm–MPTMS microgels were successfully prepared through free radical precipitation polymerization technique. The formation scheme of the temperature-sensitive PNIPAAm–MPTMS microgels is illustrated in Scheme 1. At 70 °C, APS decomposed and generated free radicals to initiate the copolymerization of NIPAAm with MPTMS. At the same time, the hydrolysis/condensation of methoxysilane groups were catalyzed to form crosslinking points by the acid environment due to the decomposition of APS (pH=3, determined by a pH meter). With both reactions proceeding, monodispersed PNIPAAm–MPTMS microgels formed. After 45 min of polymerization/crosslinking, the transparent solution turned into a “milky” dispersion; the solution still remained “milky” even though the solution was kept at room temperature after 6 h of polymerization/crosslinking, indicating the formation of microgels [16]. This “milky” appearance is due to a change of light scattering caused by a change in the dimension of the microgel. The incorporation of MPTMS into the microgels has been confirmed by X-ray photoelectron spectroscopy. The peak of binding energy at 101.4 eV is ascribed to the existence of Si atoms, and the concentration of Si is 0.6, from which the MPTMS content was calculated. The mol ratio of MPTMS in the microgels is about 5%, which is well in agreement with the fed composition.

Many papers have reported the reaction kinetics and new synthesis of PNIPAAm-related microgels. For example, Wu et al. have studied the reaction kinetics of PNIPAAm microgels crosslinked by BMAAm [21]; it was found the reactions were very fast and high conversion was obtained within the first hour. In addition, many PNIPAAm-based microgels were prepared by carrying out the polymerization for 2 h [22], 4 h [23], or 6 h [24]. Therefore, we chose the reaction time to be 6 h, which should be enough for the reaction. In the current study, the reaction kinetics was studied and the average hydrodynamic diameter of the microgels as a function of reaction time is shown in Fig. 1, from which it can be observed that the diameter of the microgels increased with reaction time within 1.5 h, then decreased slightly to reach stability in the following time. This is probably because the polymerization/crosslinking mechanism of MPTMS is different from that of MBAAm. Unlike the di-vinyl crosslinkers, such as MBAAm and EGDMA, the reaction rates of the two functional groups of MPTMS are different because they belong to different reaction types. During the polymerization/crosslinking process, the hydrolysis/condensation of methoxysilane groups might not be as fast as the radical copolymerization of the NIPAAm with the methacryloxyl groups. From Fig. 1, it is also seen that the derived count rate increases greatly within 1.5 h and becomes stable after the first stage. This implies that the conversion of the monomers and the particle number remarkably increased at the beginning stage and the particle nucleation stopped after 1.5 h. Within 1.5 h, the hydrolysis/condensation of siloxane groups inside

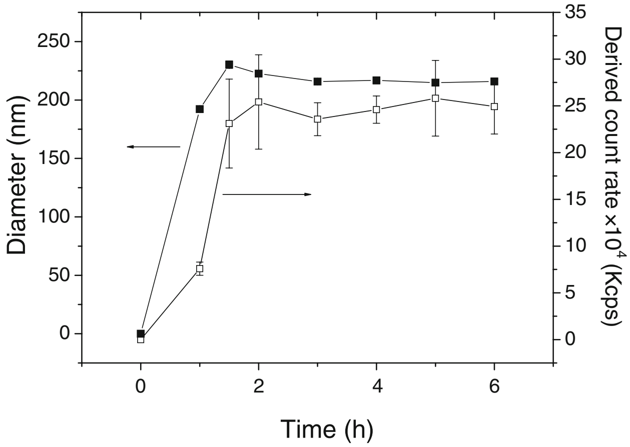


Fig. 1 The average hydrodynamic diameter and the derived count rate of the microgels as a function of reaction time. During the polymerization, 50 µl reaction solution was taken out at given time points and was diluted with 20 folds water. Then the diameter and the scattering intensity (derived count rate) were immediately measured by PCS at 22 °C

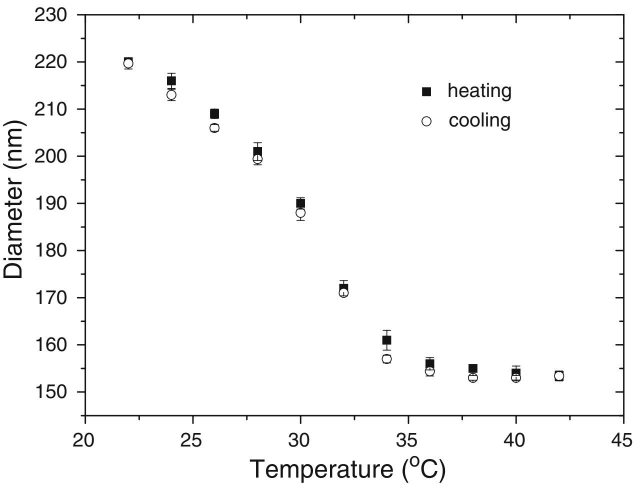


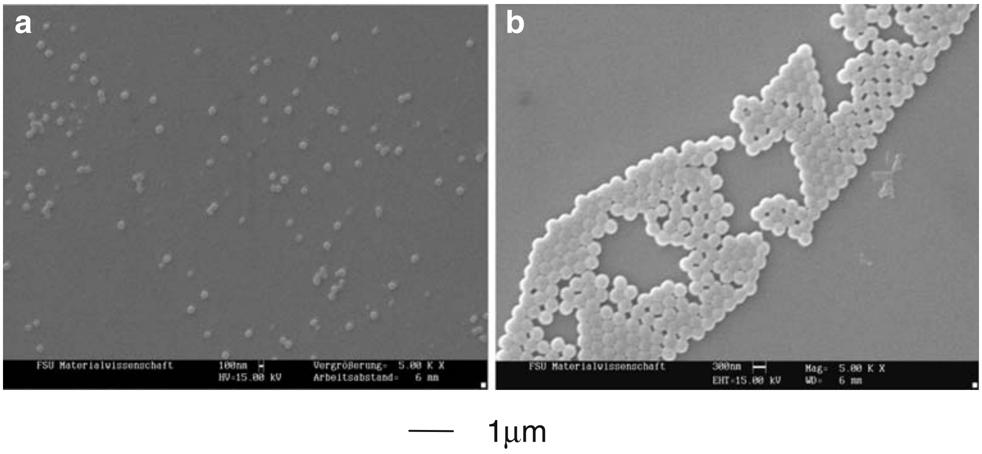
Fig. 2 Hydrodynamic diameter of the microgel particles as a function of temperature as measured by PCS

the particles might not be sufficient and there are some free methoxysilane or silanol groups, which are not crosslinked to form crosslinking points. With prolonging reaction time, the crosslinking density of the microgels probably increased, leading to a slight decrease of the diameter. Note that in this study, MPTMS acted as the co-monomer as well as the crosslinker, and the polymerization and crosslinking belong to different reaction types, which might provide an alternative way to prepare hybrid materials.

The hydrodynamic diameter as a function of temperature was measured by PCS and the results are displayed in Fig. 2. The measurements were carried out under equilibrium conditions after maintaining the sample for 5 min at each temperature point. At 22 °C, the microgels are in a swollen state and have an average hydrodynamic diameter of 220 nm as measured by PCS. At 42 °C, the diameter decreases to 154 nm. The transition temperature of the microgels, where the diameter decreases sharply, is about 31 °C, which is slightly lower than that of conventional PNIPAAm microgel crosslinked by MBAAm [12, 21]. MPTMS is more hydrophobic than NIPAAm and copolymerization of hydrophobic MPTMS with NIPAAm would shift the delicate hydrophobic/hydrophilic balance to the hydrophobic direction. Therefore, the phase transition of the microgels, which is governed by this balance, occurred at a lower temperature. When cooling the temperature from 42 to 22 °C, the diameter exhibited similar temperature dependence and the diameters during both heating and cooling processes almost overlapped, indicating the temperature sensitivity of the microgels is reversible. The polydispersity measured by PCS randomly fluctuated between 0 and 0.05 in the experimental temperature range, suggesting that the microgels are monodispersed and no aggregates form as the dispersion temperature was raised above LCST. The use of APS affords particles that have an anionic surface charge, which prevents microgels from aggregating together through electrostatic repulsion even though the temperature is higher than LCST.

The dilute dispersion of PNIPAAm–MPTMS microgels was dispersed onto mica substrate. After drying in atmosphere, the morphology of the microgels was observed under SEM after having been coated with gold vapor and the image of the microgels is shown in Fig. 3a. It is obvious that microgel particles have spherical structures and the particle size distribution is quite narrow. The diameter of the dry microgels is about 150 nm, which is about 70% of the hydrodynamic diameter determined in swollen state in water at 22 °C. Although swollen microgels would collapse onto the substrate and change their shape to form pancake/disc or oblate spheroids [5, 25, 26], it is not difficult to understand that water evaporation during the drying process leads to the volume shrinking. Therefore, the diameter of the microgels determined by SEM is much smaller than that measured by PCS. Note that the addition of SDS to reaction solutions has great influence on the final diameter of the PNIPAAm–MPTMS microgels. A SEM image of the microgels without adding SDS is shown in Fig. 3b. The

Fig. 3 SEM images of the microgels prepared with (**a**) or without (**b**) SDS as the stabilizer during the polymerization



diameter is about 300 nm, which is lower than the hydrodynamic diameter in water solution at room temperature (599 nm, determined by PCS). The diameters in both dry and swollen states of the microgels prepared without SDS are much larger than those of the microgels prepared with SDS as stabilizer. This is because during the polymerization/crosslinking, SDS is prone to absorb onto the surface of the PNIPAAm–MPTMS particles and increases the colloidal stability of the precursor particles, thus lowers the diameter of the final microgels [25]. More experimental and detailed characterization will be reported in the near future.

Conclusion

In conclusion, a novel method was reported to prepare temperature-sensitive PNIPAAm–MPTMS microgels by precipitation polymerization method. MPTMS acted as the co-monomer to form temperature-sensitive copolymer, as well as the crosslinker to obtain crosslinked microgels. The phase transition temperature of the microgels is about 31 °C and the sensitivity is almost reversible. The diameter in dry state is smaller than the value in water due to the shrinking of the particles in drying process. Because the reactions of copolymerization and crosslinking are ascribed to different types, e.g., the carbon–carbon radical copolymerization of vinyl groups and the sol–gel condensation of siloxane groups, the approach reported here provides a promising option to modify the inorganic nanoparticles or synthesize new hybrid materials. Additionally, due to the uniform dispersity, temperature sensitivity and possible degradability, these microgels could be utilized as versatile templates to prepare porous polymeric materials.

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