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The effect of the annealing on the poly(vinyl alcohol) obtained by freezing–thawing

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ABSTRACT

In the present work poly(vinyl alcohol) (PVA) hydrogels were obtained by freezing/thawing technique. The effect of thermal treatment on its performance was studied by annealing the hydrogels at five different temperatures, all of them between the water evaporation and the polymer melting ones, for 1 h. The main characteristics of hydrogels (glass transition temperature, crystallinity degree, equilibrium swelling degree, bound water content, gel fraction, water vapour transmission rate and diffusion exponent) were determined and the effect of annealing temperature was analyzed. Two different solution concentrations (5 and 10 wt.% of PVA) were used to prepare the hydrogels. It was clearly demonstrated that the studied properties markedly changed as a function of annealing temperature: the maximum swelling degree, the thickness change and the bound water content decreased whereas the gel fraction increased when annealing temperature was raised. An exponential relationship between gel fraction and crystallinity degree was found and the characteristics of hydrogels were correlated with both parameters.

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1. Introduction

Hydrogels have been extensively used in a variety of biomedical applications, including cartilage replacement [1], contact lenses [2], drug delivery devices [3], microorganism immobilization [4] and also in biotechnological field [5].

Traditional methods to crosslink PVA used to produce hydrogels employ irradiation [6] or chemical agents such as glutaraldehyde or sodium borate [7,8]. However, these methods, and particularly the chemical crosslinking one, may produce undesirable side effect in the final devices derived from the residual crosslinking agent or the reaction toxic waste. To avoid the ensuing toxicity, a novel method to obtain strong hydrogels from aqueous solution of poly(vinyl alcohol) (PVA) was developed. This method, based on freeze and then thaw a solution of PVA several times, was firstly reported by Nambu [9,10] and thoroughly studied by Peppas [5,11–13]. It results in the formation of crystallites that serve as physical crosslinks making an insoluble in water three-dimensional network. Nevertheless, Hernandez et al. [14] have suggested that some chemical crosslinking could take place, probably arising from the creation of free radicals due to the shearing produced when the water crystals grow within the polymer solution.

It has been proposed that the structure of PVA hydrogels obtained by freezing/thawing (F/T) technique consists in three

phases: a water phase (with low PVA concentrations), an amorphous phase and a crystalline phase that partially restricts the motion of amorphous PVA chains [15].

PVA molecules are aggregated during ice formation and hydrogen bonding is established between molecular chains. By increase of freezing and thawing cycle, residual free molecular chains are successively included in link zones [16]. Due to the modification of the polymer structure after water sorption, the mechanical and the physical properties of hydrophilic polymers can vary significantly with the water activity in the surrounding medium [12]. Upon water absorption, small or less perfect polymer crystallites can be destroyed [17]. In addition, the glass transition temperature (T_g) of these kinds of materials sharply decreases with the water content increases [18].

Heat treatments above the T_g [12,13] as well as repeated F/T cycles, are also used as means of achieving the same results mainly by increasing the amount of crystals of the polymer, which act as a physical crosslinkers of the network.

On the other hand, the degree of crystallinity, as well as the size of crystallites, depends on the drying conditions [19]. It has been found that the faster dry the faster formation of crystals demonstrating the effect of the drying time and drying rate on the process of crystal formation [12,13]. When PVA films are annealed at constant temperature (between the glass transition and the melting temperatures), the macromolecular chains have enough mobility to align themselves and fold to form crystals [13]. It is well known that the increasing in the polymer crystallinity degree, resulting in a more resistant material [20]. The swelling and mechanical properties of PVA hydrogels were also examined. In addition, it has been

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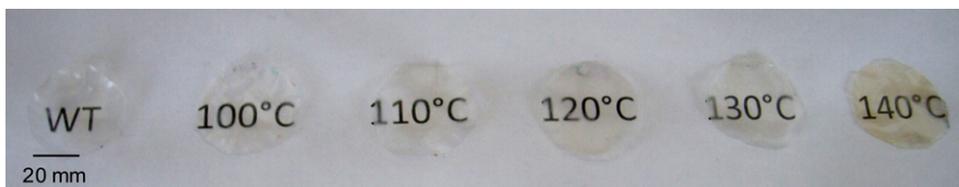


Fig. 1. Photograph of PVA hydrogels annealed at different temperatures. WT: without temperature treatment.

found that the degree of swelling of PVA hydrogels depends on the annealing temperature [21]. Finally, the dehydration rate also influences the degree of crystallinity and the crystallization rate [22].

The aim of this work was to investigate the effect of the annealing temperature on the structural and swelling characteristics of the PVA hydrogels obtained by F/T technique. For this purpose, thermal properties, degree of crystallinity, equilibrium swelling degree, gel fraction and bound water of untreated and treated PVA hydrogels were determined and analyzed.

2. Experimental

2.1. Materials

The PVA used in this study is a commercial product purchased from Sigma–Aldrich with a degree of hydrolysis higher than 98–99%

and a molecular weight of 31,000–50,000 g/mol. The sodium azide was supplied by Biopack.

2.2. Preparation of hydrogels

Aqueous solutions of 10 wt.% PVA (hydrogels with 5 wt.% were also prepared in order to verify some obtained results) were prepared by dissolving the polymer in distilled water at 85 °C and slowly stirred (with magnetic stirrer) for 4 h, using sodium azide at 0.2 mg/ml as a biocide. After that, the solutions were placed in an ultrasonic bath for 30 min to remove all bubbles. The polymer was entirely dissolved and the transparent solutions were allowed to reach room temperature. Then the PVA solutions were cast onto anti-adherent containers and frozen for 12 h, cooling down to –18 °C and afterward placed at room temperature (25 °C, thawing process) for the same time in order to produce crosslink. This procedure was repeated 4 times.

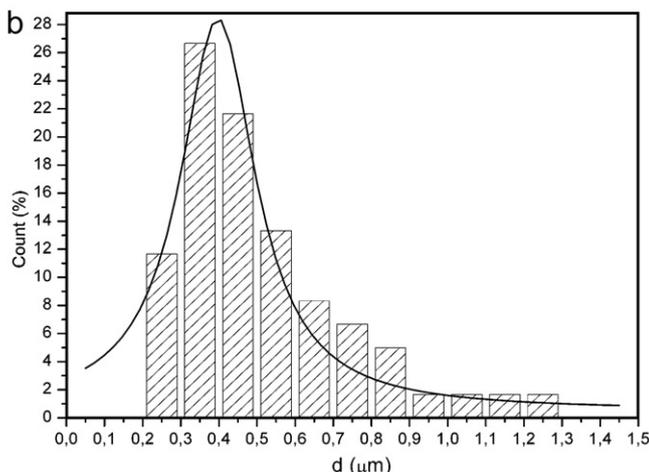
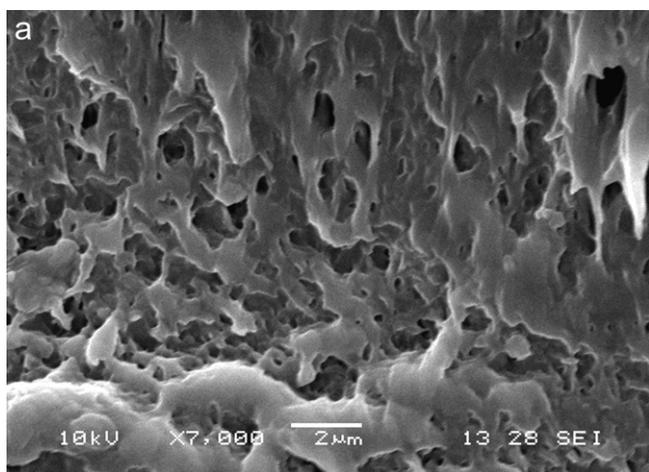


Fig. 2. (a) SEM microphotograph (7000×) of 5 wt.% PVA hydrogel treated at 130 °C. (b) Porous diameter distribution obtained from SEM microphotograph.

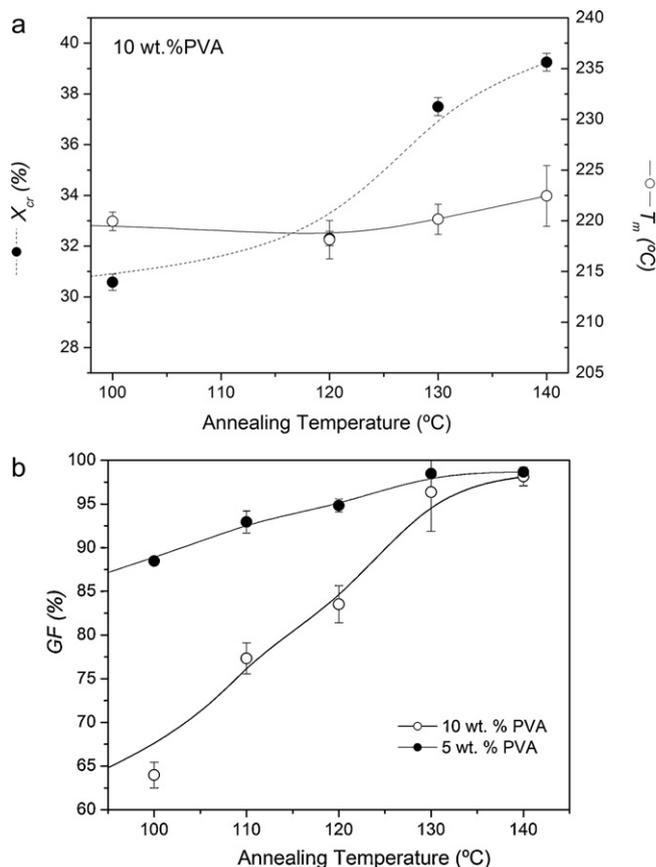


Fig. 3. (a) Crystallinity degree (X_{cr}) and melting temperature (T_m) of hydrogels prepared from 10 wt.% PVA solution as a function of annealing temperature; (b) Gel Fraction (GF%) of hydrogels prepared with both solution concentrations as a function of annealing temperature.

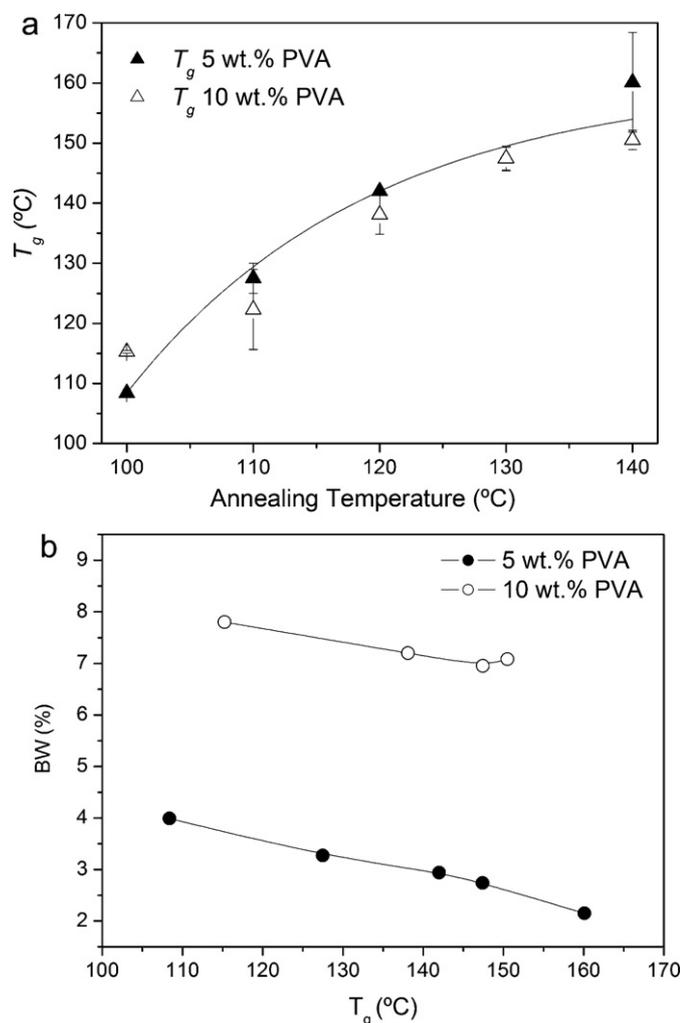


Fig. 4. (a) Effect of annealing temperature on the glass transition temperature (T_g) of hydrogels and (b) Bound water content (BW%) as a function of the glass transition temperature (T_g) of hydrogels prepared from 5 and 10 wt.% solutions.

2.3. Annealing treatments

PVA hydrogel samples were annealed at different temperatures: 100, 110, 120, 130 and 140 °C in an oven for 1 h. These temperatures were selected because they were over the water evaporation temperature, and they were between the glass transition temperature and the melting point of the polymer. The samples were dried in an oven for 24 h at 37 °C before annealing.

2.4. Methods

2.4.1. Scanning electron microscopy (SEM)

In order to analyze the hydrogels morphology SEM micrographs were obtained in a JEOL JSM-6460 LV instrument. The samples were dried in an oven for 24 h at 37 °C then cryo-fractured in liquid air and gold-coated. Tests were carried out in dry stage.

2.4.2. Differential scanning calorimetry (DSC) studies

Measurements were carried out in a Shimadzu DSC-50. Samples were scanned from room temperature to 250 °C at a heating rate of 10 °C/min, under nitrogen atmosphere. Before DSC analysis, hydrogel samples were dried for 24 h at 37 °C.

The glass transition temperature (T_g), and the melting temperature (T_m) were determined from the obtained curve. The degree of

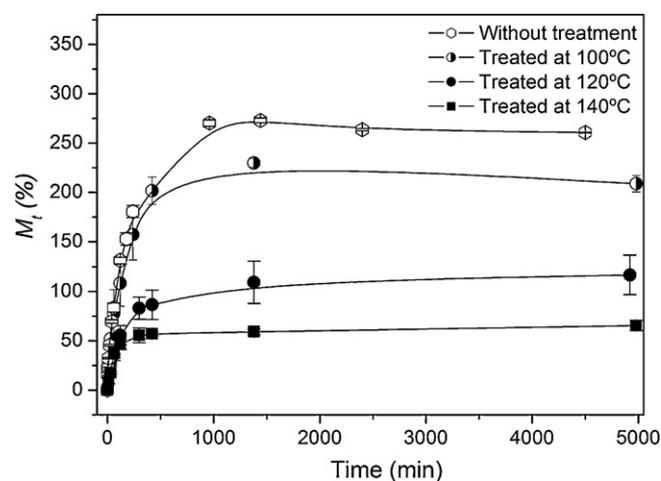


Fig. 5. Absorbed saline solution (%) at 37 °C as a function of time for untreated and annealed 5 wt.% hydrogels.

crystallinity (X_{cr}) was calculated from the following equation:

$$X_{cr} \% = \frac{\Delta H}{\Delta H_c} \times 100 \quad (1)$$

where ΔH was determined by integrating the area under the melting peak over the range 190–240 °C and ΔH_c was the heat required for melting a 100% crystalline PVA sample (138.6 J/g) [12,13].

2.4.3. Thermogravimetric analysis (TGA)

Thermogravimetric studies carried out in a Shimadzu TGA-DTGA 50. All dried samples (37 °C, until constant weight) were scanned from room temperature to 600 °C at 10 °C/min under nitrogen atmosphere. The bound water content (BW%) was obtained from the obtained curves. The bound water content was calculated by using the following equation [23]:

$$BW \% = \frac{W_0 - W_1}{W_0} \times 100 \quad (2)$$

where W_0 and W_1 are the weights of the dried hydrogel extracted from TGA curves before and after 190 °C, respectively.

2.4.4. Gel fraction

The weight ratio of the dried hydrogels in rinsed and un-rinsed conditions can be assumed as an index of the degree of crosslinking or gel fraction (GF%) [24]. To perform gel fraction measurements, a slice of each sample was placed in an oven before and after rinsing at 37 °C until no change on its mass was observed. After that, each sample was immersed in distilled water at room temperature for 4 days to rinse away unreacted species. Subsequently, the immersed sample was removed from distilled water and dried at 37 °C until constant weight was reached. Therefore the gel fraction can be calculated as follows:

$$GF \% = \frac{W_f}{W_i} \times 100 \quad (3)$$

where W_i and W_f are the weights of the dried hydrogels before and after immersion, respectively.

2.4.5. Swelling studies

Gravimetric water uptake measurements are the most commonly used method to evaluate the effect of crosslinking on water transport in PVA [25]. Swelling determinations were carried out in saline solution using a thermostatic water bath at 37 °C. All samples were dried before immersion at 37 °C until constant weight. The

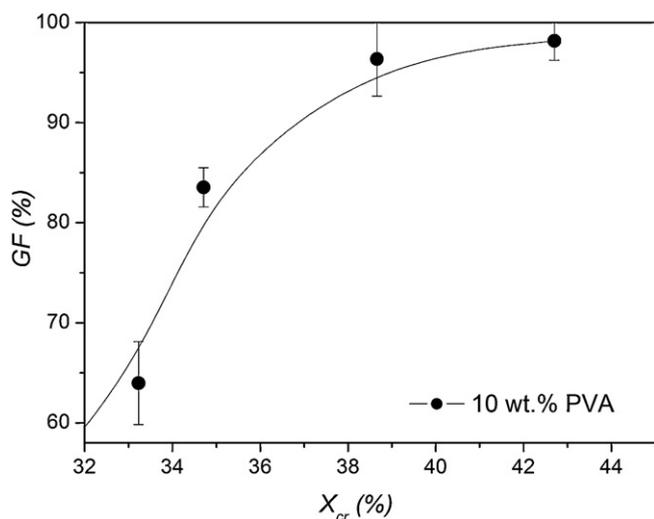


Fig. 6. Gel Fraction (GF%) as a function of (X_{cr} %) for annealed hydrogels obtained from 10 wt.% PVA solution.

swelling degree (M_t) percentage was determined by the following equation:

$$M_t \% = \frac{M_f - M_i}{M_i} \times 100 \quad (4)$$

where M_i and M_f are the weights of the sample before and after immersion, respectively. The thickness of dried and equilibrium swollen hydrogel were also registered by using an optical microscope Olympus SZ-10.

2.4.6. Determination of the diffusion exponent

The diffusion exponent (n) can be obtained from the log M_t/M_∞ vs log t curve. A simple semi-empirical equation can be used to analyze data of controlled release of water soluble drugs from polymers [26]. The general form of the equation is:

$$\frac{M_t}{M_\infty} = kt^n \quad (5)$$

where M_t/M_∞ is the fractional release, k is the kinetic constant, M_t is the swelling degree and M_∞ is the equilibrium swelling degree (the maximum swelling degree which remains constant over time).

2.4.7. Water vapor transmission rate (WVTR)

For these measurements, dried hydrogels (maintained in a humidity chamber at 60% RH for 10 days, until constant weight) samples with a diameter of 28 ± 2 mm and a thickness of 0.16 ± 0.04 mm were cut and then put as a cap with adhesive on the mouth of a flask with a diameter of about 26 mm containing 20 ml of distilled water. The flask was then placed in a constant temperature-humidity homemade chamber for 72 h (37°C at 75% RH). The mass loss of the system was considered as an index of WVTR. The WVTR of each sample was calculated by using the following equation [24]:

$$WVTR \left(\frac{\text{g}}{\text{m}^2 \times \text{h}} \right) = \frac{M_0 - M_1}{72 \times A} \times 10^6 \quad (6)$$

where A is the area of flask mouth (mm^2), M_0 and M_1 are the mass of the system (flask and hydrogel cap) before and after placing in the chamber, respectively.

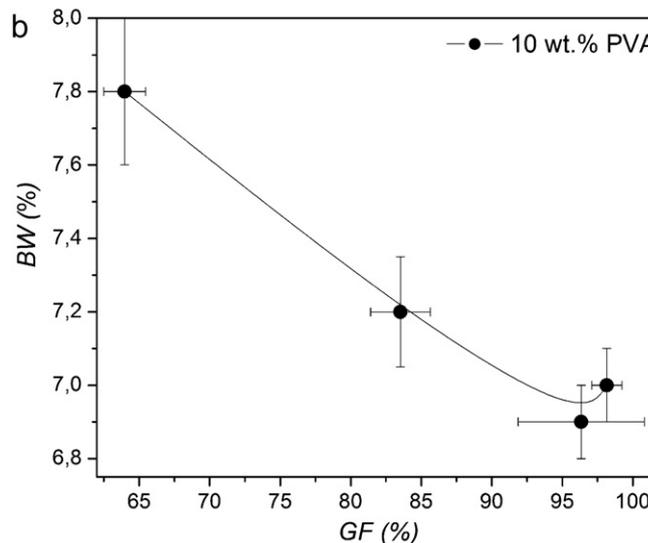
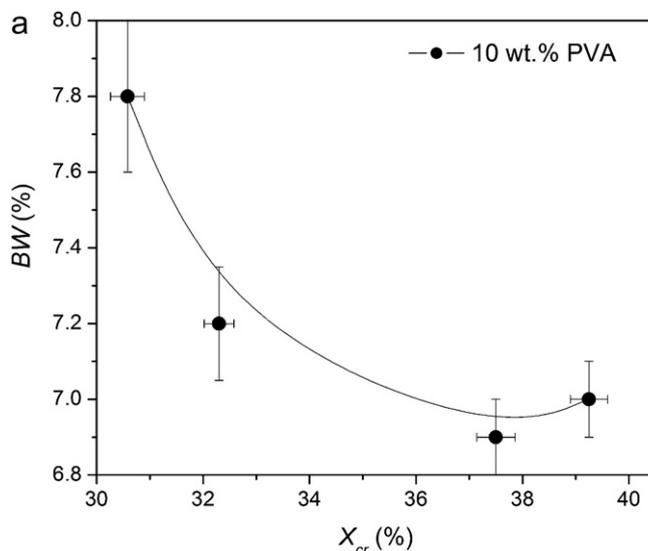


Fig. 7. Shows the Bound Water Content as a function on (a) crystallinity degree and (b) Gel Fraction.

3. Results and discussion

3.1. Structure of untreated and annealed hydrogel: degree of crystallinity, melting temperature, glass transition, gel fraction and bound water content

Fig. 1 shows the final aspect and transparency of PVA hydrogels annealed at different temperatures.

A macroscopical observation indicates that the material becomes less transparent, more brittle and it was more difficult to manipulate without generate a fracture with the increasing temperature treatment.

Fig. 2 shows the SEM micrograph of PVA cryogel annealing at 130°C . A typical porous structure can be observed in the following pictures. A similar structure was displayed for all treated hydrogels.

The porous size measured from 30 porous by the previous microphotography was $0.51 \pm 0.22 \mu\text{m}$.

The crystalline nature of PVA has been of specific interest particularly for physically crosslinked hydrogels prepared by freezing-thawing technique.

It was pointed out that the annealed samples were studied in the dry stage, changes in crystallinity during the drying process were considered.

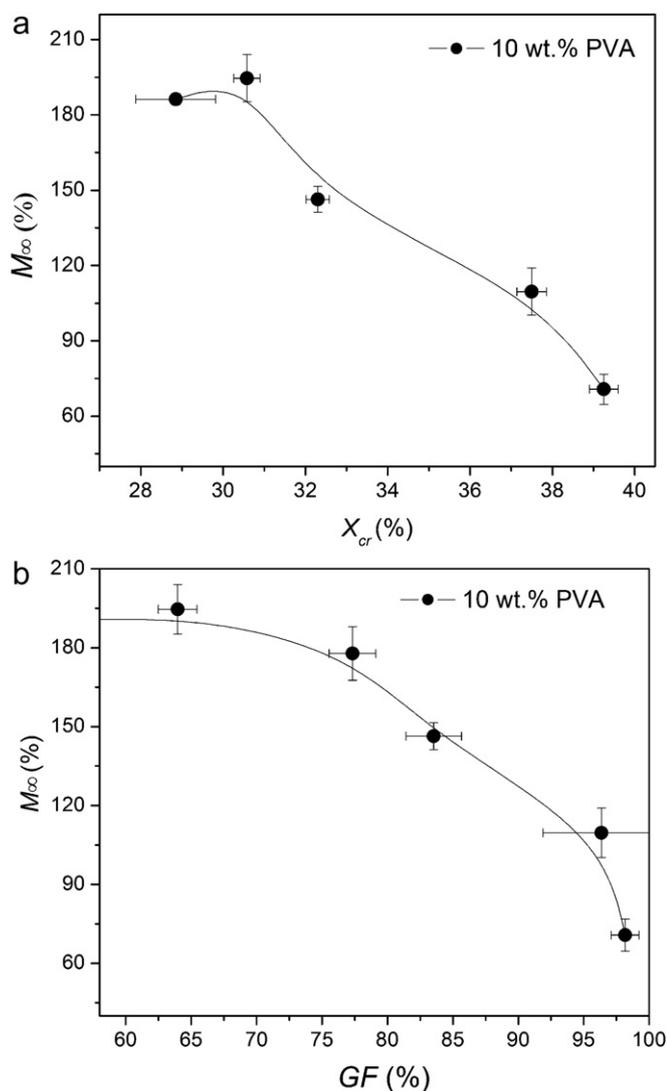


Fig. 8. Shows the Swelling equilibrium degree as a function on (a) crystallinity degree and (b) Gel Fraction for 10 wt.% solution.

Fig. 3a shows the crystallinity degree (X_{cr}) of studied hydrogels as a function of annealing temperature; melting temperature (T_m) was also included in the same figure. In addition, the GF as a function of annealing temperature for hydrogels obtained from both solution concentrations is included in Fig. 3b. From Fig. 3a it can be seen that the quantity (X_{cr}) and the size of crystals (directly related with T_m) [27] increased as a function of the annealing temperature.

The effect of drying time on the crystallinity of chemically crosslinked hydrogels has been previously studied [12] being the main result that this parameter increased as a function of drying rate. On the other hand, in the case of F/T hydrogels the freezing rate affects the size of ice crystals and, therefore, the number of formed crosslinks [28].

It has been found, investigating the drug release from PVA, that the mucoadhesive and drug release behavior could be adjusted by degree of crystallinity, which was affected by the number of cycles and the time of freezing of the solutions [5,29]. Nevertheless, the effect of drying temperature on crystallinity degree and on the glass transition temperature (T_g) of physically crosslinked PVA hydrogels is still unknown.

Fig. 4 shows the effect of annealing temperature on the glass transition temperature and bound water of PVA hydrogels prepared from both solution concentrations.

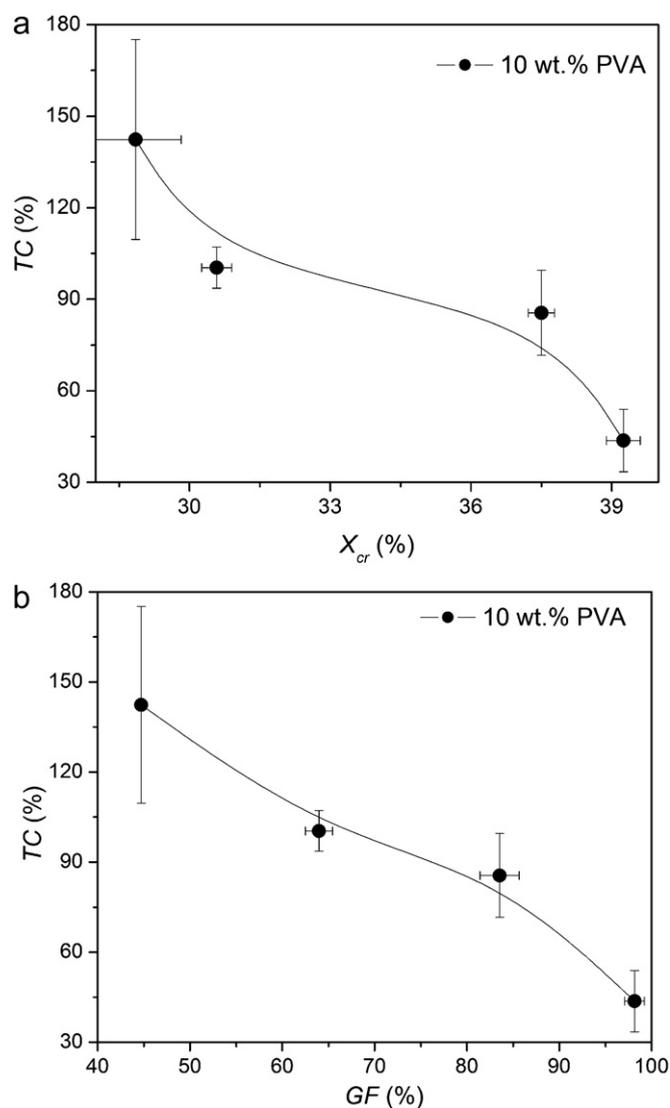


Fig. 9. Shows the thickness change (TC) as a function on (a) crystallinity degree and (b) Gel Fraction for 10 wt.% solution.

It can be noted that the behavior of T_g with the annealing temperature was independent of the polymer concentration (for concentrations studied here) increasing exponentially with annealing temperature. T_g is related to the crosslinking degree and with the plasticized content, so that, the previous result can be attributed to a raise on the crosslinks and a decrease on water content (bound and unbound) [30]. It is known [31] that the presence of water produces a significant decrease on T_g . To clarify the obtained results, the swelling behavior will be analyzed in the following section.

3.2. Swelling behavior of untreated and annealed hydrogels: swelling equilibrium degree, the effective diffusion coefficient and the water vapor transmission rate

Fig. 5 shows the sorption curve (M_t vs t) for untreated and annealed hydrogels.

It can be observed that the absorbed saline solution decreased in the treated PVA hydrogels and this phenomenon is more evident as the annealing temperature increases. PVA, which is a hydrophilic polymer, contains a large number of hydrophilic -OH groups, which can easily form hydrogen bonds with free water molecules [32], water and other small molecules, can easily penetrate into the space between the PVA crystallites [33]. After being put into phys-

Table 1
Swelling characteristics of PVA hydrogels as a function of annealing temperature.

Annealing temperature (°C)	Sample, 10 wt.%PVA			Sample, 5 wt.%PVA		
	M_{∞} , %	GF, %	TC, %	M_{∞} , %	WVTR, g/m ² h	TC, %
None	186.26 ± 2.26	44.71 ± 0.10	142.38 ± 32.81	262.7 ± 0.3	20.00 ± 0.38	471.20 ± 71.25
100	194.62 ± 9.41	63.97 ± 1.47	100.38 ± 6.73	208.8 ± 8.3	18.62 ± 2.90	256.68 ± 8.65
110	177.78 ± 10.21	77.33 ± 1.78	^a	191.2 ± 10.1	16.84 ± 2.52	234.10 ± 20.07
120	146.37 ± 5.18	83.53 ± 2.12	85.57 ± 13.95	116.8 ± 19.9	15.95 ± 1.95	146.39 ± 40.33
130	109.61 ± 9.39	96.35 ± 4.48	^a	80.4 ± 6.4	16.63 ± 1.82	104.60 ± 17.83
140	70.77 ± 6.05	98.16 ± 1.07	43.69 ± 10.21	65.5 ± 5.2	13.91 ± 1.92	95.46 ± 7.89

^a It was not possible to measure.

iological saline the network spaces are quickly permeated because there are more spaces for small molecules to inhabit. Then, as time passes, the swelling rate decreases until an equilibrium state is reached, as shown in Fig. 5. The thickness changes measurements and the maximum saline solution uptake (M_{∞}) are displayed in Table 1.

The previous table clearly shows that the maximum amount of saline solution absorbed decreased with the increase of the annealing temperature. This behavior can be due to the reduced space for small molecules to occupy and a longer distance for PVA chains to penetrate into the pore spaces, which leads to a smaller swelling degree. This effect corresponds with the increase on the crosslinking degree as a function of heat treatment temperature [29].

It is known that n is an important parameter to describe the kind of mechanisms that govern the drug swelling or release [34–38]. There exist several mechanisms by which different drugs can be released from polymer matrices; one of them is diffusion, which occurs when an active agent goes through the polymer. It was previously reported [12] that the rate of swelling of these hydrogels linearly increases with the square root of time. In our case, the Fickian exponent values were around 0.34 ± 0.05 which are close to the Fickian exponent value ($n = 0.5$ characterizes Fickian diffusion [34–37]). The variety of deviations from Fickian kinetics observed in glassy polymer-penetrant systems is commonly attributed to the slow viscous structural relaxations of the swelling polymer in response to penetrate induced osmotic stresses, which occur on time scales comparable to those of the diffusion process [38].

WVTR and thickness change (TC) displayed in Table 1 decreased as a function in treatment temperature, it can be attributed to an enhancement in crosslinking density as seen in the GF% changes.

3.3. Influence of gel fraction and crystallinity degree on the studied parameters

It is well known that the X_{cr} has a direct relationship with the improvement in the mechanical properties [20] and that GF is a measurement of the crosslinking degree. So that it is important to reveal if one of these parameters have a higher influence or control on the final properties of PVA hydrogels produced by F/T. Fig. 6 shows the correlation on the two main variables: gel fraction and crystallinity degree for the two analyzed polymer concentration.

It is known that the crystallites essentially served as additional crosslinks [11–13] to redistribute external stresses, so that, the results displayed in Fig. 6 are coherent; in addition, an exponential correlation between X_{cr} and GF is evident. The pseudo-plateau in X_{cr} –GF curve could be attributed to the saturation of zones available to produce crystallinities and to a decrease on the free volume.

The following figures (Figs. 7–9) show the most important characteristics of the hydrogels (the bound water content and the swelling behavior measured by M_{∞} and TC) as a function of both parameters (X_{cr} and GF).

A clear result of the above figures is that the tendency of the characteristics with the crystallinity degree and the gel fraction

is the same. However, it is seen that the curves are different as a function of each variable.

4. Conclusions

It can be concluded that the thermal annealing of PVA hydrogels have a direct influence on its relevant characteristics. Both, the crystallinity degree and the T_g , which are measurements of crosslinking degree, increased as a function of the annealing temperature. Moreover all the most important properties of the hydrogels were influenced by these changes: the maximum swelling degree, the thickness change and the bound water content decreased whereas the GF increased as a function of annealing temperature. An exponential relationship between the main characteristics GF and X_{cr} was found. All these results were independent of the polymer concentration and indicate that hydrogels with desired characteristics can be obtained by means of a thermal treatment.

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