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Preparation and Characterization of Poly(vinyl alcohol)-poly(vinyl pyrrolidone) Blend: A Biomaterial with Latent Medical Applications

Andres Bernal,[1,2] Ivo Kuritka,[1,2] Petr Saha[1,2]

[1]Polymer Centre, Faculty of Technology, Tomas Bata University in Zlin, nam. T.G. Masaryka 275, 762 72 Zlin, Czech Republic
[2]Centre of Polymer Systems, University Institute, Tomas Bata University in Zlin, Nad Ovcirnou 3685, 760 01 Zlin, Czech Republic

Correspondence to: I. Kuritka (E-mail: ivo@kuritka.net)

ABSTRACT: Aqueous solutions of poly(vinyl alcohol) and poly(vinyl pyrrolidone) are blended and films are produced by casting method with the further intention of being used as bio-materials with latent medical application. Glutaraldehyde, 4,4′-diazido-2,2′-stilbenedisulfonic acid disodium salt tetra-hydrate are used as crosslinker agents, whereas lactic acid is the plasticizer in the blend. The obtained films are characterized by differential scanning calorimetry (DSC), mechanical properties, swelling and solubility behavior. DSC measurements show that the blends exhibit a single glass transition temperature indicating that they are miscible, even in the presence of the plasticizer and crosslinker agents. By the combination of all mentioned additives, a relevant enhancement of the swelling is observed, accompanied by a stabilization of the solubility during the tested time. Finally, mechanical properties show an appropriate performance in the studied parameters. As a consequence, the obtained films could be suitable for use as medium or long-term implants. © 2012 Wiley Periodicals, Inc. J. Appl. Polym. Sci. 000: 000–000, 2012

KEYWORDS: biomaterials; mechanical properties; thermal properties; poly(vinyl alcohol); poly(vinyl pyrrolidone)

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INTRODUCTION

Polymers are widely acknowledged as being some of the most versatile materials due to their broad physical and mechanical properties. This allows them to be used for different proposes, including medical applications such as tissue engineering, implants, artificial organs, prostheses, ophthalmology, dentistry, bone repair,[1] or as a temporary scaffold, a temporary barrier, and a drug delivery system.[2]

Among synthetic polymers, both poly(vinyl pyrrolidone) (PVP) and poly(vinyl alcohol) (PVA) have been intensively studied as biomaterials. Researches have found for the former that it is very useful in pharmacy and medicine due to its outstanding absorption and complex abilities.[3] Despite the fact that the human body is not able to degrade PVP, this polymer can be gradually excreted into the urine without concentrating in the kidneys,[4] when the molar mass does not exceed 30,000 g mol^{-1}, which is an interesting attribute for biomedical uses. Numerous attractive features have been reported for PVA, such as high hydrophilicity, recognized biodegradability, biocompatibility, and good processability on film formation.[5] Both polymers are water soluble,[6] an important property for processing, although this characteristic could be a disadvantage when being used as a long-term implant. Blends, on the other hand, might represent an appropriate solution for material design. They have been investigated in order to satisfy the needs of specific sectors within the polymer industry. Generally, they show superior performance in relation to the individual components and, as a result, the range of applications grows continuously for this class of materials.[7] The combination of PVA and PVP in blends has emerged as a new tool for preparation of biomaterials,[8] and there are abundant amount of reports which describe the multifunctional utilities for these kind of blends.[9–12] As a consequence of the very small entropy of mixing and usually positive heats of mixing, any pair of polymers will be immiscible unless some strong interactions such as hydrogen bonding, ionic and dipole, π electrons and charge-transfer complexes appear.[13] In the case of PVA and PVP blends, the ring of pyrrolidone contains a proton accepting carbonyl group, while PVA has hydroxyl groups and therefore, hydrogen bonding is expected among them. Moreover, the use of modifiers can change the properties of PVA/PVP blends in many aspects. In fact, the water solubility of single components could be modified by blending PVA/PVP or by the use of some additives even if it is

not common.[14] In this context, glutaraldehyde (GA) has been chosen as a crosslinker agent for PVA because it forms an excellent polymer network in which the mechanical and swelling properties can be controlled. These crosslinking reactions can be conducted under mild conditions because of the lack of ability for crosslinking PVP.[15–17] For PVP, a common crosslinker is 4,4′-diazido-2,2′-stilbenedisulfonic acid disodium salt tetrahydrate (DAS) which is not indeed an effective PVA crosslinker.[15] Hence, the possibility to independently control the crosslinking mechanism for both polymers is considered as the main reason for the selection of the agents. By crosslinking, a reduction of hydrophilicity can be utilized as a valuable alternative to improve the water resistance of the blend for specific medical uses. Mechanical test, swelling, and solubility degree are determined in this study since biomedical polymers must be used in the biological environment. Water adsorption can influence the dimensional stability and mechanical properties of the prosthetic element and, moreover, water by itself can be a powerful degrading agent. It is evident that a careful characterization of the bulk properties is fundamental for determining the structure–properties correlation.[18]

The aim of this work was to prepare and characterize PVA/PVP blends using specific additives in order to obtain suitable films with prospective medical application. Information about mechanical properties, degree of swelling, solubility degree, and thermal properties were obtained in this research. On the basis of the requirements for biomaterials, PVA/PVP blend with LA, GA, and DAS, has showed appropriate mechanical performance and water resistance. As a result of those characteristics, the material may be considered as a suitable candidate for further investigation as a long or medium-term implant in the medical field.

EXPERIMENTAL

Materials

Poly(vinyl alcohol) (PVA, M_w = 47,000 g mol^{-1}) with a polymerization degree of 1000 and 98% hydrolysis, poly(vinyl pyrrolidone) (PVP, M_w = 40,000 g mol^{-1}), 4,4′-diazido-2,2′-stilbenedisulfonic acid disodium salt tetrahydrate (DAS) of analytical grade and a 50% water solution of glutaraldehyde (GA) were provided by Sigma Aldrich, The Czech Republic. Lactic acid (analytical grade) (LA) was produced by Lachema, The Czech Republic, hydrochloric acid, and acetic acid (analytical grade) were supplied by Penta, The Czech Republic. They were used without further purification.

Sample Preparation

PVA and PVP Films. A PVA solution at 5 wt % was prepared by dissolving the polymer in distilled water at 80°C for 12 h under continuous magnetic stirring. Once, the solution was obtained, GA at 0.25 wt % related to the total amount of polymer was added as crosslinker agent and the solution was heated up to 80°C during 20 min as a crucial step in the crosslinking mechanism. A second set of samples were prepared with GA and hydrochloric acid (indicated as H^+ hereafter) at 1.2 wt % was added. Finally, PVA solution and LA at 15 wt % related to the total amount of the polymer was blended and stirred for 15 min. The solutions were cast on polyethylene substrates and allowed to dry at 35°C for 4 days in air circulating oven. Films with a thickness of about 200 μm were obtained. Table I summarizes, designs, and describes each sample.

PVP was dissolved by adding slowly the polymer to water at room temperature, always under vigorous magnetic stirring. Simultaneously, in distilled water a 4 wt % aqueous solution of DAS was prepared in a dark room and it was added to the polymer solution. After removal of the bubbles, the blend was cast on polyethylene substrates and it was allowed to dry at 35°C for 4 days in air circulating oven. Films with a thickness of about 200 μm were obtained. Once samples with DAS were dried, they were irradiated for 5 min by a home made instrument with four Sylvania black-light F8W/T5/BL350 lamps. The samples were stored in polyethylene bags and kept on a dark place at laboratory conditions, i.e., temperature 21–23°C and relative humidity 40–60%.

PVA/PVP Blends. Blends of 1 : 1 wt/wt ratio of PVA and PVP solutions were blended under magnetic stirring using the same additives as for the single components. Blends with DAS were always kept in dark room. All the samples were allowed to dry for four days at 35°C.

Characterization

Differential Scanning Calorimetry. Calorimetric measurements were carried out in a DSC 1 calorimeter, Mettler Toledo (Greifensee, Zurich, Switzerland), under nitrogen flowing at a rate 30 mL min^{-1}. The specimens were pressed in unsealed aluminum pans. Heating cycle was performed in order to obtain glass transition temperature (T_g) and melting temperature (T_m). The samples were cooled down by air at an exponentially decreasing rate. The heating of the cycle was performed from 25 to 240°C at a rate of 20°C/min. The T_g was determined as the midpoint temperature by standard extrapolation of the linear part of DSC curves using Mettler-Toledo Stare software and the T_m as the maximum value of the melting peak. The relative crystallinity (X_c) was estimated from the endothermic area using eq. (1):

$$X_c = \Delta H_f / \Delta H_f^0, \quad (1)$$

where ΔH_f is the measured enthalpy of fusion from DSC thermograms and ΔH_f^0 is the enthalpy of fusion for 100% crystalline PVA (138.6 J g^{-1}).[19]

Degree of Swelling and Solubility Degree. As PVA and PVP are water soluble polymers, gravimetric method was used to calculate the degree of swelling and the solubility of the films. Squares of 1.5 cm^2 were cut and dried at 60°C until constant weight (W_1). After that, they were immersed into 5 mL of distilled water at 37°C (normal human temperature) at different time intervals (1, 3, 5, 10, 20, and 30 min). Subsequently, the samples were taken out from the water and the surface moisture was carefully removed by paper napkin. They were weighted again (W_2). Finally, samples were allowed to dry until constant weight at 60°C and weighted once more (W_3). The degree of swelling (DS) and the solubility of the film (SF) were calculated according to the eqs. (2) and (3), respectively. Five replicate tests were done for each sample and these values were undergone to Dixon test for identification and rejection of outlier data with 95 % of

Table I. Prepared Films

No.	Name	Description
1	PVA	PVA at 5 wt %
2	PVA/LA	PVA at 5 wt % and LA at 15 wt % related to the total amount of polymer
3	PVA/GA/H^+	PVA at 5 wt %, GA at 0.25 wt % related to the total amount of polymer and 50 μL of hydrochloric acid
4	PVA/GA/LA	PVA at 5 wt %, GA at 0.25 wt % and LA at 15 wt % both related to the total amount of polymer
5	PVA/GA/H^+/LA	PVA at 5 wt %, GA at 0.25 wt %, LA at 15 wt % both related to the total amount of polymer and 50 μL of hydrochloric acid
6	PVP	PVP at 5 wt %
7	PVA/PVP/GA/H^+	PVP at 5 wt %, PVA at 5 wt %, GA at 0.25 wt % related to total amount of polymer and 50 μL of hydrochloric acid
8	PVA/PVP/GA/H^+/LA	PVA at 5 wt %, PVP at 5 wt %, GA at 0.25 wt %, LA at 15 wt % both related to the total amount of polymer and 50 μL of hydrochloric acid
9	PVA/PVP/DAS/GA/H^+	PVA at 5 wt %, PVP at 5 wt %, GA at 0.25 wt %, DAS at 4 wt % both related to total amount of polymer and 50 μL of hydrochloric acid
10	PVA/PVP/DAS/LA/GA	PVA at 5 wt %, PVP at 5 wt %, DAS at 4 wt %, LA at 15 wt % and GA at 0.25 wt % all of them related to total amount of polymer
11	PVA/PVP/DAS/GA/H^+/LA	PVA at 5 wt %, PVP at 5 wt %, DAS at 4 wt %, LA at 15 wt % and GA at 0.25 wt % all of them related to total amount of polymer and 50 μL of hydrochloric acid

confidence and no data was rejected. For all the measurements, an analytical balance with the accuracy 0.0001 g was used. (Denver Instrument SI-64, Goettingen, Germany).

$$\mathrm{DS}(\%) = \frac{W_2 - W_3}{W_3} \times 100 \quad (2)$$

$$\mathrm{SF}(\%) = \frac{W_1 - W_3}{W_1} \times 100 \quad (3)$$

Lactic Acid Leaching Analysis. From the leaching media of the samples containing LA, one aliquot of 1 mL was collected and diluted until 10 mL in distilled water. The total acidity was obtained by titration with a total acidity minititrator and pH meter for water analysis (Hanna Instrument HI84430, Woonsocket, Rhode Island).

Mechanical Properties. Mechanical properties of PVA and PVP blends, including Young Modulus (E), stress at break (σ), and elongation at break (ε) were tested on five specimens per sample. Rectangular test specimen specified in ISO 527-3[20] with a length of 100 mm, width of 10 mm and thickness of about 200 μm were used. The experiment was carried out using an Instron-type tensile testing machine (Testometric M350-5CT, Lincoln Close, Rochdale, England) and the rate was 50 mm/min. The test conditions are specified in ISO 291.[21] The thickness of the samples was measured by a micrometer with the accuracy of 0.01 mm and specimens were kept in polyethylene bags, in a dark room and at controlled temperature and relative humidity.

RESULTS AND DISCUSSION

Differential Scanning Calorimetry

The thermograms for PVA blends are depicted in Figure 1 and the obtained thermal parameters are shown in Table II. The graphs were vertically shifted for better presentation. The characteristic melting temperature (T_m) for PVA at 211°C and the glass transition temperature (T_g) at 80°C were clearly manifested in the thermogram. Nevertheless, the thermal relaxations for PVA include the α-relaxation temperature (T_α) which is observed in the thermogram as a small exothermic effect at 100°C associated with conformational changes caused by either thermal motion or by the action of an external field without rupture of the chemical bonds.[22,23]

PVA/LA presented a noticeable reduction in the crystallinity related to the neat PVA by about 30% due to the influence of LA on the hydrogen bonding strength among PVA chains. As a result, a lesser amount of lattices were present, causing a decrease of 21°C in T_m. Furthermore, the increasing of PVA chain mobility was a consequence of the plasticizing effect, which was proven by a significant decrease in the recorded T_g

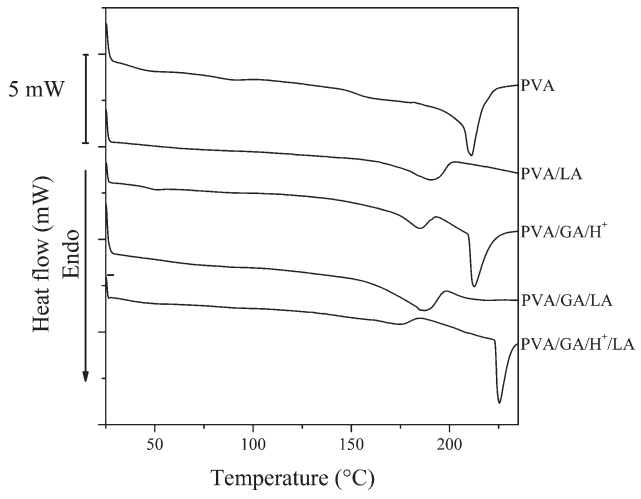

Figure 1. DSC thermograms for PVA and its blends.

Table II. Thermal Parameters of PVA and PVA/PVP Blends

Sample	Temperature °C		Enthalpy	Crystallinity
	T_g	T_m	ΔH_f (mJ g^{-1})	%
PVA	80	211	49	36
PVA/LA	55	190	35	25
PVA/GA/H$^+$	46/82	185/213	25/63	16/46
PVA/GA/LA	60	186	26	19
PVA/GA/H$^+$/LA	40/140	175/224	9/53	7/38
PVP	110	-	-	-
PVA/PVP	51	218	42	29
PVA/PVP/GA/H$^+$	51	174/205	78	57
PVA/PVP/GA/H$^+$/LA	48	167	51	37
PVA/PVP/DAS/GA/H$^+$	54	178/224	5/64	4/46
PVA/PVP/DAS/LA/GA	51	178	18	13
PVA/PVP/DAS/GA/H$^+$/LA	39	165/186	8/55	5/40

from 80°C to 55°C.[24] LA could be at least partially grafted causing disruption or attenuation of hydrogen bonding between parallel PVA chains, as well as disturbing the regularity of chain stacking by the presence of randomly distributed lactide groups pendant to the polymer chain. The α-relaxations in PVA did not manifest in this sample because LA modified the crystalline regions in PVA. Consequently, the polymer chains presented a higher degree of mobility or there were not significant restricted movements, as well as the changes in the crystalline structure affected the orientation of crystals, morphology, density, and perfection packing.[25]

The thermogram for PVA/GA/H$^+$ exhibited two endothermic peaks, which were attributed to the morphological effects caused by GA/H$^+$ into the matrix.[26] The peak centered at 213°C is related to T_m and practically did not change in comparison to the T_m for PVA, due to the relatively low GA concentration. The effect of crosslinker molecules on the crystal structure and the degree of crystallinity is manifested as the second peak related to the melting of the other minor crystalline phase at 185°C. PVA/GA/LA presented notably lower T_m and T_g than PVA, but just slightly different from PVA/LA. For that reason, it was possible to deduce that the stronger action is owed to the plasticizing effect of LA, which is in agreement with the swelling and solubility results as will be showed further in this text.

Two phenomena were identified in the PVA/GA/H$^+$/LA samples. In the first one, the T_m was sparingly higher than the same transition for pure PVA and PVA/GA/H$^+$. This might mean that the extra consumed energy was needed to overcome the intermolecular forces, which held the polymer molecules together, not as a crosslinked, but perhaps as a grafted material. The second phenomenon was that the matrix was partially crosslinked by GA/H$^+$, with the consequent reduction of the number of hydroxyl groups and hydrogen bonding interaction.[27] On the other hand, the increase of T_g could have occurred due to the presence of big bulky pendant groups.[28] Also, if mono-functional reaction is present,[26,29] the free volume is bigger, the chains of the matrix have more freedom, and a lower T_g can be expected. The combination of crosslinking and the presence of pendant groups influences the crystallinity and it will be virtually lost with the extent of crosslinking.[30]

The DSC thermograms for the PVA/PVP blends are shown in Figure 2 and their thermal transitions are exhibited in Table II. As interesting characteristic was that, of all the studied samples, just one T_g was exhibited. This might be a signal that the blends were miscible, albeit, it could indicate that the blends were only compatible.[15,31–33] The PVP themogram showed a very broad step at 110°C, which can be attributed to water evaporation, although it could indicate the T_g. This value is in concordance with some works,[34,35] while values of T_g for PVP ranging from 54 to 175°C were found in other sources; this may be attributed to the large influence of adsorbed moisture due to the hygroscopic nature of the material,[36] or to the differences in molecular weight.[37,38]

The addition of PVP to PVA evidenced a reduction of T_g, which implied that PVP plasticized PVA probably as a result of PVA/

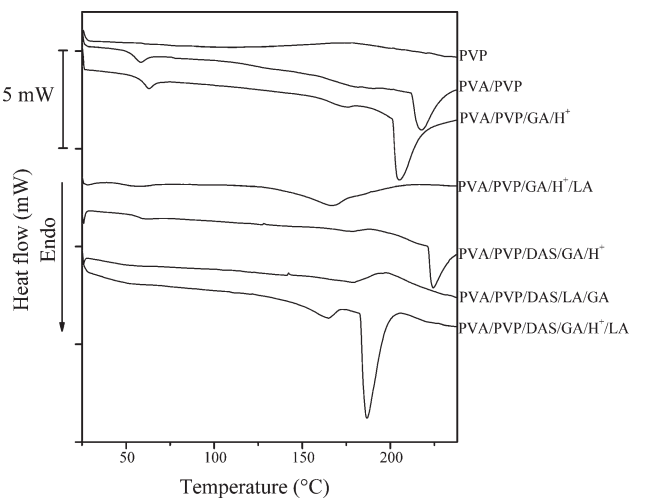

Figure 2. DSC thermograms for PVP and its blends.

PVP bonding, which disrupted the crystalline phase of PVA. The crystalline regions of PVA were more accessible to PVP and therefore, the PVA/PVP interactions were readily formed.[6] The film showed a small endothermic transition at about 51°C ascribed to T_g resulting from micro-Brownian motion of the main chain backbone. This decrease in comparison with PVA indicated that PVP was miscible with PVA in the amorphous phases.[39] The endothermic peak centered at 218°C corresponded to T_m.[40]

The PVA/PVP/GA/H^+ thermogram showed a small endothermic transition at 51°C assigned to T_g. This value was lower than the T_g exhibited by PVA/GA/H^+ and the explanation is founded in the plasticizing effect of PVP in the sample. The presence of two endothermic peaks at 174 and 205°C resembling the shape and proportion of the two peaks recorded for the melting of PVA/GA/H^+ testified for similar effect of GA. However, both T_m values were lower due to PVPs effect on semicrystalline PVA component.[41] By comparing PVA/PVP/GA/H^+ and PVA/PVP/GA/H^+/LA thermograms, significant differences appeared including that PVA/PVP/GA/H^+/LA presented only one T_m centered at 167°C. PVP reduced the endothermic curve of PVA, the peak become broader and it was shifted to lower temperatures by the combined action of PVP in the PVA crystallinity region[42,43] and LA as indicated above. The slight decrease in T_g was a consequence of the compensation of the plasticizing effect attributed to LA by the crosslinking action proportioned by GA/H^+. A broad exothermic region presented at 100°C can be ascribed to α-relaxations as evidence of a wide range of crystallite sizes and morphologies, which were affected by the additives in terms of intermolecular and intramolecular forces causing a "multi-phase" matrix.[23]

The thermograms for PVA/PVP/GA/H^+ and PVA/PVP/DAS/GA/H^+ presented minor differences, although an increase in T_m in the sample with DAS was the most significant. Even though DAS did not crosslink PVP, its presence reduced the mobility and fewer active points for interacting with the PVA chains were available. As a consequence, the crystallinity region of PVA was not affected at the same level and a higher T_m was manifested. Moreover, it has been established that the T_m for PVA depends on the PVP content which is obviously related to the decrease of the PVA crystallinity in the blend.[31,33,44] PVA/PVP/DAS/GA/H^+/LA exhibited a lower T_m because LA affected the crystalline region of PVA and plasticized the sample.

Finally, samples with DAS showed color changes before and after irradiation. If a bi-molecular reaction of DAS occurs, the efficiency of crosslinking decreases and a bronze color appears.[15] However, the thermal properties of photo-irradiated samples did not show relevant changes, which can be interpreted as DAS did not crosslink efficiently PVP or significantly affecting the crystallinity of PVA, and most importantly, DAS did not change the polymer compatibility.

Degree of Swelling

PVA Samples. As can be seen in Figure 3, during the first 10 min PVA/LA exhibited a higher degree of swelling than PVA. After that period, the swelling values for PVA/LA were slightly lower than for PVA but within the error bars. In both cases, the highest achieved degree of swelling was limited by the dissolution of the samples. A higher initial rate of swelling observed for PVA/LA can be interpreted as a consequence of the plasticizing effect of LA, which can be explained by the water molecules initially diffusing through the amorphous region of the polymer and attaching themselves to the hydroxyl side groups, disrupting inter- and intramolecular hydrogen bonding, and thereby swelling the polymer.[45,46] Hence, hydrophilic additives increase the swelling rate due to an increase of the free volume in polymer. For semicrystalline polymers such as PVA, a network of amorphous chains is formed with the crystallites acting as junction points and it may therefore be deduced that an increase in the initial rate of swelling is a consequence of the decrease of crystallinity,[24] as well as the rate of relaxation of the amorphous regions.[47,48]

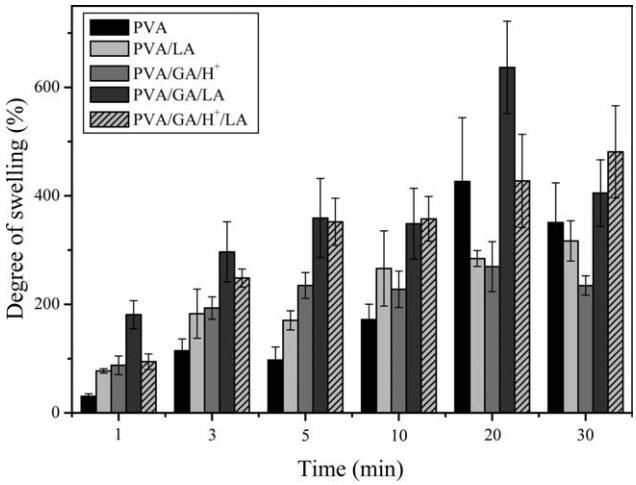

Figure 3. Degree of swelling for PVA and its blends

The combination of GA/H^+ and PVA crosslinked the polymer and thus, there were less free hydroxyl groups which reduce the hydrophilicity were expected. A decrease in the hydroxyl groups after the crosslinking reaction significantly reduced the affinity of the polymer for water leading to a reduction in the swelling ratio.[49] However, the concentration of GA/H^+ was relatively low in the prepared materials. Therefore, there was no decrease in the hydrophilicity, including PVA/GA/H^+ sample, which indeed showed a higher swelling degree than pure PVA in the first part of the experiment. For a low GA content sparse crosslinking was not able to promote a suitable dense network to totally prevent its solubility in water and the film had a high swelling value.[50] Another contribution to the initial swelling rate can be attributed to the increased disorder of the amorphous polymer matrix and the presence of hydrophilic components of the crosslinking system which could promote the diffusion of water, solvation, and unfolding of polymer chains. After that, the equilibrium swelling–deswelling was reached and the value of solubility was stabilized after 5 min of the process, when all soluble components were leached out from the specimen. In the case of pure PVA material, the swelling process passes continuously into dissolution of the polymer. On the other hand, crosslinking process causes a physical barrier limiting the disassociation of the macromolecules and the process ends in the stage of a swollen gel.

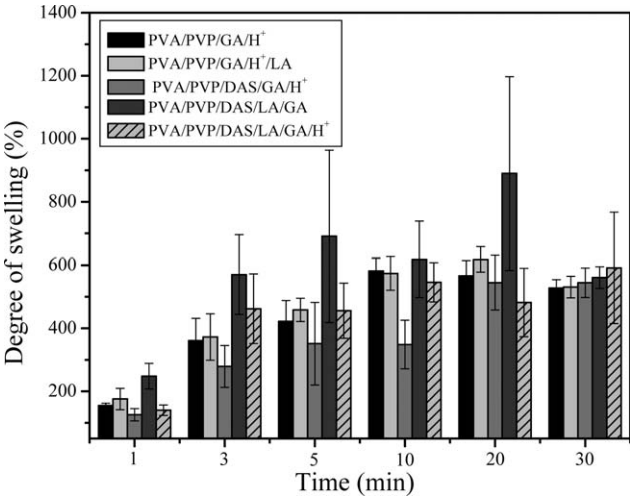

Figure 4. Degree of swelling for PVP/PVA and its blends

As it was observed in Figure 3, PVA/GA/LA material swelled to a greater extent than PVA/GA/H^+. This difference can be explained by the prevailing plasticizing effect of LA over its poor catalytic efficiency in the crosslinking of PVA by GA when compared with H^+. The comparison between PVA/GA/H^+ and PVA/GA/H^+LA showed that the former presented much lower values during the entire treatment which could corroborate that the plasticizing effect of LA was predominant in the system.

PVA/PVP Samples. The degree of swelling for PVA/PVP films in Figure 4 was higher than those of the analogous PVA films in Figure 3. This fact can be caused by the reduction of crystallinity in the blend due to the crystalline segments of the PVA chain having less chain solvation and greater stability than amorphous regions in a PVA network as a consequence of the interruption of PVA crystal formation by bulky pyrrolidone rings.[51] Furthermore, PVP as an amorphous polymer has a higher affinity for water than PVA, which makes it to swell to a greater extent.[10] The swelling of crosslinked PVP includes a very fast absorption as a consequence of hydrophilicity and capillarity, which are the basis for the notable higher values in comparison to PVA. The second step includes a typical diffusion mechanism and finally, in the third step, a minor increase in the water content occur based on very slow network relaxation.[52] Therefore, the addition of PVP promotes the swelling of PVA/PVP based blends significantly. In fact, PVA/PVP dissolved readily and it was not even possible to handle and take out as a single piece from water without dropping the slim. Indeed, the PVP/DAS specimens presented several inconveniences for determination of the swelling and solubility degree as a consequence of the quick dissolution process and the lack of strength to be manipulated in contact with water. These factors make the film unsuitable for medical applications. As a result, only crosslinked samples are discussed here. A fundamental relationship exists between the swelling of a crosslinked polymer in a solvent and the nature of the polymer and solvent. The additives can change and/or disturb the hydrogen-bonded structure of water and the molecular association of the water-soluble polymer in aqueous media, as well as the swelling behavior of the crosslinked PVP chains.[53] As an example, the values for PVA/PVP/GA/H^+ were around two times higher than PVA/GA/H^+ in all the tested times, which indicates that the swelling for PVA/PVP blends depend on the presence of PVP. On the contrary, a different phenomenon was detected for samples with DAS that were irradiated by ultraviolet light. Figure 4 depicts the degree of swelling for all PVA/PVP samples, although important attention is paid to PVA/PVP/GA/H^+ and PVA/PVP/DAS/GA/H^+. The photo-irradiated sample exhibited a lower degree of swelling in comparison to samples that did not undergo this process. The results could suggest that the DAS reaction with functional groups of PVP diminished the contribution of PVP to swelling in comparison to that in the GA crosslinked samples only. On the other hand, molecular chain length of PVP was relatively short, and a low degree or no crosslinked PVP structures of samples were obtained, therefore films were not compact enough to resist the dissolution of water, as discussed in the next section and supported by the literature as well.[54] Similar tendency was observed in PVA/PVP/GA/H^+/LA and PVA/PVP/DAS/GA/H^+/LA, which reinforces the idea that DAS did not effectively crosslink the samples.[15] As a significant result, PVA/PVP/DAS/LA/GA exhibited the highest degree of swelling for all studied samples, which is a signal of the predominant influence of LA in the blend, as well as the limited effectiveness of DAS for crosslinking PVP in the studied system. Nevertheless, PVA/PVP/DAS/LA/GA/H^+ revealed a combination of the efficiency of GA/H^+ as crosslinker of PVA and the plasticizing effect of LA, which is considered as an interesting behavior since this sample swelled to a relatively high level, but it properly resisted the dissolution during this time.

Solubility Degree

The initial statement which should be mentioned is that the solubility of PVA depends on the degree of hydrolysis, the molecular weight, and the tendency to form hydrogen bonding in aqueous solutions. In this matter, any alteration of those factors will have repercussions on the solubility of the film. Figure 5 shows the solubility degree for PVA samples and the first observed result was that LA increased the solubility of PVA film markedly during the tested period which can be attributed to the plasticizing effect caused by changes in the free volume of PVA.[55] Moreover, LA can contribute to the initial fast weight loss of the sample by its leaching. The addition of GA/H^+ to PVA presented a slight, but evident diminution on the solubility of the film in comparison to the neat polymer film during the first part of the experiment, followed by a marked decrease at the end of the tested time, which is a strong crosslinking signal. The explanation is related to the number of chains that were joined to the matrix because GA was able to promote a suitable network to prevent solubility in water, and the reaction on both edges of the GA molecule reduced the free volume of the material, which improved the water resistance of the films.[50] These kind of crosslinked polymers form gels which have the ability to absorb a solvent and swell, still keeping their three-dimensional structure which might help them become a possible candidate for long-term implantations.[56] As a noteworthy corresponding result, a difference between PVA/GA/H^+ and PVA/GA/LA was

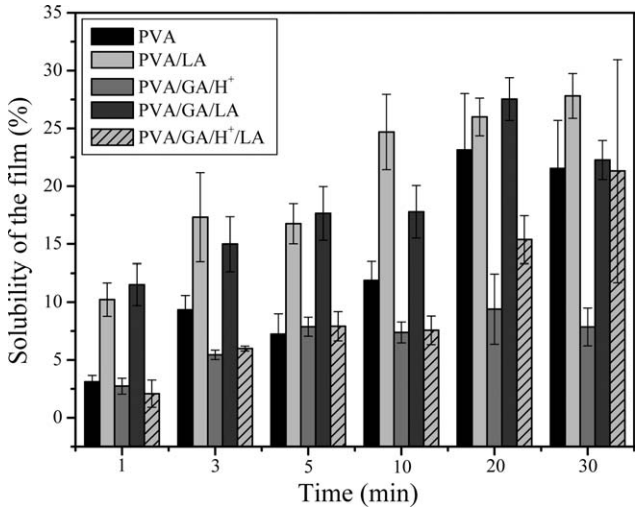

Figure 5. Solubility degree for PVA and its blends

observed and the films obtained by the combination of GA/LA exhibited a noticeably higher solubility than those with GA/H^+ which means that LA in contact with GA activated the crosslinking process to a much lower level than hydrochloric acid, and LA just plasticized the sample. Moreover, for PVA/GA/H^+/LA, every additive brought its own effects. GA/H^+ reduced the amount of hydroxyl side groups in PVA and is responsible for crosslinking, whereas LA increased the free volume of the matrix. As a consequence, the sample exhibited lower solubility than PVA/GA/LA and higher than PVA/GA/H^+.

The ease in which PVA and PVP is blended is attributed to hydrogen bonding which may take place between the proton-accepting carbonyl moiety in pyrrolidone rings and the hydroxyl side groups of PVA. Hydrogen bonding is also responsible for solubility of both PVA and PVP in water.[14,48] PVP is more hydrophilic than PVA, therefore its presence in the blends caused higher solubility values in comparison with the blends formed by PVA. The solubility degree for PVA/PVP samples is depicted in Figure 6 and it can deduced that in all the samples in which LA was present, the values were notably higher in comparison with samples where LA was absent. It was manifested once more, that the plasticizing effect of LA was preponderant in the system and dominated the dissolving mechanism. GA/H^+, on the other hand, was able to proportionate water resistance to the blend, and thus, the solubility showed lower values for PVA/PVP/GA/H^+ and PVA/PVP/DAS/GA/H^+.

By comparing the solubility of PVA/PVP/GA/H^+ and PVA/PVP/DAS/GA/H^+ there were not significant differences between them which lead to the conclusion that DAS did not crosslink efficiently to PVP. The same effect on solubility was observed for the couple formed by PVA/PVP/GA/H^+/LA and PVA/PVP/DAS/LA/GA/H^+. An explanation can be found in the low molecular weight of the PVP used in the studied materials, which caused the relative inefficiency of the DAS crosslinking process.[54] However, it cannot be excluded that the concentration of DAS was relatively high, and its decomposition rate was high as well. Furthermore, a higher probability of bimolecular coupling lead to a large dinitrilene concentration. Another adverse effect of the relatively high amount of DAS in the presence of inactive PVA virtually diluting PVP, could be intrachain crosslinking. In both ways, the solubility is not reduced, and even increased, because of a loss of interchain interactions.[15]

Lactic Acid leaching Analysis. The leaching of the samples with LA was analyzed and pH was obtained. For all the samples and intervals, the pH decreased slightly from 3.60 in the first minute to 3.10 after 30 min. This reduction in pH could indicate that the LA molecules, not strongly linked with the polymer, were delivered to the system within the first 2 min after the film was immersed in water. As a consequence of the changes in pH were not significantly exceeding physiologically values, the presence of LA will not negatively influence the tissues considering indeed, that it is well know that LA exhibits antibacterial properties. This characteristic also makes the films suitable for utilization in medical applications.[55]

Mechanical Properties

Young Modulus (E), stress at break (σ), and elongation at break (ε) were chosen for evaluation of the influence of LA, GA, and DAS on the mechanical properties of the obtained films. The results are reported in Table III, although it must to be mentioned that PVP and PVP/DAS were excluded here because the materials were too brittle and it was not possible to obtain suitable specimens for the test. It was found that LA in PVA and PVA/PVP blends considerably reduced the Young's Modulus and at the same time, the tensile strength and the elongation at break was noticeably increased. The reason can be founded in the plasticizer effect of LA.[55] On the contrary, PVA/GA/H^+ exhibited reduced mechanical properties as a result of crosslinking and because the concentration of GA was too low in comparison to LA and it did not cause softening of the material. However, if LA is accompanied by GA or GA/H^+, the elongation was higher as a consequence of the plasticizing effect. The expectable effect of an increase due to chain bonding by

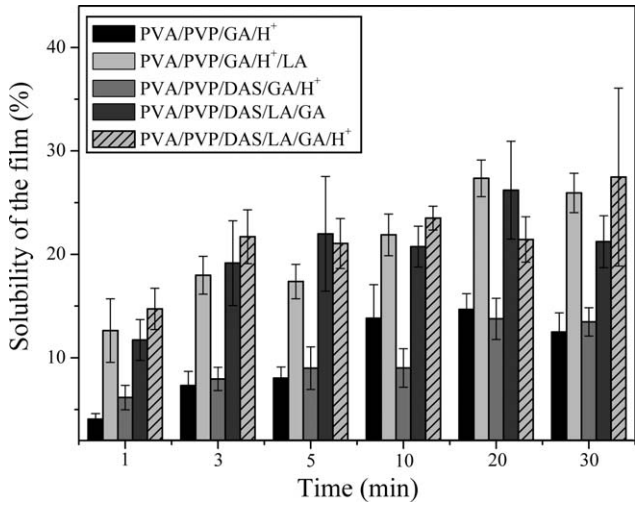

Figure 6. Solubility degree for PVA/PVP and its blends.

Table III. Mechanical Properties for PVP and PVA Blends

Sample	Thickness (mm)	Young's modulus (MPa)	Tensile strength (MPa)	Elongation at break (%)
PVA	0.236 ± 0.017	1100 ± 170	14 ± 3	38 ± 7
PVA/LA	0.274 ± 0.018	229 ± 18	21 ± 2	205 ± 11
PVA/GA/H^+	0.120	360 ± 60	8.5 ± 1.1	32 ± 5
PVA/GA/LA	0.274 ± 0.057	240 ± 20	22 ± 3	195 ± 18
PVA/GA/H^+/LA	0.286 ± 0.064	140 ± 15	26 ± 5	224 ± 8
PVA/PVP	0.270 ± 0.028	2460 ± 140	21 ± 4	5 ± 1
PVA/PVP/GA/H^+	0.226 ± 0.006	2420 ± 100	16 ± 3	4.6 ± 0.2
PVA/PVP/GA/H^+/LA	0.244 ± 0.013	460 ± 70	12.9 ± 1.8	99 ± 8
PVA/PVP/DAS/GA/H^+	0.276 ± 0.011	1580 ± 80	14 ± 2	32 ± 14
PVA/PVP/DAS/LA/GA	0.300 ± 0.025	770 ± 70	11 ± 4	79 ± 19
PVA/PVP/DAS/GA/H^+/LA	0.286 ± 0.008	745± 158	18 ± 2	58 ± 27

crosslinking is hidden within the overlap of error intervals for both materials, PVA/LA and PVA/GA/H^+/LA. It is important to point out that PVP dramatically increased the Young's modulus of PVA which could reinforce the idea that interactions between carbonyl and hydroxyl groups were present and caused brittleness of the prepared films. Furthermore, the low elongation at break is a result of the poor mechanical features of PVP, even if it is blended with PVA. Besides, LA does not influence PVP by chain grafting; its presence in the blend with PVA improves the film's elongation, which could confirm that LA contribution is due to the creation of hydrogen bonds.

It has been shown crosslinking PVA with DAS was not effective.[15] For that reason, the influence of DAS is focused on PVP. Mechanical properties of the PVA/PVP blends are governed by PVP, therefore it can be expected that DAS reduces the Young's Modulus and the tensile strength but increases the elongation. The DAS/GA mixture must specifically crosslink the two polymer components into intermingled PVA and PVP networks.[15] However, due to the low molecular weight of PVP, DAS did not crosslink the polymer, although it affected the mechanical properties. As a result, PVP/PVA/DAS/GA/H^+ had a higher Young's Modulus, lower tensile strength, and less elongation than PVP/PVA/DAS/GA/H^+/LA, because in this case, the concentration of LA was high enough for plasticizing the blend.

CONCLUSIONS

The casting method, as a simple polymer production technique was chosen for obtaining PVP/PVA films as versatile candidates for medical applications. GA/H^+ crosslinked effectively PVA whereas LA plasticized this polymer as well as the blend formed by PVA/PVP. Although DAS did not crosslink PVP due to the low molecular weight of the polymer, its presence did not negatively affect the blend regarding to the examined characteristics. Compared with raw materials, the crosslinked PVA/PVP films exhibited superior performance in terms of the properties which were analyzed by DSC, degree of swelling, solubility degree, and mechanical properties, as is explained as followed. DSC thermograms showed just one T_g for PVA/PVP samples which means that the films were miscible even with the use of LA, GA and DAS. The reported modifications of T_g and T_m suggested that the additives used did not negatively affect the thermal behavior within the studied temperature range. The crosslinked PVA/PVP films swelled to a greater extent than PVA, showing significantly higher values for water resistance. These characteristics provide the material with the ability to properly resist to biological systems and it could be considered as an interesting approach for a prospective material used in medicine. In addition, the chosen combination of the additives GA/H^+/LA/DAS seemed to fulfill the crosslinking and plasticizing needs for the PVA/PVP blends, representing an additional advantage. Furthermore, the additives used are commonly blended in polymers for medical applications and it is expected that LA would provide some supplementary benefits to the blend, due to its antibacterial properties. For all of the given reasons, the crosslinked PVA/PVP films should undergo further analysis in order to determine its applicability in medicine as a prospective material for medium or long-term implants.

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