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Hydrogels based on PAAm network with PNIPAAm included: hydrophilic–hydrophobic transition measured by the partition of Orange II and Methylene Blue in water

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Abstract

This work describes the transition from hydrophilic to hydrophobic in hydrogels of Polyacrylamide (PAAm) having Poly(*N*-isopropylacrylamide) (PNIPAAm) included. The transition was measured through the partition coefficient, *K*, Orange II and Methylene Blue dyes at several temperatures, using different amount of Acrylamide (AAm), Methylene-bis-acrylamide (MBAAm), as cross-linking agent, and PNIPAAm. The dye concentration in the gel and the solution were measured using UV–Vis spectroscopy. Values of partition coefficient, *K*, were determined as the ratio of the dye concentration in hydrogel relative to water. Methylene Blue, the less hydrophilic dye, showed higher *K* values when compared to Orange II, more hydrophilic one. Value of *K* depends on the temperature and on the PNIPAAm content. The PNIPAAm chains are solvated by water and randomly distributed at temperatures below 32 °C, the LCST of PNIPAAm, but collapse near or above the LCST. The collapsed PNIPAAm chains induce a more hydrophobic environment that increases the solubility of Methylene Blue and decreases the solubility of Orange II in the hydrogels of PAAm with PNIPAAm included. These hydrogels show potential application concerning the separation processes, where the temperature and/or the hydrophilicity control the diffusion.

Keywords: Hydrogel; Partitioning; LCST

1. Introduction

In general, hydrogels are biocompatible [1] and may be applied in drug delivery systems [2–10], immobilization of enzymes [11–15], cell culture [16–20], etc. Hydrogels are made of hydrophilic three-dimensional polymer networks able to take up large amounts of water [21–24]. The water inside of the hydrogel, in high content, fills up the mesh (or pores) and allows selective diffusion of solutes through the hydrogel polymeric matrix. These characteristics allow guided hydrogels to be used in a membrane separation process [1].

Hydrogels that respond to temperature changes have been used in many applications, particularly in processes related to drug delivery [1,25]. Tanaka and co-workers were the pioneers [26] in investigating the effect of temperature on gels of N-substituted acrylamides. They observed that hydrogels of poly(*N*-isopropylacrylamide), PNIPAAm, when heated above 32 °C exhibits a volume collapse associated with a hydrophilic–hydrophobic transition [25, 26] This phenomenon was widely investigated and several synthesis of such hydrogels were proposed as well as their applications [25]. However, a serious limitation of PNIPAAm hydrogels in many applications is the low mechanical strength of such gels when highly swollen [27]. To overcome this problem, thermo-sensitive hydrogels based on PNIPAAm were prepared with satisfactory mechanical properties by trapping PNIPAAm in the network to form a semi-interpenetrating network, semi-IPNs [27–30]. According to literature, semi-IPNs hydrogels having PNIPAAm entangled in polyacrylamide, PAAm, network are mechanically stable and their response to temperature, due to the presence of PNIPAAm, is preserved [28–30].

There is interest in systems like PNIPAAm-based hydrogels for drug delivery applications [25]. Changes in the swelling ratio of PNIPAAm gels by raising the

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temperature influence seriously the diffusion of solutes from the interior of gels to outside aqueous medium [30]. So, the value of Lower Critical Solution Temperature (LCST) of PNIPAAm-based hydrogels may be adjusted to be close to the human body temperature (37 °C) [25].

Hoffman and co-workers developed a system for delivering vitamin B12 [31]. The collapsed PNIPAAm hydrogel was incubated overnight in a cold (4 °C) solution containing B12 to maximize the loading of the drug into hydrogel network. Placing the gel in water and heating the system above the LCST of PNIPAAm led to a release of the vitamin as monitored by UV–Vis spectroscopy.

Membranes of cross-linked polyacrylamide having poly(*N*-isopropylacrylamide) included, like semi-IPN hydrogels, were studied by Muniz and Geuskens [30]. The permeability to Orange II was determined at temperatures ranging from 25 to 40 °C. Around 32 °C the permeability to Orange II increases sharply, indicating that the PNIPAAm influences the average mesh size of the membrane, in comparison to PAAm hydrogels without PNIPAAm, used as control.

It is well established that the solute transport in hydrogels occurs in filled regions in the space delimited by the polymer chains [32,33]. Any factor that reduces the size of this space, or pores, will have an effect on the transport of solute through the membrane. Kiso [32] studied the combination of these factors analyzing the influence of the hydrophobicity and the molecular size in aromatic pesticide rejection in membranes for nanofiltration. This effect can be studied through the determination of the partition coefficient [32,33], K, which can be defined as the ratio between solute solubility in the gel phase and the solute solubility in the water phase [34]. Thus, when the value of K approaches to 1, it can be assumed that the solute–water and solute–hydrogel interactions are equivalent.

To investingate the affinity between Orange II and Methylene Blue with PAAm–PNIPAAm semi-IPN hydrogels, in different formulations, we measured the partition coefficient (K) of both solutes as a function of temperature, cross-linking degree, amount of PNIPAAm and polyacrylamide, PAAm.

2. Experimental

2.1. Synthesis of PNIPAAm

The *N*-isopropylacrylamide (NIPAAm) monomer (Acros Organics, 2210-25-5) was recrystallized in hexane. Aqueous solution (100 ml) containing 442.0 μmol ml^{-1} of NIPAAm and 16.8 μmol ml^{-1} of sodium persulfate ($Na_2S_2O_8$, Aldrich, 21,623) was prepared. The solution was nitrogen purged for at lest 30 min and 0.7 ml of N,N,N'N'-Tetramethylenediamine (TEMED, Aldrich, T2-250-0) 7 μmol ml^{-1} aqueous solution, used as an accelerator, was added. The flask was closed, covered with aluminum foil and kept under agitation for 24 h at room temperature. The PNIPAAm from aqueous solution was purified by precipitation in water at 60 °C.

2.2. Preparation of hydrogel

Semi-IPNs hydrogels, based on PAAm networks and having PNIPAAm included, were obtained by polymerizing acrylamide, AAm, (Aldrich, 14,866-5) in aqueous solution containing PNIPAAm, Methylene-bis-acrylamide (MBAAm, Plusone, 17-1304-02) as the cross-linking agent. To perform the hydrogels synthesis, two solutions were prepared. Solution A contains AAm, MBAAm, PNIPAAm and TEMED. The concentrations of AAm, MBAAm and PNIPAAm in the synthesis are described in Table 1. The concentration of TEMED was maintained in 3.2 μmol ml^{-1}. Aqueous solution B contains sodium persulfate in the concentration of 42.0 μmol ml^{-1}. After N_2 purging the solutions during 20 min, 18 ml of solution A and 2 ml of solution B were mixed and the resultant solution was quickly inserted between two glass plates (12 × 12 cm^2) separated by a rubber gasket (0.6 mm thick). The system was kept at room temperature during 24 h. The notation (M–X–P), used to characterize the gels, means: M = molality of AAm in the feed aqueous solution used to synthesis of the gel; X = amount of cross-linking agent denoted as the ratio of MBAAm to AAm (in mol %), and P = concentration (in wt%) of the PNIPAAm in the feed aqueous solution used.

2.3. Partition coefficient measurements

Aqueous solutions of Methylene Blue (Synth, Brazil, 32214) and Orange II (Fluka, 75370) were prepared, in the concentrations of 148 μmol ml^{-1} and 140 μmol ml^{-1}, respectively. After that, the hydrogels were immersed in

Table 1
Concentrations of AAm, MBBAm and PNIPAAm of feed solutions used for the synthesis of the hydrogels (2.5-1-P), (5-1-P) and (5-5-P)

	AAm (μmol ml^{-1})	MBAAm (μmol ml^{-1})	PNIPAAm (wt%)
System 2.5-1-P			
(2.5-1-0)	2500	25	0
(2.5-1-1.3)	2500	25	1.3
(2.5-1-2.5)	2500	25	2.5
(2.5-1-5)	2500	25	5.0
System 5-1-P			
(5-1-0)	5000	50	0
(5-1-1.3)	5000	50	1.3
(5-1-2.5)	5000	50	2.5
(5-1-5)	5000	50	5.0
System 5-5-P			
(5-5-0)	5000	250	0
(5-5-1.3)	5000	250	1.3
(5-5-2.5)	5000	250	2.5
(5-5-5)	5000	250	5.0

25 ml of the dye solutions. The volume of the hydrogel was evaluated by measuring its thickness and area. After 24 h of immersion, the concentration of the reminiscent dye in the aqueous solution was determined by UV–Vis spectroscopy. The hydrogels were kept immersed in carefully closed recipients to prevent water from entering or evaporating. Spectra of dye in water were obtained and the readings were done at wavelength 486 and 664 nm for Orange II and Methylene Blue, respectively. Partition coefficients were determined at temperatures from 25 to 40 °C, basing in the initial and final concentrations of the dyes. The partition coefficients were determined as the ratio between the solubility of the dye in the hydrogel and in the water.

3. Results and discussion

3.1. Hydrophilic–hydrophobic properties of the dyes

The difference in the hydrophilic character between Methylene Blue and Orange II can be understood by comparing their structures. In the Methylene Blue molecule presented in Fig. 1, there are three nitrogen atoms that could interact with water through H-bonds. However, the methyl groups linked to the two non-aromatic nitrogen atoms decrease the capability of such interactions due to the stabilization provided by its electron donating character and by stereo hindrance. The molecule of Orange II, as depicted in Fig. 2, presents the azo-conjugated group in which two nitrogen atoms are involved. Thus, the unpaired electrons are dispersed along the molecular chain where four oxygen atoms enhance the electronic density. This way, the formation of H-bonds is more favored in the Orange II molecule. Concerning these aspects, it can be pointed out that Orange II presents higher hydrophilic character than Methylene Blue. The molar mass is similar: 350.33 and 373.90 g mol^{-1}, respectively. This fact allows us to study the effect of the affinity of the dyes with the hydrogel in aqueous media, without significant influences on the size of these molecules.

The hydrophilic–hydrophobic dye capabilities were evaluated by measure the partition coefficient, K, in solvents of different polarity relative to water at 25 and 40 °C. The values of K obtained to *tert*-amyl alcohol, methylene chloride and hexane are presented in Table 2. The data of Table 2 shows that Methylene Blue is less hydrophilic than Orange II because it is more soluble in methylene chloride, of intermediate polarity, than in *tert*-amyl alcohol, a polar one, or in hexane completely non polar. On the other hand, Orange II is only barely soluble in hexane or methylene chloride. An increase on temperature from 25 to 40 °C decreases the dyes solubility in those solvents and enhances the dyes solubility in water.

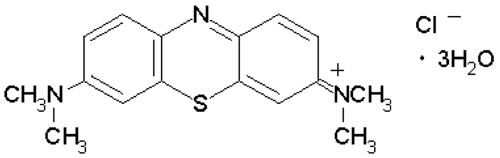

Fig. 1. Molecular structure of Methylene Blue.

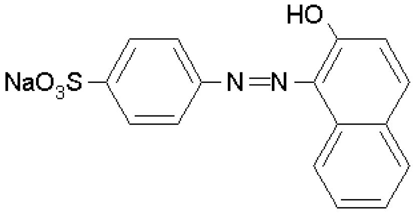

Fig. 2. Molecular structure of Orange II.

3.2. Partition coefficients of dye in hydrogels relative to water

The dependence of partition coefficient, K, of Orange II in (2.5-1-P) hydrogel relative to water on temperature is presented in Fig. 3. A decrease in the solubility of the Orange II in swollen hydrogels of (2.5-1-P) was observed when heated from 25 to 40 °C. This means that the hydrogels become less hydrophilic when heated, even in the swollen state. The effect is sharper when the (2.5-1-P) semi-IPNs hydrogels are heated above the LCST of PNIPAAm. When the content of PNIPAAm in hydrogel is increased, the curves of K vs. temperature are S-shaped and their inflexion is close to 32–33 °C, the LCST of PNIPAAm in water. When Methylene Blue is used, a quite different behavior was observed and the results are illustrated in Fig. 4. The solubility of Methylene Blue in the hydrogels increases by raising the temperature, but only to semi-IPN. For the (2.5-1-0) hydrogel the solubility of Methylene Blue decreases. This means that the raise in the hydrophobic character is not due to the PAAm network but it is probably due to the presence of PNIPAAm. As observed in Fig. 4, the curves are S-shaped and the transition is close to the LCST of PNIPAAm. Other aspect to be highlighted here is the dependence of K of Methylene Blue on the PNIPAAm content. The values of K for Methylene Blue are not proportional to the PNIPAAm content below the LCST, but they became almost the same at 40 °C.

In Fig. 4, we can observe the effect of the hydrophilic–hydrophobic transition of the PNIPAAm on the solubility of Methylene Blue. In temperatures above the LCST of the

Table 2
Partitioning of Orange II and Methylene Blue dye in phase equilibrium of non-polar solvent–water (1:1) at temperatures of 25 and 40 °C

Non-polar solvent	Partition coefficient, Kx10^2			
	Orange II		Methylene Blue	
	25 °C	40 °C	25 °C	40 °C
tert-Amyl alcohol	25.0 ± 8.0	20.0 ± 1.0	31.0 ± 9.0	9.0 ± 1.0
Methylene chloride	2.0 ± 0.1	2.0 ± 0.1	127.0 ± 1.9	99.0 ± 1.5
Hexane	0.1 ± 0.0	0.1 ± 0.0	26.0 ± 2.0	28.2 ± 2.0

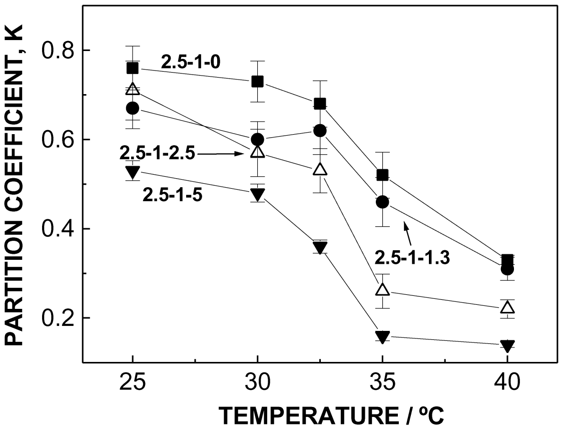

Fig. 3. Partition coefficient of Orange II as a function of temperature for PAAm/PNIPAAm semi-IPN hydrogels of (2.5-1-P) system.

PNIPAAm, an increase in the solubility of Methylene Blue in the semi-IPN hydrogels was noticed. The heated semi-IPN hydrogels are less hydrophilic, which favors the interaction with the Methylene Blue. It is important to emphasize that the transition from hydrophilic to hydrophobic through heating is due to the re-orientation of PNIPAAm chains. Above 32 °C the solubility of Methylene Blue in the PAAm network decreases. This can be compared to the results found by Muniz and Geuskens [30] in hydrogels based on polyacrylamide network having PNIPAAm included. They observed a less swollen degree of the PNIPAAm semi-IPNs hydrogels for temperatures above LCST. In Fig. 4, the (2.5-1-5) hydrogel, richer in PNIPAAm for the (2.5-1-P) system, presented a sharp variation in the values of *K* in the immediacy of the LCST of PNIPAAm. In contrast, the hydrogel (2.5-1-0), without PNIPAAm, presented only a slight interaction with Methylene Blue, when compared to the other hydrogels of the (2.5.1-P) system. This is due to the high hydrophilicity of the PAAm network.

The dependence of *K* on the amount of PNIPAAm, for Orange II and Methylene Blue in different temperatures, for the (2.5-1-P) system is presented in Figs. 5 and 6, respectively. When PNIPAAm is added in the hydrophilic PAAm network, the solubility of Orange II within the hidrogel decreases. This effect becomes more intense when the hidrogel is heated above the LCST. Such lowering of Orange II solubility is more important in warmed hydrogels having high amounts of PNIPAAm. However, according to the results observed in Fig. 6, the behavior for Methylene Blue is the opposite of that found for Orange II. By heating semi-IPN hydrogels of (2.5-1-P) system, as represented in Fig. 6, the solubility of Methylene Blue in the polymeric matrix increases abruptly.

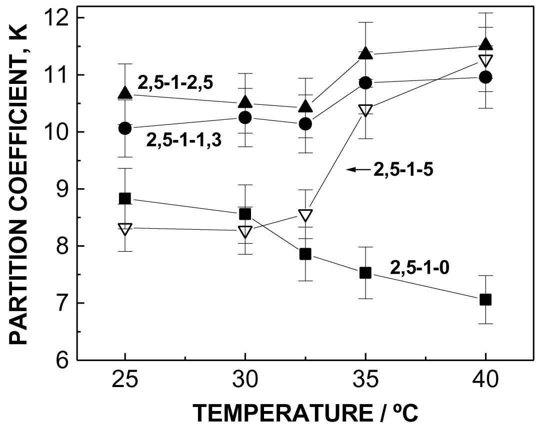

Fig. 4. Partition coefficient of Methylene Blue as a function of temperature for PAAm/PNIPAAm semi-IPN hydrogels of (2.5-1-P) system.

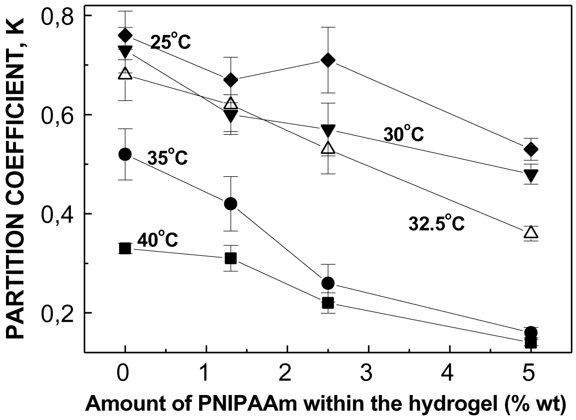

Fig. 5. Partition coefficient of Orange II as a function of amount of PNIPAAm within PAAm/PNIPAAm semi-IPN hydrogels of (2.5-1-P) system.

Orange II showed higher solubility in the (5-1-0) hydrogel (Fig. 7) than in the (2.5-1-0) hydrogel (Fig. 3). It should be pointed out that this finding is due to the high concentration of PAAm in the polymer matrixes of (5-1-P) hydrogels. Another important factor to be observed is the decrease in the solubility of Orange II in the hydrogels by increasing the temperature and raising the PNIPAAm content. From the curves of hydrogels from the (5-1-P) system, presented in Fig. 7, it can be observed that the richer

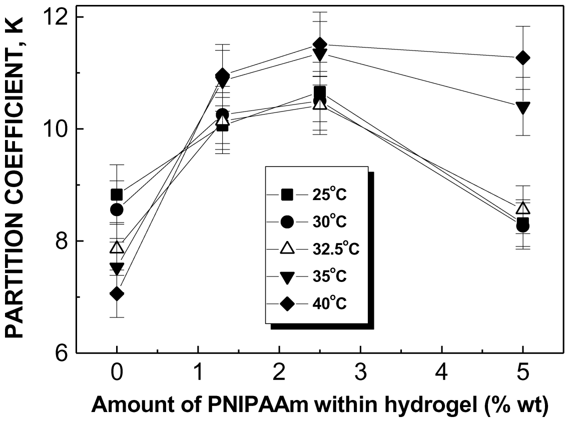

Fig. 6. Partition coefficient of Methylene Blue as a function of amount of PNIPAAm within PAAm/PNIPAAm semi-IPN hydrogels of (2.5-1-P) system.

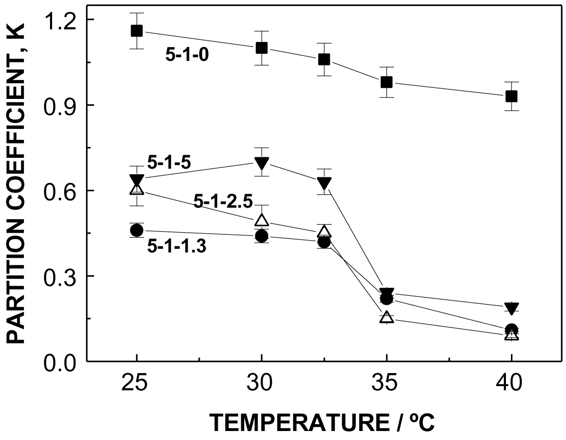

Fig. 7. Partition coefficient of Orange II as a function of temperature for PAAm/PNIPAAm semi-IPN hydrogels of (5-1-P) system.

in PNIPAAm the hydrogel is the sharper is the variation of *K* in the vicinity of LCST.

Curves of *K* obtained for Methylene Blue using hydrogels from (5-1-P) system are displayed in Fig. 8. The curve relative to (5-1-0) hydrogel in Fig. 8 decreases with the temperature. This may be connected to the fact that Methylene Blue is more soluble in hot water than in warmed PAAm network. When the PNIPAAm content is around 1.3 wt%, a slight affinity of semi-IPN hydrogel with the dye may be observed. When the PNIPAAm content is 2.5 wt%, a slight increment in *K*, near and above the LCST, was observed. However, when the PNIPAAm content is 5 wt% and the temperature is raised, a sharp increase in *K* for Methylene Blue was observed. This way, the addition of PNIPAAm into PAAm network favors the solubility of the Methylene Blue within the warmed hydrogel. This behavior was not observed in the experiments using Orange II. Another important aspect is that the water molecules are more organized within the polymer network, compared to the water outside of the hydrogel. In fact, only a fraction of water in hydrogel is considered as free water [35]. Organized water in the hydrogel experiences several orientations, leading to different behavior relative to the free water molecules [35]. The solubility of Orange II and Methylene Blue rises in free warmed-water outside the hydrogel, but the capability of water inside of PAAm hydrogel to solvate the dye is not increased at same level, then, it results in a decrease in *K* values.

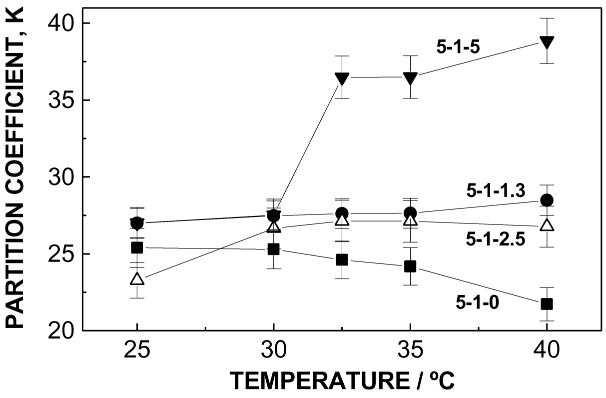

Fig. 8. Partition coefficient of Methylene Blue as a function of temperature for PAAm/PNIPAAm semi-IPN hydrogels of (5-1-P) system.

Curves of *K* obtained for Orange II as a function of temperature for the (5-5-P) system are represented in the Fig. 9. The curve related to the hydrogel (5-5-0) showed a non-linear decreasing as a function of the temperature. In the case of semi-IPNs hydrogels, the values of *K* also decrease, but it is more evident in temperatures above LCST.

The dependence of *K* on the temperature for Methylene Blue within hydrogels from the (5-5-P) system is depicted in Fig. 10. The (5-5-0) hydrophilic hydrogel showed less affinity with Methylene Blue, as expected. The behavior of the (5-5-1.3) and (5-5-2.5) hydrogels is quite similar and different to those of (2.5-1-P) and (5-1-P) systems. It may be due to the fact that hydrogels of the (5-5-P) system are highly cross-linked and thus, more compacted. In the compacted hydrogels, the mobility of the PNIPAAm chains is decreased and, thus, its re-orientation. Then, near or just above the LCST no sharp variation in *K* occurs anymore. In this system, the affinity Methylene Blue with the hydrogel increases as the PNIPAAm content is raised.

The presence of PNIPAAm inside PAAm hydrogel decreases considerably the values of *K* for Orange II, namely in the hydrogels from the (5-1-P) system. The PNIPAAm chains occupy spaces that would be occupied by water, as do the water in hydrogels of PAAm having no PNIPAAm included. Thus, the addition of PNIPAAm decreases the mesh size. In temperatures above LCST of PNIPAAm, the solubility of Orange II in the polymeric matrix decreases abruptly. When heated, the PNIPAAm chains change from hydrophilic to hydrophobic character [34] and, consequently, the non-polar groups reduce the diffusion of Orange II into the hydrogel, decreasing the solubility of the dye. The decrease in *K* for Orange II in PAAm hydrogels as the temperature is raised may be connected to the increase in the solubility of the dye in hot water. For better understanding, we quantified the solubility

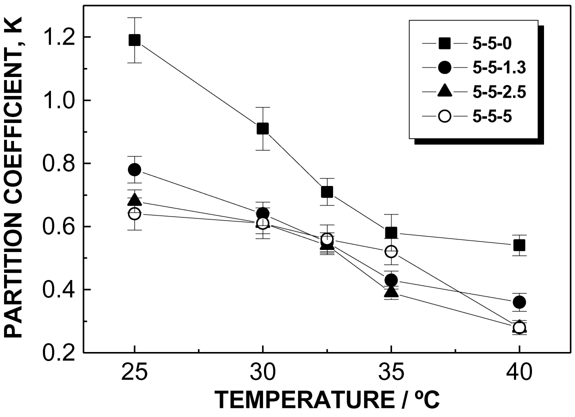

Fig. 9. Partition coefficient of Orange II as a function of temperature for PAAm/PNIPAAm semi-IPN hydrogels of (5-5-P) system.

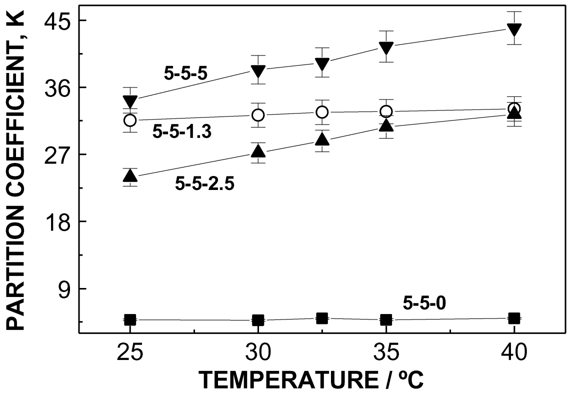

Fig. 10. Partition coefficient of Methylene Blue as a function of temperature for PAAm/PNIPAAm semi-IPN hydrogels of (5-5-P) system.

of Orange II in water at different temperatures. It was observed that the maximum solubility of Orange II is 64.5 mg ml^{-1} in water at room temperature. However, at 60 °C the solubility in water is 139 mg ml^{-1}. Thus, the Orange II is more soluble in hot water.

According to literature [30], the permeability of PAAm hydrogels increases as the temperature is raised and in addiction, PAAm hydrogels having PNIPAAm included should present lower permeability to Orange II at temperatures above the LCST of the PNIPAAm due to the predominance of hydrophobicity. However, an opposite behavior was verified: a considerable increase of the permeability to Orange II on PAAm/PNIPAAm semi-IPN hydrogels when the temperature is close to LCST [30]. The collapsed-PNIPAAm chains are mechanically supported by PAAm network and this fact provides an increase of the average mesh size. Guilherme and Muniz [34] recently developed membranes based in alginate-Ca^{2+} having PNIPAAm included. The authors observed that the permeability of such hydrogels to Orange II decreases in temperatures above the LCST. The interpretation of the data was based in the complex formation involving H–N< groups (of the PNIPAAm) and carboxyl groups (of alginate). According to that approach, the complex would exposure non-polar groups of the PNIPAAm towards the pores of hydrogel, decreasing the interaction between the hydrogel and Orange II. The results obtained in the present work, concerning the measure of partition coefficient for Orange II and Methylene Blue, match very well the conclusions pointed out for the membranes from alginate-Ca^{2+}/PNIPAAm.

Despite of hydrogels from the (5-1-P) and (5-5-P) systems to be 2 and 10 fold more cross-linked than the (2.5-1-P) system, respectively, the values of *K* for Orange II fell in the same range, from 0.15 to 1.2. In fact, the dependence of *K* on the cross-linking degree is more important in hydrogels having 5 wt% of PNIPAAm included. Curves of *K* obtained for Orange II and Methylene Blue as a function of MBAAm content, in different temperatures, are presented in Figs. 11 and 12, respectively.

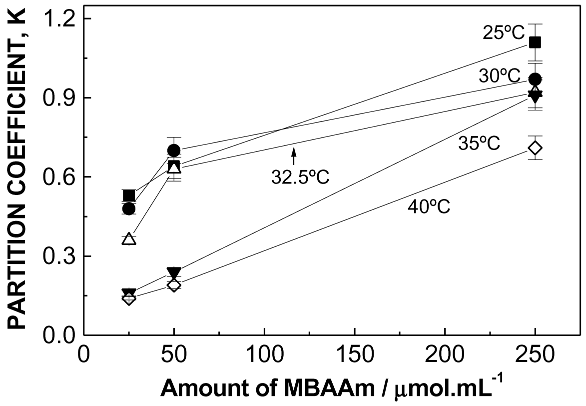

Fig. 11. Partition coefficient of Orange II as a function of amount of MBAAm in different temperatures for PAAm/PNIPAAm semi-IPN hydrogels (AAm-MBAAm-5) system.

According to the curves of Fig. 11, the solubility of Orange II in the PAAm/PNIPAAm hydrogels increases almost linearly to the cross-linking degree. This means that the affinity of Orange II with the hydrogel is not strongly dependent on the cross-linking degree. Taking into account that the size of the dye is much smaller than the average mesh size of the polymeric matrix, it could be pointed out that the diffusion of the dye in the hydrogel is more dependent on the hydrophilic or hydrophobic environment. To reinforce this analysis, we can observe in Fig. 11 that the solubility of Orange II in the polymeric matrix is not significantly affected by the increase of the cross-linking degree when compared to the sharp dependence of *K* on the amount of MBAAm, found for the Methylene Blue (Fig. 12). The Methylene Blue is easily soluble in the hydrogel due to the presence of PNIPAAm inside the matrix because the solubility of Methylene Blue is higher in semi-IPN than the respective PAAm hydrogel. This indicates that the hydrophobicity, enhanced by the presence of PNIPAAm, is a predominant factor and that the *K* is not strongly dependent of the mesh size. For this reason, the solubility of the Orange II is larger when the polymeric matrix becomes more

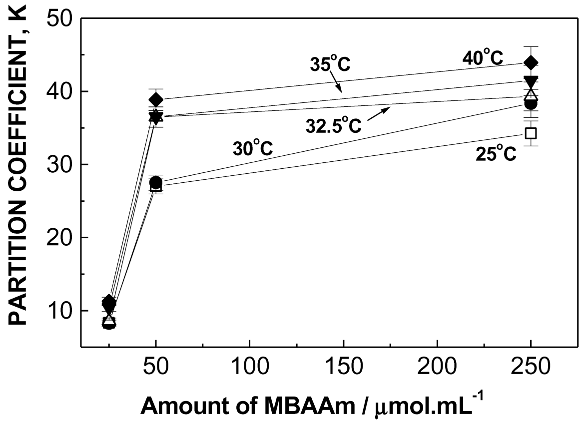

Fig. 12. Partition coefficient of Methylene Blue as a function of amount of MBAAm in different temperatures for PAAm/PNIPAAm semi-IPN hydrogels (AAm-MBAAm-5) system.

hydrophilic. The dependence of *K* for Methylene Blue to the cross-linking degree for hydrogels having 5 wt% included increase suddenly as the amount of MBAAm reaches 50 μmol L^{-1} and the effect is more intense at 40 °C. The increase of the mesh size induced by the collapsing of the PNIPAAm chains and presence of great amount of non-polar groups facilitate the diffusion of Methylene Blue into the polymeric matrix.

4. Conclusions

The transition from the hydrophilic character to the hydrophobic one by warming the hydrogels of PAAm having PNIPAAm included was characterized by measuring the partition coefficient, *K*, of Orange II and Methylene at several temperatures, changing the amount of PAAm, cross-linking degree and PNIPAAm. Methylene Blue, a less hydrophilic dye, showed higher *K* as compared to Orange II, a more hydrophilic one. The effect is dependent on the temperature and on the PNIPAAm content. The cross-linking degree has more influence on the *K* of Methylene Blue than that of the Orange II. The results were explained taking into account that the PNIPAAm chains are water soluble and randomly distributed at 32 °C, the LCST of PNIPAAm, but became collapsed near or above the LCST. At that condition, the PNIPAAm chains became more hydrophobic, but greater shrinking is avoided by the presence of PAAm network. The collapsed PNIPAAm chains induce a more hydrophobic environment that increases the solubility of Methylene Blue and decreases the solubility of Orange II in the hydrogels of PAAm with PNIPAAm included. The results summarized in this work, suggest a potential application of PAAm/PNIPAAm hydrogels in separation processes where the diffusion could be controlled by temperature or by the environment hydrophobicity.

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