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Preparation of Filled Temperature-Sensitive Poly(*N*-isopropylacrylamide) Gel Beads

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Summary: Temperature-sensitive filled poly(*N*-isopropylacrylamide) (PNIPAAm) gel beads with diameters in the range of millimeters were prepared using the alginate technique. The polymerization and cross-linking reaction of NIPAAm in the presence of inorganic filling particles was performed in spherical networks of Ca-alginate forming interpenetrating networks (IPN). Thermosensitive gel beads could be obtained by washing these IPN with EDTA solution.
The PNIPAAm gel beads were analyzed by optical methods to observe there swollen diameter in dependence on the temperature. The diameters of the swollen gel beads were in the range of 0.1 – 2 mm. The influence of the monomer to cross-linker ratio (MCR) and the filling materials (ferrofluid, $BaTiO_3$, TiO_2, and Ni,) were studied. The phase transition temperature (T_{pt}) was only weakly influenced by the MCR and the filling material remaining at around 34 °C.

Keywords: alginate technique; ferrofluid; filler; gel beads; PNIPAAm hydrogels; temperature-sensitive polymers

Introduction

Novel polymer gels that are responsive to external stimuli have been developed in the past decade [1-3]. The stimuli that induces change in polymer gels include temperature, pH, solvent and ionic composition, electric field, light intensity and the recognition of specific molecules. The discovery of a discontinuous volume phase transition in gels, which is often called the collapse transition, has made such soft materials of technological interest [4,5]. The behavior of these gels can be utilized in mechanical devices, controlled release delivery and separation systems [6-8].

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Poly(*N*-isopropylacrylamide) (PNIPAAm) hydrogel is one of the most frequently studied temperature-responsive gel [4]. Above the transition temperature the network chains are in the collapsed state. This transition is called the lower critical solution temperature (LCST) behavior. For PNIPAAm gels swollen in water the LCST was found to be 34 °C. Several other gels show reversible swelling and shrinking transitions with different LCST as well. These gels were often used to immobilize enzymes and as carriers of certain functional groups important for biochemical or biomedical applications [5]. For those applications gel beads were usually used in the size range from approximately 0.1 μm to several mm. These gels were heated by a surrounding heat source to control the degree of swelling. A more efficient heating method was proposed recently. Takahashi and his coworkers immobilized needle like iron oxide (γ-Fe_2O_3) powders with 0.5-0.8 μm length into polymer gels for magnetic heating [9,10]. Due to the hysteresis loss of the hard magnetic material in the presence of an alternating magnetic field, the magnetic energy was converted into heat inside the gel, which increased the temperature. This method is energetically efficient as only the gel beads are heated and not the entire environment.

Magnetic field sensitive gels were also developed to increase the rate of shape change [11-13]. Magnetic nanoparticles of Fe_2O_3, called magnetite, were incorporated into chemically cross-linked poly(vinylalcohol) hydrogels. It was established that the peculiar magnetic and magneto-elastic properties of these gels could be used to target magnetic gel beads to a certain place or to create a wide range of motions to control the shape of the gels.

Fe_2O_3 nanoparticles with a typical size of 10 nm are magnetically soft materials. They exhibit superparamagnetic behavior [14]. The mono-domain ferromagnetic particles of colloidal size are the elementary carriers of a magnetic moment in the ferrogel. In the absence of an applied field they are randomly oriented due to thermal agitation and thus the ferrogel has no net magnetization. As soon as an external field is applied, the magnetic moments tend to align with the field to produce a bulk magnetic moment (M). With ordinary field strengths the tendency of the dipole moments to align with the applied field is partially overcome by thermal agitation. As the strength of field increases, all the particles eventually align their moments along the direction of the field leading to the magnetisation saturates. If the applied field is turned off, the particles quickly randomize, and M is again reduced to zero. This means that the magnetization curve shows no hysteresis at all and can be fitted by a Langevin function corrected with the distribution of the magnetic dipole moments.

The properties of magnetic beads containing hard magnetic particles in their gel matrix differ significantly from those containing soft magnetic particles. If the gel is loaded with a magnetically hard filler material, it behaves like a permanent magnet. As a consequence - due to the magnetic interactions - the gel beads form aggregates, even without the application of an external magnetic field. Intensive stirring is required to counterbalance the magnetic interactions and prevent aggregation. If magnetic soft particles are introduced into the gel, then the beads have no permanent magnetization and as a result they form aggregates only in the presence of an external magnetic field.

The aim of the present work is the synthesis of temperature sensitive hydrogel beads by the alginate technique. They were characterized to their temperature sensitivity in dependence on the cross-linking ratio. Filled PNIPAAm gel beads have been synthesized by incorporating inorganic filling materials, too. The influence of the fillers on the swelling behavior was analyzed.

Preparation of Filled PNIPAAm Beads

The gel beads were prepared according to the method developed by Park and Choi [15]. An interpenetrated network (IPN) was prepared by the simultaneous gelation of Ca-alginate to form spherical bead shapes and the concomitant free radical polymerization of the NIPAAm and cross-linker (N,N'-methylene bisacrylamide) within the beads. The beads were then incubated in ethylenediamine tetraacetate (EDTA) solution to chelate Ca-ions and extract the alginate from the IPN beads. The molar cross-linking ratio (molar ratio of monomer to cross-linker (MCR)) was varied between 24 and 75 at a constant monomer concentration of 7.68 wt-%. At a constant cross-linking ratio (MCR 50) the monomer concentration was varied between 7.68 and 4.07 %. A schematic procedure is shown in Figure 1.

Ca-ions formed an ionotropic complex with the alginates backbones leading to the formation of a water swollen gel network. The monomer, cross-linker, filling material and the redox initiator were kept in these Ca-alginate gel beads, the co-initiator (ammonium persulfate) in the medium rapidly diffused into the gels and initiated the polymerization. The cross-linked PNIPAAm in the Ca-alginate gel could be described as an interpenetrating network (IPN) structure, in which the two polymer networks were entangled in each other. Homogeneous PNIPAAm gel beads could easily be formed from the IPN gel in large spherical shapes, when the alginate polymer was dissolved by addition of Ca-chelating agents.

A magnetic field sensitive gel is a special type of filler loaded gel, where the finely divided filler particles have strong magnetic properties. Preparation of such gels does not require a special polymer or a special type of magnetic particle. As a polymer network one may use every flexible chain molecule, which can be cross-linked. The filler particles can be obtained from ferro- as well as ferrimagnetic materials.

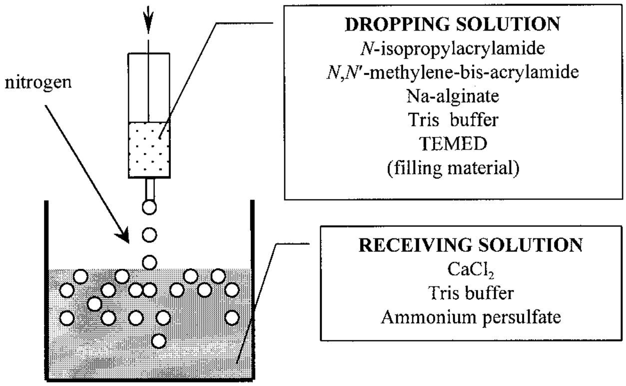

Figure 1: A schematic procedure for the preparation of PNIPAAm gel beads

The preparation of a magnetic PNIPAAm gel (MPNIPAAm) was similar to that of other filler-loaded elastomeric networks. Well-dispersed particles were precipitated in the polymeric material. This "in situ" precipitation can be made before, during and after the cross-linking reaction [16,17]. Firstly, a ferrofluid, which contained magnetite sol particles, was prepared from iron (II) chloride and iron (III) chloride in aqueous solution. In order to counter-balance the van-der-Waals attraction and the attractive part of the magnetic dipole interactions, colloidal stability was maintained by a small amount of perchloric acid, which induced peptization. The purified and stabilized magnetite sol with a concentration of 15.7 wt-% was used for further preparative work. During the preparation the dropping solution contained 0.5 ml of the ferrofluid (corresponding to 0.94 wt-% magnetite content) [18]. For the preparation of the with inorganic particles filled PNIPAAm gels the particles were suspended in the solution with a total concentration of 10 wt-%. The structure of the inorganic particles is shown in Figure 2. The MCR was varied between 24 and 50 at a constant monomer concentration of 7.68 wt-%.

The bead size can to some extent be controlled by using different sized needles on the string. In this manner beads ranging from 0.5 to 4 mm may be conveniently prepared. Here, gel beads with an average diameter of d = 2.0 mm and narrow size distribution were prepared to enable for accurate measurements. It should, however, be mentioned that none of these properties are size dependent. The preparation of smaller beads requires another technique.

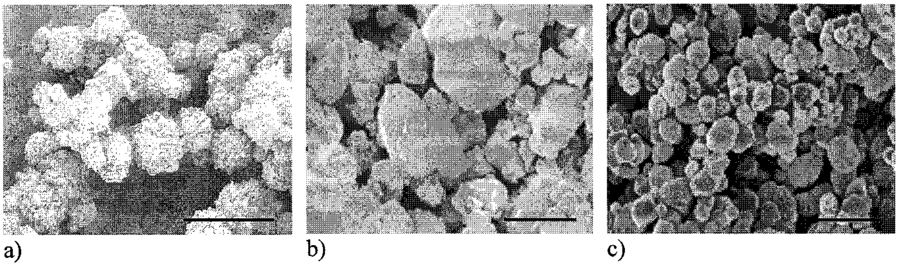

Figure 2: SEM of the a) Ni particles (bar = 10 μm), b) $BaTiO_3$ particles (bar = 1 μm), and c) TiO_2 particles (bar = 0.5 μm)

In order to determine the temperature dependence of the degree of swelling the experiments were monitored using a digital video system. This method enables the measurement of very small changes in the diameter (one pixel on the screen) on the real time video image.

Collapse Transition of Non-Magnetic and Magnetic PNIPAAm Gel Beads

The temperature dependence of the PNIPAAm gel and MPNIPAAm gel beads was studied. The behavior of MPNIPAAm gel was similar to that of the non-magnetic PNIPAAm gels. An abrupt volume change in response to temperature change was observed in both cases (Figure 3). d_0 is the diameter of the gel beads at approximately 10 °C.

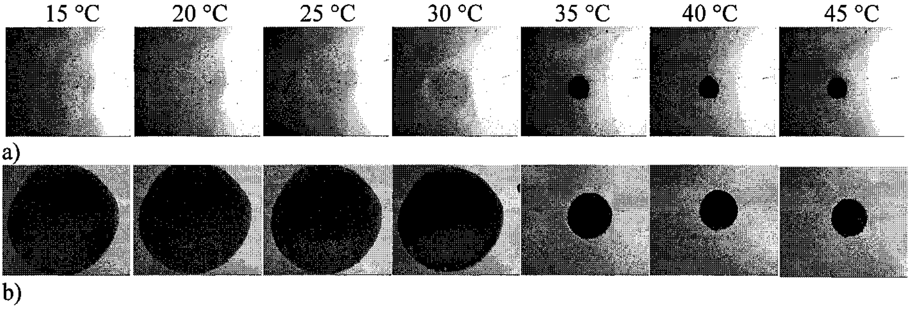

Figure 3: Thermo shrinking phenomenon of a) non-magnetic PNIPAAm gel bead, and b) magnetic PNIPAAm gel bead

An increase of the temperature led to a significant decrease in the volume of the gel beads (Figure 4). The swelling ratio changed from 1 to 0.2 in every case. It can be seen that the cross-linking ratio does not affect the phase transition temperature, which was around 34 °C.

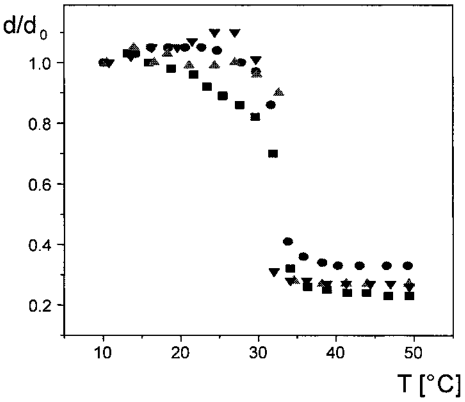

Figure 4: The effect of different cross-linking ratio on the LCST of PNIPAAm gel beads (■ - MCR 24, ● - MCR 32, ▲ - MCR 50, ▼ - MCR 75)

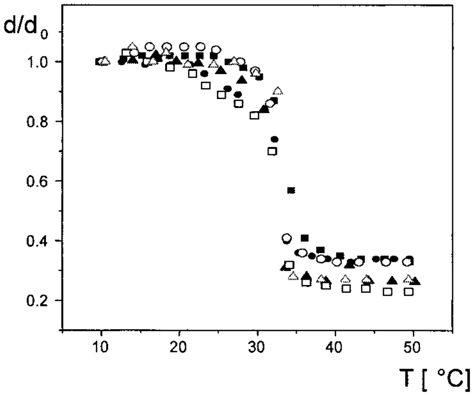

Figure 5: The effect of different cross-linking ratio on the LCST of PNIPAAm and MPNIPAAm gel beads (open symbols - PNIPAAm gel, solid symbols - MPNIPAAm gel) (■- MCR 24, ● - MCR 32, ▲ - MCR 50)

The influence of larger filling particles (in the range of some μm) was analyzed by incorporating other inorganic particles ($BaTiO_3$, TiO_2 and Ni). Figure 6 shows the temperature sensitive behavior of the filled gel beads. A shift in the phase transition temperature was not observed at the analyzed gels (T_{cr} = 34 °C) due to low interactions between the filling material and the cross-linked PNIPAAm. However, the differences in the degree of swelling were effected by the nature of the filler particles.

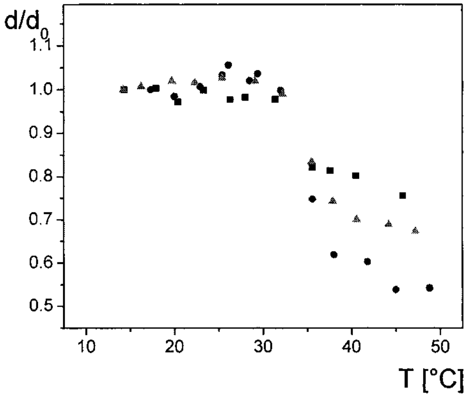

Figure 6: The effect of incorporated inorganic particles on the temperature sensitivity of the PNIPAAm gels (■- $BaTiO_3$, ● - TiO_2, ▲ - Ni)

Conclusion

This work was carried out in order to describe the preparation of filled temperature sensitive PNIPAAm gel beads. The temperature sensitivity of filled PNIPAAm gels is quite similar to that of the same gel containing no nanoparticles. Consequently the collapse transition is not affected by the presence of the nanoparticles. The special magnetic properties of these gels may be used to target and orient the temperature responsive gel beads and enables their easy separation from the environment through the use of non-uniform magnetic field.

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