Degradable Polymer Films Made from Poly(salicylic-acid-co-sebacic acid) and Poly(sebacic anhydride)/Poly(adipic anhydride) Blends: Degradation Kinetics and Use as Sacrificial Layers for Polymer Multilayer Systems

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Abstract

Two approaches to obtain fast-degrading polymer films based on poly(sebacic anhydride) (PSA) are presented, both of which target polymer films with a lower degree of crystallinity than pure PSA homopolymer: first, thin films were prepared from poly(adipic anhydride)/poly(sebacic anhydride) blends at different ratios, and second, films were made from the copolymer poly(salicylic acid-co-sebacic acid). These films are intended as sacrificial layers for self-regenerating functional coatings, for example to regenerate antimicrobial surface activity. The degradation kinetics of these films were analyzed by surface plasmon resonance spectroscopy (SPR). The results of the blends approach indicate that the blend degradation rate was accelerated only in the initial degradation phase (compared to PSA). The degradation kinetics study of the poly(salicylic-acid-co-sebacic acid) film shows that this copolymer degraded faster than poly(sebacic anhydride) initially, releasing antimicrobial salicylic acid in the process. However, its degradation rate slowed down at a mass loss > 60% and approached the PSA degradation curve at longer degradation times. When tested as sacrificial layer in self-regenerating antimicrobial polymer stacks, it was found that the degradation rate was too low for successful layer shedding.

Keywords
blends; degradable polymers; degradation; polymer coatings; thin films

1 Introduction

Degradable polymers are well-known from studies in the context of drug delivery, implant materials, and tissue engineering.\cite{1} In particular, the degradation and drug release profiles, biocompatibility, physical-chemical properties, and mechanical properties of polyanhydrides and polyesters were studied in great detail.\cite{2} As has been extensively discussed in literature, polymer degradation is a complicated process where hydrolysis (i.e. molar mass reduction of the polymer chains forming the material) and erosion (i.e. mass loss by detachment

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of material from a sample) take place in parallel. Depending on the ratio of the water diffusion rate and the polymer hydrolysis rates, polymer degradation takes place either throughout the material volume (bulk erosion), or only at its surface (surface erosion). The transition of the degradation mechanism from surface erosion to bulk erosion is characterized by the critical length \( l_c \). Above \( l_c \), the material undergoes surface erosion; for sample dimensions lower than \( l_c \), bulk erosion dominates. For example, the critical length of polyanhydrides is 75 μm; that of polyorthoesters is 0.6 mm.

The rate of water diffusion is mostly affected by two parameters: the degree of crystallinity and the hydrophobicity of the material. For polysteres like poly(DL-lactide), poly(glycolide), or poly(L-lactide-co-glycolide), and polyanhydrides like poly(1,3-bis(p-carboxyphenoxy) propane-co-sebacic acid), it was found that a higher degree of crystallinity reduces the water diffusion rate and thus the polymer degradation rate. In semi-crystalline polymers, degradation starts in the more easily accessible amorphous regions, where acidic degradation products further accelerate the hydrolysis rate. The effect of hydrophobicity on polymer degradation rates was also quantified in a number of studies. For example, when poly(sebacic anhydride) (PSA) was hydrophobically modified, e.g. by copolymerizing sebacic anhydride with long-chain aliphatic or aromatic moieties in different ratios, the resulting copolymers degraded slower than the PSA homopolymer. In another study, poly(adipic anhydride) degraded faster than its more hydrophobic homologue poly(sebacic anhydride). In general, the lower the water solubility of the polymer chain, the slower its degradation kinetics. Because water diffusion is a transport phenomenon, polymer degradation rates are also affected by the sample dimensions. In polymer films, the film thickness can be orders of magnitude smaller than the other two film dimensions. Thus, when the film thickness is lower than the critical length \( l_c \), the predominant degradation mechanism may also change from surface erosion to bulk erosion.

We recently investigated the degradation rate of PSA and found that free-standing PSA pellets with a thickness of 190-670 μm degraded substantially slower than thin substrate-attached PSA films with a thickness < 1 μm, thus demonstrating the thickness effect on the degradation rate. With a \( l_c \) of ~ 75 μm for polyanhydrides, it is plausible that surface erosion dominated in the PSA pellets, while the films underwent bulk erosion. These previous studies were performed in the context of polymer multilayer materials containing degradable polymer films as sacrificial layers for the regeneration of surface properties by layer shedding. These multilayers consist of ca. 100-300 nm thick polymer layers stacked on top of each other. Each functional layer is separated by a sacrificial layer. The material design is such that the topmost functional layer can delaminate once the sacrificial layer underneath is removed, which allows self-regeneration of the surface properties of the polymer stack. To obtain sacrificial layers with faster degradation rates than poly(sebacic anhydride), we continued our work on degradable polymer thin films with two further approaches: degradable films made from polyanhydride blends (blends approach), and from a poly(ester anhydride) (copolymer approach), as presented herein. While the effect of blending and copolymerization on degradation of macroscopic samples has been previously investigated, no such studies exist for very thin samples (thickness below \( l_c \)), so that the extent of the effect of the overall degradation process of these materials is yet unknown.
The blends approach was chosen because mixing two polymers lowers their degree of crystallization and yields a material with increased degradation rates.\textsuperscript{15}\textsuperscript{16}\textsuperscript{17} For example, blending poly(adipic anhydride) with poly(trimethylene carbonate) gave a material with faster mass loss than pure poly(adipic anhydride).\textsuperscript{18} The copolymer approach was selected because different co-repeat units of the same copolymer do not co-crystallize, even if they are structurally as similar as in poly(ethylene-co-butene) or poly(ethylene-co-octene).\textsuperscript{15} This reduces the degree of crystallinity of the resulting material. This effect depended mostly on the molar fraction of co-repeat units used, and less on their chemical nature. \textsuperscript{15}\textsuperscript{19}\textsuperscript{20}

In this work we study the degradation kinetics of films made from a) poly(sebacic anhydride)/poly(adipic anhydride) blends, and b) poly(sebacic acid-co-salicylic acid) copolymers (Figure 1). In addition to studying the separate films, we investigate their usefulness as sacrificial layers for self-regenerating antimicrobial polymer multilayer systems. For this, the degradable layers here presented where combined with polymer networks made from the antimicrobial polymer poly(guanidinium oxanorbornene) (PGON), and the antimicrobial activities of the poly(sebacic acid-co-salicylic acid) copolymers and the PGON after removal of the sacrificial layers were tested.

2 Experimental Section

General information on chemicals sources and instrumentation used is given in Section 1 and 2 of the Supporting Information.

2.1 Synthesis of Poly(anhydrides)

The homopolymers poly(adipic anhydride) (PAA) and poly(sebacic anhydride) (PSA) were synthesized by polycondensation as reported previously.\textsuperscript{6}\textsuperscript{23}\textsuperscript{24} Details (including NMR Spectra, Figures S1 and Figure S2) are given in Section 3 of the Supporting Information. The poly(adipic anhydride) obtained had a number average molar mass ($M_n$) of 2,500 g mol\textsuperscript{-1} and a polydispersity index (PDI) of 2.0, as determined by gel permeation chromatography (GPC, Figure S3, Supporting Information). The poly(sebacic anhydride) had a $M_n$ of 20,000 g mol\textsuperscript{-1} and a PDI of 3.1 (Figure S4 in the Supporting Information). GPC was measured in chloroform using SDV columns (SDV 5 μm, SDV 5 μm 100 Å, SDV 5 μm 10000 Å) and poly(methyl methacrylate) standards.

2.2 Synthesis of Poly(salicylic acid-co-sebacic acid)

Poly(salicylic acid-co-sebacic acid) was synthesized by adapting a literature procedure.\textsuperscript{25} The detailed synthesis and characterization (NMR spectra, Figure S5 to S7) are described in Section 4 in the Supporting Information. The copolymer obtained had a $M_n$ of 4,300 g mol\textsuperscript{-1} and a PDI of 2. GPC was measured in chloroform using SDV columns (SDV 5 μm, SDV 5 μm 100 Å, SDV 5 μm 10000 Å) and poly(methyl methacrylate) standards. The elugrams is given in Figure S8 in the Supporting Information. The MALDI-TOF mass spectrum (Figure S9) confirmed the structure and the degree of polymerization. The exact structural analysis of the polymer fragments can be found in Table S1.
2.3 Substrate Pre-treatment

Double-side polished silicon wafers (for Fourier-Transform infrared spectroscopy (FTIR) measurements) were functionalized with 4-[(3-triethoxysilyl)propoxy-benzophenone] (3-EBP) as reported previously.[26] For surface plasmon resonance spectroscopy, home-made LaSFN9 substrates were functionalized with lipoic acid 4-benzophenone ester (LS-BP) as described in earlier publications.[26] A detailed description of the substrate pre-treatments was given in Sections 5 and 6 in the Supporting Information.

2.4 Blends made from Poly(adipic anhydride) – Poly(sebacic anhydride)

Poly(adipic anhydride) and poly(sebacic anhydride) were dissolved in dichloromethane at different mass ratios. The solvent was then slowly evaporated. The thermal properties of the resulting blends were studied by differential scanning calorimetry (DSC) to assess their degree of crystallinity. To obtain films, PAA : PSA blends (mass ratio 2:1 and 3:1) were re-dissolved in dichloromethane at a total concentration of 15 mg mL\(^{-1}\) and spin-coated (rotation speed: 3000 rpm; acceleration: 1000 rpm\cdot s\(^{-1}\); spin time: ten seconds) onto LS-BP functionalized gold substrates.

2.5 Homopolymer and Copolymer Films

Poly(adipic anhydride), poly(sebacic anhydride) or poly(salicylic acid-co-sebacic acid) solutions (35 mg mL\(^{-1}\) in chloroform) were spin-coated onto LS-BP functionalized gold substrates for the SPR measurements (rotation speed: 3000 rpm; acceleration: 1000 rpm\cdot s\(^{-1}\), spin time: ten seconds). For the other experiments, the polymer solutions were spin-coated (rotation speed: 3000 rpm; acceleration: 1000 rpm\cdot s\(^{-1}\), spin time: 30 seconds) onto 3-EBP functionalized silicon substrates.

2.6 Degradation Kinetic Studies

Surface-plasmon resonance spectroscopy and FTIR measurements were used to study degradation of the polymer films. This has been described in great detail in a previous publication.[13] In short, the polymer-coated substrates were immersed into triethanolamine hydrochloride buffer solution (simulated physiological conditions, pH 7.4, see also Section 7 in Supporting Information) at 37 °C and retrieved after defined time points. They were blow-dried before the FTIR measurements. For the SPR measurements, the cell-mounted samples were placed under constant flow of triethanolamine hydrochloride buffer at 37 °C, and the thickness changes of the sample was determined by measuring full angular reflectivity curves. After data acquisitions, the thickness \(d_t\) obtained at the different time points was normalized to the initial thickness \(d_0\) to obtain relative thickness values for each time point (i.e. relative thickness = \(d_t/d_0\)). These relative values were then plotted versus time. Since only one data point per time point was obtained by SPR, no error bars are given.

3 Preparation of Two-Layer Stacks

A-B Stack. To assemble the poly(guanidinium oxanorbornene) (PGON)-poly(salicylic acid-co-sebacic acid) stack (A-B), a solution of the PGON in a water-methanol mixture (0.02 mL/0.08 mL) was spin-coated onto a silicon substrate pre-treated with 3-EBP (rotation speed: 3000 rpm; acceleration: 1000 rpm\cdot s\(^{-1}\); rotation time: ten seconds). The resulting layer was
UV irradiated (wavelength: 254 nm; energy dose: 0.2 J cm\(^{-2}\)) to form a surface-attached polymer network. The PGON network was extracted in water overnight to remove the sol content. A solution of the poly(salicylic acid-co-sebacic acid) in chloroform was spin-coated on top of the A layer to form the B layer (rotation speed: 3000 rpm; acceleration: 1000 rpm·s\(^{-1}\); rotation time: 30 seconds).

**B-A Stack.** To assemble the poly(salicylic acid-co-sebacic acid)-PGON stack (B-A), a solution of poly(salicylic acid-co-sebacic acid) in chloroform was spin-coated onto a 3-EBP pre-treated silicon substrate. On top of this layer, a solution of PGON in a water-methanol mixture (0.02 mL/0.08 mL) was deposited by spin-coating (rotation speed: 3000 rpm; acceleration: 1000 rpm·s\(^{-1}\); rotation time: ten seconds). This resulting two-layer stack was then irritated by UV-light to form a PGON-network as upper layer A.

## 4 Results

### Study Design

The aim of this study was to obtain degradable polymer layers based on poly(sebacic anhydride) (PSA) with a faster degradation rates than the PSA homopolymer. For this, the degradation of polymer films made from poly(sebacic anhydride) and poly(adipic anhydride) (PAA) blends, and of poly(ester anhydride) films made from sebacic acid and salicylic acid were investigated. First, the degradation rate of the polyanhydride blends was investigated and compared to the parent homopolymers films. Second, the degradation of the poly(ester anhydride) was studied as a single polymer film. These films were then assembled into bilayer systems with an antimicrobial polymer layer (poly(guanidinium oxanorbornene), PGON), and the degradation behavior of the resulting system was studied (Figure 1).

### Polyanhydride Blends

Polyanhydride blends were obtained from PAA and PSA as described in the Experimental Section. Differential scanning calorimetry (DSC) studies were performed to assess the crystallinity of the thus obtained materials compared to the PAA and PSA homopolymers. The melting temperatures and the enthalpies of fusion (\(\Delta H_{\text{fus}}\)) thus obtained are shown in Figure 2 and Table 1. The corresponding DSC curves are shown in Figures S10-S15 in the Supporting Information (Section 8). The DSC curves showed two melting points for blends made from PAA and PSA and even three melting points for pure PSA homopolymer. The phenomenon of multiple melting peaks is frequently observed in semi-crystalline polymer systems, including homopolymers, copolymers and blends.\([27][28][29][30][31]\) It is explained by the presence of different crystal types or morphologies in the sample, or the reorganization of the crystallites during thermal analysis. The enthalpy of fusion \(\Delta H_{\text{fus}}\) was calculated by integrating the total area under these endotherms (see also Figures S10-S15 in the Supporting Information). The data indicates that PAA : PSA blends with a mass ratio of 2 : 1 and 3 : 1 had the lowest enthalpy of fusion per unit mass (63-65 J g\(^{-1}\)), corresponding to a much lower degree of crystallinity than the PSA homopolymer with \(\Delta H_{\text{fus}} = 109 J g^{-1}\).\([23]\) They were thus the materials with the potentially fastest degradation rates in this sample set.
Polymer films were obtained from these blends by spin-coating as described in the Experimental Section. Hydrophobically modified gold layers on high refractive index glass slides were used as substrates, as these are suitable for surface plasmon resonance spectroscopy (SPR) studies. The degradation of these films and films cast from their parent homopolymers was investigated by SPR (Figure 3: a) relative film thickness $y_t = \frac{\text{thickness at time } t}{\text{thickness at } t = 0}$ and b) $\ln y_t = \ln \left( \frac{\text{thickness at time } t}{\text{thickness at } t = 0} \right)$ versus time for PSA, PAA, and two PAA:PSA blends). The half-logarithmic plot indicates that the degradation of the homopolymers proceeds with a steady thickness loss initially. The apparently slower thickness loss of PSA at a relative thickness < 0.1 can be attributed to physisorption of the remaining material at the interface. In contrast to this, the thickness loss of the blends consists of two distinct phases with a rather abrupt change of gradient at a relative thickness between 0.3 and 0.4 (-1.2 to 1.0 on the ln scale in Figure 3b). The degradation rate constants of the two phases were determined by fitting each data set from Figure 3a separately with an exponential function ($y_t = y_0 - a \cdot e^{k_{app} \cdot t}$, where $y_t$ the relative thickness at different time points, $a$ is a fitting constant, and $k_{app}$ is the apparent degradation rate constant. These fits are shown in Figure S16 the Supporting information Section 9.) For example, in the range of 0-4 h, the relative layer thickness of PAA : PSA 2:1 decreased rapidly with a degradation rate constant of $0.42 \pm 0.05 \text{ h}^{-1}$. Afterwards, it slowed down by two orders of magnitude to a degradation rate constant of $0.02 \pm 0.01 \text{ h}^{-1}$. The rate constants of all samples are summarized in Table 2.

The data shows that both blends initially indeed had a faster degradation rate than the parent PSA homopolymer ($0.45 \pm 0.05 \text{ h}^{-1}$ and $0.90 \pm 0.52 \text{ h}^{-1}$, respectively, compared to $0.20 \pm 0.02 \text{ h}^{-1}$). The rate of the latter blend more closely resembled the degradation rate of poly(adipic anhydride) films, which was $1.26 \pm 0.05 \text{ h}^{-1}$. However, after about 70% mass loss, the rate constant of the blends dropped to $0.02 \pm 0.01 \text{ h}^{-1}$ for PAA : PSA (2:1) and $0.03 \pm 0.02 \text{ h}^{-1}$ for PAA : PSA (3:1), which is even slower than PSA film degradation ($k_{app} = 0.20 \pm 0.02 \text{ h}^{-1}$). Apparently, the PAA-rich domains of the blend degraded first, followed by the remaining PSA-rich domains. Overall, the remaining material seems to be firmly adhering to the substrate, as mass loss becomes extremely slow at about 12% remaining material. Thus, using PAA : PSA blends as sacrificial layers would have no advantage over using neat PAA homopolymer, which demonstrates near-quantitative mass loss after 10 hours.

Poly(salicylic acid-co-sebacic acid) Copolymers

Poly(salicylic acid-co-sebacic acid)[21][22] was synthesized by adapting a literature procedure,[25] and polymer films spin-cast from this copolymer and the parent PSA homopolymer onto hydrophobically modified substrates were analyzed after different degradation times by Fourier-transform infrared spectroscopy (FTIR) and SPR. FTIR spectra of PSA and poly(salicylic acid-co-sebacic acid) films are shown in 4. PSA featured the expected two carbonyl bands corresponding to the anhydride group (at 1810 cm$^{-1}$ and 1749 cm$^{-1}$),[32] which are widely separated (Figure 4a). In a previous study, these signals were used to quantify PSA degradation.[13] Since poly(salicylic acid-co-sebacic acid) is a poly(ester anhydride), the carbonyl region of its FTIR spectrum (Figure 4b) is populated by additional peaks from the different possible repeat units of the copolymer.
These overlapping multiple peaks make FTIR degradation studies of this copolymer extremely difficult, even if peak deconvolution methods are applied. Therefore, only SPR was used to quantify the degradation rates of these films. For this, the relative film thickness was determined at different degradation times and plotted versus time.

The plots of relative film thickness vs. time of PSA and poly(salicylic acid-co-sebacic acid) determined by SPR are shown in Figure 5, with the plot of ln (relative film thickness) vs. time as an inset. This semi-logarithmic plot features two sections with different gradients and thus cannot be fitted with a single exponential. Using the fitting functions $\ln y_t = a_2 - k_{\text{slow}} \cdot t$ and $\ln y_t = a_2 - k_{\text{fast}} \cdot t$ for each plot section (with $y_t = \ln$ (relative film thickness), $a_1$ and $a_2$ = fitting constants), the apparent degradation rate constants $k_{\text{fast}}$ and $k_{\text{slow}}$ were determined (Table 3). Poly(salicylic acid-co-sebacic acid) had a $k_{\text{fast}}$ of $0.080 \pm 0.003 \text{ h}^{-1}$. Compared to the one of PSA ($k_{\text{fast}} = 0.032 \pm 0.002 \text{ h}^{-1}$), it was two and half times faster within the first six hours. $k_{\text{slow}}$ of poly(salicylic acid-co-sebacic acid) was less than $0.001 \text{ h}^{-1}$, whereas that of the PSA was $0.011 \pm 0.001 \text{ h}^{-1}$. Overall, the mass loss of poly(salicylic acid-co-sebacic acid) was 64% after 12 hours, whereas PSA had only lost 29% of its initial thickness after 11 hours. FTIR spectra at 0 h, 48 h and 96 h degradation time (Figure 6) were used to identify the chemical components of the relatively large fraction of material that remained on the surface after degradation. From this data, it is clear that the anhydride groups were hydrolyzed after 48 h (disappearance of the characteristic peak at 1790 cm$^{-1}$). The peak at 1612 cm$^{-1}$ could be from the aromatic C=C bond of a salicylate unit, indicating that at least part of the remnant on the surface are salicylates. In the light of the better solubility of salicylic acid ($2.48 \text{ g L}^{-1}$ at 25 °C$^{[33]}$) compared to sebacic acid ($0.25 \text{ g L}^{-1}$ at 25 °C$^{[34]}$), it is assumed that the other remaining unspecific IR peaks are from a mixture of sebacic and salicylic acid.

### Bilayer Systems Consisting of a Functional and a Degradable Polymer Layer

One aim of this work was to test if fast degrading polymer layers can be used as sacrificial layers in self-regenerating multi-layer systems. These systems are built alternatingly from functional layers and sacrificial layers. By design, in these materials the removal of a sacrificial layer triggers shedding of the functional layer on top of it, and thus potentially regenerates a surface function. In the system investigated by us, the functional layer to be shed was an antimicrobial layer made from a cross-linked, polycationic polyelectrolyte hydrogel with antimicrobial activity (poly(guanidium oxanorbornene), PGON). Since poly(salicylic acid-co-sebacic acid) releases antimicrobial salicylic acid during degradation, it was also hoped that the release of salicylate would maintain the antimicrobial activity of the material during ongoing shedding of the active layer. To test the suitability of poly(salicylic acid-co-sebacic acid) as a sacrificial layer, two different bilayer system made from this polymer and the antimicrobial PGON hydrogel were assembled. First, the degradation of the copolymer in the presence of PGON was investigated. For this, a stack consisting of a PGON bottom layer (layer A, Figure 7a, prepared on a silicon substrate by previously reported methods (see Figure S18 and S19 in Supporting Information for complete data sets))$^{[6]}$ and a poly(salicylic acid-co-sebacic acid) top layer B (Figure 7b) was assembled. The surface-attached layer A had a thickness of $70 \pm 0.7 \text{ nm}$, as determined...
by ellipsometry. The bilayer stack had a total thickness of 197 ± 0.4 nm, i.e. B was about 130 nm thick. The analytical data obtained during build-up and disintegration of this stack are summarized in Figure 7. In the FTIR spectra, the most characteristic peak of PGON is the imide signal at 1700 cm\(^{-1}\). Poly(salicylic acid-co-sebacic acid) has the characteristic anhydride signals at 1790 and 1740 cm\(^{-1}\), the ester at 1760 cm\(^{-1}\), and the aromatic C=C bonds at 1612 cm\(^{-1}\). When the bilayer stack was disassembled in triethanolamine buffer at 37 °C, the signal at 1790 cm\(^{-1}\) (highlighted by the green arrow in Figure 7) vanished. The layer thickness was reduced to 78 ± 1.4 nm, which is slightly more than the original thickness of the bilayer system. This is due to some remnant of salicylate, as indicated by the remaining peak at 1612 cm\(^{-1}\) in the FTIR spectrum of the disassembled material.

Photoelectron spectroscopy (XPS) analytics of the bilayer stack and the left-over material indicated that the nitrogen content increased from 0% to 8%. As this method is sensitive to the top few nanometers of a material, this indicates the presence of PGON imide and guanidinium groups, and thus identifies PGON as the major component of the degraded material. The antimicrobial activity of the degraded materials against *Escherichia coli* bacteria was also tested using a previously reported standard protocol.[35] The data (see Figure S20 in Supporting Information) confirms that the degraded material (Figure S20 c)) was still antimicrobially active, but not as strongly as the fresh PGON layer (Figure S20 a)), possibly due to the presence of remnant sebacic acid fragments on top of the degraded layer.

To test the suitability of poly(salicylic acid-co-sebacic acid) as a sacrificial layer, a B-A stack consisting of a PGON as top layer (A) and a poly(salicylic acid-co-sebacic acid) bottom layer (B) was assembled (Figure 8). The bottom layer had a thickness of 109 ± 6.3 nm (determined by ellipsometry, Figure 8a). The thickness of the two-layer stack was 291 ± 3.5 nm, from which a thickness of about 182 nm for the A layer was calculated. Again, the presence of the characteristic peaks of both materials in the bilayer was confirmed by FTIR measurements (Figure 8b). After degradation in triethanolamine buffer for 96 hours, the remaining material had a thickness of 87 ± 9.1 nm (determined by ellipsometry, Figure 8c), which was significantly thinner than either the original A or B layer. FTIR spectra (Figure 8c) showed the complete hydrolysis of the anhydride groups (previously at 1790 cm\(^{-1}\)) after degradation. Also, the salicylate peak at 1612 cm\(^{-1}\) vanished. XPS analytics showed that the chemical composition of the remaining layer was close to that of PGON. This leads to the conclusion that material from the B layer underneath the A layer was gradually removed during degradation. However, instead of shedding, the PGON layer collapses onto the substrate – a phenomenon also observed in a previous publication.[6] The thickness reduction of the A layer of the degraded material compared to the initial A layer can be explained by extraction of unbound polymer chains (sol content) from that layer. The result of the antimicrobial assay (see Figure S21 in Supporting Information) showed that the remnant on the substrate was still active against *E.coli* (Figure S21 c)), however to a lesser extent than the fresh material (Figure S21 a)).

## 5 Conclusion

In this work, two approaches to suppress crystallization in degradable polymer films derived from poly(sebacic anhydride) (PSA) are presented. It was anticipated that these films would have faster degradation kinetics than the respective PSA homopolymer, and thus would be
useful as sacrificial layers in surface-regenerating polymer multilayers. In the polymer blend approach, the two polyanhydrides PSA and PAA were blended in different weight ratios to obtain less crystalline materials. The resulting blend had indeed less crystallinity than the pure polyanhydrides, as shown by DSC. However, the erosion rate of the blends was only faster during the first four hours and then stagnated. Thus, the blends showed two distinct degradation phases, where the fast phase can be presumably attributed to the PAA domains, and the slow phase to domains rich in PSA. Overall, these materials were not superior in degradation speed to PAA homopolymer, which kept degrading continuously until a very high mass loss was observed.

In the copolymer approach, the degradation kinetics of a copolymer consisting of salicylic acid and sebacic acid were compared to the PSA homopolymer. Indeed, the initial degradation rate of this copolymer was faster than that of pure PSA, with 64% mass loss within 12 h. However, similarly to the blend approach the mass loss then stagnated. To test whether this was sufficient to work as a sacrificial layer, the copolymer was incorporated into a polymer bilayer stack (as a model for self-regenerating polymer multilayers) consisting of a functional top layer and the copolymer as bottom layer. When trying to shed the top layer through degradation of the bottom layer, it was observed that the top layer remained attached to the stack even when the bottom layer degraded. This phenomenon was observed previously in other systems and can be related to a too low mass transfer from the degrading layer. This allows re-attachment of the functional top layer to the substrate, and thus prevents layer shedding. Thus, other mechanisms for layer shedding from polymer multilayers, including depolymerizable sacrificial layers, are currently investigated. Nevertheless, both the blend and the copolymer film might be useful matrices for drug delivery, with two distinct degradation kinetics and thus two phases of drug release. As one of the reviewers pointed out, the introduction of branching might further suppress crystallization and thus further accelerate the degradation kinetics of these materials compared to the parent linear PSA homopolymers.

Supporting Information is available from the Wiley Online Library.

**Supplementary Material**

Refer to Web version on PubMed Central for supplementary material.

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Figure 1.
Synthesis and structures of polymers used in this study: a) Poly(sebacic anhydride) (PSA) and poly(adipic anhydride) (PAA). Degradation of PSA and PAA blends was studied in comparison to the parent homopolymers. b) Poly(salicylic acid-co-sebacic acid) degradation was studied in the copolymer approach. c) Poly(guanidinium oxanorbornene) (PGON) with 10 mol% of diazoester-functionalized repeat units was used to build functional layers for PGON-poly(salicylic acid-co-sebacic acid) bilayer systems.
Figure 2.
DSC curves of poly(adipic anhydride) (PAA), poly(sebacic anhydride) (PSA), and PAA : PSA blends at different mass ratios. a) PAA homopolymer (1:0), PAA : PSA blends (3:1 and 2:1); b) PAA : PSA blends (1:1 and 1:3), and PSA homopolymer (0:1).
Figure 3.
Degradation of polymer films made from poly(adipic anhydride) (PAA) and poly(sebacic anhydride) (PSA) homopolymers, and PAA : PSA blends at a ratio of 2:1 and 3:1. PSA homopolymer data from ref. [13]. Film thickness was determined by surface plasmon resonance spectroscopy and is plotted as a) relative film thickness $y_t = \frac{\text{thickness at time } t}{\text{thickness at } t = 0}$ versus time, and b) $\ln y_t = \ln \left( \frac{\text{thickness at time } t}{\text{thickness at } t = 0} \right)$ versus time. Degradation conditions: aqueous triethanolamine hydrochloride buffer, 37 °C.
Figure 4.
FTIR spectra of a) PSA homopolymer, with well-separated carbonyl bands at 1810 cm\(^{-1}\) and 1749 cm\(^{-1}\), and b) of poly(salicylic acid-co-sebacic acid) at \(t = 0\) h, with carbonyl bands at 1810 cm\(^{-1}\) and 1749 cm\(^{-1}\), each with additional peaks.
Figure 5.
Degradation of poly(salicylic acid-co-sebacic acid) films (green circles) compared to PSA homopolymer films (blue squares) studied by SPR. Relative thickness is plotted vs. time, with a plot of ln (relative thickness) vs. time as inset.
Figure 6.
FTIR spectra of poly(salicylic acid-co-sebacic acid) films at $t = 0$ h, and after 48 h and 96 h degradation. The pure components of the copolymer (salicylic acid and sebacic acid) are shown for comparison. The vertical line at 1612 cm$^{-1}$ highlights the single unambiguous peak of the spectra (1625 – 1590 cm$^{-1}$), originating from a salicylic acid derivative.
Figure 7.
Assembly and disassembly of the PGON-poly(salicylic acid-co-sebacic acid) bilayer system A-B studied by ellipsometry (thickness data in the left column), FTIR (middle column) and XPS (right column). The checkered layer A (blue) represents the cross-linked PGON hydrogel, the green layer is the degradable B layer. a) characterization of the PGON layer, b) characterization of the assembled A-B stack, c) characterization of the disassembled material.
Figure 8.
Assembly and disassembly of the system B-A studied by ellipsometry (thickness data in the left column), FTIR (middle column) and XPS (right column). The checkered layer A (blue) represents the cross-linked PGON hydrogel, the green layer is the degradable poly(salicylic acid-co-sebacic acid) B layer. a) characterization of the poly(salicylic acid-co-sebacic acid) layer, b) characterization of the assembled B-A stack, c) characterization of the disassembled material.
Table 1

Thermal properties of poly(adipic anhydride) (PAA), poly(sebacic anhydride) (PSA), and PAA : PSA blends at different mass ratios determined by differential scanning calorimetry (DSC). \( T_m \) = melting temperature, \( \Delta H_{fus} \) = enthalpy of the fusion.

| Mass ratio (PAA : PSA) | \( T_m / ^\circ C \) | \( \Delta H_{fus} / J g^{-1} \) |
|------------------------|----------------------|-------------------------------|
| 1:0                    | 73.0 80.1            | 84                            |
| 3:1                    | 51.4 58.2            | 63                            |
| 2:1                    | 50.4 57.2            | 65                            |
| 1:1                    | 47.6 50.9            | 69                            |
| 1:3                    | 53.4 61.2            | 83                            |
| 0:1                    | 61.8 70.5 76.1       | 109                           |
Table 2

Degradation rate constants $k_{\text{app}}$ obtained from the exponential fits $y_t = y_0 - a \cdot e^{k_{\text{app}} \cdot t}$ to the SPR data shown in Figure 3.

| Sample       | Time Range | $k_{\text{app}}$ / h$^{-1}$ |
|--------------|------------|-----------------------------|
| PAA : PSA (2:1) | 0 – 4 h    | 0.42 ± 0.05                 |
|              | 4 – 150 h  | 0.02 ± 0.01                 |
| PAA : PSA (3:1) | 0 – 4 h    | 0.90 ± 0.52                 |
|              | 4 – 150 h  | 0.03 ± 0.02                 |
| PAA          | 0 – 9 h    | 1.26 ± 0.05                 |
| PSA          | 0 – 60 h   | 0.20 ± 0.02                 |
Table 3
Degradation rate constants $k_{\text{fast}}$ and $k_{\text{slow}}$ obtained from the fits ($\ln y_t = a_i - k_i \cdot t$) to the SPR data shown in Figure 5

| Sample type & initial thickness | Method | $k_{\text{fast}}$   | $k_{\text{slow}}$  |
|-------------------------------|--------|---------------------|---------------------|
| PSA 121 nm                    | SPR    | $0.032 \pm 0.002$ h^{-1} | $0.011 \pm 0.001$ h^{-1} |
| Poly(salicylic acid-co-sebacic acid) 131 nm | SPR    | $0.080 \pm 0.003$ h^{-1} | < 0.001 h^{-1} |