ACETAL MOIETIES AS BIODEGRADABLE FUNCTIONALITY IN PHOTOPOLYMERS FOR BONE REGENERATION

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INTRODUCTION

The most critical and costly problems in human health care is the loss or failure of an organ or tissue. Currently, the loss of an organ or tissue is treated by transplant autografts (originating from patient) or from one individual into another (allografts). This is an imperfect solution, because transplantation is limited by a critical donor shortage. Due to that the discipline of tissue engineering (TE) in life science has emerged over the last two decades. It allows to restore, maintain or improve the function of lost, damaged or diseased tissue. It is applicable for a wide range of injuries and diseases ranging from cardiovascular, skin and bone diseases. Attention lies on the biocompatibility and biodegradability of scaffolds. The scaffold completely takes over the mechanical function of the organ. In the meantime the tissue regenerates, the scaffold degrades and gives way to the new formed tissue (Figure 1). Since individual implants are necessary for each patient, the technology of additive manufacturing (AMT) was established in TE (Figure 2). This technology enables the production of complex geometries with defined porosity.[3] These properties are important for the above mentioned requirements of Tissue Engineering.

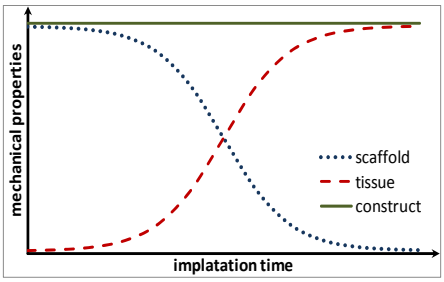

Figure 1: Ideal mechanical behaviour of the manufactured scaffold during the time of degradation and the regeneration of natural tissue.[1]

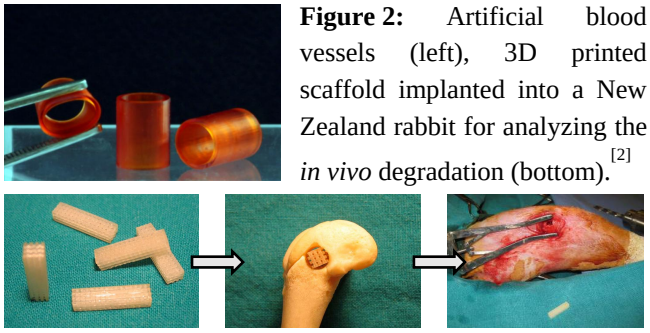

Figure 2: Artificial blood vessels (left), 3D printed scaffold implanted into a New Zealand rabbit for analyzing the *in vivo* degradation (bottom).[2]

FUNDAMENTAL OF THE PROBLEM

In this work, new bone replacement materials are developed. During bone regeneration, cells, the so called osteoclasts, degrade the bone at a pH value of about 4.5 and other cells, the osteoblasts build up new tissue.[4] The standard materials for bone replacement are polyesters, however, degrade quite slow under acidic conditions. Therefore, fast degradation should be ensured by incorporation of acetals into the polymer backbone. Acetals have the property of being stable under neutral and basic conditions but degrade fast under acidic pH value.[5]

MATERIALS AND METHODS

Acetals were synthesized by conversion of an aldehyde or ketone, e.g., terephthalaldehyde, with an alcohol, e.g., 2-hydroxyethylmethacrylate (HEMA). This way, acetal moieties were also provided with photopolymerizable groups. Methacrylates were chosen as reactive groups. Compared to acrylates, they are less toxic and have sufficient reactivity to be used in photopolymer based AMTs. The molecular structures were approved by NMR spectroscopy. In order to investigate the reactivity of the synthesized monomers, photo-DSC measurements are conducted. In addition, photorheology coupled with real-time IR measurement was chosen to determine parameters relevant for 3D printing applications. Furthermore, the degradability of photopolymerized methacrylates was tested *in vitro* at a pH typical for the osteoclasts microenvironment. Therefore, the samples were placed into an aqueous HCl (pH of 4.5) and were weighed after certain intervals.

RESULTS AND DISCUSSION

In the course of this work, monomers with acetals as cleavable moieties were be prepared in good yields with sufficient purity. These monomers were tested for their reactivity and show values expected for this class of monomers. The degradation characteristics of according polymers is promising. In Figure 3, the sample mass during degradation of the crosslinked acetal based on glycerol monomethacrylate and terephthalaldehyde (T5MA) is shown. There, a steep increase of the mass in the initial phase can be seen. It is assumed that this is the result of spontaneous swelling. The continuous mass increase in the second phase is expected to be caused by water uptake into the network owing the decreased network density as a consequence of acetal cleavage. In the third phase, elution of small molecules out of the polymer network overcompensates the mass increase by swelling and a mass decrease is finally observable.

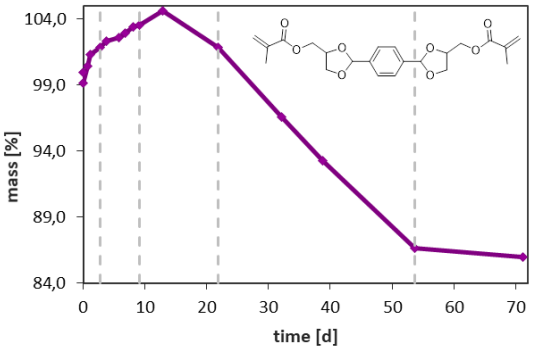

Figure 3: Degradation of T5MA under acidic pH

CONCLUSION

The synthesis of monomers with acetals as cleavable moieties was successful. Methacrylate as functional group has shown a good reactivity as investigated by Photo-DSC and real-time infrared photorheology measurements. The *in vitro* degradability tests have shown a swelling followed by a mass-erosion of photopolymerized networks. These results proof the applicability of acetals as degradability motifs in polymer networks. In addition to methacrylates as model class of photopolymerizable monomers, biocompatible vinyl esters and vinyl carbamates will be considered in future.

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