# Characterization of Degraded Hydrogels Based on Poly(vinyl alcohol) Grafted with Poly(lactide-*co*-glycolide)

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**ABSTRACT:** Poly(vinyl alcohol) (PVA) grafted with poly(lactide-*co*-glycolide) and cross-linked as a material of increased hydrophobicity relative to PVA was produced. The properties were examined with respect to the mass loss, water uptake, hydrophilicity, and mechanical characteristics upon hydrolytical degradation. The hydrogels investigated display water uptake increasing with degradation time because of increasing hydrophilicity. The mass loss amounts up to 15% after eight weeks of degradation. The mechanical properties of the hydrogels are within the range of those of natural tissue, the *E* modulus is 18 MPa, or even 100–200 MPa, depending on the structure of material. The mechanical characteristic and their dependence degradation show the most recognizable correlation with the chemical structure. Studies of the topography of degraded samples (scanning electron microscopy) and IR measurements demonstrate the degradation to occur at slow rate due to the high degree of grafting. The mass loss is rather low and a bulk degradation mechanism takes place. © 2010 Wiley Periodicals, Inc. J Appl Polym Sci 119: 1322–1329, 2011

**Key words:** hydrogels; poly(vinyl alcohol); poly(lactide-*co*-glycolide); mechanical properties; degradation

## INTRODUCTION

Poly(vinyl alcohol) (PVA) for quite some time has been recognized as a material for wide pharmaceutical applications as drug-delivery matrices[1,2] as well as in a number of biomedical applications including soft contact lenses,[3,4] implants,[5–7] and artificial organs[8] because of its inherent nontoxicity, noncarcinogenicity, good biocompatibility, and desirable physical properties, such as soft nature and high degree of swelling in aqueous solutions. This broadens its anyway wide application to its use in emulsions and suspension polymerizations and in processes for the binding of pigments and fibers, protective coatings and the production of solution cast films, beside of its original use in the textile industry.

If PVA is used as a biomaterial, most commonly, it comes in the form of a hydrogel which means that the linear structure has been transferred into a three-dimensional crosslinked one. Physical crosslinking is achieved by performing freeze-thaw cycles or similar methods[9–11] that allow for introduction of partial crystallinity.[12,13] This presents an additional possibility to the traditional methods for chemical crosslinking by irradiation or reaction with bifunctional crosslinking agents. Common crosslinking agents include glutaraldehyde, acetaldehyde, formaldehyde, and other monoaldehydes or sodium borate and boric acid.[5,12,14] A huge advantage of PVA when considered as a biomaterial and compared to other materials, apart from the readiness of the body to accept it, presents its ability of simulating native tissue. Therefore, a great deal of work has been devoted to the examination of PVA hydrogels as a material for the potential replacement for soft tissue. Thus, Oka et al.[15] reported on the biocompatibility as well as the mechanical properties of PVA gels in relation to their usefulness as artificial articular cartilage. They examined such aspects as lubrication, load bearing, and attachment of the material to the bone to look at the overall biomechanics of the material. PVA hydrogel formulations with different water content were tested and displayed values of compressive and shear moduli similar to those of human articular cartilage.[6] Artificial meniscus based on PVA hydrogel was manufactured and has shown viscoelastic behavior similar to that of human meniscus in mechanical tests. The shape of the stress-strain curve displayed a strong dependence on the water content of the PVA hydrogel.[7] Moreover, after a first study considering the state of implanted articular cartilage

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**TABLE I**
**Theoretical and Experimental Composition and Degree of Grafting (DG) of Poly(vinyl alcohol)-*graft*-[poly(D,L-lactide-*co*-glycolide)] Hydrogels**

| | | *N* | | LA : GA | | DG, % | |
|---|---|---|---|---|---|---|---|
| Network | Polymer | Theor[a] | Exp[b] | Theor[a] | Exp[b] | Theor[a] | Exp[b] |
| A | PVA-PLGA16$_{25}$ | 16 | 16 | 75 : 25 | 75 : 25 | 15 | 15 |
| B | PVA-PLGA8$_{25}$ | 8 | 8 | 75 : 25 | 75 : 25 | 15 | 14 |
| R[24] | PVA-PLA9$_{50}$ | 8 | 9 | 50 : 50 | 50 : 50 | 15 | 13 |

[a] Theoretical number of repeating ester units.
[b] Number of repeating ester units as determined by NMR.

covering 8–52 weeks,[16] an extended study was performed after two years whereas it was established that the state of the implanted PVA hydrogel as knee joint meniscus was good.[11]

Since the properties of PVA hydrogels depend on the water content of the three-dimensional crosslinked structure, and having in mind that the hydrogel structure is determined by the cross-linking density it is challenging to perform crosslinking of PVA by using α-hydroxy acids. It enables multiple impacts onto the system. Accordingly, chemical crosslinking occurs that assures stability of the three-dimensional structure and the ester groups formed upon crosslinking allow for biodegradability as a consequence of hydrolysis. Also, due to the higher hydrophobicity of aliphatic polyesters as compared to PVA the hydrophobicity/hydrophilicity characteristics of material are influenced by the crosslinking moiety.[17] Furthermore, aliphatic polyesters such as polylactide (PLA), polyglycolide (PGA) and their copolymers (PLGA) or blends,[18–21] among other advantages that contribute to their use as biodegradable materials, are characterized by high mechanical strength. Thus, thermoplastic high molecular mass PLA shows a mechanical behavior comparable to that of synthetic polymers like polystyrene and polyethylene terephthalate. However, studies have shown that mechanical properties of these polymers depend strongly on molecular weight, degree of crystallinity and chain architecture.[18–21] A similar influence of the length of aliphatic esters blocks was observed in the case of copolymers of LA/GA with various hydroxy acids as comonomers.[22,23]

In this report two hydrogels prepared from PVA grafted with poly(lactic-*co*-glycolic) esters were evaluated regarding their structure, composition, surface and mechanical properties, mass loss, water uptake and related material's topography upon the degradation process. The knowledge of the degradation behavior of a material is crucial for its medical application as a biomaterial.

## EXPERIMENTAL

### Polymers

Films based on PVA grafted with poly(D,L-lactide-*co*-glycolide) oligomers of different length were synthesized as previously described.[17] Briefly, poly(D,L-lactide-*co*-glycolide) with a molar lactide to glycolide ratio of 3 : 1 and with a methacrylate at one end and a carboxylate end group at the other end were grafted onto PVA via the carboxylate group. The graft copolymers were crosslinked via the methacrylate groups using a free radical initiator. The materials investigated here are listed in Table I, named by the acronym PVA-PLGAx$_y$, where x is the total number of ester units in grafts and y is the molar percentage of the glycolide content.

### Analytical methods

IR spectra were recorded with a NEXUS FTIR spectrometer using the photoacustic method (FTIR-PAS). For each sample, scans were recorded between 4000 $cm^{-1}$ and 400 $cm^{-1}$, with a resolution of 8 $cm^{-1}$.

**TABLE II**
**Characteristic IR Absorption Bands, the Band Areas and their Ratios of Poly(vinyl alcohol)-*graft*-poly(D,L-lactide-*co*-glycolide) Networks A and B**

| | | Characteristic signals | | | | | | Area ratio | |
|---|---|---|---|---|---|---|---|---|---|
| Sample | Week | O—H$_{str}$ ($cm^{-1}$) | $A_{O-H}$[a] | C—H$_{str}$ ($cm^{-1}$) | $A_{C-H}$[a] | C=O$_{str}$ ($cm^{-1}$) | $A_{C=O}$[a] | $A_{O-H}$[a]/$A_{C-H}$[a] | $A_{O-H}$[a]/$A_{C=O}$[a] |
| A | 0 | 3380 | 1910 | 2940 | 932 | 1760 | 2580 | 2.049 | 0.741 |
| | 4 | 3390 | 1462 | 2943 | 667 | 1759 | 2100 | 2.192 | 0.696 |
| | 8 | 3383 | 1441 | 2943 | 711 | 1759 | 2253 | 2.027 | 0.640 |
| B | 1 | 3383 | 3350 | 2939 | 1079 | 1775 | 2412 | 3.105 | 1.389 |
| | 4 | 3375 | 3528 | 2939 | 1085 | 1755 | 2486 | 3.252 | 1.419 |

[a] Area in relative units of the particular stretching band.

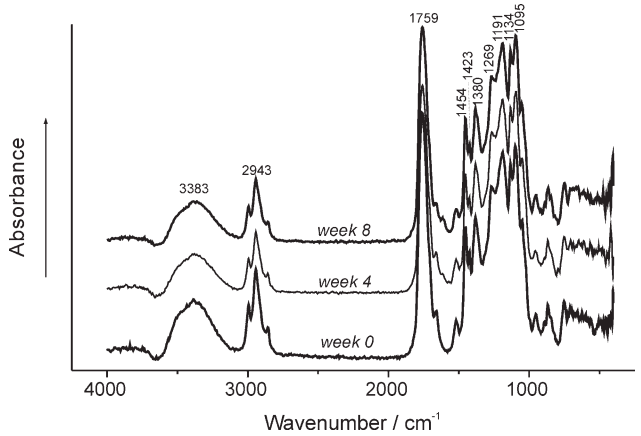


**Figure 1** IR spectra of network A before and after 4 and 8 weeks of hydrolytical degradation in PBS (pH 7.4) at RT.

The tensile tests were performed with the low-load horizontal tensile test machine Minimat 2000 (Rheometric Scientific). The strain rate was 10 mm/min. The tests for each measuring point are performed on five samples.

The captive bubble contact angle technique was used to study the hydrophilicity of the surface of the highly hydrated polymers. The smaller the contact angle is, the greater is the hydrophilicity of the polymer surface. For measuring purpose the swollen hydrogels were cut into pieces of ca. 2–3 $cm^2$ and fixed on microscope slides.

The surface and cross section morphologies of networks before and during hydrolytical degradation were depicted using a scanning electron microscope (Cambridge S360, Leica), operated at an accelerating voltage of 15 kV and different magnification (×300, ×5000). The cross-sectional samples were prepared by fracturing the samples after being frozen in liquid nitrogen. Before morphology observations, the samples were coated in argon atmosphere with gold using a sputter coater (S 150B Sputter Coater, Edwards).

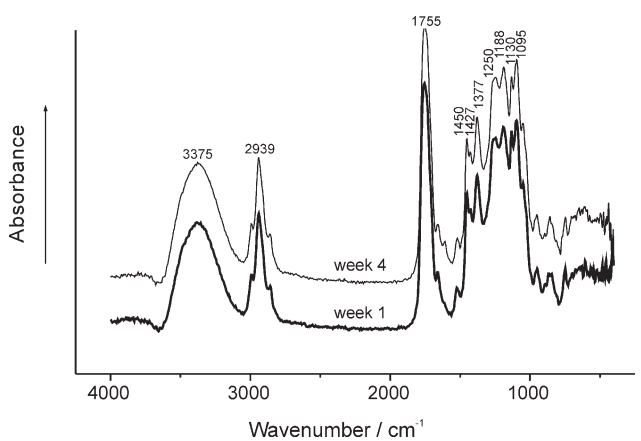


**Figure 2** IR spectra of network B after 1 and 4 weeks of hydrolytical degradation in PBS (pH 7.4) at RT.

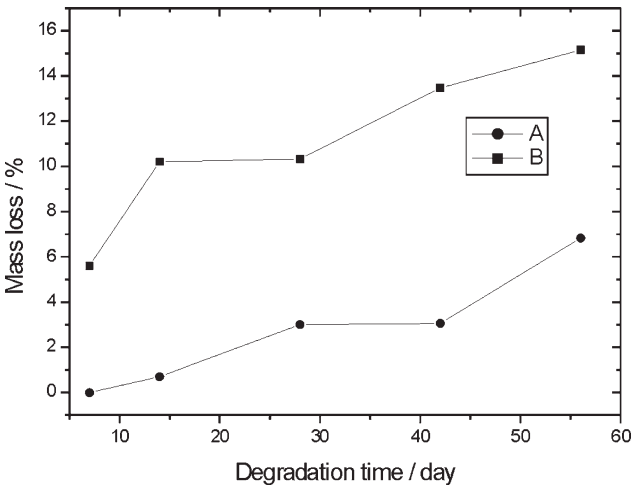


**Figure 3** Mass loss of networks A and B in hydrolytical degradation experiments at pH 7.4, room temperature.

### Degradation studies

Film specimens shaped depending on the foreseen testing method were placed in vials and immersed in phosphate buffer solution (PBS) (0.05 *M*, pH 7.4 containing 0.004% sodium azide, to prevent the growth of microorganism). The pH value was measured after 4–7 days and as the value sank below 7.2, the buffer solution was exchanged. The degradation was followed at room temperature for various periods of time.

Circular disks of 15 mm diameter and a thickness of around 0.3 mm prepared by punch cutting were provided for water uptake and mass loss measurements. At a given point of time, the discs were removed, three at each point, and weighed after the removal of surface water. The samples were then dried for at least 48 h in a lyophilizer.

The water uptake and mass loss were calculated using the following equations:

$$\text{Water uptake } (\%) = 100\,(W_w - W_d)/W_d$$

$$\text{Mass loss } (\%) = 100\,(W_o - W_d)/W_o$$

where $W_w$ and $W_d$ represent the mass of film in wet and dry state, respectively. $W_o$ is the film weight determined initially.

The hydrogel films were cut into stripes of a width of 8 mm and a length of 50 mm for tensile strength measurements. The dimensions were measured in the swollen state. Five parallel samples were tested for each type of film.

## RESULTS AND DISCUSSION

The objective of this study was to compare two different materials from our laboratory to size their

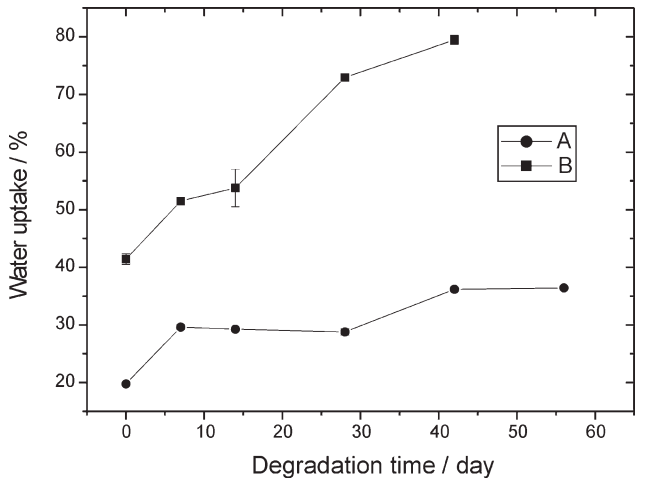


**Figure 4** Water uptake of networks A and B in hydrolytical degradation experiments at pH 7.4, room temperature.

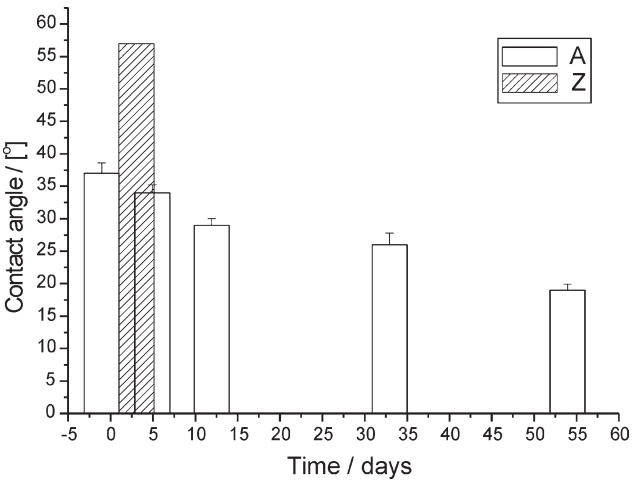


**Figure 6** Contact angle of hydrogel A hydrolytically degraded in water at room temperature and sample Z, measured in water using the captive-bubble method.

potentials regarding mechanical and other properties as tissue replacement. Since the performance of these materials is based on their mechanical properties, special attention was given to its change with the advancement of degradation. The composition of the copolymers was determined using $^1$H-NMR spectroscopy, comparing peaks representative of each of the constituents of the copolymer. Therefore, in case of hydroxyethyl methacrylate (HEMA)-poly(lactide-*co*-glycolide) oligomers, the peaks compared were the following: (a) the vinyl protons of the methacrylate end group, at 5.6 or at 6.1 ppm and (b) the methyl protons of the lactide units (six protons) at 1.4–1.6 ppm and (c) the glycolide methylene protons (four protons) at 4.5–5.0 ppm. Besides, the experimental degree of grafting ($DG_{exp}$) was calculated from the ratio (d) of the integrals of the resonance lines of the methacrylate methyl protons at 2.05–1.95 ppm, and (e) the acetate methyl protons at 1.85 ppm.[17] To clarify the influence of the length of the polyester grafts the films were analyzed by means of IR spectroscopy and, moreover, contact angle measurements and scanning electron microscopy. In Table II values of a few characteristic bands in the IR spectra of films are given that were observed before erosion, as well as subsequently.

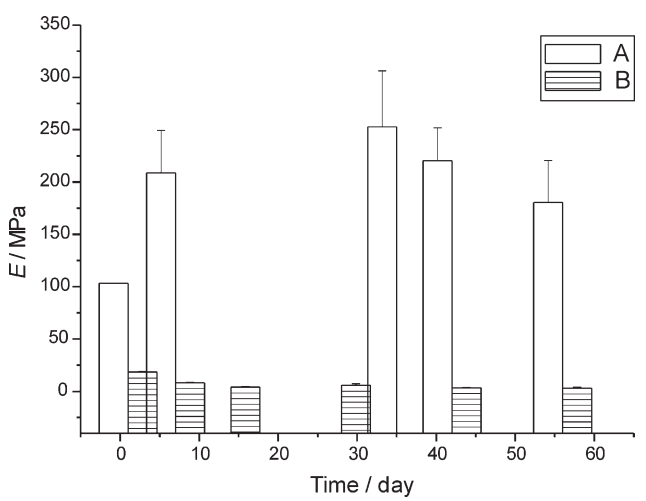


**Figure 5** *E* modulus of networks A and B during hydrolytical degradation at pH 7.4, room temperature.

The IR spectrum of network A, before and after hydrolytical degradation for 4 and 8 weeks in phosphate buffer solution at room temperature, is presented in Figure 1. The high content of polyesters in network A shifts the C=O band toward higher wave numbers relative to its value in the pure PVA sample (1740 $cm^{-1}$). During degradation, this band shifts only slightly downward indicating the high stability of this sample, while samples of lower stability displayed a much stronger shift.[24] Furthermore, network A, after four weeks of degradation, in the fingerprint region shows a split band at 1452/1424 $cm^{-1}$ as a consequence of the glycolide content in the grafts. The strongest band is at 1093 $cm^{-1}$, followed by a slightly weaker band at 1190 $cm^{-1}$ while the band at 1245 $cm^{-1}$ is much weaker and is not so well separated. After another four weeks of degradation (Week 8) there is no significant change of the spectrum: the band at 1452/1424 $cm^{-1}$ is still split, the differences between the bands at 1240 $cm^{-1}$, 1190 $cm^{-1}$ and 1090 $cm^{-1}$ are similar to the differences obtained for the former sample, which demonstrates its slow degradation as a consequence of its long polyester grafts and high degree of grafting. The IR spectrum of network B after hydrolytical degradation for 1 and 4 weeks is shown in Figure 2. After 1 week of degradation, this network shows a slightly split band at 1452 $cm^{-1}$ due to the glycolide content. The strongest band, in the fingerprint region, is at 1097 $cm^{-1}$ and two smaller bands are at

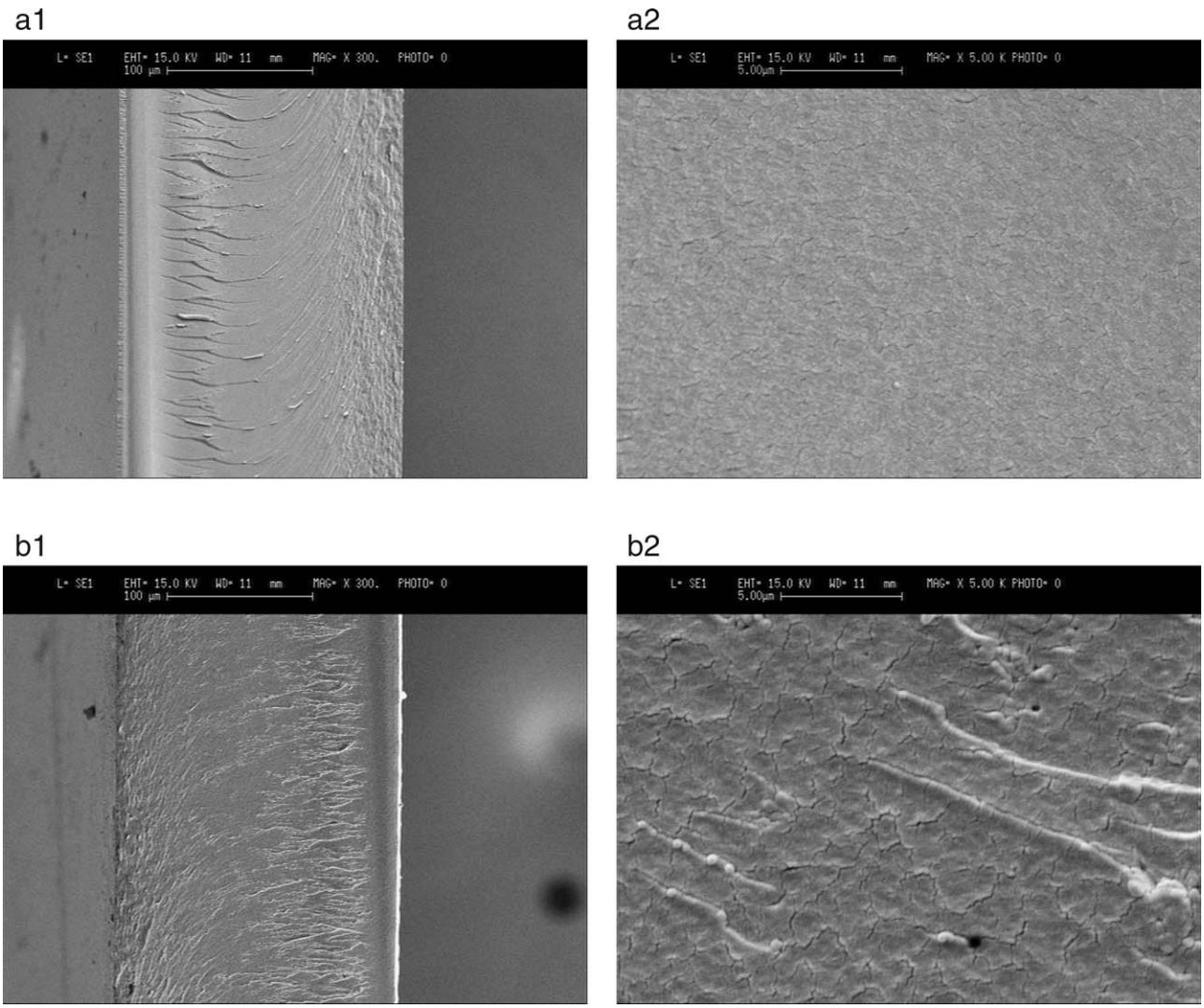


**Figure 7** SEM micrographs of network A, (a) before hydrolytical degradation: cross section at MAG ×300 (1) and ×5000 (2), (b) after eight weeks of hydrolytical degradation: cross section at MAG ×300 (1) and ×5000 (2).

1190 $cm^{-1}$ and at 1245 $cm^{-1}$. After 4 weeks of degradation the band at 1190 $cm^{-1}$, characteristic of the polyester, gradually diminishes relative to the other two bands. This is a confirmation of slow degradation which is still faster than that of sample A.

The mass loss is an indicator of the degradation process.[19] As Figure 3 shows, the mass loss with degradation of samples A and B begins simultaneously, indicating good water diffusion into the polymer networks. The mass loss rate depends on the length of polyester side chains in the network. Hence, sample B with shorter polyester grafts, combined with a slightly smaller degree of grafting, shows faster mass loss due to its higher hydrophilicity than hydrogel A. Thus, hydrogel B displays 10% mass loss within less than one week, while for hydrogel A the same mass loss is reached after seven weeks. Experiments were conducted to determine the water uptake in buffer (Fig. 4). The water absorption of the hydrogels increases steadily with time because the degradation causes an increase in polymer hydrophilicity. Moreover, the removal of ester units increases the hydrophilicity of the hydrogel due to a relative increase of hydroxylic groups on the PVA backbone. The longer polyester grafts of hydrogel A make it more hydrophobic and less prone to water absorption. Therefore, hydrogel B swells more than hydrogel A despite the higher content of polyester grafts that can undergo hydrolysis. Thus, after 8 weeks the water uptake in hydrogel A is less than 40% while in hydrogel B it is around 80%.

The mechanical properties of the hydrogels vary with the polyester content of the copolymer. Overall, relative high values of the $E$ modulus are observed for the hydrogels A and B, Figure 5 (initial $E$ value 103 and 18 MPa, respectively), due to the influence of the polyester grafts with 16 and 8 repeating units, respectively, combined with the high degree of grafting that results in a high crosslinking density. When

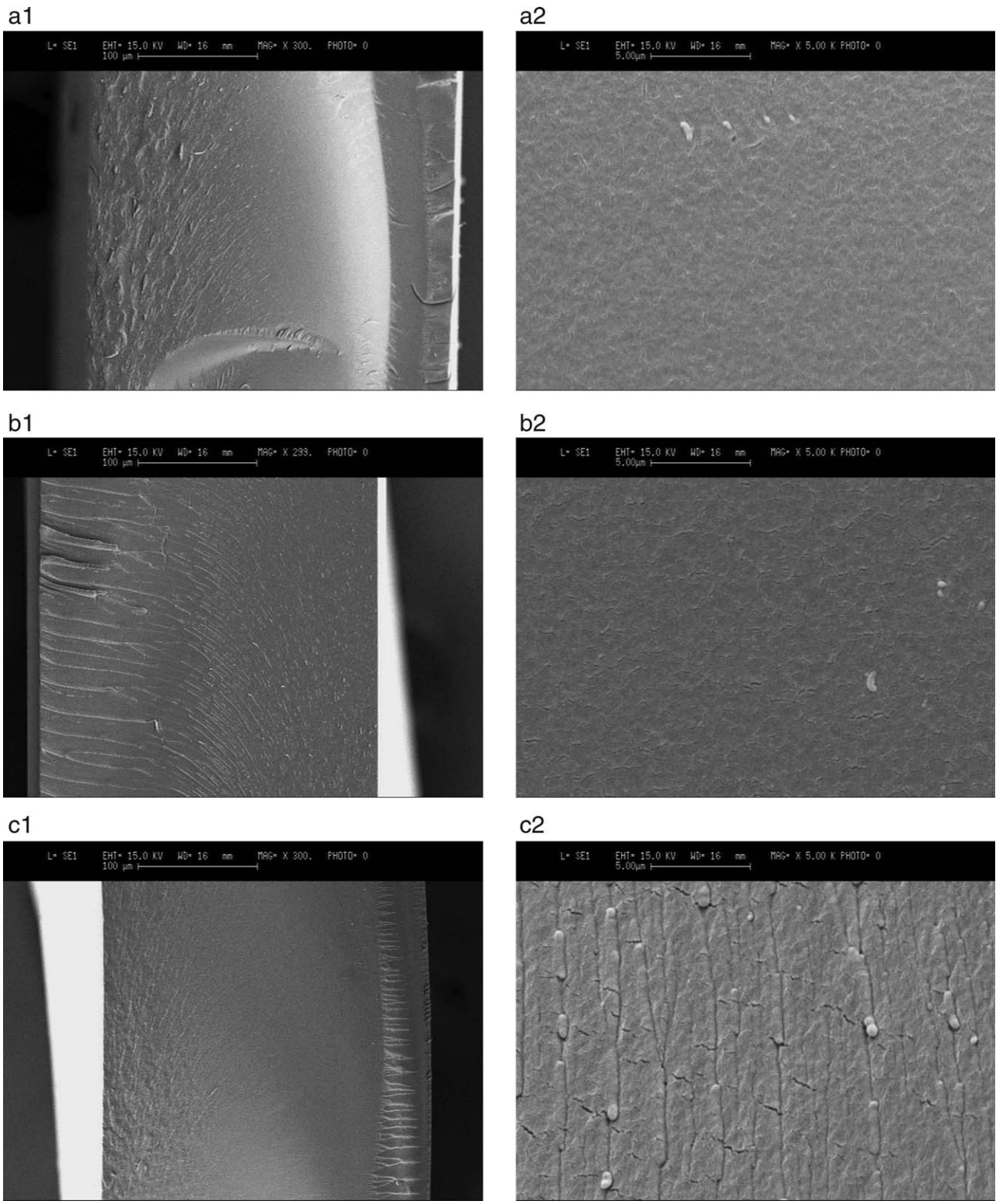


**Figure 8** SEM micrographs of network B, (a) before hydrolytical degradation: cross section at MAG × 300 (1) and × 5000 (2), (b) after 4 weeks of hydrolytical degradation: cross section at MAG × 300 (1) and × 5000 (2), (c) after 8 weeks of hydrolytical degradation: cross section at MAG ×300 (1) and ×5000 (2).

hydrogel B is compared with hydrogel R (Table I), $E \approx 2$ MPa[25]) a significantly lower modulus can be assigned to the smallest difference in degree of grafting since the influence of the glycolide portion in the polymer on mechanical properties was shown to be small in literature.[26] One can conclude that the small

difference in glycolide content between hydrogel B and hydrogel R can be considered to have a negligible influence on the mechanical properties although accompanied with small differences in grafts length. It is necessary to emphasize that the *E* modulus of hydrogel A approaches the value of a thermoplastic polymer (>100 MPa).[27] As aliphatic polyesters such as PLA, polyglycolide (PGA) and their copolymers (PLGA) or blends[18–21] are widely studied, examination of their mechanical characteristics shows their high mechanical strength. It is necessary to emphasize its dependence on the molecular weight, however. Thus, poly(L-lactide) ($M_w$ = 137,000) displays an elastic modulus of ca. 20 MPa ± 3 MPa, while its 40/60 w/w blend with poly(D-lactide) displays an *E* modulus of 22 ± 3.4 MPa and poly(D,L-lactide) displays an *E* modulus of 2.8 ± 0.4 MPa.[20] On the other hand, PVA hydrogels were proposed as promising biomaterials to replace diseased or damaged articular cartilage since the compressive modulus of PVA hydrogels increases from ~ 1 to 18 MPa, when measured over a strain range of 10–60%, which is within the range of the modulus of articular cartilage.[6] In case of hydrogel A, an interesting phenomenon takes places, which is surprising at first sight: the *E* modulus increases to a certain extent during degradation but decreases afterwards. A possible explanation might be that some kind of rearrangement occurs within the polyester domains which strengthen the material and lead to the increased modulus, because it was shown that crystallinity that appears in α-hydroxy acid oligomers depends on their nature and degree of polydispersity.[22] That phenomenon has to be more closely examined and explained with the assistance of alternative methods within a framework of the following work. Hydrogel B, on the other hand, displays a continuous reduction of the modulus during hydrolytical degradation from 18 MPa to 3 MPa.

In Figure 6 values of the contact angle of the swollen hydrogel A, initially and during hydrolytical degradation, using the captive-bubble method, are given. When applying this technique, using water as the measuring medium, a smaller contact angle value corresponds to higher hydrophilicity. Poly(rac-lactide) (Z), used here as a standard, displays a significantly higher value of the contact angle than hydrogel A, i.e. 57° which indicates lower hydrophilicity. The general tendency of the contact angle of hydrogel A to decrease as the degradation process proceeds (from 35° to 20°) demonstrates the increase of hydrophilicity with degradation time.

The topography of cross sections of films of the networks was examined by means of SEM to monitor the degradation. The SEM images of the cross section of hydrogels A and B, before and during the hydrolytical degradation, are shown in Figures 7 and 8. Samples before degradation, at low magnification (×300) show a smooth surface. At higher magnification (×5000) the cross section is smooth as well. During hydrolytical degradation there is no change in the thickness of sample A [comparing Fig. 7(a-1) and (b-1)]. After eight weeks of hydrolytical degradation network A shows still smooth surfaces. The roughness of the cross section increases just slightly after degradation as it is revealed by images at high magnification [Fig. 7(a-2) and (b-2)]. Network B shows, after four weeks of hydrolytical degradation, stable shape of the sample and smooth surfaces [Fig. 8(a-1) and (b-1)]. The thickness of the sample changes just slightly, even after eight weeks [Fig. 8(a-1) and (c-1)]. Only images at high magnification show a rougher surface of the cross section [Fig. 8(c-2) relative to (a-2) and (b-2)]. This indicates a bulk degradation mechanism which takes place at slow rate due to the high degree of grafting and resulting in a high cross-linking density.

## CONCLUSIONS

Copolymers based on the PVA and poly(lactide-*co*-glycolide) of different structure were synthesized. Due to their hydrophilicity hydrogels display good water uptake from the onset. These materials are prone to hydrolytical degradation. During degradation, the hydrophilicity increases accompanied by increasing water uptake. Furthermore, as the degradation proceeds mass loss of material occurs. The degradation process as evidenced by the slight changes of characteristic bands of the IR spectra. Additionally, SEM images are in line with it and support a steady degradation process. Hydrogel samples with low mass loss display no deterioration of the material, while hydrogels displaying a significant mass loss reveal negligible thinning of the samples due to the bulk degradation. Moreover, the large difference of the *E* modulus of these materials as a consequence of their different structure indicates their potentials for various applications especially concerning the relatively constant values in the course of several weeks of degradation.

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