

Effect of Annealing on the Crystallization of Poly Vinyl Chloride for Drug Delivery System

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Abstract

Poly vinyl alcohol has been studied for its ability to form crystallites by using annealing method. Semicrystalline films of poly vinyl alcohol (PVA) were prepared by casting 11.5 wt. % and 13 wt. % PVA aqueous solution onto glass slides at annealing temperature range 90 -120°C and duration time 15- 60 minute. This allowed the macromolecules to form crystallites, small regions of folded and compacted chains separated by amorphous regions where single PVA chain may pass through several of these crystallites. Degree of crystallinity of PVA films (hydrogels) was determined by method of density; on the other hand the swelling behavior was conducted by the determination of water uptake, wet degree of crystallinity, gel fraction and solubility. The results of PVA films showed that water uptake decreased with increasing temperature, time of annealing and PVA concentration, while degree of crystallinity increased, and gel fraction and solubility decreased with increasing temperature and time of annealing. The maximum dry and wet degree of crystallinity was 64% and 36% respectively at 120°C and 60 min.

Key words: poly (vinyl alcohol)–annealing–swelling- crystallinity.

Introduction

Advances in polymer science have opened up possibilities for using a wide variety of polymeric materials as drug delivery systems. Biodegradable polymers, by virtue of their ability to degrade in the body naturally, offer enormous advantages over conventional drug delivery systems [1,2]. It eliminated the need for surgery and also does not elicit any adverse reactions from the body. Polymeric drug delivery systems are mainly intended to deliver the drug over a period of time. Some of the materials that are currently being used/studied for controlled drug delivery include

poly methyl methacrylate, poly vinyl alcohol, polyacrylamide, polyethylene glycol, polylactic acid, polyglycolic acid, polylactideglycolic acid, and polyanhydrides [3]. Hydrogels of polymer are gaining increasing popularity in the area of controlled-release drug delivery. These polymers are generally glassy in the dehydrated state but swell to become an elastic gel upon water penetration. The entrapped drug within the swelling matrix concomitantly dissolves and diffuses through the swollen network into surrounding aqueous environment. The rate of drug release from hydrogels is regulated by cross-linking density and the extent of swelling [4]. Poly vinyl

alcohol (PVA) is a hydrophilic polymer with unique properties. It absorbs water, swells easily and it has extensively been used in controlled release applications [5]. Several methods have been explored to form semicrystalline PVA for use in biomedical applications. One early method studied by Peppas [6] explored crystallization by a slow dehydration process. Peppas *et al.* [7] studied formation of crystallites by a freeze-thaw process. Thin amorphous films of PVA were frozen for 8 h at -20°C and then thawed for 4 h at 25°C . This cycle was repeated several times. They showed that as the number of freeze-thaw cycles increased the stability of the crystallites during swelling increased. However, the total number of crystals in the hydro gel did not necessarily increase with increased freeze-thaw cycles. They also added PEG [8] to hydro gels formed by the freeze-thaw process, and showed that the resulting hydro gels exhibited increased stability during swelling. Other studies have used a combination of cross-linking and crystallization techniques to probe the characteristics of PVA hydro gels under various crystallization and swelling conditions. Mallapragada and Peppas [9] studied the effect of swelling on the crystalline regions of PVA hydro gels. The PVA networks were created by first cross-linking aqueous solutions of PVA using electron-beam irradiation, followed by annealing to form crystallites. Using IR spectroscopy to compare the crystallinity before and after swelling, they showed that the swelling process did not affect the crystallites in the semicrystalline PVA; only the amorphous regions of the hydro gel were penetrated by the water molecules. Another technique for crystallization of PVA is annealing at a temperature between the glass transition temperature and the melting

point; Mallapragada *et al.* [10] conducted some of the earliest experiments using this annealing process. These studies also explored dissolution mechanisms of PVA hydro gels that had been crystallized using annealing. Unlike previous works, these annealed films were not previously cross-linked, so the sole source of stability was the crystalline structure formed during annealing. Peppas N.A., and Tennenhouse D. [11] study the preparations Semicrystalline films of poly vinyl alcohol by annealing amorphous PVA films at temperature $90, 100, 110^{\circ}\text{C}$ for 60 min, the degree of crystallinity of the dry films was measured by differential scanning calorimetry [12,13].

In this work, special emphasis is given to the methods of preparation, the optimization of the preparation process and the swelling behavior of the associated systems.

Experimental Work

1. PVA Film Preparation

The films produced were made from a 13% and 11.5% aqueous PVA solution. To prepare 13% PVA solution, 35 ml of deionized water was added to 5.3 g PVA ($M_w=14000$, degree of hydrolysis=99.8%). To prepare 11.5% PVA solution, 45 ml of deionized water was added to 5.3 g PVA ($M_w=14000$, degree of hydrolysis 99.8%). The PVA solution was stirred and heated at $85-90^{\circ}\text{C}$ for 4 to 6 h by using a water bath. The solution was allowed to cool for several minutes before use. The solution was then cast on to six 25.4×76.2 mm glass slides and spread uniformly over the slides using a glass rod. The films were allowed to dry at $25-30^{\circ}\text{C}$ for at least 24 h.

2. Annealing of the films

The amorphous PVA and films were annealed in an oven at temperatures 90,110 and 120°C for 15,30 and 60 min with concentrations of 13% and 11.5% aqueous PVA films. Once the films were removed from the oven and then peeled off from the glass slides and stored at room temperature. The resulting hydro gels were tested for their crystalline, swelling behavior, gel fraction and solubility.

Tests of the Films

1. Water Uptake

The samples were submerged in deionized water at 37°C (the last level simulates water absorption at the temperature of the human body) until they reached equilibrium, which occurred after three to four days. After swelling, the weight and volume of the samples were again measured. The water uptake, or percent water incorporated into the hydrogel was calculated from Eq.1.

$$w_{eq}(\%) = \frac{w_s - w_d}{w_s} \times 100 \quad \dots(1)$$

where w_d is the weight of dry sample and w_s is the weight of swollen sample.

The swelling behavior of PVA films was studied by measuring the amount of water incorporated into the sample. After the annealing process, the samples were weighted then swollen in water, later the swelling samples were weighted after swollen every two days nearly until the amorphous PVA was soluble.

2. Calculation of the Samples Volume

Volumetric measurements were taken by suspending the sample in heptane (a non-solvent), weighing, and calculating the volume, V, based on the weight of the heptane displaced. First

the samples were weighing in air and then volumetric measurements were taken by suspending the sample in n-heptane, weighing, and calculating the volume, V, based on the weight of the heptane displaced. The volume, V, was calculated by Eq.2.

$$V = (W_{air} - W_{heptane}) / \rho_{heptane} \quad \dots(2)$$

Where W_{air} is the weight of the sample in air, $W_{heptane}$ is the weight of the sample in heptane and $\rho_{heptane}$ is 0.6840g/ml.

3. Density of Gels

The density of dry gels was determined by hydrostatical weighing by [kit YDK OILP in n-heptane (EN 1183-1:2004)]. The density of gels was calculated by Eq.3.

$$\rho = w_a \cdot \rho_h / w_a - w_h \quad \dots(3)$$

where w_a is the weight of the sample in air, ρ_h is the density of the liquid (n-heptane), and w_h is the weight of the sample in the liquid.

4. Degree of Crystallinity

The semicrystalline films were characterized by measuring the degree of crystallinity, X, after annealing. The degree of crystallinity of the samples was calculated by Eq.4:

$$\frac{1}{\rho_g} = \frac{X}{\rho_c} + \frac{(1-X)}{\rho_a} \quad \dots(4)$$

Where a $\rho_c=1.345$ g/cm³ for 100% crystalline PVA, $\rho_a=1.269$ g/cm³ [89] for 100% amorphous PVA, and ρ_g is the density of the sample. The “wet degree of crystallinity” X_{wet} , was calculated by Eq.5. This value indicates the volume of crystallites in the hydrogel compared to the total volume of the swollen hydrogel.

$$X_{wet} = X * V_{dry} / V_{swollen} \quad \dots(5)$$

To calculate the degree of crystallinity X of the samples, first the dry annealing films were weighted in air and then in n-heptane; after that the were samples swollen in water by using magnetic stirrer for 4h, and later the swollen samples were weighted in air heptane once more.

Results and Discussion

Effect of Annealing Temperature on the Water Uptake of PVA Films

Thin films of PVA were annealed at temperatures of 90, 110 and 120°C (above the glass transition temperature of 85°C) for 15 min to investigate the effect of annealing temperature on water uptake of the films. Fig.1 and Fig 2 show that water uptake increased with time until it reached nearly constant value after 20 day. Water uptake was decreased with increasing annealing temperature for 13% and 11.5% PVA related to the effect of density of the films.

The increasing of density was caused by the effect of annealing temperature on the inner composition of the polymer. Increasing the temperature of annealing caused in compacting of polymer molecules which result in decreasing the voids among polymer molecules. Consequently the porosity decreased and the permeability of the polymer for liquids and gases decreased [14]. This behavior indicates clearly the increase in the crystalline phase in comparison with the amorphous one, or it can be said that the system is more packed with crystallite.

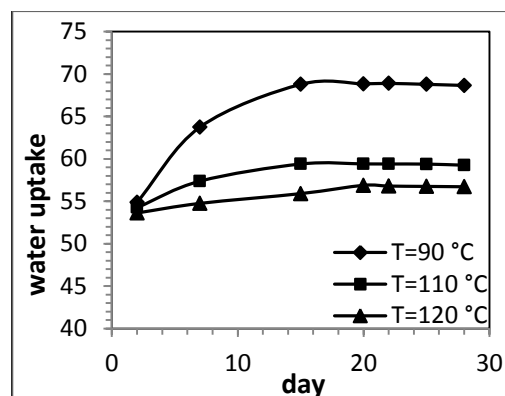


Fig.1, Relation between water uptake and time of swelling for different annealing temperature, $t=15$ min, 13% PVA

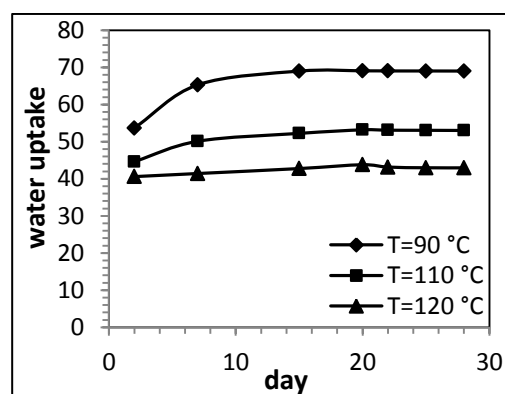


Fig.2, Relation between water uptake and time for different annealing temperature, $t=15$ min, 11.5% PVA

Effect of Annealing Time on the Water Uptake of PVA Films

The effect of annealing time on the water uptake of polyvinyl alcohol films was investigated. The films of PVA were annealed for different times (15, 30 and 60 min) at annealing temperature of 120°C. Figures 3 and 4 show the effect of annealing time on the water uptake with constant annealing temperature using 13% and 11.5% PVA, respectively. These figures illustrate that increasing the annealing time causes decreasing the water uptake, which can be attributed to the increase in density.

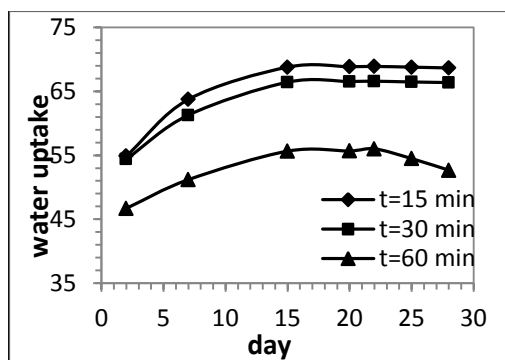


Fig.3, Relation between water uptake and annealing time for T=120°C, and 13% PVA

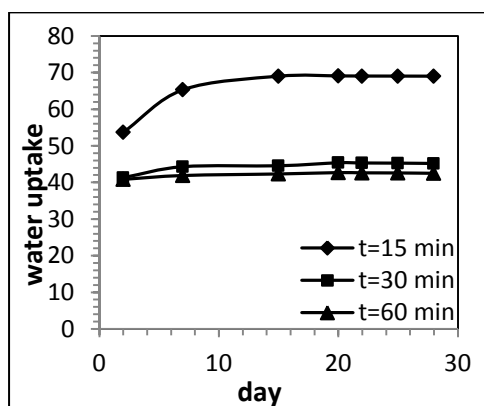


Fig.4, Relation between water uptake and annealing time for T=120°C and 11.5% PVA

Effect Concentration of PVA on the Water Uptake of PVA Films

The effect of the concentration of PVA on the water uptake of polyvinyl alcohol films with time was investigated. The PVA films were annealed at constant temperature of 120°C for constant annealing time of 30 min to investigate the effect of the concentration of PVA on the water uptake of the films. Figure 5 shows the effect of increasing concentration of PVA on water uptake with time of swelling. The increase in polymer concentration leads to a decrease in the water uptake of the films. From the results of the previous sections, increasing the density caused the decreasing of the water uptake of the polymer; increasing the concentration means the increasing of the density, thus the increasing of the polymer concentration carried out the decreasing of the water up take which

was caused by the decreasing of the permeability of the polymer. The increase in the density means that the interstitious distance between the adjacent molecules will become less leading to less porosity and hence less water uptake. During the annealing process, some of the amorphous phases changes into folded compact chains which are distributed through the amorphous phase. This can be considered as crosslinking but of physical type. These points of physical crosslinkings are considered as crystals or crosslinking agents or centre.

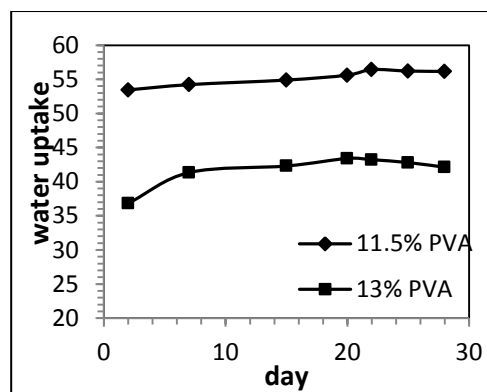


Fig.5, Relation between water up take and swelling time for different concentration of PVA at annealing temperature of 120°C and annealing time of 30 min

Effect of Annealing Temperature on the Degree of Crystallinity of PVA Films

The effect of annealing temperature on the degree of crystallinity of polyvinyl alcohol films was investigated. Fig.6 shows the effect of the annealing temperature on the degree of crystallinity with different annealing time. The increase in the annealing temperature leads to the increase of the degree of crystallinity, which results from increasing the density of the polymeric samples. The annealing process causes the appearance of aggregation of the polymer chains; consequently the crystal regions will grow with the increase of annealing temperature [10,13]. The physical

crosslinking causes the polymer to be packed with crystals with less inner distances.

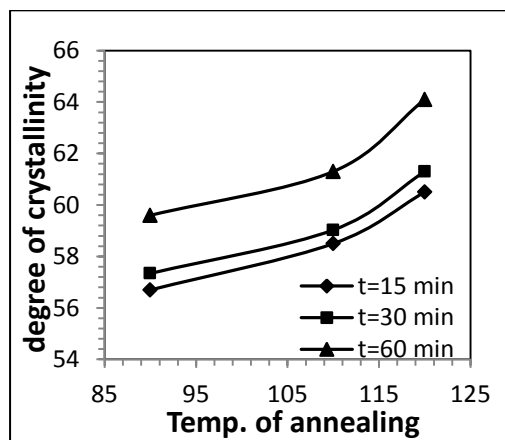


Fig.6, Relation between the degree of crystallinity of PVA and annealing temperature for different annealing time, 11.5% PVA

Effect of Annealing Time on the Degree of Crystallinity of PVA Films

The Effect of annealing time on the degree of crystallinity of polyvinyl alcohol films was investigated as show in Fig.7. The degree of crystallinity increased with increasing time of annealing.

Comparison Between Dry and Wet Crystallinity of PVA Films

A comparison between dry and wet crystallinity of polyvinyl alcohol films at different temperatures and constant annealing time was investigated as shown in Fig.8, while Fig. 9 shows a comparison between the dry and wet crystallinity of the samples annealed for different annealing times at constant temperature. As expected, the rate of swelling differs in both dry and wet films. The wet crystallinity of the samples was much lower than that of the dry crystallinity. This was readily explained by the water incorporated into the polymer network during swelling. The amorphous regions of the hydrogel swelled, allowing water to penetrate the network and became entrained in the hydrogel. This expansion of the network and

incorporation of water caused the overall weight and volume of the hydrogels to increase during swelling.

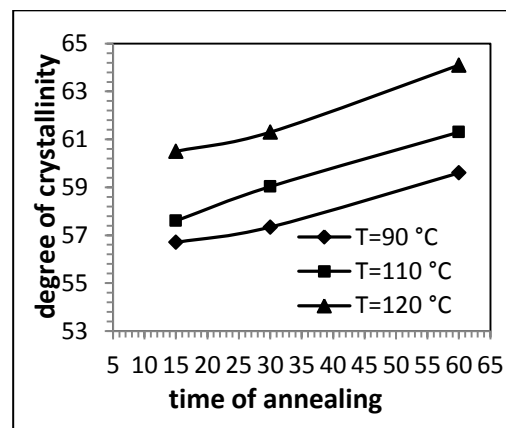


Fig.7, Relation between the degree of crystallinity and time of annealing for different annealing temperature, 11.5% PVA

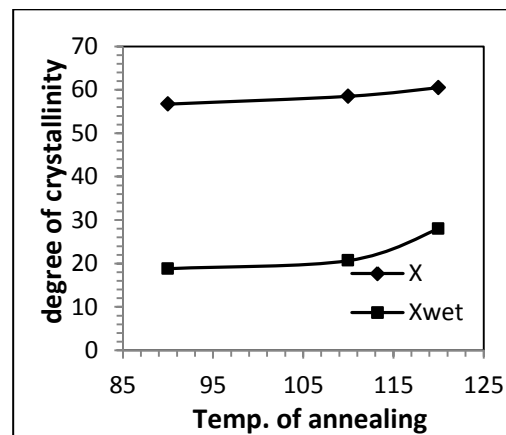


Fig.8, Relation between the degree of crystallinity and temperature of annealing for dry and wet films

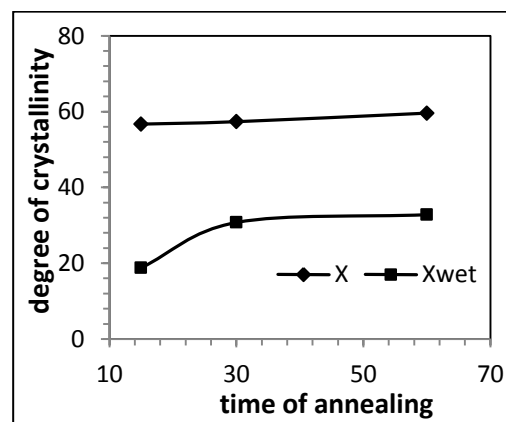


Fig.9, Relation between the degree of crystallinity and time of annealing for dry and wet films

Long-Term Stability of Hydrogels

Long term stability of hydrogels was investigated. As noticed from the previous results, the increasing of annealing temperature and time of annealing causes the decreasing of the water uptake, and since the gel fraction is a function of the water uptake; therefore the gel fraction behaves exactly the same as the water uptake. On the other hand the solubility is inversely proportional to the crystallinity, or it behaves inversely. Fig. 10 shows the effect of annealing temperature and time of annealing on gel fraction of PVA films, where the increasing of annealing temperature and time of annealing causes the decreasing of the gel fraction. Fig.11 shows the effect of annealing temperature and time of annealing on the solubility of the PVA films, where the increasing of annealing temperature and time of annealing results in the decreasing of the solubility.

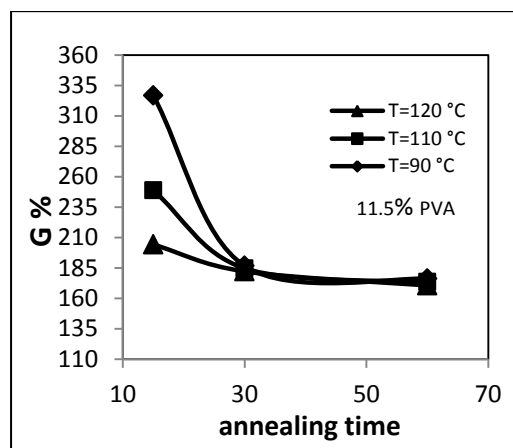


Fig.10, Relation between Gel fraction of the polymer and annealing time at different annealing temperature, 11.5% PVA

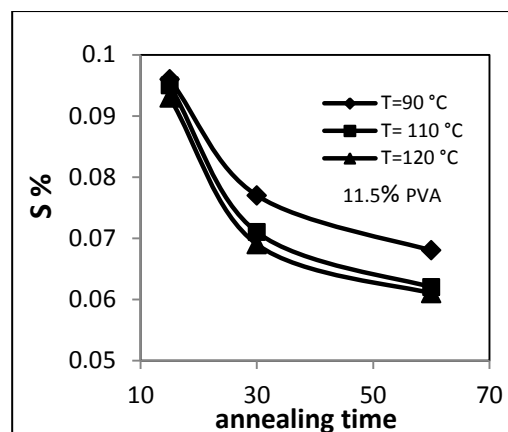


Fig.11, Relation between Solubility of the polymer and annealing time at different annealing temperature, 11.5% PVA

Conclusions

Increasing the annealing temperature leads to a decrease in water uptake, an increase of density, and an increase of the crystallinity of PVA films with constant time of annealing. Increasing time of annealing leads to decreasing in the water uptake, increasing density and increasing of the crystallinity of PVA films at constant annealing temperature. Increasing density leads to decreasing in the water uptake and increasing crystallinity of the PVA films. The wet crystallinity of the samples was much lower than that of the dry crystallinity for the PVA films. The results show that increasing the annealing temperature and annealing time causes the decrease of the gel fraction and solubility for the PVA films.

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