

Stefan Oschatz*, Thomas Reske, Jana Markhoff, Thomas Eickner, Klaus-Peter Schmitz, Niels Grabow and Sabine Illner

Degradable dual co-electrospun polyester based nonwovens for guided tissue regeneration

Abstract: In this study, initial experiments are presented regarding the suitability of polyester based nonwoven composite materials for guided tissue regeneration based on degradation. The *in vitro* degradation of poly(lactic-co-glycolic acid)/polydioxanone and polycaprolactone/polydioxanone mats has been performed under accelerated condition in alkaline glycine buffer at 50 °C for 21 days. The degradation of the materials has been characterized regarding total mass loss and macroscopic morphological changes, as well as determination of the molecular weight degradation *via* GPC experiments.

Keywords: dual co-electrospinning, polyester nonwoven, degradation, guided tissue regeneration

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1 Introduction

Polymer based nonwoven materials are promising candidates for guided tissue regeneration (GTR), especially for the treatment for periodontal damages, as they fulfill several functions. On the one hand, they serve as a barrier for fast growing cells (e.g. gingival cells versus bone cells) into the site of action, as those cells would compete with the target cells.[1] On the other hand, nonwovens may provide a

necessary supporting structure for cells and apatite formation to regenerate bone defects.

Electrospinning, in particular, is a versatile tool for the generation of such biomaterials and allows the usage of a vast variety of substrates. Polyesters are especially promising candidates due to their biodegradation ability.

Several approaches for the application of biodegradable nonwovens for GTR have been reported in the literature. As an example, YIN *et al.* reported on the manufacturing of electrospun poly(lactic acid)/silk fibroin-gelatin scaffold for GTR.[2] These scaffolds showed good cell adhesion for 3T3 mouse fibroblasts and the formation of a cell monolayer in 12 days. In 2016, the group of YAO reported the successful fabrication of a nonwoven from a PDLLA/PLGA blend with an adjustable degradation rate depending on the amount of incorporated PLGA.[3] A different approach was made by ZHANG *et al.* using an aqueous solution of gelatin to create a degradable nonwoven.[4] MAGIERA *et al.* went a step further and performed concurrent-electrospinning of PLA with gelatin to create a composite nonwoven structure. The use of this technique resulted in reduced hydrophobicity of the material compared to pure PLA, leading to a faster degradation rate.[5]

In 2019, our group reported on the successful generation of a biostable co-electrospun nonwoven from polyurethane and polyamide.[6] The materials accessible in such a way exhibited distinct fibers of the respective polymer. The approach of this work is the combination of polymers with distinctly different degradation times in a dual co-electrospun composite nonwoven. Such a material may offer a sufficient barrier effect, but, due to the faster degradation of one type of fiber, may still allow for the time delayed migration and colonization of cells. The residual slow degrading polymer acts as supporting scaffold and the opened pores between the fibers enables cell infiltration.

In this work, the degradation behavior of nonwovens consisting of two different polyester fibers is presented. Polydioxanone (PDO) has been combined with poly(lactic-co-glycolic acid) (PLGA) and polycaprolactone (PCL). PDO

Corresponding author: Stefan Oschatz, Institute for Biomedical Engineering, Rostock University Medical Center, 18119 Rostock-Warnemünde, Germany

E-Mail: stefan.oschatz@uni-rostock.de

Thomas Reske and Klaus-Peter Schmitz, Institute for Implant Technology and Biomaterials e.V., 18119 Rostock-Warnemünde, Germany

Sabine Illner, Jana Markhoff, Thomas Eickner and Niels Grabow, Institute for Biomedical Engineering, Rostock University Medical Center, 18119 Rostock-Warnemünde, Germany

(Resomer X) is a relatively fast degrading polymer, with degradation times of < 6 months, according to manufacturer's information. Compared with this, PLGA (Resomer LG 857) exhibits a degradation time of 1 - 2 years and PCL > 2 years.[7] The degradation has been observed in respect to total mass loss and molecular mass degradation.

2 Materials and Methods

2.1 General information:

Resomer LG 857 S (PLGA) and Resomer X 206 S (poly-dioxanone) were provided by Evonik. Poly-caprolactone (PCL) was provided by Aldrich.

2.1.1 Dual co-electrospinning:

Dual co-Electrospinning was performed on a Contipro 4SPIN C4S LAB2 (Dolní Dobrouč, Czech Republic). The setup used was 24 cm collector distance, 43 kV high voltage and a feed rate of 50 $\mu\text{L}/\text{min}$ for both polymer solutions. All polymers were dissolved in CHCl_3 (PDO: 10 w/w%, PLGA: 6 w/w%, PCL 7 w/w%) prior to spinning. The obtained nonwovens were thermally annealed for 24 hrs at 80 $^{\circ}\text{C}$ after the spinning process.

2.1.2 Accelerated degradation:

Circular samples of 11 mm diameter were taken from the generated nonwoven and placed in degradation medium without further treatment under decent shaking. For degradation, glycine buffer adjusted to pH = 8.7 with NaOH was used at 50 $^{\circ}\text{C}$. Medium was replaced after 12 days of degradation. At the selected time points, the degradation medium was removed and the samples were washed twice for 15 min with distilled water. Finally, the samples were dried at 40 $^{\circ}\text{C}$ under reduced pressure. Mass loss during degradation was investigated by using a Radwag micro balance MYA 0.8/3.4Y.

2.1.3 GPC-measurements:

The molecular weight of the polymer nonwoven samples was determined using a PSS SECcurity SEC system (Polymer Standard Services GmbH, Mainz, Germany) including a RI detector combined with a WGE Dr. Bures g 2010 viscosity detector (WGE Dr. Bures GmbH, Dallgow, Germany) equipped with three PSS SDV columns (103, 105 and 106 \AA , respectively). Chloroform stabilized with ethanol was chosen as mobile phase at a flow rate of 1 mL/min. The samples were dissolved in chloroform giving a final concentration of 1.5 mg/mL, with 0.2 $\mu\text{L}/\text{mL}$ hexylbenzene as internal standard. MW was calculated using twelve polystyrene

calibration standards (376 - 2,570,000 g/mol). Column temperature was set to 30 $^{\circ}\text{C}$.

3 Results and Discussion

The degradation behaviour in respect to mass loss can be found in Figure 1. Notably, a distinct difference between the two polymer combinations investigated in this work can be observed. Whereas the PCL/PDO system temporarily stabilizes at around 12% mass loss after 14 days under the described degradation conditions, the investigated PLGA/PDO composite nonwoven showed a considerably higher mass loss of $\sim 80\%$ in the same time range.

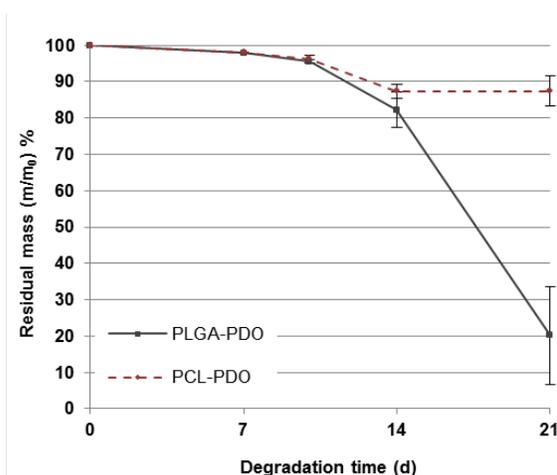


Figure 1: Mass loss during accelerated degradation of PLGA/PDO (grey) and PCL/PDO (red/dashed) composite nonwovens in glycine buffer at pH = 8.7 and 50 $^{\circ}\text{C}$ (n = 3)

However, the observed mass loss of PLGA/PDO composite nonwoven was significantly higher than expected based on data from pure PDO and PLGA film material. This can be explained on the different surface-area-to-volume ratio of bulk materials compared to fibrous structures. Since degradation of these materials is based on hydrolysis of the ester groups, a larger surface promotes the diffusion of water soluble molecular fragments at late stages of degradation [8] and may decrease mechanical resilience. In accordance to this, the PLGA/PDO nonwoven showed strong disintegration, leading to an increase in the observed mass loss due to the fact that fragments of the material may have been lost during media changes. To visualize this effect, macro images at the different degradation stages were taken (Figure 2).

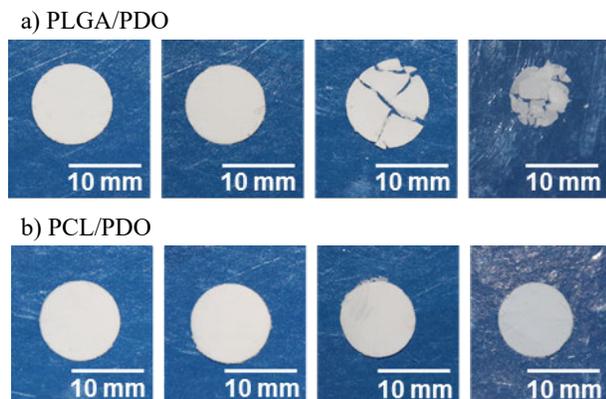


Figure 2: Macro photography of the nonwovens at different degradation time points (from left to right: 7, 10, 14 and 21 days). The scale bar represents 10 mm.

For a more detailed insight on the underlying chemical processes during the degradation, the nonwoven samples were further analysed *via* GPC to determine the loss in molecular weight. As it can be seen in Figure 3, both composite materials show a similar behavior regarding degradation of the polymer chains in a time range of 0 – 14 days. This, however, is in strong contrast to the results of the total mass lost experiment. We assume that this contradiction is based on a more pronounced macroscopic cleavage of the nonwoven fibers for the PLGA/PDO nonwoven compared to the PCL/PDO system. However, this observation has to be addressed more in detail in the on-going work.

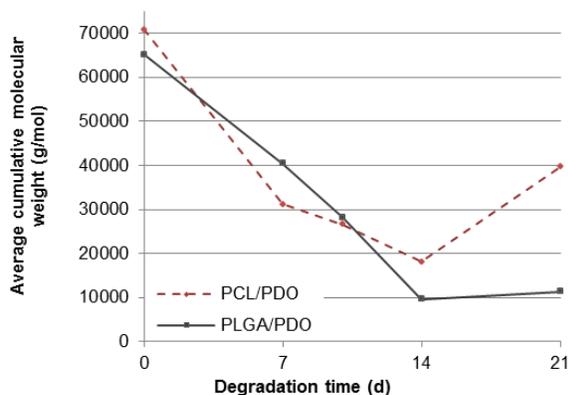


Figure 3: Cumulative molecular weight loss during accelerated degradation of PLGA/PDO (grey) and PCL/PDO (red/dashed) composite nonwoven in glycine buffer at pH = 8.7 and 50 °C (n = 2 with 3 repetitive measurements each)

Regarding the last data point, the GPC measurements showed an increase in MW for both composite materials at

21 days. This observation can be explained by the composition of the materials. The nonwovens consist of two fiber types from two distinct polymers which exhibit different degradation behaviors, whereas one polymer degrades more slowly compared to the other. This leads to the formation of two overlapping signals in the chromatogram, causing a distortion on the outcome of the MW determination. A representative image of such a chromatogram is shown in Figure 4.

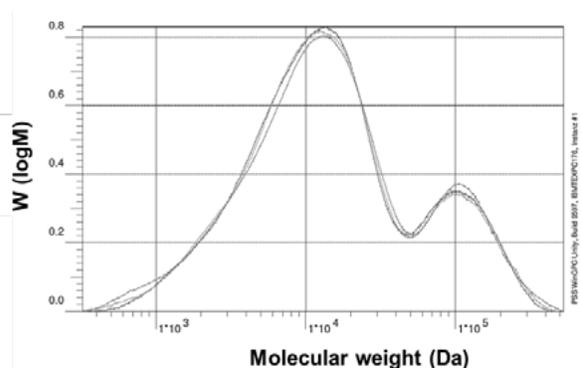


Figure 4: Overlapping gel permeation chromatograms for PCL/PDO composite nonwoven after accelerated degradation for 21 d. The image shows the results for all three repetitive measurements for one sample.

4 Conclusion

The combination of two different polymers to form a composite nonwoven *via* dual co-electrospinning is a promising way to generate matrices for GTR. Our initial experiments showed that the choice of the combined polymers crucially alters the degradation behavior of such nonwovens. Although the molecular mass loss is comparable, PLGA/PDO showed a distinctly higher degree of fragmentation and total mass loss compared to a PCL/PDO composite.

Follow-up work of our group will focus more on these effects, e.g. by SEM imaging of the degrading samples to investigate changes in fiber morphology, which may be responsible for the observed differences in behaviour. Furthermore, cell seeding experiments will be conducted to evaluate the suitability of polyester nonwoven composites for possible *in vivo* applications.

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