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THERMORHEOLOGICAL AND GLASS TRANSITION PROPERTIES OF PNIPA/PVP AND PNIPA/CARBOPOL BLENDS

*M. Mayo-Pedrosa, C. Alvarez-Lorenzo and A. Concheiro**

Departamento de Farmacia y Tecnología Farmacéutica, Facultad de Farmacia, Universidad de Santiago de Compostela, 15782-Santiago de Compostela, Spain

Abstract

The miscibility of poly(N-isopropylacrylamide) (PNIPA) with poly(vinyl pyrrolidone) (PVP) and a cross-linked poly(acrylic acid) (Carbopol® 971P) was evaluated from the rheological data of aqueous dispersions and the temperature of glass transitions of films made of binary mixtures. PNIPA has a low critical solubility temperature (LCST) of about 33°C, below which 1% dispersion behaves as a viscous system. At temperatures above LCST, the hydrophobic interactions among the isopropyl groups initially provide transient networks of greater elasticity. The LCST of PNIPA as well as its T_g (144°C, estimated by DSC and MTDSC of films) were not modified by the presence of PVP. The immiscibility of PNIPA and PVP was confirmed by the absence of interaction between both polymers as shown by FTIR analysis of the films. In contrast, PNIPA and carbopol were miscible and the behaviour of their mixtures differed significantly from that of the parent polymers; i.e. a strong synergistic effect on the viscoelasticity of the dispersions was observed below the LCST. As temperature increased, the blends showed a decrease in the loss and storage moduli, especially those with greater PNIPA proportions. The fall was smoother as the PNIPA proportion decreased. This behaviour may be explained as the result of the balance between PNIPA/carbopol hydrogen bonding interactions (as shown in the shift of C=O stretch in FTIR spectra) and PNIPA/PNIPA hydrophobic interactions. The T_g values of the films of the blends showed a positive deviation from the additivity rule; the mixtures containing more than 1:1 amide:carboxylic acid groups have a notably high T_g (up to 181°C). This increase is related to the stiffness induced in the films by the PNIPA/carbopol interactions.

Keywords: carbopol, FTIR, MTDSC, polymer miscibility, polymer–polymer interactions, poly(N-isopropylacrylamide)/poly(acrylic acid) mixtures, poly(N-isopropylacrylamide)/PVP mixtures, viscoelasticity

Introduction

Physical blending of different polymers can result in new materials that exhibit a variety of properties depending on the characteristics of the parent homopolymers and the blend composition. The study of the properties of these systems is receiving increasing atten-

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* Author for correspondence: E-mail: ffancon@usc.es

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tion since adequate mixtures can make it possible to optimise the performance of polymer-based systems, in a cheaper and quicker way than synthesising new polymers [1]. In this sense, the largest commercial exploitation of polymer blending has occurred in the plastics area with the attempt to improve the processability and the strength of the materials [2]. In the pharmaceutical field, preparation of solid and semisolid drug dosage forms usually implies coprocessing of several polymeric excipients to provide adequate mechanical and/or drug release properties [3]. Appropriate mixtures of different cellulose ethers have been shown to be particularly useful to increase the viscosity, to extend the drug release time and even to modify the release kinetics of gels and tablets, compared to those made of only one of the polymers [4, 5]. Blends of poly(vinylpyrrolidone) with polyvinyl acetate phthalate can be useful to obtain enteric formulations [6]. Interactions between polymers can also serve to optimise the bioadhesive force of the drug delivery systems [7, 8]. Finally, the potential of applications of polymers mixtures, with different glass transition temperatures (T_g), is also relevant in the film coating of pellets and tablets [9–11].

Whether the behaviour of the blend is intermediate between the properties of the components or considerably different will be determined by the miscibility and phase behaviour of the blend. Miscibility, i.e. interpenetration of components at the molecular level [12], is only possible when the different polymers are capable of establishing specific interactions between their chains, causing negative enthalpy and Gibbs free energy of mixing [1]. Complex formation occurs in a cooperative way, leading to compact structures. Four main types of polymer–polymer interactions can be distinguished: van der Waals, hydrophobic, electrostatic, and hydrogen bonding [13].

Polymer systems that modify their structure and, in consequence, their properties in response to changes in the physical and chemical characteristics of the physiological medium have become an important area of research and development in the fields of medicine, pharmacy, and biotechnology [14, 15]. In these fields, polymers with a low critical solubility temperature (LCST) or with ionisable groups, which provide networks able to experiment reversible phase transitions, are attracting special attention. Poly(N-isopropylacrylamide) (PNIPA) is widely used to prepare gel systems that undergo a volume-phase transition when heated to a temperature above its LCST. PNIPA cross-linked gels are swollen at temperatures lower than 33°C and collapsed when the temperature is raised [16, 17]. The influence of copolymerisation with hydrophobic or ionic monomers on phase transition temperature of cross-linked PNIPA hydrogels, and on its consequences on drug delivery, has been the subject of several studies [18–20]. In contrast, scarce attention has been paid to the behaviour of mixtures of PNIPA with other preformed polymers of technological interest [21]. PNIPA, through its amide groups (proton-acceptor), could interact with polymers with proton-donor groups, such as carboxylic, phenolic, or hydroxyl groups [22–24]. Experimental evidence of these interactions has been shown in blends and copolymers of N-isopropylacrylamide with methacrylic acid, P(NIPA-co-MAA). Hydrogen bonding formation, the intensity at which is a function of the monomers ratio, alters the coil-to-globule transition temperature in solution and the T_g of the copolymers. The plot of T_g *vs*. composition of P(NIPA-co-MAA) copolymers presents an Sshaped curve; this non-linearity suggesting that the structural units interact strongly amongst themselves [25, 26].

In this study, the miscibility and thermal properties of PNIPA blends with two commonly used pharmaceutical grade polymers, poly(vinylpyrrolidone) and Carbopol® 971, a slightly cross-linked poly(acrylic acid) derivative, are evaluated. The complex formation ability of PVP and carbopol with other several polymers has been previously reported [9–11, 27]. To carry out the work, the temperature responsive behaviour of both aqueous dispersions and films of PNIPA/PVP and PNIPA/carbopol was analysed using oscillatory rheometry and differential scanning calorimetry (DSC and MTDSC). Fourier transform infrared spectroscopy (FTIR) was used as a complementary technique to elucidate the nature of the possible interactions. The main aim was to obtain information about the mixtures of PNIPA with these polymers with a view to their potential use as components of responsive systems and, in particular, as agents able to modulate the viscoelastic behaviour of aqueous dispersions and the mechanical properties of films.

Experimental

Materials

Carbopol® 971P NF (molecular mass $1.25 \cdot 10^6$ Da, batch CC7NAAJ041) was provided by BFGoodrich Europe, UK. Poly(vinylpyrrolidone) (PVP) Kollidon® 30 (molecular mass 44000–54000 Da, batch 08–0097) was from BASF, Germany. Purified water obtained by reverse osmosis (MilliQ®, Millipore Spain) was used. Poly(N-isopropylacrylamide) (PNIPA) was synthesised by an aqueous redox polymerisation method adapted from a procedure reported by Schild and Tirrell [28]. Briefly, 22.2 g of monomer was dissolved in 15 mM phosphate buffer (600 mL of distilled water, 0.6914 g of Na_2HPO_4, 0.9094 g of NaH_2PO_4, and 5.09 g of NaCl; titrated with ca. 50 mL of 0.1 M NaOH to pH 7.4). Then, 12 mL of N,N,N',N'-tetramethyl ethylenediamine (TEMED) and 2.3 g of ammonium persulphate in 5 mL of water were added under stirring. The reaction mixture was stirred for 15 h under nitrogen. Precipitation was carried out by dropwise addition of the polymerisation mixture to 800 mL of methanol. The resulting polymer was dissolved in 150 mL of distilled water, and again precipitated in methanol (200 mL) and vacuum-dried. Mean molecular mass of each batch of PNIPA synthesised was estimated from intrinsic viscosity in water at 25°C, applying the Mark–Houwink equation:

$$[\eta]=KM^a \tag{1}$$

where $[\eta]$ is intrinsic viscosity, and K and a are constants assigned values of $2.26 \cdot 10^{-4}$ and 0.97, respectively [29]. PNIPA mean molecular mass was for all batches 3700±50 Da.

Preparation and characterization of polymer aqueous dispersions

Preparation

Aqueous dispersions of each polymer and binary mixtures of PNIPA/PVP and PNIPA/carbopol (Table 1) were prepared by adding solid PNIPA, when necessary, to aqueous solutions of the other component. Total polymer concentration was 1%. The mixture was shaken for 6 h and then left to stand for 24 h at room temperature.

Table 1 Composition of PNIPA/PVP and PNIPA/carbopol aqueous dispersions

Blend #	PNIPA/%	Other polymer/%	PNIPA/other polymer
1	1.00	0.00	6:0
2	0.00	1.00	0:6
3	0.50	0.50	3:3
4	0.17	0.83	1:5
5	0.33	0.67	2:4
6	0.67	0.33	4:2
7	0.83	0.17	5:1

Oscillatory rheometry

The temperature dependence of the storage and loss moduli (G' and G'', respectively) of the aqueous dispersions was recorded in a Rheolyst AR1000N rheometer (TA Instruments, New Castle, DE, USA) equipped with an AR2500 data analyser and a steel cone of 2° and 6 cm diameter. The experiments were carried out in duplicate for an angular frequency of 0.1 rad s^{-1} by measuring these parameters while increasing the temperature from 15 to 60°C at 3°C min^{-1}.

Cloud point

The cloud point was determined, in duplicate, by measuring transmittance (800 nm, HP Agilent 8453, Germany) at increasing temperatures; 1°C steps until close to cloud point, then 0.1°C steps.

Preparation and characterisation of films

Preparation

To obtain the films, the dispersions were poured onto a Teflon plate and maintained at 40°C for 48 h.

DSC and MTDSC studies

Differential scanning calorimetry experiments were carried out, in duplicate, using a DSC Q100 (TA Instruments, New Castle, DE, USA) with a refrigerated cooling accessory (RCS) and modulated capability. Nitrogen was used as the purge gas at a flow rate of 50 mL min^{-1}. The calorimeter was calibrated for baseline using no pans, for cell constant and temperature using indium (melting point 156.61°C, enthalpy of fusion 28.71 J g^{-1}), and for heat capacity using sapphire standards. All experiments were performed using non-hermetic aluminium pans, in which 5–10 mg film samples were accurately weighed, and then just covered with the lid. The samples were loaded on an autosampler tray. Samples for DSC study were program-heated from 30 to 180°C (films with carbopol) or to 200°C (films with PVP), then cooled to 0°C, and finally heated again up to 200°C, always at the rate of 20°C min^{-1}. MTDSC experimental conditions were as follows: after equilibration at 30.0°C, the temperature rises up to 200°C, at 5°C min^{-1}, using a modulation amplitude of ±0.5°C every 30 s. The total heat flow signal was separated (applying the Fourier transform algorithm; Universal analysis 2000, v.3.3B, TA Instruments) into a heat capacity component (reversing heat flow) and a kinetic component (non-reversing heat flow), as shown in the following expression,

$$\frac{\mathrm{d}Q}{\mathrm{d}t} = C_\mathrm{p}\frac{\mathrm{d}T}{\mathrm{d}t} + f(t,T) \qquad (2)$$

where $\mathrm{d}Q/\mathrm{d}t$ is the total heat flow, C_p is the heat capacity, $\mathrm{d}T/\mathrm{d}t$ is the heating rate, and $f(t,T)$ represents the heat flow from events which are a function of time and absolute temperature (kinetic events) [30–32]. T_g is reported as the midpoint of the glass transition.

Fourier transform infrared spectroscopy (FTIR)

Spectra were recorded by a FTIR Mattson ATR Spectra-Tech spectrometer (Germany) over the range 400–4000 cm^{-1}, using the KBr pellet technique.

Results and discussion

PNIPA/PVP systems

Figure 1 shows the influence of temperature on G' and G'' of 1% PNIPA and 1% PVP aqueous dispersions, and their 50:50 mixture. At temperatures below LCST, PNIPA dispersion showed a viscous behaviour; the storage modulus being negligible. In contrast, around 34°C the dispersion became turbid (see cloud point values in Table 2) and a brusque increase in the values of G' and G'' occurred. The increase in temperature promotes hydrophobic interactions between the isopropyl groups of different polymeric chains, which may provide transient networks of greater elasticity. A further increase in temperature results in a decrease in viscosity owing to the decrease in the hydrodynamic radius of the polymer [33]. This effect should be more evident for low polymer proportions. Considering the intrinsic viscosity of the PNIPA synthesised (~0.65 dL g^{-1}), 1% proportion is already above the overlapping concentration [34].

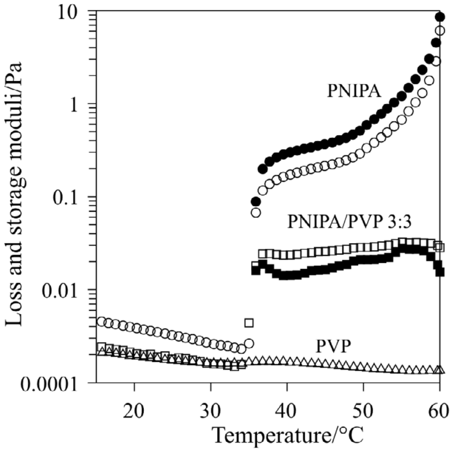

Fig. 1 Influence of temperature on the storage (G', full symbols) and the loss (G'', open symbols) moduli of 1% PNIPA, 1% PVP, and 1% PNIPA:PVP 3:3 aqueous dispersions

PVP dispersions did not show temperature-sensitivity, and the G'' values remained practically constant. PNIPA/PVP mixtures showed an intermediate behaviour. In the concentration range studied, no dependence of LCST on PNIPA concentration was observed. Below the LCST, G'' values were coincident with those of PVP dispersions, while around LCST, a jump in the rheogram is observed. Just above the LCST, the G'' values were slightly higher than those of G', and similar to those predicted by the sum of the contribution of each component of the blend. Beyond 45°C, a significant decrease in both moduli, especially for G', was observed for blends containing less than 50% PNIPA (Table 2). As mentioned above, this observation may be related to the coil-to-globule transition of the thermosensitive polymer.

For amorphous polymers, the miscibility is usually associated with the presence of a single glass transition for the blend. The glass transition for PNIPA films is at

Table 2 Cloud point of PNIPA/PVP aqueous dispersions and storage (G') and loss (G'') moduli at different temperatures

Blend #	Cloud point/ °C	G'/ mPa at 37°C	G''/ mPA at 37°C	G'/ mPa at 50°C	G''/ mPa at 50°C
1	33.8	197	116	589	332
2	–	–	1.6	–	1.4
3	33.8	19	24	21	28
4	33.8	8.8	11	6.3	18
5	33.8	12	21	7.7	14
6	33.7	59	39	21	34
7	33.7	62	37	40	44

about 144°C, according to the value found by Kuckling *et al.* [33] of 142°C; although, lower values have also been reported [21, 26]. T_g for PVP films is at about 167°C, which is coincident with the value reported by Nyamweya and Hoag [10]. All blends exhibited the two glass transition temperatures, although the second one appeared at slightly greater temperature (Fig. 2). The DSC (second heating run) and MTDSC measurements gave similar results. Both polymers showed enough change in heat capacity to be readily determinable using conventional DSC. However, the remanence of some moisture in the films causes an endothermic event that overlaps the T_gs; the second heating run being necessary to visualise them. No changes in the integrity or the composition of the sample are expected to occur during the first heating/cooling run, owing to the thermal stability of both polymers [23, 25]. The MTDSC reversing heat flow curves (obtained in a single run) provided a similar pattern. In this case, the main advantage of using the MTDSC technique is its quickness. The fact that the second T_g of the blends (171–175°C) was slightly greater than for pure PVP (167°C) may be due to a limited amount of phase mixing [1], owing to some hydrogen bonding (the amide nitrogen of PNIPA could be partially protonated) or hydrophobic association between both polymers above the LCST.

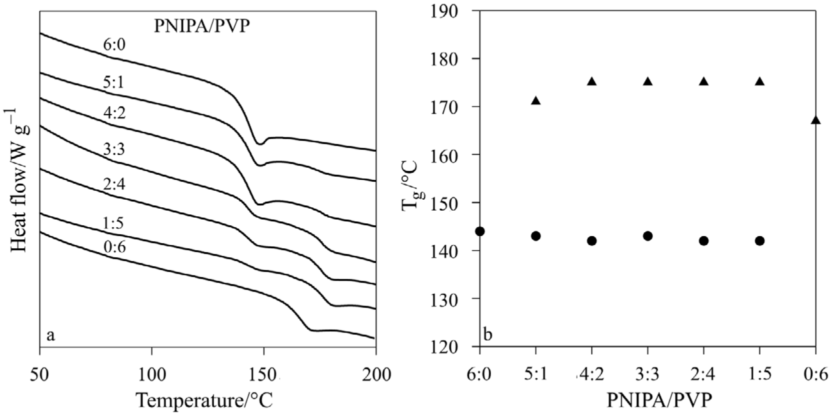

Fig. 2 a – DSC curves and b – T_g values of PNIPA:PVP films. T_g values were reproducible to about ±1°C

The FTIR spectra of the films showed the characteristics bands of both polymers without significant changes (Fig. 3). In the spectra of PNIPA, the amide I band (C=O stretch) appears at 1650 cm^{-1}, the amide II band (N–H vibration) at 1544 cm^{-1}, and the methyl groups (in isopropyl group) at 1386–1367 cm^{-1} [24]. The characteristic peaks of the vinyl group at 995–905 cm^{-1} were not observed. This indicates that the N-isopropylacrylamide was successfully polymerised [35]. The characteristic peaks of PVP in the FTIR spectra appeared at 1672, 1425, 1288 and 650 cm^{-1} [3].

Overall, these results indicate that no relevant interaction occurs between PNIPA and PVP, which are both of them proton-acceptors and do not form complexes, i.e. they are compatible but practically immiscible.

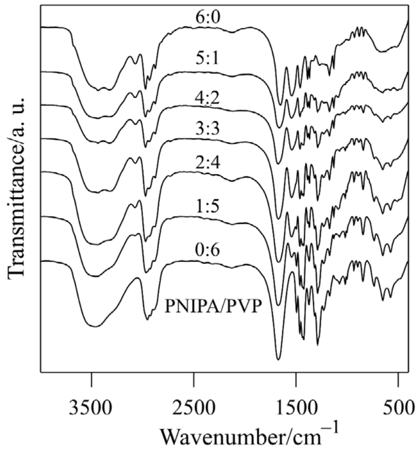

Fig. 3 FTIR spectra of PNIPA:PVP films

PNIPA/Carbopol systems

PNIPA/carbopol blends behaved very differently from PNIPA/PVP blends. 1% Carbopol® 971P aqueous dispersion showed G' andG'' values practically constant in the temperature range analysed, and considerably greater than those observed for 1% PNIPA dispersion (Fig. 4). Carbopol® 971P is constituted by high molecular mass poly(acrylic acid) chains loosely cross-linked (fishnet conformation), resulting in a network of lower cross-linking density than other Carbopol® varieties, such as 974P and 934 P (fuzzball structure) [36]. The pK_a of carboxyl acid groups is around 4.5 and, therefore, most acid groups are not ionised in water. Nevertheless, the entanglement of adjacent microgels provides a significantly elastic character to the aqueous dispersion [37].

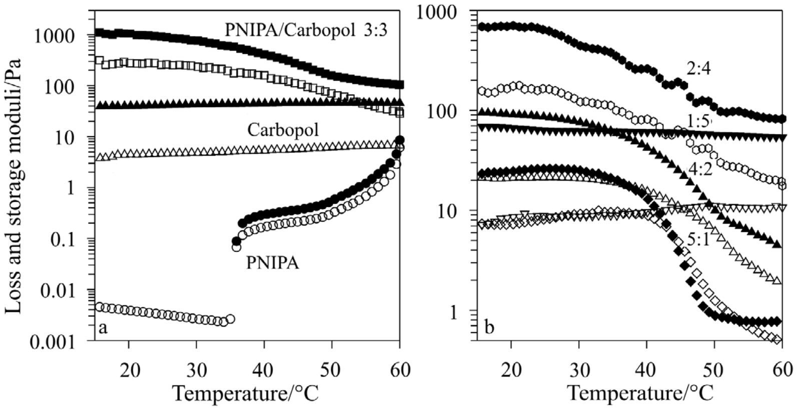

Fig. 4 Influence of temperature on the storage (G', full symbols) and the loss (G'', open symbols) moduli of 1% PNIPA, 1% carbopol, and 1% PNIPA:carbopol aqueous dispersions

Interestingly, a synergistic effect was observed for the aqueous dispersions of the blends of PNIPA and carbopol. Those dispersions were macroscopically homogeneous but turbid. The cloud points of the blends could not be determined. Only in the case of blend #6, was a precipitate observed after 24 h of storage. At room temperature, the blends showed greater G' and G'' values than the carbopol alone dispersions. The maximum increase was observed for the 3:3 PNIPA:carbopol aqueous dispersion (Fig. 4).

When temperature increased, the blends showed a decrease in G' and G'' instead of the jump that is characteristic of the PNIPA alone dispersion. The temperature sensitivity was higher for the blends with greater PNIPA proportions; e.g. G' and G'' of 5:1 PNIPA:carbopol dispersion markedly decreased at around 37°C. The fall was smoother as the PNIPA proportion decreased. This behaviour may be explained as the result of the balance between PNIPA/carbopol interactions and, above its LCST, PNIPA/PNIPA hydrophobic interactions. At room temperature, PNIPA is hydrophilic and may increase the connections among carbopol microgels, through interactions of the amide group with the carbopol carboxylic acid groups. The FTIR spectra of films (Fig. 5) showed changes in the absorption peaks of carboxylic acid groups from 1714 cm^{-1} (carbopol) to 1735 cm^{-1} (4:2 blend).

The increase in the links among both polymer chains explains the greater consistency of the dispersions. When temperature rises above the LCST, the hydrophobic interactions among isopropyl groups of PNIPA chains may play a role. For cross-linked P(NIPA-co-MAA) copolymers, the ionisation of MAA carboxyl groups or the establishment of hydrogen bonds between the amide groups of N-isopropylacrylamide and those carboxyl groups may hinder the coil-to-globule transition, increasing the LCST [18, 25, 26]. Nevertheless, in the cases of PNIPA/carbopol blends, the hydrophobic interactions among the isopropyl groups of PNIPA should be enough to induce the coil-to-globule transition. This explains the decrease in G' and G'' as temperature rises. The aggregation of the PNIPA chains above LCST may

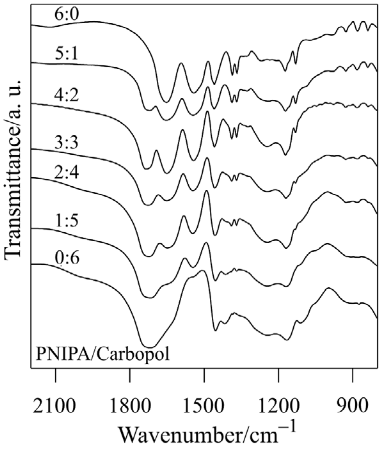

Fig. 5 FTIR spectra of PNIPA:carbopol films

also induce the shrinking of carbopol microgels (providing a microscopically heterogeneous system with zones rich in both polymers) and could cause the detaching from carbopol network (resulting in a system formed by independent polymer structures). Any of these phenomena results in a decrease in G' and G''. The temperature-sensitivity of the rheological parameters should be related to the relative proportion of the polymers. Considering the molecular mass of the repeating units of each polymer, a 1:1 amide/carboxylic acid molar ratio is reached for a blend 4:2.5 PNIPA/carbopol; i.e. blends #3, #4 and #5 can have all amide groups forming hydrogen bonds and an excess of free carbopol. Therefore, these blends are less temperature-sensitive. In contrast, when there is an excess of PNIPA, the collapse and the phase separation are more evident.

The DSC (second heating run) of PNIPA/carbopol films are shown in Fig. 6. MTDSC curves showed a similar pattern. Pure carbopol film had a T_g at 126°C. Since the T_g of PNIPA is around 144°C, applying the Gordon–Taylor equation [38] the blends might be expected to have a T_g in between both values.

$$T_{\mathrm{gmix}} = \frac{w_1 T_{\mathrm{g1}} + K w_2 T_{\mathrm{g2}}}{w_1 + K w_2} \tag{3}$$

where w is the mass fraction of each polymer and K (originally a function of the cubic expansion coefficient and the specific volume) is an adjustable parameter that informs about positive or negative deviations of the T_{gmix} from the values predicted by the free volume additive rule [12].

Only the film obtained by desiccation of dispersions containing the lowest proportion of PNIPA (blend #4) showed a unique T_g at 130°C. The films of blends PNIPA:carbopol 2:4 and 3:3 (blends #5 and #3) showed in addition to this T_g another one at much greater temperature (176–181°C). The films in which PNIPA proportion was greater than carbopol proportion also presented a T_g greater than those of the par-

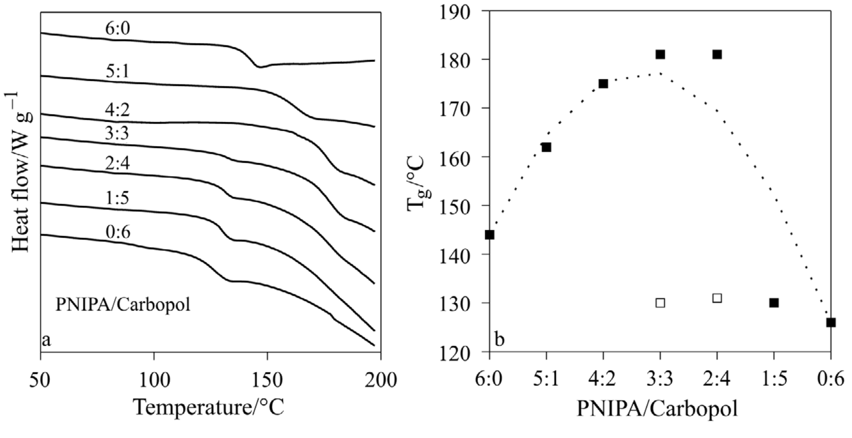

Fig. 6 a – DSC curves and b – T_g values of PNIPA:carbopol films. T_g values were reproducible to about ±1°C. Dashed line represents the relationship predicted by non-linear regression using Eq. (4) (b=9.3633; s.e. 1.2967; 2.5 DF, r^2= 0.8150)

ent polymers (Table 3). This suggests that PNIPA/carbopol interactions result in much more rigid networks. As can be seen in Fig. 7, the plot of T_g *vs*. composition is convex; showing two T_gs when there is an excess of carbopol carboxylic acid groups compared to PNIPA amide groups. This indicates that the complex is not miscible with the excess of carbopol. The pattern of the plot of the T_g *vs*. composition of the complexes was not fitted by Eq. (3), but by a modification of the additivity rule that includes the contribution of specific interactions:

$$T_{\mathrm{gmix}}=w_1T_{\mathrm{g1}}+w_2T_{\mathrm{g2}}+b(T_{\mathrm{g2}}-T_{\mathrm{g1}})w_1w_2 \tag{4}$$

where b is a fitting parameter [38].

Table 3 Glass transitions (T_g) and wavenumber of the C=O stretch observed in PNIPA/carbopol films. T_g values were reproducible to about ±1°C (n=2)

Blend #	T_{gDSC}/°C	T_{gMTDSC}/°C	FTIR C=O/cm^{-1}
1	144	144	–
2	126	126	1714
3	130, 181	132, 176	1726
4	130	130	1716
5	131, 181	131, 181	1722
6	175	177	1735
7	162	165	1720

Positive deviations of T_g from additivity are related to stiffening effects induced by attractive interactions between the different components. On the other hand, negative deviations indicate repulsions [39]. Convex, concave and sigmoidal shapes have been reported for the plots of T_g *vs.* composition of copolymers [40]. In particular, hydrogen bonding in mixtures and copolymers has been found to be responsible for large deviations of T_g values from those predicted by the classical models [21, 38, 41].

This interaction phenomenon is clearly shown in the FTIR spectra shift of the carbonyl stretch of carbopol. The infrared spectrum of carbopol is characterised by a broad band of carbonyl stretch of the carboxylic group at 1714 cm^{-1} [42]. The broadening of this band is attributed to the existence of two carbonyl populations, one corresponding to the intra- and intermolecular hydrogen bonding and another due to free carbonyl groups. This band moves to a higher vibration frequency (1730 cm^{-1}) with the increase of PNIPA (Fig. 5), indicating the diminution of the internal hydrogen bonding of carbopol and the formation of new bonds with the other polymer. A similar effect has been observed for the interaction of carbopol with non-ionic surfactants [42].

Conclusions

Blends of PNIPA with an immiscible polymer, such as PVP, modified neither the temperature response of PNIPA dispersions nor its T_g; the blends having values of the storage and loss moduli intermediate between those of the parent polymers. In contrast, interaction of PNIPA with a proton donor such as a poly(carboxylic acid) derivative, through hydrogen binding, enhances the thickening capacity of the polymers as well as the temperature of glass transition of the films. The T_g dependence on composition of the blends showed a convex pattern, which cannot be described by simple additive models. Such a synergistic effect is a result of the stiffness of the films caused by the strong interactions between PNIPA and carbopol. These results indicate that the combination of PNIPA with other polymers, miscible or immiscible, opens a new way to modulate the properties of their aqueous dispersions and films.

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