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# Degradation Behavior of the Hydrogel Poly(vinyl alcohol)-*graft*-Poly[(*rac*-lactide)-*co*-Glycolide)] under Different Conditions

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**Summary:** The hydrogel poly(vinyl alcohol)-*graft*-poly[(*rac*-lactide)-*co*-glycolide)] [PVA-*g*-P(LGA)], containing nine ester groups in the polyester grafts (lactide:glycolide ratio 50:50) grafted onto PVA to an extent of 13%, and crosslinked via terminal acrylate groups was subjected to degradation experiments in phosphate buffer solution (pH 7.4) at room temperature and at 37 °C during 8 weeks. In the course of degradation, the properties of the hydrogel change as a result of the decrease of the polyester content. The increased temperature has a significant influence on the degradation rate but its amount varies with the methods applied. Thus, a large drop of the elastic modulus takes place in samples degraded at 37 °C with time and relative to RT. Thermal and IR analysis show changes while the initial difference between two sets of samples in contact angle is reduced with time.

**Keywords:** aliphatic polyesters; biomaterials; degradation; hydrogels; hydrophilic polymers

## Introduction

Biocompatibility is the main criterion for selecting a polymer for the use as a biomaterial. Furthermore, biodegradability is another characteristic of materials for certain applications which has caused their intensive investigation. In the 1960s, a huge potential of these materials was realized for application in medicine, pharmacy, agriculture etc.[1–3] Since then, polymers prepared from glycolic acid, lactic acid and their copolymers have undergone a revival. Diverse polymers based on lactic and glycolic acid - and on other polymers, e.g. poly (ε-caprolactone)[4–7] have been accepted for use as medical devices. The resulting materials display excellent properties with regard to the requirements of a diversity of applications such as in the medical industry, beginning with the biodegradable sutures. However, though this materials demonstrate a number of excellent properties after their extensive study deficiencies emerged as well. Thus, for some cases, e.g. absorbable sutures or orthopedic fixation, the degradation pathway and control of degradation time is necessary to be defined.[1,8–11] Mechanical properties as a function of degradation time are most important criteria for selecting a polymer to be used as a biomaterial for a special application. There are numerous factors affecting the mechanical performance of biodegradable polymers, such as monomer composition, initiator, process conditions, and the presence of additives. These factors in turn influence the polymer's hydrophilicity, crystallinity, melting temperature and glass transition temperature, molecular weight, molecular weight distribution, sequence distribution. This indicates the importance of the understanding of the materials' degradation behavior.[12–14]

In this paper we report on the influence of degradation temperature for a copoly-

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mer consisting of hydrolysable hydrophobic lactide and glycolide units in the side chains and a hydrophilic poly(vinyl alcohol) backbone. This hydrogel has a potential to be used in wound closure and cardiovascular applications.

## Characterization

### Hydrolytical Degradation Experiment

For degradation experiments samples of ca. 1.5 cm$^2$ or ribbons of ca. 0.8 cm width and 3–5 cm length were prepared. The thickness of the samples was of ca 0.03 cm. All dimensions were measured in the swollen state. The samples were placed in plastic vials of 10 ml and in Eppendorf's tubes of 50 ml which were filled with phosphate buffer solution (PBS) pH 7.4. In order to prevent the growth of microorganisms, sodium azide was added (40 mg kg$^{-1}$). The degradation was followed at room temperature and in a mechanical stirring incubator with 40 turns per min at $37 \pm 0.1\,^\circ$C, for comparison reason, during a period of eight weeks. The pH value was measured after four to seven days and if the value was below 7.2, the buffer solution was exchanged. During the degradation, at a given point of time, samples were taken and analyzed.

IR spectra were recorded with a NEXUS FT-IR spectrometer using the photoacustic method (FTIR-PAS). For each sample, scans were recorded between 4000 and 400 cm$^{-1}$, with a resolution of 8 cm$^{-1}$. TGA measurements were performed with a Netzsch TG 209 instrument in nitrogen atmosphere. Thermograms were taken in the range between 30 °C and 600 °C. The mass loss of the samples as a function of temperature was followed at a heating rate of 10 °C min$^{-1}$. The mechanical properties of degraded hydrogels were examined 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 were performed on five samples. *Captive bubble* contact angles were measured to determine the relative hydrophobicity of the uppermost surface layer of the sample. The smaller the contact angle is, the greater is the hydrophilicity of the polymer surface.

## Results and Discussion

The hydrogel synthesized from poly(*rac*-lactide-*co*-glycolide) grafted along a poly (vinyl alcohol) (PVA) chain, [PVA-*g*-P(LGA)] (molar lactide/glycolide ratio 1:1, 9 polyester repeating units per graft 9, degree of grafting 13%),[15] was characterized before and after hydrolytical degradation for up to 8 weeks at RT and 37 °C in PBS buffer in order to follow the influence of the different conditions. IR measurements of the samples before and after 4 weeks of degradation are presented in Figure 1. The sample before degradation shows an OH band at 3380 cm$^{-1}$ while the sample degraded at RT shows the same band at 3370 cm$^{-1}$ and the sample degraded at 37 °C displays it at 3390 cm$^{-1}$.

The absorption band characteristic of the C-H bond shows the smallest deviation ($2939 \pm 1$ cm$^{-1}$). In the fingerprint region the sample before degradation shows bands of equal intensity at 1180 cm$^{-1}$ and at 1100 cm$^{-1}$ and a slightly weaker band at

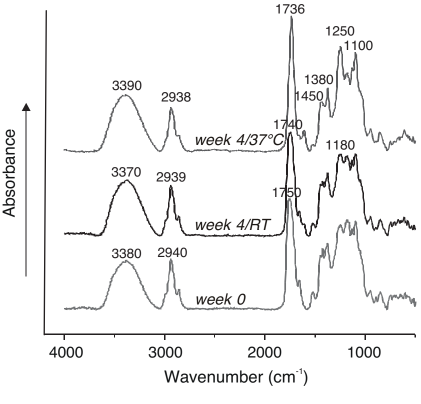

**Figure 1.**

FTIR-PA spectra of PVA-*g*-P(LGA): original sample (week 0), after four weeks at RT and after 4 weeks at 37 °C in PBS buffer.

1250 $cm^{-1}$ (this band is strongly expressed in the PVA spectrum and is attributed to the acetate group present).[15] The band around 1450 $cm^{-1}$ is split as a consequence of both glycolide and lactide content in the copolyester chain.[16,17] The sample degraded at RT shows a decrease of the intensity of the band at 1184 $cm^{-1}$ due to the reduction of the ester content, and its intensity is slightly below that of the band at 1248 $cm^{-1}$ and 1096 $cm^{-1}$. The band around 1450 $cm^{-1}$ is still split. On the other hand, the spectrum of the sample degraded at 37 °C shows a much larger decrease of the intensity of the band at 1180 $cm^{-1}$ relative to the bands at 1246 $cm^{-1}$ and at 1095 $cm^{-1}$. The band at 1246 $cm^{-1}$ in this sample is significantly stronger than the band at 1095 $cm^{-1}$ indicating the reduction of the ester content relative to the PVA. content [18] The band around 1440 $cm^{-1}$ shows a weak shoulder. In this highly degraded sample a new band appears at 1610 $cm^{-1}$ which is difficult to assign.

In the thermal analysis, network PVA-*g*-P(LGA) shows only a slightly steeper onset of thermal decomposition after 4 weeks of degradation, while the same sample, after 8 weeks of hydrolytical degradation, shows an immediate weight loss, but the main decomposition process takes place at about the same rate as in the sample before degradation (Figure 2). The thermal analysis of the PVA-*g*-P(LGA) network, after 4 weeks of hydrolytical degradation at room temperature and at 37 °C is shown in Figure 3. The curves have similar shape. In Table 1 the characteristic values obtained by thermal analysis are given. In the first thermal degradation regime of the sample hydrolytically degraded at 37 °C, $T_{10\%}$ is located at 229 °C compared to 251 °C for the network degraded at RT. In the second regime of the main mass loss, the two curves have similar shape. The difference between them is most evident when their differentiated curves in the third decomposition regime are observed. Thus, the curve of the sample degraded for 4 weeks at RT displays a smaller peak that appears at a lower temperature of 402 °C and the main peak at 426 °C. In the sample degraded for 4 weeks at 37 °C, the main transformation in the third regime appears at 405 °C, but a new smaller peak appears at higher temperature of 432 °C. This indicates different volatile degradation products.[4,19,20]

The temperature at which the hydrolytical degradation of the PVA-*g*-P(LGA) sample is performed influences the contact angle, Figure 4. The sample degraded at room temperature displays the main increase in surface hydrophilicity within the first 7 days and the subsequent change is small. Within the first week, the orientation

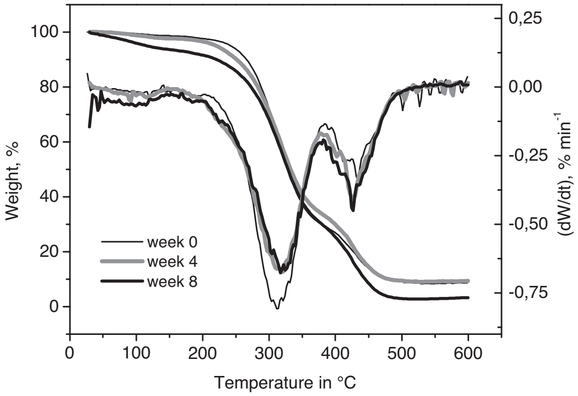

***Figure 2.***
TGA and DTGA plots of PVA-*g*-P(LGA) network before and after hydrolytical degradation at room temperature, measured at a heating rate of 10 °C $min^{-1}$.

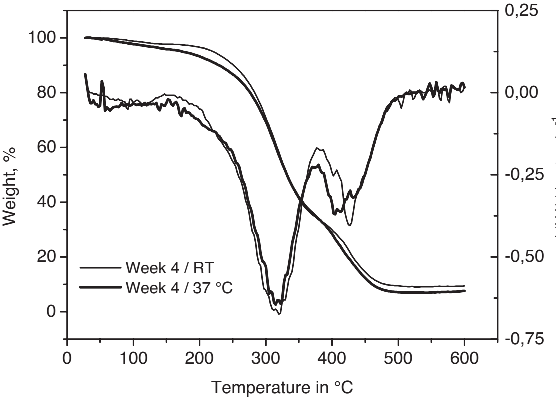

***Figure 3.***
TGA and DTGA plots of PVA-*g*-P(LGA) network after four weeks of hydrolytical degradation at room temperature and at 37 °C, measured at a heating rate of 10 °C $\text{min}^{-1}$.

of OH groups to the surface takes place causing a significant decrease of the contact angle. Since degradation at RT is a slow process, the further increase of hydrophilicity proceeds slowly. On the other hand, the decrease of the contact angle of the sample degraded at 37 °C is partially compensated by reorientation, resulting in a much slower decrease of the contact angle.

After 50 days of hydrolytical degradation all samples showed similar hydrophilicity irrespective of the degradation conditions. The mechanical tests showed significant mechanical deterioration of the hydrogels after hydrolytical degradation at RT, as well as at 37 °C. The change in the *E* modulus is shown in Figure 5. The *E* modulus decreases with degradation, indicating the loosening of the network structure. The sample degraded at room temperature shows an approximately linear decrease of the *E* modulus in the course of five weeks which reached a minimum after six weeks. At the same time, the sample degraded at 37 °C shows a significant decrease of the *E* modulus after one week which strongly further decreases after two weeks. Upon further degradation the *E* modulus change in the sample was negligible and its determination was limited to samples degraded for four weeks because of strong deterioration.

***Table 1.***
Thermal characterization of the network PVA-*g*-P(LGA) hydrolytically degraded for 4 and 8 weeks at RT and for 4 weeks at 37 °C, obtained by TGA at a heating rate of 10 °C $\text{min}^{-1}$; $T_{10\%}$, 10% loss of weight temperature; $T_{\text{max1}}$ and $T_{\text{max2}}$, temperature of maximum rate of weight loss; $\Delta W_1$ and $\Delta W_2$, weight loss at $T_{\text{max1}}$ and $T_{\text{max2}}$; $Y_{600\,°\text{C}}$, residual at $T = 600$ °C.

| | 37 °C[a)] | RT[a)] | RT[b)] |
|---|---|---|---|
| $T_{10\%}$/ °C | 229 | 251 | 221 |
| $T_{\text{max1}}$/ °C | 317 | 317 | 322 |
| $\Delta W_1$/% | 60 | 64 | 61 |
| $T_{\text{max2}}$/ °C | 405 | 426 | 426 |
| $\Delta W_2$/% | 28 | 24 | 27 |
| $Y_{600\,°\text{C}}$ | 7 | 9 | 3 |

a) Measured after 4 weeks of hydrolytical degradation.

b) Measured after 8 weeks of hydrolytical degradation.

The polyester portion, relative to the poly(vinyl alcohol), has a strong influence on the mechanical properties, in agreement with data in the literature where it was shown that poly(lactide) [11,21,22] displays a much higher *E* modulus than poly(vinyl alcohol).[23–25] The mechanical properties of aliphatic polyesters depend greatly on molecular weight.[26] It is important to emphasize that high values of the *E* modulus are found typically for poly(lacitde) of high molecular weight while the polyester grafts in this work have low molecular weight. The influence of the glycolide portion in the polymer on mechanical properties in literature.[27] was

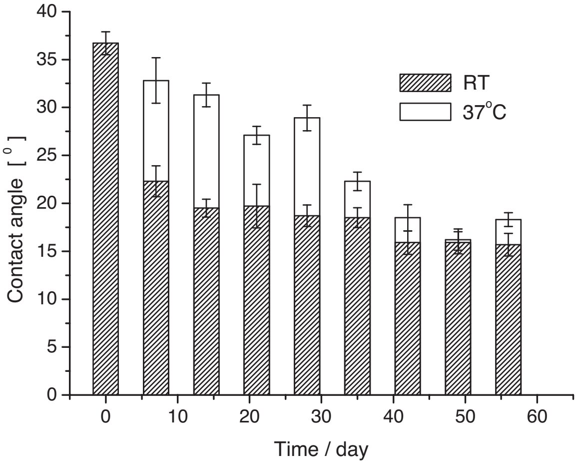

***Figure 4.***
Contact angle of the hydrogel PVA-*g*-P(LGA) hydrolytically degraded at RT and at 37 °C, measured in water using the *captive-bubble* method.

shown to be small Semi-crystalline poly(lactide)s of high molecular weight have excellent mechanical properties, but exhibit long degradation periods and might induce long term complications in vivo. On the other hand, low molecular weight amorphous poly(D,L-lactide) fully degrades at much faster rate but suffers from poor mechanical properties.[28] Poly(L-lactide) ($M_w = 137\,000$) displays an elastic modulus of ≈20 ± 3 MPa, while poly(D,L-lactide) displays an elastic modulus of 2.8 ± 0.4 MPa.[29] Poly(vinyl alcohol) hydrogels were proposed as promising biomaterials to replace diseased or damaged articular cartilage. Kobayashi et al.[30] performed mechanical tests on PVA hydrogels of different water content. They showed that adjusting the water content in the gel provides viscoelastic characteristics ($0.27 \leq E/\text{MPa} \leq 5$) similar to those of articular cartilage.[31]

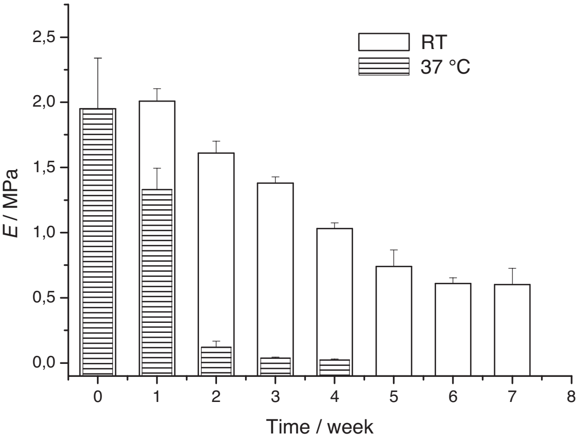

***Figure 5.***
*E* modulus of hydrogel PVA-*g*-P(LGA), hydrolytically degraded at RT and at 37 °C, as a function of degradation time.

## Conclusions

The hydrogel based on poly(vinyl alcohol) grafted with low molecular weight poly-[(*rac*-lactide)-*co*-glycolide)] chains with terminal acrylate groups serving as cross-linkers was degraded in experiments performed at room temperature (RT) and at 37 °C in PBS buffer solution for up to 8 weeks. The influence of increased temperature was evident but to different extent. In the course of degradation the polyester content decreases as seen from the fingerprint region of the IR spectra. Thermogravimetric analysis shows a larger mass loss for samples which were hydrolytically degraded at lower temperatures. The hydrophobicity (monitored by contact angle) decrease is immanent during eight weeks of hydrolytical degradation where at 37 °C of degradation the decrease in hydrophobicity is a continuous process while at RT a large decrease in hydrophobicity appears initially and changes upon further degradation are rather small. Mechanical properties display the largest influence of the degradation temperature where a significant decrease in properties appears already after the first week.

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