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Large Swelling Capacities of Crosslinked Poly(N-isopropylacrylamide) Gels in Organic Solvents.

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ABSTRACT

PNIPAM hydrogels are widely studied materials which swell in a great extent in water and water like solvents (e.g. alcohols). The hydrophilic nature of PNIPAM networks is very attractive however it is an important disadvantage at the moment of encapsulating hydrophobic drugs, which minimize their use in other fields. In this work we studied the swelling in different solvent mixtures with water and also in pure nonaqueous solvents, some of them immiscible with water. Accordingly, PNIPAM gels swell strongly in highly polar solvents (e.g. chloroform) but it does not swell in slightly polar solvents (e.g. toluene). The main interaction between the solvent and the polymer chain seems to involve the hydrogen bonding with the amide group, according to the calculated Hansen parameters (δ_h). It is possible to swell the gel in binary or ternary mixtures containing toluene. In that way, non-polar substances can be loaded inside the gel to change its properties. As a proof of concept, polyaniline (PANI) solubilized in chloroform using camphorsulfonate as solubilizing counterion. The obtained nanocomposites become sensitive to pH changing colour and conductivity when exposed to basic or acidic aqueous solutions.

Hydrogels area made of cross-linked networks of hydrophilic polymer chains where the free polymer is solvated by water. In that way, hydrogels swell strongly (100-30000 %) in water.[1,2,3] Poly(N-isopropylacrylamide) (PNIPAM) is one of the most studied hydrogels, since it shows large swelling capacities. It is also thermosensitive, since show a hydrophilic to hydrophobic phase transition at ca. 32-34 °C. Since the hydrogels swell in water, it is difficult to load substances insoluble in water inside PNIPAM gels[4,5,6]. On the other hand, PNIPAM hydrogels can swell in organic solvent/water mixtures, (ethanol/water, methanol/water,[7] acetone/water,[8] and dimethylsulfoxide (DMSO)/water,[9]). In this work, we study the swelling of PNIPAM hydrogels not only in different solvent mixtures with water but also in pure nonaqueous solvents (alcohols, ketones, amides, chlorocarbons). Some of them (e.g. chloroform) are even immiscible with water. Differential Scanning Calorimetry (DSC) measurements of

PNIPAM gels swelled in different solvents show strongly different transitions. If a gel (e.g. PNIPAM) swell in two different solvents (e.g. $CHCl_3$ and water), any substance loaded in one solvent (e.g. $CHCl_3$) is retained when the solvent is removed and the dry gel is swollen in the other solvent (e.g. water). Moreover, the loaded substance is exposed to the solvent where it is insoluble and could interact with ions in the solution. As a proof of concept, we load polyaniline (PANI) from its solution in chloroform (aided by doping with camphorsulfonate counterions) and show that the modified gel, swollen in aqueous solution, is sensitive to external pH.

EXPERIMENTAL DETAILS

N-isopropylacrylamide (NIPAM) used as monomer was obtained from Scientific Polymer Products. N,N-methylenebisacrylamide (BIS), N,N,N',N'-tetramethylenediamine (TEMED) and ammonium peroxydisulfate (APS) were purchased from Sigma-Aldrich. N-methyl pyrrolidone (NMP)(S. Aldrich, 99%), ethanol (Cicarelli, 99.5%), tetrahydrofuran (THF)(S. Aldrich, 99.9%), chloroform ($CHCl_3$)(Cicarelli, 99%), acetone (Cicarelli, 99.5%), formic acid (Biopack, 85%), cyclohexane (Cicarelli, 99 %), acetonitrile (ACN)(Aldrich, 99.5%), toluene (Biopack, 99.5%), carbon tetrachloride (Aldrich, 99.5%) dimethylsulfoxide (DMSO)(Sintorgan, 99.9%), isopropanol (Cicarelli, 98%) and polyethylene glycol (PEG 200)(Aldrich) were used as received. Water used in this work was bi-distilled. All other reagents are of analytical quality. PNIPAM gels were synthesized via free-radical polymerization of N-isoprpylacrylamide (NIPAM) using bisacrylamide (BIS) as cross-linking agent. Ammonium persulfate and tetramethylethylenediamine were used as the initiator system of polymerization. The synthesis was done following the procedure described elsewhere.[10] BIS (2% molar ratio of NIPAM) was dissolved in aqueous solution of NIPAM (0.5 M) in water. The solution was purged by bubbling N_2 gas to eliminate O_2. The polymerization initiator system (APS (0.001 g/mL) with TEMED (10 µL/mL)) was added. The polymerization was carried out in a closed glass flask at 20 °C for 3 h. The gel samples are extracted, washed with flushing distilled water at room temperature for 48 h in order to remove unreacted chemicals. Then, the gels were dried at 50 ^oC under dynamic vacuum for 48 hs and stored in a desiccator. Swelling capacity measurements were carried out for PNIPAM hydrogels in different pure solvents. Dried hydrogel samples, previously weighed, were placed in the solvent at room temperature (20 °C). The sample was removed from solution, at certain time intervals, and the excess solvent wiped with tissue paper. Then it was weighed in an analytic balance and placed back in the bath. When the gel reaches the equilibrium condition, the weight of gel (Weq) does not change with the time so the percentage of equilibrium swelling ($\%Sw_{eq}$) is calculated by the following equation:

$$\%S_{weq} = 100 * Weq/W_0 \qquad \text{(eq. 1)}$$

The studied solvents were: water, N-methyl pyrrolidone (NMP), ethanol, tetrahydrofuran (THF), chloroform ($CHCl_3$), acetone, formic acid, cyclohexane, acetonitrile, toluene, carbon tetrachloride, dimethylsulfoxide, isopropanol and polyethylene glycol (PEG 200).

The incorporation of polyaniline (PANI) inside PNIPAM hydrogel was made by sorption from its solution in $CHCl_3$. PANI is insoluble in water and $CHCl_3$ but it can be solubilized in the later by doping with camphorsulfonate counterions.[11] To do that, 0.1 g of solid PANI (emeraldine base), synthesized as described before,[12] was immersed in 1 M camphorsulfonic acid/$CHCl_3$ and stirred for 2 hs. The loading was carried out by swelling the dry PNIPAM gel in the PANI solution with constant stirring

during 24 h, enough time to reach maximum swelling. Differential Scanning Calorimetry measurements were performed in a 404 F1 DSC (Netzch) with a 10 °C/min ramp beginning at -20 °C. Electrical Conductance was measured on nanocomposite cylinders using two gold film electrodes pressed on the extremes and a digital multimeter (Brymen BM202).

RESULTS & DISCUSSION

The swelling at equilibrium of PNIPAM gels was measured in several organic solvents and water. (Fig. 1)

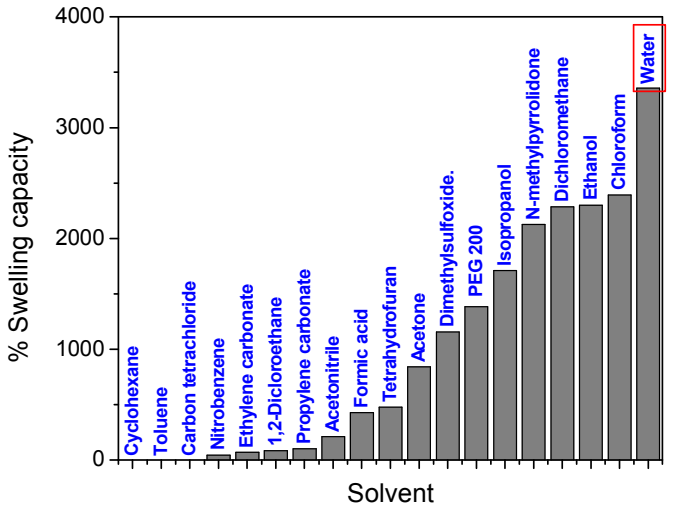

Figure 1. Percentage of equilibrium swelling ($\%Sw_{eq}$) of PNIPAM in different solvents at 20 °C during 48 h. The reported data was the averaged of three measurements.

Water is the best solvent for PNIPAM swelling but other solvents swell significantly PNIPAM gels. (Fig.1) $CHCl_3$ and CH_2Cl_2, non-aqueous solvents which are immiscible with water, show a large swelling capacity, similar to ethanol, a water-like solvent. It seems that hydrogen bonding of solvent molecules with the amide group in PNIPAM monomer units is relevant to the swelling capacity.

Table 1. Effect of solvent nature on the kinetics of PNIPAM swelling.

Solvent	n	k	Type of Diffusion	Correlation coefficients
H_2O	0.47 (+/- 0.1)	0.0409 (+/- 0.0001)	Non-Fickian	0.99
EtOH	0.49 (+/- 0.1)	0,0516 (+/- 0.0002)	Fickian	0.96
$CHCl_3$	0.63 (+/- 0.2)	0,0464 (+/- 0.0001)	Non-Fickian	0.94
THF	0.49 (+/- 0.1)	0,1080 (+/- 0.0005)	Fickian	0.91
NMP	0.43 (+/- 0.2)	0,0453 (+/- 0.0001)	Non-Fickian	0.97

The alcohols and water could build donor hydrogen bonds with >C=O group and acceptor H bonds with N-H. On the other hand, secondary amides (e.g. DMF or NMP) and ketones only have acceptor bonds with >N-H. In the case of chloroform and dichloromethane, donor hydrogen bonding seems to exist. The kinetic measurement of gel swelling, can be interpreted using a power law model,[13]:

$$W_t/W_{oo} = k\, t^n \qquad \text{(eq. 2)}$$

The measurements made for selected solvents (Table 1) show a strong effect of solvent nature on the mass transport (Fickian or anomalous) of solvent inside the gels.

PNIPAM is a thermosensitive gel which has an hydrophilic to hydrophobic phase transition at 32 ^{o}C.[14] The LCST transition shows as a clear endothermic peak in the differential scanning calorimetry scan (Fig. 2). PNIPAM swollen in ethanol shows an exothermic transition peak (called upper critical solution temperature (UCST)) at 59 °C. These results are in good agreement with those reported by other authors[15]. No peak is observed in the 0-50 ^{o}C (Fig. 2, green line) in chloroform. PNIPAM swelled in NMP show two weak lower critical solution temperatures (LSCT) transition peaks at 42 °C and 62 °C. It was reported before that to PNIPAM-co-2%AMPS hydrogels swollen in NMP,[16] show a LSCT at ca. 56 °C. Since NMP is highly hygroscopic, the transition at 42 ^{o}C could be due to remaining water.

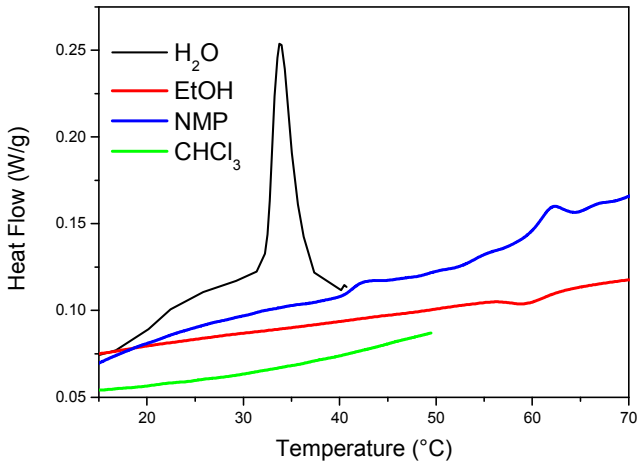

Figure 2. DSC thermograms of: PNIPAM swelled in water (black line), ethanol (red line), N-methylpyrrolidone (blue line) and chloroform (green line).

The possibility of swelling PNIPAM gels in nonaqueous solvents allows loading molecules which are insoluble in water inside the gel. Upon removal of the nonaqueous solvent and swelling of the modified gel in water, the loaded molecule could be exposed to aqueous media. As a proof of concept, a conducting polymer (polyaniline, PANI) was dissolved in $CHCl_3$ using camphorsulfonate as solubilizing counterion. Then, pieces of dry PNIPAM gels were swelled in the solution, loading PANI-CSA inside PNIPAM.(Fig. 3). When chloroform is removed from PNIPAM-PANI-CSA nanocomposites and they are swelled in water, PANI chains are exposed to aqueous solution. This is evident since changing the pH of the external solution alters de protonation state of PANI (Fig. 4) as it can be seen by changes in optical absorption and conductivity. It is well known that protonated PANI (emeraldine salt, pH < 3) presents a green colour (Fig. 4.A) while deprotonated PANI (emeraldine base, pH >5) show a blue colour (Fig. 4.B).

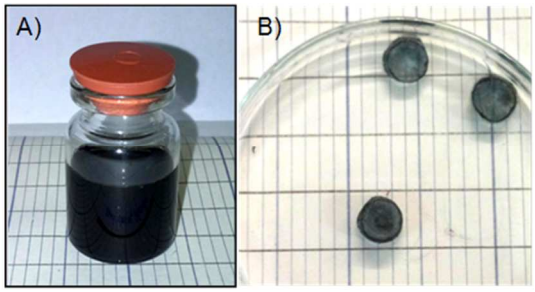

Figure 3. (A) Swelling solution of polyaniline (PANI) in 1 M camphorsulfonic acid(CSA)/$CHCl_3$. (B) PNIPAM gel pieces loaded with PANI-CSA.

The color changes are due to the different optical absorption spectra of the different PANI forms.[17]

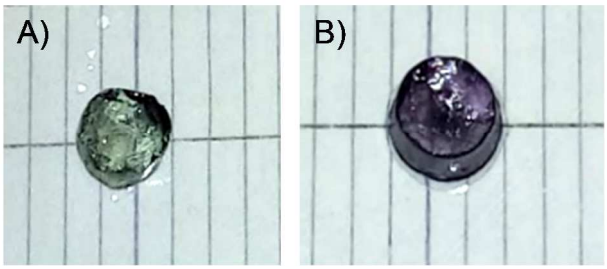

Figure 4. PNIPAM gel pieces loaded with PANI-CSA exposed to aqueous solutions of pH=1 (A) and pH = 10 (B).

A PNIPAM-PANI-CSA gel cylinder show a conductance ca. 45 times larger when exposed to pH 1 solution, than the same gel exposed to pH 10 solution (Table 2). This is expected since protonated PANI chains bear mobile charge carriers (polarons) while deprotonated PANI, albeit conjugated, is a neutral molecule.[18]

Table 2. pH effect on the electrical conductance of PNIPAM-PANI-CSA nanocomposites.

Material	pH	Conductance (mS)
PNIPAM-PANI-CSA	1	1.97
PNIPAM-PANI-CSA	10	0.043

A similar loading with PANI (emeraldine base) can be made from its solution in N-methylpyrrolidone.[16]. It was suggested that a true semi-interpenetrated network of PANI inside PNIPAM is produced since both PANI and the free segments of PNIPAM (between crosslinks) are dissolved in the solvent.[16] The procedure shown here should also produce a true semi-interpenetrated network of PANI-CSA inside PNIPAM gel. The loading from nonaqueous solvents could also be used to load different molecules into the PNIPAM gels.[19]

CONCLUSIONS

Although, there are some studies about the swelling capacity in solvent mixtures, in this work we proved for the first time, their ability of swelling in different pure solvents from ethanol to chloroform, allowing the material to be defined as a solvogel. Additionally, the same PNIPAM gels can swell water, making the material an amphigel.While DSC measurements of PNIPAM swelled in water show the well-known endothermic LCST transition at 32-34 ^{o}C, no transition was observed in chloroform. In N-metyhylpyrrolidone a weak peak is observed at 62 ^{o}C while in ethanol, an exothermic peak (UCST) can be found at 59 ^{o}C. Therefore, the nature of the swelling solvent affects strongly the kind of transition. The ability to swell in nonaqueous solvents is used to load polyaniline (PANI) inside PNIPAM gels from solutions in camphorsulfonic acid/$CHCl_3$. When $CHCl_3$ is removed and the nanocomposite is swelled in water, PANI is exposed to aqueous solution as it is shown by its sensitivity to pH which affects the optical absorption and electrical conductivity. A true semi-interpenetrated network of PANI-CSA into PNIPAM gel seems to be produced.

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REFERENCES

[1] M. Verhulsel, M. Vignes, S. Descroix, L. Malaquin, D. M. Vignjevic and J.-L. Viovy, *Biomaterials*, **35**, 1816-1832, (2014).
[2] E. S. Dragan, *Chemical Engineering Journal*, **243**, 572-590 (2014).
[3] E. Caló and V. V. Khutoryanskiy, *European Polymer Journal*, **65**, 252-267. *(*2015*)*
[4] H. Ozay and O. Ozay*, Chemical Engineering Journal*, **232**, 364-371, (2013).
[5] W. Yun Zhang and C. James Yang, *Chemical Communications*, **47**, 9312-9314, (2011).
[6] R. Nishiyabu, S. Ushikubo, Y. Kamiya and Y. Kubo, *J. Mater. Chem.A*, **2**, 15846-15852 (2014).
[7] I. Bischofberger, D. C. Calzolari and V. Trappe, *Soft Matter*, **10**, 8288-8295(2014).
[8] A. Hüther, X. Xu and G. Maurer, *Fluid Phase Equilibria*, **219**, 231-244, (2004).
[9] M. M. Ozmen and O. Okay, *European Polymer Journal*, **39**, (2003) 877-886.
[10] M. V. Martínez, C. R. Rivarola, M. C. Miras and C. A. Barbero, *Sensors and Actuators B: Chemical*, **241**, 19-32, (2017).
[11] S.S. Jeon, C. Kim, T.H. Lee, Y.W. Lee, K. Do, J. Ko, S.S. Im, *J. Phys. Chem. C*, **116**, 22743–22748, (2012).
[12] G.M. Morales, M. Llusa, M.C. Miras, C. Barbero, *Polymer*, **38**,5247-5250, (1997)
[13] F. Ganji, S. Vasheghani-Farahani, E. Vasheghani-Farahani, Iran. Polym. J., **19**,375-398, (2010)
[14] R.E. Rivero, F. Alustiza, N. Rodríguez, P. Bosch, M.C. Miras, C.R. Rivarola, C.A. Barbero, *React. Funct. Polym.*, **97**,77-85, (2015)
[15] R.O. Costa and R.F. Freitas, *Polymer* **43**, 5879-5885 (2002)
[16] M.V. Martínez, S. Bongiovanni Abel, R. Rivero, M.C. Miras, C.R. Rivarola, C.A. Barbero, *Polymer*, **78,** 94-103, (2015)
[17] S. Bongiovanni Abel, E.I Yslas, C.R. Rivarola, C.A Barbero, *Nanotechnology,* **29**, (2018) Nr. 125604
[18] D. A. Acevedo, A. F. Lasagni, C. A. Barbero, F. Mücklich*, Adv. Mater.,* **19**, 1272- 1275 (2007)
[19] M.V. Martinez, M. Molina, C.A. Barbero, *J. Physical Chemistry, B*, in press (2018). DOI: *10.1021/acs.jpcb.8b07625*.