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Hydrolytic and enzymatic degradation of flexible polymer networks comprising fatty acid derivatives

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ABSTRACT

In this study a degradation process of flexible polymer networks fabricated from telechelic macromonomers comprising methacrylic functionalities and dimer fatty acid derivatives were discussed. Hydrolytic degradation in simulated body fluid (SBF) as well as enzymatic degradation with a lipase of six different systems comprising ester, anhydride and urethane bonds was investigated. In parallel, in order to make a comparison with other analogous polymeric systems, reference materials were also considered. The degradation process was monitored by determining the weight loss and water uptake, FT-IR analysis and changes in pH of degradation medium as a function of time. A rapid progress of degradation of the network containing anhydride bonds was observed. Furthermore, polymer networks showed low water absorption from 10 to 2 wt.%. Polymer networks did not release acidic degradation products in an amount that causes acidification of the medium except the anhydride network. The IR analysis of characteristic bands showed degradation of specific bonds leading to formation of possible hydrolysis products of these networks such as poly(methacrylic acid), macromonomer precursor molecules and derivatives of the macromonomers having terminal carboxylic and hydroxyl groups. We demonstrated that the referred polymeric networks undergo a controlled gradual degradation in the presence of lipase. This study provides an example of how the susceptibility of cross-linked polymers to degradation can be tailored by varying their molecular structure, depending on the needs.

1. Introduction

Sustainable and balanced development involve, in the largest number of areas of human activity, the replacement of petrochemical raw materials by using materials from renewable resources [1–3]. The group of renewable materials includes fatty acids, in the form of triglycerides which are a component of oils present in the seeds of plants such as canola, corn, soybeans, flax, sunflower [4]. Fatty acids and their derivatives are often used for the preparation of polymeric bio-based materials. The industrial applications of fatty acids include binders and film-forming agents in coatings and paints, hydraulic fluids, lubricants, inks, rubbers [5–9]. Due to the natural origin and the associated biocompatibility potential fatty acids are also used in materials contacting with living tissue. The latest scientific literature abounds with reports on biomaterials containing derivatives of fatty acids [10–13]. Effects of the introduction of fatty acids in the structure of (bio)materials include: increasing the hydrophobicity [14], improving the flexibility and elastic recovery after deformation [15,16], lowering the glass transition temperature and melting point, as well as reducing the degree of crystallinity [17–19], or improving the resistance to oxidative degradation and heat resistance (stability strongly depends on the degree of unsaturation) [20–22].

One very important aspect of using biomaterials for *in vivo* applications is that they should persist in a robust state long enough to allow the formation of new tissue or to serve as an artificial lifelong replacement. In both cases, as well as for its successful implementation in applications such as tissue engineering scaffolds, hydrolytic degradation is of crucial importance [23]. There are three types of polymer chain breakdown, that lead to molecular mass reduction. These include the processes of destruction, depolymerization and degradation. In the process of destruction low molecular weight products other than the monomer are released. It can be caused by physical factors such as heat, high energy radiation or chemicals. Depolymerization in contrary to the polymerization, leads to thermal decomposition of macromolecules [24,25].

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Degradation is in turn the process of disintegration of the polymer chain into shorter oligomeric units under different physical agents (radiation, heat, stress), or chemicals.

Aliphatic polyesters such as PLA, PLGA copolymers [26], PCL are widely known and used in tissue engineering. A lot of efforts have been done to investigate this group of polymers. FDA approval has been granted to various medical devices made of these polyesters [27]. Nevertheless, applications of these crystalline polyesters might be limited due to relatively slow degradation and resorption, as compared with other aliphatic polyesters [28]. Therefore, a large number of research contributed to the exploration and synthesis of new materials able to comprise an artificial substitute in tissue engineering has been performed [29–33]. A significant step forward in the field of aliphatic polyesters for medical application has been done creating copolymers of commercial polyesters with materials from biocompatible renewable resources such as fatty acids [34,35]. Introducing fatty acid moieties influences the degradation profile of such multiblock copolymers. The changes are associated with specific molecular structure. Hydrolysis of ester bonds in such copolymers causes fas less acidification of the environment as compared to other polyesters. This effect is associated with the lower concentration of ester bonds in the polymeric chain [36]. In this aspect great attention is paid to cross-linked polymers, especially photopolymerizable systems [37,38]. Recently, we developed telechelic macromonomers with α,ω-dihydroxy, α,ω-dicarboxy or α,ω-diamine functionalities and used such "cores" to build up different structures *via* simple organic chemistry [39]. Our primary goal was to obtain unique photocurable macromonomers with fatty acid derivatives, that are able to form flexible polymer networks with potential in soft tissue engineering.

In this paper, we present a hydrolytic and enzymatic degradation study of polymer networks fabricated from telechelic macromonomers. The networks under consideration contain one or more moieties from among anhydride, ester and urethane groups. All of these groups may undergo hydrolytic degradation, and the mechanisms of this process is shown in Fig. 1.

The degradation process was monitored by determining the weight loss and water uptake, FT-IR analysis and changes in medium pH as a function of degradation time.

2. Experimental

2.1. Materials and methods

A series of 9 materials: six telechelic macromonomers containing fatty acid moieties, one telechelic macromonomer synthesized without fatty acid derivatives, namely from poly[(di(ethylene glycol) adipate] containing urethane groups (PDEGA-UR), and 2 commercially available reference materials – poly(caprolactone) (PCL), PURASORB® PC12 (Purac Biomaterials, Gorinchem, the Netherlands), M_n = 124 kDa and poly(D,L-lactide-glycolide) 50:50, Resomer® RG 509 S (Evonik Industries AG, Essen, Germany), were used for degradation studies. Six telechelic macromonomers were prepared according to procedure described in Ref. [39]. The structural formulae of macromonomers comprising ester, anhydride and urethane bonds is shown in Fig. 2.

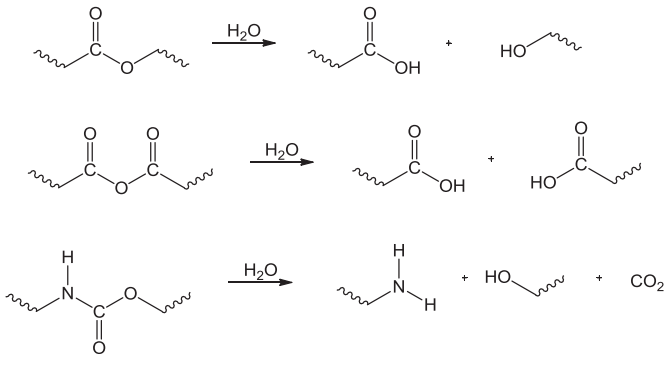

Fig. 1. Simplified hydrolytic degradation mechanisms of: ester, anhydride and urethane bonds.

The dimerized fatty acid fragment was marked as grey dot. Possible structures of the fatty acid compound are illustrated in Fig. 3.

Each macromonomer was terminated with reactive methacrylic groups. The molecular masses as well as dispersity index of the macromonomers were determined by GPC as reported in Ref. [39], and are given in Table 1.

The cross-linked polymers were prepared according to the following procedure. The solution of photoinitiator, Irgacure 819 (BASF, Ludwigshafen, Germany) in methylene chloride was added to the appropriate amount of macromonomer in order to achieve a desired macromonomer:photoinitiator weight ratio. Unless otherwise stated, the ratio was 50:1. After dissolution of the macromonomer, the viscous solution was poured into a Petri dish, and then methylene chloride was evaporated under reduced pressure. Then, the composition was irradiated with UV light with a narrow spectral range and maximum intensity at the wavelength λ_{max} of 365 nm in an air atmosphere. A flashlight Labino® UVG2 was used as a light source. The intensity of the radiation was controlled with the help of radiometer AktiPrint (Technigraf GmbH) and was 20 mW/cm^2. The exposure time was 200 s.

2.2. Estimation of the cross-linking density

Two methods were used to estimate the cross-linking density of the polymer networks from telechelic macromonomers, namely gel fraction measurement and differential photo-calorimetry (DPC). Gel fraction was measured in dichloromethane which was found to be great solvent for the macromonomers. The cross-linked samples were refluxed for 1 h. After that the samples were dried under vacuum to constant mass. The gel fraction G_F was calculated as the ratio of mass after drying to initial mass of the samples.

DPC measurements were performed on Q100 differential calorimeter (TA Instruments) equipped with UV Omnicure 2000 module. The macromonomer was polymerized in air and the content of initiator (Irgacure 819) was 2 wt. %. The degree of conversion C was calculated from the formula:

$$C = \frac{M \cdot \Delta H}{\Delta H_p \cdot n} \quad (1)$$

where M is the molecular weight of the macromonomer, ΔH is the enthalpy of reaction, ΔH_p is the standard enthalpy of methacrylate polymerization equal to 58.6 kJ/mol [40] and n is the number of reactive groups per molecule.

2.3. Degradation of polymer networks

In order to investigate stability of the obtained polymer networks, hydrolytic and enzymatic degradation has been performed. Hydrolytic degradation was carried out for all prepared materials, and for enzymatic degradation two cross-linked polymers, namely P1838-DMA and P1838-UR, were selected. The degradation process was carried out in polystyrene microplates. The polymer discs used in this study were cut using manual die cutter from polymer films cross-linked as described above. They were of 6 mm in diameter and weighted 15–20 mg. Each disc was immersed in 2 cm^3 of the