The Sol-Gel Approach towards Thermo-Responsive Poly(N-isopropyl acrylamide) Hydrogels with Improved Mechanical Properties

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Summary: A new type of thermo-responsive hydrogels based on the polymer poly(N-isopropyl acrylamide) (PNIPAA) has been synthesized with the sol-gel technology. For the preparation of this type of nano-structured hydrogels, the inorganic silica phase was synthesized by the sol-gel process in the presence of an aqueous solution of high molecular weight PNIPAA. This combination of the organic and inorganic phases forms hybrid hydrogels with a semi-IPN morphology. The unique structure of these hydrogels improves the mechanical stability to a great extent as compared to conventional PNIPAA-hydrogels. This was shown by stress-strain experiments and the capability to absorb and desorb large amounts of water. The silica only slightly influences the transition temperature of the hydrogels but allows us to vary the thermo-responsive properties of the materials to a great extent.

Keywords: hydrogels; lower critical solution temperature; nanocomposites; poly(N-isopropyl acrylamide); silicas

Introduction

The hybrid hydrogels, produced by a sol-gel process, are a new kind of hydrogels, where nano-sized inorganic particles act as physical or chemical cross-links of the networks based on water-borne synthetic polymers. Although several silica composites based on water-soluble polymers have been reported in the literature, they mostly consist of an inorganic matrix and little attention is paid to their hydrogel properties.[1,2]

In general, these hybrid hydrogels represent a new class of materials where the advanced features of both hydrogels and an inorganic nano-particulate structure are combined.[3,4] Just like ordinary polymer hydrogels, they easily swell in water, exhibit good elasticity and high optical transparency. At the same time, they possess good mechanical properties, in particular high

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strength characteristics.

For the production of the hybrid hydrogels, the well known sol-gel technology is applied.[5] Generally, this method can be represented as a two step network-forming process based on two fundamental chemical reactions - hydrolysis and condensation (Figure 1). Usually, tetrafunctional silicates such as tetramethoxysilane (TMOS) are used, but also other metal alkoxides (Al, Ti or Zr alkoxides). These two reactions are concurrent and interdependent and proceed under mild conditions. A number of variables influence the structure of the SiO_2-network: pH, solvent, water-to-alkoxide ratio and the type of the alkoxide used. Recently the sol-gel process has received much attention with respect to the design and preparation of polymer-inorganic hybrid materials. So far the most promising applications are based on novel characteristics and enhanced properties such as improved toughness, strength, modulus, impact and scratch resistance, optical transparency, thermal stability and electrical conductivity.[6-9] The structure of the inorganic phase can be controlled by changing the parameters of the sol-gel reactions.

$$Si(OR)_4 + 4\,H_2O \xrightarrow{\text{hydrolysis}} Si(OH)_4 + 4\,ROH$$

$$Si(OH)_4 \xrightarrow{\text{condensation}} SiO_2 + 2\,H_2O$$

Figure 1. Reaction scheme of the sol-gel process: hydrolysis and condensation of alkoxy derivatives of Si.

The goal of the present work is to apply the sol-gel process for the preparation of thermo-responsive hybrid hydrogels. In these "intelligent" gels, the thermo-responsive properties are introduced by the incorporation of a polymer that shows a "lower critical solution temperature" (LCST) in aqueous medium. For this research the well-known thermo-responsive polymer, poly(N-isopropyl acrylamide) (PNIPAA) has been chosen. PNIPAA possesses an LCST that is located at temperatures of 32-33°C.[10] These physiological temperatures open perspectives for numerous biomedical applications and drug delivery systems.[11-13]

The first PNIPAA-SiO_2 hybrid hydrogels have been reported by Kurihara et al.. In their system, PNIPAA and silica domains were linked through covalent bonds.[14] More recently Chujo et al. reported on conventional cross-linked PNIPAA networks that are combined with silica particles.[15]

In our work on the other hand, the principle of the hydrogel formation was to perform the sol-gel

process in the presence of high molar mass polymer, without covalent bonds between the organic and inorganic phase. In this way, the silica particles act as physical cross-links for the polymer molecules and can be represented as a semi-interpenetrating polymer network (semi-IPN). In a previous report we already demonstrated that hybrid hydrogels as semi-IPNs based on another polymer with LCST-behaviour, poly(N-vinyl caprolactam) (PVCL), can better withstand the mechanical stress created during the swell and shrinkage processes in response to temperature changes in comparison to conventional hydrogels.[3] Compared to PVCL, PNIPAA shows a much different phase behaviour in water (Type II), leading to a discontinuous and more extensive shrinking of the corresponding hydrogels.[10] In this report, the reaction conditions and thermo-responsive properties of PNIPAA-containing hybrid hydrogels will be reported.

Experimental Part

Materials

Tetramethoxysilane (TMOS) (Acros, 99%), 2,2'-azobisisobutyronitrile (AIBN) (Merck-Schuchardt, >98%), ammonium persulfate ($(NH_4)_2S_2O_8$) (Aldrich, 98%) and N,N,N',N' tetramethylethylenediamine (TEMED) (Aldrich, 99%) were used as received. Benzene (Aldrich, 99+%) was refluxed over a sodium/benzophenon solution. N-isopropyl acrylamide (NIPAA) (Acros, 99%) was purified by recrystallization on hexane, followed by drying under vacuum and stored at 4°C.

Synthesis of Linear Poly(N-isopropyl acrylamide) (PNIPAA)

The high molecular weight PNIPAA (PNIPAA-1,2) were obtained by performing the radical polymerization in benzene with AIBN as initiator at an elevated temperature of 60°C. Lower molar mass PNIPAA (PNIPAA-3) was synthesized in water with the redox system $(NH_4)_2S_2O_8$ / TEMED.[16]

Synthesis of PNIPAA Organic/Inorganic Hybrid Materials

The synthesis of PNIPAA hybrid hydrogels was carried out in a test tube with a magnetic stirring rod. An aqueous solution of PNIPAA (distilled water) at pH equal to 12 is added together with a certain amount of TMOS. The reaction mixture is stirred for 5 minutes before being poured

between two silylated glass plates, separated by a 3 mm thick spacer. By performing the gelation in the glass mould, the evaporation of water is prevented. The hydrogels have been investigated at least 24 hours after their preparation.

In order to explain the nomenclature in the discussion part, one synthetic procedure is described in detail: 0.4g TMOS (d = 1.02 g/ml) is added to a solution of 4 ml water containing 0.4g PNIPAA (9.1 wt.-% PNIPAA solution), thus V_{PNIPAA}/V_{TMOS} = 10/1 and the initial TMOS to water ratio in wt.-% is 9.1. The resulting ratio PNIPAA/SiO_2 is 50/50 (wt.-%) and the total composition, indicated as the ratio water/PNIPAA/silica (wt.-%), is equal to 84/8/8.

Methods of Analysis

Soluble fractions (SF) of the PNIPAA hybrid hydrogels are determined gravimetrically and are defined as $SF = 100.(W_0 - W_e)/W_0$. W_e and W_0 respectively denote the weight of extracted and dry hybrid material. The extraction proceeded in acetone during 6h.

The swelling degrees of the PNIPAA hybrid hydrogels in distilled water are determined gravimetically as a function of time and temperature. The equilibrium weight of the swollen samples is determined after a weight change of less than 1 wt.-%. The degree of swelling was defined as $S = 100.(W_{sw} - W_0) / W_0$, where W_{sw} and W_0 respectively denote the weight of the swollen and dried sample (vacuum, 60°C, 24 hours).

Stress-strain curves are determined at room temperature, at constant elongation speed (15mm/min) on 3 mm thick samples (width : 4mm).

Results and Discussion

Synthesis of Linear Poly(N-isopropyl acrylamide) (PNIPAA)

In the introduction part, the necessity for high molecular weight polymers to obtain stable hydrogels was already mentioned. The molecular weights and nomenclature of PNIPAA are shown in Table 1. The synthetic details are described in the experimental part.

Table 1. Molecular weights of PNIPAA.

Sample	M_v PNIPAA[1)]
	g/mol
PNIPAA-1	1.650.000
PNIPAA-2	1.050.000
PNIPAA-3	560.000

[1)] Molecular weights were determined by viscosimetry in water at 25 °C, using the Mark Houwink equation : $[\eta] = K \cdot M_v^a$ with $K = 14.5 \cdot 10^{-2}$ ml/g and $a = 0.5$.[17]

Synthesis and Characterization of PNIPAA-Silica Hybrid Materials

Regardless the fact that there are no covalent bonds present in the hydrogels, there are strong interactions between the two phases, i.e. the inorganic silica phase and the organic polymer phase. This is a consequence of both hydrogen bonds and physical entanglements. The existence of hydrogen bonds between the carbonyl groups of PNIPAA and the remaining silanol groups of the inorganic domains could be demonstrated by FTIR-spectroscopy. For example a shift of the carbonyl peak of PNIPAA from 1665 cm^{-1} for pure PNIPAA to 1639 cm^{-1} for PNIPAA present in a specific hybrid hydrogel is detected. This is due to the presence of silanol groups and thus the formation of hydrogen bonds.

The model to visualise the morphology has been described extensively in the previous report and is based on the work of Wilkes et al.[18] Instead of covalent bonds in the Wilkes model, the hybrid hydrogel can be represented as a semi-IPN consisting of cross-linked silica particles with entanglements and hydrogen bonds in between the particles and the high molar mass PNIPAA chains.

Another way to determine the stability of the physical cross-linked hydrogel is by the measurement of the soluble fraction and the equilibrium swelling degree (Table 2). From this table, one can see that the soluble fractions are quite low in the case of hybrid hydrogels with high molecular weight PNIPAA (PNIPAA-1 and -2) and TMOS weight fractions exceeding 4%. Under these conditions the number of physical entanglements and hydrogen bonds between both phases prevents the extraction of polymer chains and provides highly stable hydrogel materials in spite of the equilibrium swelling degrees up to 3000%. On the other hand, for lower molecular weight

PNIPAA (PNIPAA-3), much of the organic material is extracted from the gels and equilibrium swelling degrees could not be determined due to their instability.

Table 2. Soluble fractions and compositions of the PNIPAA hybrid hydrogels.

	Weight fraction TMOS to H_2O in reaction mixture	PNIPAA / SiO_2	Soluble fraction	Equilibrium swelling degree in water (20°C)
	wt.-%	wt.-%	%	%
PNIPAA-1	8	70/30	1.3	1800
	6	70/30	2.1	2400
PNIPAA-2	9	50/50	0	2200
	9	60/40	3.7	1800
	8	70/30	0.3	2200
	6	70/30	3.1	2900
	6	60/40	2.5	2500
	4	70/30	11.3	5400
	4	80/20	17.7	5100
PNIPAA-3	8	70/30	55	/
	6	70/30	58	/

As reported earlier for PVCL hybrid hydrogels, the swelling degrees can be tuned by the variation of the reaction conditions. The equilibrium swelling degree increases with the PNIPAA/SiO_2 ratio (up to 5000%), whereas it lowers with a higher TMOS concentration in the reaction mixture. The TMOS weight fraction determines the cross-linking density of the inorganic silica phase. Similar to conventional hydrogels, the equilibrium swelling degrees lower with increasing cross-linking density.

Mechanical Properties of the Hybrid Hydrogels

In order to demonstrate the enhancement of the mechanical stability of the hydrogels, the most obvious technique was to perform stress-strain tests (Table 3). As expected, the elasticity modulus increases with increasing silica fraction or decreasing water fraction. The good elasticity

properties are demonstrated by the values of the elongation at break that vary from 160 up to 465%. Former investigations showed that stress-strain tests were impossible to perform on conventional PNIPAA-hydrogels with equal swelling degrees, indicating the improvement of mechanical stability of these hybrid hydrogels.

Table 3. Stress-strain data of PNIPAA hybrid hydrogels (PNIPAA-2).

Composition hybrid hydrogels : H_2O/PNIPAA/ SiO_2 (PNIPAA/ SiO_2)		Young modulus	Elongation at break
wt.-%		kPa	%
78/15.5/6.5	(70/30)	28	465
80/12/8	(60/40)	24	170
86/8.5/5.5	(60/40)	18	160
84/8/8	(50/50)	15	300
80/16/4	(80/20)	15	450
83/12/5	(70/30)	7.5	290

Thermo-responsive Properties of the Hybrid Hydrogels

The hybrid hydrogels owe their thermo-responsiveness to the nature of the organic phase, i.e. the LCST-polymer PNIPAA. In an aqueous solution at temperatures above the cloud point (T_{cp}) this polymer releases water molecules and undergoes a transition from a hydrophilic to hydrophobic state. This process generally results in two visually observable phenomena: a volume decrease and the appearance of turbidity.

The phase diagram of some PNIPAA hybrid hydrogels is shown in figure 2. It clearly shows the expulsion of water above the T_{cp} of PNIPAA. When the amount of silica is higher in comparison to PNIPAA, the expulsion is larger and, analogously to conventional cross-linked systems, it can be derived that the shrinkage effect is lower at higher cross-linking densities, i.e. higher TMOS weight percentage.

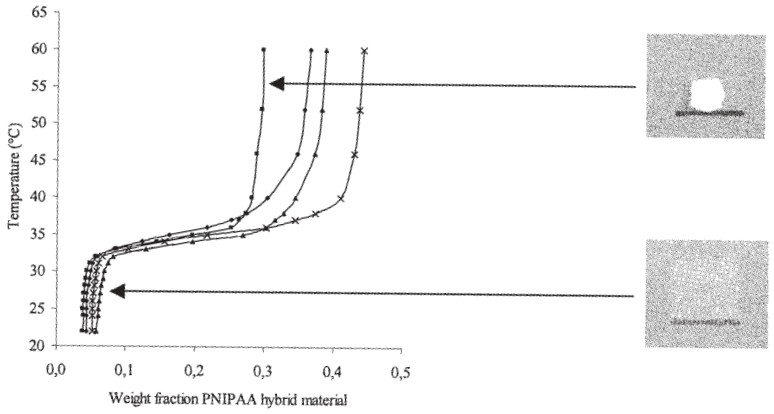

Figure 2. Phase diagram of PNIPAA hybrid hydrogels (PNIPAA-2) with composition: (a) PNIPAA/SiO_2 = 70/30; TMOS = 6 wt.-%, (b) 60/40; TMOS = 9 wt.-%, (c) 60/40; TMOS = 6 wt.-% en (d) 70/30; TMOS = 8 wt.-%. The shrinkage effect is illustrated for a gel with composition (a).

Although it is difficult to observe in figure 2, light transmission measurements showed that, in comparison to pure PNIPAA solutions, the presence of silica domains in the hybrid materials slightly lowers the LCST with about 2°C. Thus, the thermo-responsive behaviour still expresses itself above room temperature. The explanation of the decrease of the phase transition temperatures in the presence of the inorganic phase, is the competition between water and silanol groups to form hydrogen bonds with the carbonyl groups of PNIPAA. If these carbonyl groups no longer can freely interact with water molecules below the T_{cp}, the phase transition temperature of PNIPAA decreases.

Conclusion

Mechanically improved thermo-responsive hybrid hydrogels based on PNIPAA were developed by making use of the sol-gel technology. The synthesis was achieved by the in situ formation of an inorganic silica phase in the presence of high molecular weight PNIPAA. This methodology leads to micro-heterogeneous systems in which silica particles of nanometer dimensions act as physical cross-links for the PNIPAA molecules. Hydrogen bonds between the silica particles and

PNIPAA, together with physical entanglements are responsible for the strong interactions between the inorganic and organic phase. Stress-strain tests on highly swollen materials demonstrated that the unique structure of these hybrid hydrogels improves the mechanical stability to a great extent as compared to conventional hydrogels. The properties of the hydrogels can be easily tuned by changing the reaction conditions, whereas the influence of silica on the phase transition temperatures of PNIPAA is negligible.

As a general conclusion, it can be stated that the synthesis of organic/inorganic hybrid hydrogels is a successful concept to develop thermo-responsive hydrogels with improved mechanical properties.

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