

# Tunable temperature behaviour of water-soluble polyamidhydroxyurethane

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One promising class of polymers are water soluble polymers which presents a polymer-based phase separation that is stimulus – sensitive. The tunable behaviour with respect to temperature and non-solvent concentration of poly(amidhydroxyurethane) is presented. The molecular architecture of studied polymer gives rise to a coil to micelle demixing scenario. Obtained results show that 37 °C particularly interesting for biomedical applications temperature can be achieved in specific conditions. Turbidimetric method was employed for obtaining the useful experimental parameter range.

(Received March 15, 2006; accepted May 18, 2006)

*Keywords:* Water-soluble polymer, Temperature tunable polymers, Polyamidhydroxyurethane

## 1. Introduction

Water-soluble polymers (WSP) are promising materials for various applications: smart/responsive materials such as sensors and actuators, cell patterning [1,2] and smart/controlled drug-delivery systems [3,4]. WSP are divided in two main types: polyelectrolytes (PWS) and neutral polymers (NWSP) [5].

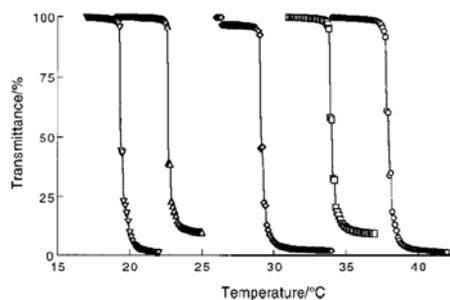
Solubility of PWS is mainly driven by charge type interactions between polymer and solvent, meanwhile the solubility of NWSP is controlled mainly by hydrogen bonding. NWSP can be obtained by controlling the amounts of hydrophilic and hydrophobic parts in the polymer following two main synthesis strategies. One of the NWSP synthesis strategies conduct to an alternating sequence of hydrophilic and hydrophobic segments in the polymer backbone and the second to a hydrophobic polymer backbone with hydrophilic branches.

An important class of NWSP presents a polymer-based phase separation that is stimulus – sensitive. This behaviour usually originates from the existence of a lower critical solution stimulus (LCSS) beyond which the polymer becomes insoluble in water. A typical example is the temperature – sensitive solubility polymer that usually originates from the existence of a lower critical solution temperature (LCST) (Fig. 1).

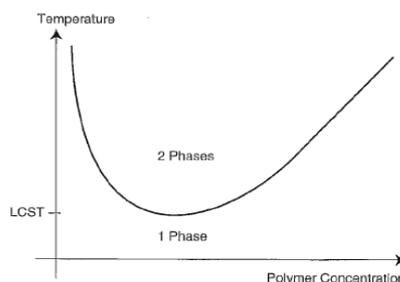
Solubility of NWSP is tunable by various stimuli: pH, temperature, pressure, ion strength and non-solvent concentration. Polymers that exhibit a response in water at about 37 °C, are particularly interesting for biomedical applications.

The water solvency behaviour of organic polymers can be generally classified into two types. One is where the increase of the temperature or the presence of a non-solvent, significantly worsens the solvent quality which, in turn, leads to the occurrence of a phase separation between the polymer and water. Aqueous solutions of poly(ethylene oxide) (PEO),

and poly(vinyl alcohol) (PVA) with low degrees of hydrolysis, show this type of behaviour [6]. The other type is one where the solvent quality of the polymer solutions increases, rather than decreases, under similar variations of the temperature, pressure and non-solvent concentration. The aqueous solutions of poly(acrylamide) (PAM), and PVA with high degrees of hydrolysis, belong to this type.



(a)



(b)

*Fig. 1. Specific behavior of temperature – sensitive NWSP which presents a LCST. a) tunable temperature behavior vs. concentration and b) obtained demixing temperature vs. polymer concentration.*

The reasons for these different types of behaviour are related to the characteristics of the individual polymer-chain structures and their chemistry. For aqueous solutions of polymers with relatively strong intra- and inter-chain interactions, such as those provided by the dipole interactions and hydrogen bonding, these intra- and interpolymer-chain interactions decrease with the increase of the temperature and with the addition of nonsolvents/electrolytes in water. Hence, the solvent quality increases with the increase of the temperature, and of the amount of nonsolvents/electrolytes. This type of systems is characterized by an upper critical solubility temperature (UCST). It is expected that a further reduction of the solvency and the existence of an LCST might thus occur for these solutions with the further changes of these variables, but these effects may not be achievable in practice. On the other hand, for the aqueous solutions of polymers where there is dominant hydrogen bonding between the polymer chains and water molecules, the increase of the temperature, and the addition of nonsolvents/electrolytes in water disrupt this hydrogen bonding and thus reduce the solvency. It is also to be expected that a UCST exists for these solutions under some conditions. In conclusion both UCST and LCST conditions may theoretically exist for all aqueous polymer solutions.

The synthesis and structural characterization of a new NWSP - poly(amidhydroxyurethane) (PAmHU) was previously reported [7]. This paper deals with PAmHU tunable behaviour with respect to temperature and non-solvent concentration.

## 2. Experimental

PAmHU was obtained from ethylene carbonate (EC), ethylene diamide (ED), and acrylic acid (AA). Detailed PAmHU synthesis is presented elsewhere [7,8]. Thermochemical characterization of PAmHU synthesis shows that polymerization takes places in two steps and that temperature is an important parameter for the complex kinetic process conducting to PAmHU [9]. The resulted PAmHU polymer is crystalline, very tough and soluble in water; the average molecular weight number is  $\overline{M}_n = 18,700$  g/mol.

In a previous study [7] the network structure of less water PAmHU film was determined as one with a high degree of macroscopic homogeneity consisting at a microscopic level of three phases: a water phase of low PAmHU concentration, an amorphous phase, and a crystalline phase that restricts some of the motion degree of the amorphous domains. In the network PAmHU molecule is packed as a ball and the molecules are interconnected between them by inter-molecular bonds in the bidentate or three-dimensional hydrogen bonding. The bidentate or three-dimensional hydrogen bonding is performed by hydrogen bonding of the ether oxygen, the acrylamide carbonyl oxygen and the urethane carbonyl oxygen groups. This very stable network structure provided a great capacity of swelling.

The primary structure of PAmHU is presented in

Fig. 1. The backbone of this polymer is completely hydrophobic and the water solubility is conferred by the presence of hydrophilic lateral branches on each second backbone carbon atom.

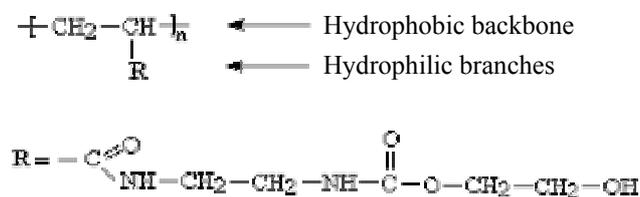


Fig. 1. Primary structure of PAmHU.

This type of structure usually induces a micelle to coil mechanism for phase separation. PAmHU-water system presents a temperature and non-solvent concentration tunable behaviour as shown bellow. The useful range of control parameters was determined by applying the turbidimetric method. This method provides direct information about phase separation against temperature and nonsolvent concentration.

Deionized distilled water was used for obtaining polymer solutions of various concentrations. The solution was stirred in a thermostat. We have used the viscosity of the solution as a criterion in deciding if a thermodynamically stable solution was formed. Cloud points were determined in  $22 \div 60$  °C temperature range, centred at 37 °C - standard biological temperature. The non-solvent used was analytical grade ethylic alcohol (S. C. Chemical Company S.A.).

The turbidimetric titration method is based on the light scattering produced by the diffusion centres from the studied solution. The increase of the system turbidity causes the decrease of the transmitted light intensity and increasing of the diffused light intensity.

Turbidity,  $\tau_\lambda$ , for a certain wave length, is defined based on the Lambert-Beer law, by the following relation:

$$\tau_\lambda = \frac{1}{L} \ln \frac{I_0(\lambda)}{I(\lambda)} = \frac{2,303}{L} \lg \frac{I_0(\lambda)}{I(\lambda)} = \frac{2,303}{L} D, \quad (1)$$

where  $L$  is the optical length,  $I_0(\lambda)$  and  $I(\lambda)$  are the incident, respectively the transmitted light intensity and  $D$  is the optical density.

The value of the system turbidity is a measure of the mass fraction of polymer which precipitated from the solution. When phase separation is triggered by titration with a nonsolvent, the dilution process should be considered.

The experimental setup used is presented in Fig. 2. The initial volume of polymer solution was 25 mL and the maximum volume of the spectral cuvette was 40 mL. The transmitted light intensity was measured with a LKB ULTROSPEC 4052 TDS spectrophotometer, which was used at constant wavelength, 395 nm. The obtained signal was recorded using a DAS 1600 data acquisition board controlled by ViewDac software.

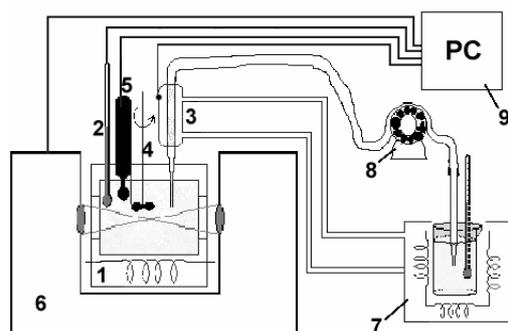


Fig. 2. Sketch of turbidimetric titration experimental set-up. 1 - main thermostat; 2 - main thermocouple; 3 - nonsolvent thermocouple; 4 - mechanical stirrer; 5 - pH electrode; 6 - spectrophotometer; 7 - nonsolvent thermostat; 8 - peristaltic pump; 9 - data acquisition system.

### 3. Results

The studied concentration range was limited by the high viscosity of the PAmHU-water system; concentration higher than 3% w/w produce a gel like system improper for turbidimetric studies. For the 37 °C, particularly interesting temperature for biomedical applications, the amount of nonsolvent needed for precipitation of very low concentration PAmHU solution ( $\leq 1\%$  w/w) exceeds the volume of spectral cuvette. Fig. 3 shows the behaviour of PAmHU-water solution at 2% w/w (a) and 3% w/w (b).

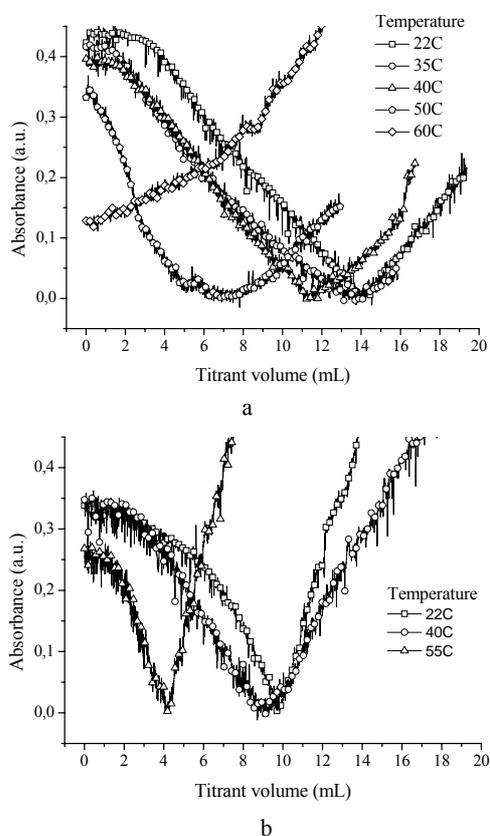


Fig. 3. Turbidimetric traces of a) 2% and b) 3% w/w PAmHU in water solution at different temperatures (as shown); nonsolvent was pure ethanol.

A typical titration curve of the PAmHU polymer presents an initial absorbance decrease due to dilution of polymer-water system followed by an absorbance increase due to phase separation. The cloud point was assigned to the minimum of the titration curve.

### 4. Discussion

Cloud point dependence on the composition of PAmHU-water-ethanol system is presented in Fig. 4. Data from Fig. 4 suggest that the PAmHU-water system presents a LCST at about 57 °C. Further it is obvious that ethanol content can tune the transition temperature in the 22-60 °C range.

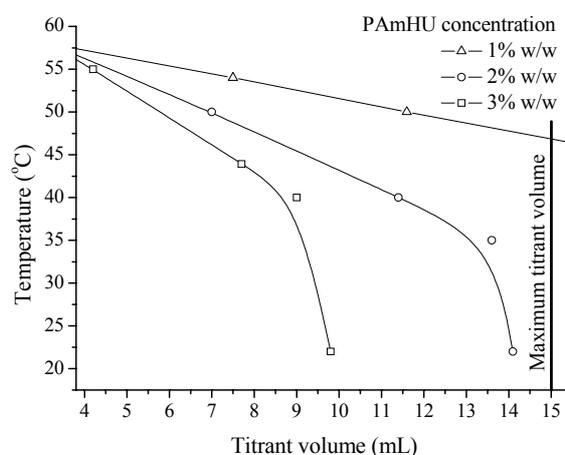


Fig. 4. Cloud point vs. composition of PAmHU-water-ethanol system.

The PAmHU water solubility is determined by the competition between different types of molecular interactions: polymer-water interactions by hydrogen bonding of the ether oxygen, the acrylamide carbonyl oxygen and the urethane carbonyl oxygen groups, intra- and inter- molecular interactions generated by the same three mentioned groups [7]. The first type of interactions induce solubility meanwhile the second type determine phase separation.

A measure of those molecular interactions strength is given by the energy of interaction,  $W$ , between the two interacting dipoles. The energy interaction between two dipoles of moments  $M_1$  and  $M_2$  is:

$$W = \frac{M_1 M_2}{r^3} (\cos \varphi - 3 \cos \theta_1 \cos \theta_2), \quad (2)$$

where  $r$  is the distance between the dipoles,  $\theta_1$  and  $\theta_2$  are the angles between the respective dipoles, and  $\varphi$  is the angle the dipoles naturally subtend with respect to each other. The value of  $W$  is zero for the case where the dipoles are orientated perpendicular to each other and has a maximum value for parallel dipoles. It is known that the water-ethanol dipole interaction is characterized by a high  $W$  value.

The general criterion for thermodynamic evolution

and stability is expressed by the fundamental law of thermodynamics:

$$\Delta G = \Delta H - T\Delta S \leq 0, \quad (3)$$

where  $G$ ,  $H$ ,  $S$  are free Gibbs energy, enthalpy and entropy of system. The evolution of the system is driven by the competition between entropic and enthalpic terms. The established thermodynamic parameters available for aqueous polymer solutions show that the enthalpy of dilution is positive; i.e. endothermic, and thus the entropy is, thereby, positive. The competition between ethanol and polymer for the water solvent lead to non-solvent properties of ethanol in PAmHU-water system. The high strength interaction between water and ethanol determines the decrease of the system entropy. When the critical balance between entropic and enthalpic terms is achieved the demixing takes place. As can be seen from Fig. 4 small amounts of ethanol drastically reduce the demixing temperature of PAmHU-water system.

As expected from the primary structure of PAmHU, the phase separation is diffuse having the characteristics for micelle to coil mechanism of separation. Further the PAmHU-water system presents a temperature and non-solvent concentration tunable behaviour.

The experimental results show that the transition temperature can be tune to the optimum biological temperature of 37 °C by ethanol addition almost for the entire solution domain.

## 5. Conclusions

The synthesis strategy used is effective in creating NWSP with hydrophobic backbone and hydrophilic lateral branches.

The analysis of interactions response to experimental parameters leads to the conclusion that the PAmHU behaviour correspond to a coil to micelle transition.

The transition temperature can be tuned from 22 to 50 °C by tailoring the composition of the PAmHU-water ethanol system, being possible to reach the optimum biological temperature of 37 °C.

By controlling the molecular mass dispersion of PAmHU is possible to improve the tunable behaviour of the system. Further optimization can be obtained by changing the primary structure of hydrophilic lateral branches.

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