



Study on the hydrolytic degradation of glycolide/trimethylene carbonate copolymers having different microstructure and composition

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ABSTRACT

Hydrolytic degradation of a series of copolymers synthesized by ring opening polymerization of trimethylene carbonate and glycolide was studied by following the weight loss and changes in molecular weight, polydispersity index and mechanical properties. Analyses of ¹H NMR and FTIR spectra taken during exposure to a pH 7.4 phosphate buffered solution were also performed. Copolymers with different microstructures (i.e. random, triblock and segmented copolymers) were synthesized. Most segmented copolymers studied had identical trimethylene carbonate content but differed in the hard segment content. Composition was also varied to demonstrate the influence of the soft segment composition.

Results were consistent with a model where degradation started in the amorphous phases and affected the glycolide units of the less compact soft segments and the regions within lamellar stacks. This degradation step led to a clear decrease of GGG triads (NMR data) and amorphous glycolide content (FTIR data), as well as an increase in Young's modulus. Degradation subsequently proceeded through the crystalline glycolide units belonging to lamellar stacks. The molecular weight of the degraded samples reached always an asymptotic value that corresponded to a solubility limit for fragments with high TMC content and for highly crystalline entities constituted by glycolide rich fragments.

Results pointed to the importance of the hard segment content and the composition of the soft segment, which logically influenced the distribution between amorphous and crystalline phases.

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1. Introduction

Much effort is currently focused on developing polymers for special purposes in the biomedical field. Polymers used as biomaterials must meet strict requirements depending on the intended use, and so an enhancement of properties is necessary to broaden their application range. Modification via copolymerization is typically considered as an appropriate strategy to provide materials with extended mechanical and degradation properties. Glycolide and its copolymers with different lactones and/or cyclic carbonates are widely employed as surgical sutures, implants, scaffolds for tissue engineering or controlled drug delivery systems due to their biodegradability, biocompatibility and physical properties [1–9]. In particular, the copolymerization of glycolide (GL) and trimethylene carbonate (TMC) is interesting since it may provide materials with the requirements for the above applications. In this sense, the stiffness characteristic of high modulus polymers like polyglycolide or polylactide can be modified by imparting flexibility into the chains

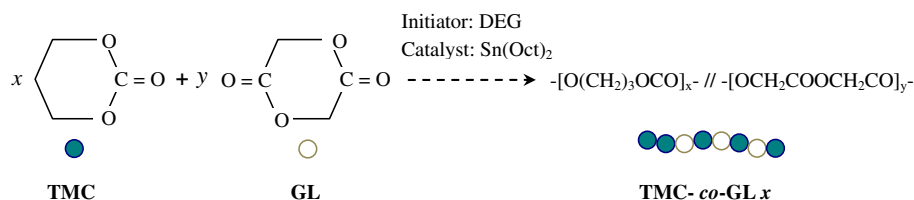
with the incorporation of monomer units of typical low T_g polymers like polytrimethylene carbonate, which is considered as an ideal softening component for brittle and biocompatible polymers [10,11].

Much research has been done on the synthesis and analysis of GL/TMC copolymers [12–14] and even of more complex systems based on three (e.g. GL, TMC, caprolactone (CL)) [15–17] or four (e.g. GL, TMC, CL and lactide (LA)) monomers [18–20]. Our recent studies have focused on the influence of microstructure (i.e. random, blocky or segmented) on thermal properties, crystallinity and crystallization processes of the GL/TMC bicomponent system [21]. Specifically, segmented copolymers composed of two polyglycolide hard segments and a middle soft segment with a statistical distribution of both monomers (Fig. 1) merited special attention because of their application as commercial surgical sutures. It was concluded that the amorphous phase of this kind of copolymers show complete miscibility between both constitutive segments, and that only the semicrystalline polyglycolide end blocks are involved in the crystallization process. This is highly significant as the crystallization behavior of block copolymers has a strong influence on their mechanical performance and degradability [22], which are determining factors in biomedical applications.

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1st Polymerization step: Synthesis of the middle soft segment (TMC-co-GL_x)



2nd Polymerization step: Incorporation of polyglycolide hard segments

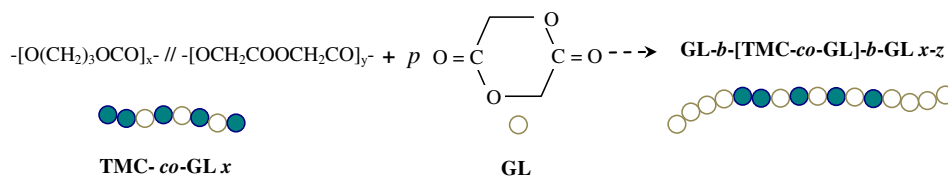


Fig. 1. Scheme of the synthesis of GL-*b*-[TMC-co-GL]-*b*-GL_{*x-z*} copolymers. The first step makes it possible to obtain a middle segment with different percentages of the two monomers (*x* refers to the TMC wt-%) while the second corresponds to the incorporation of polyglycolide hard segments.

A considerable body of literature on degradation of commercial biomaterials constituted by glycolide and trimethylene carbonate units is available [23–29]. Specifically, hydrolytic degradation studies [28] on Maxon™ (a segmented copolymer with a 32.5 wt-% content of TMC) monofilament sutures point to a two-stage bulk degradation process. The first stage mainly corresponded to the degradation of amorphous zones constituted by soft segments, resulting in slightly increased crystallinity. The second involved hydrolysis of the more crystalline hard segments, with the corresponding decrease in the glycolide content.

In this work, microstructural changes occurring during hydrolytic degradation of random, segmented and blocky copolymers of glycolide and trimethylene carbonate having a TMC wt-% close to 32.5% (like Maxon™) are mainly investigated by NMR and IR spectroscopic techniques. This analysis is extended to a segmented copolymer having a different composition (i.e. 23 wt-% of TMC) and a microstructure characterized by long polyglycolide hard segments. Results are correlated with typical *in vitro* measurements of weight loss and changes in molecular weight and tensile properties.

2. Experimental section

2.1. Materials

Monomers (glycolide and trimethylene carbonate), initiator (diethylene glycol, DEG), and catalyst (Sn(Oct)₂) were purchased from Boehringer Ingelheim, Panreac and Sigma–Aldrich, respectively. All reagents and solvents (from Sigma–Aldrich) were used as received without further purification.

2.2. Synthesis of copolymers

All polymerization steps were performed under a nitrogen atmosphere in a stainless steel jacketed batch reactor with a capacity of 250 mL at 0.2 MPa and at temperatures ranging between 180 and 220 °C.

Synthesis of segmented copolymers was performed according to a two-step polymerization strategy (Fig. 1). Middle soft segments with a theoretically random distribution were first synthesized from the appropriate monomer mixture. Two hard segments were subsequently incorporated into the soft segment previously prepared by addition of the appropriate ratio of glycolide. Triblock

copolymers were obtained when a soft segment constituted only by trimethylene carbonate was employed. Random copolymers corresponded to those attained after the first polymerization step.

All copolymers are hereafter named as GL-*b*-[TMC-co-GL]-*b*-GL_{*x-z*}, where *x* and *z* denote the theoretical TMC weight percentage in the soft segment and in the final product, respectively. According to this notation, *x* = 100 corresponds to a triblock copolymer, whereas random copolymers are particular cases where *x* = *z*. Synthesis, characterization and evaluation of the basic properties of these samples were previously performed [21]. The theoretical weight percentage of hard polyglycolide segments (*HS*) can be easily determined from the *x* and *z* values, as summarized in Table 1, together with other relevant data (sequence analysis, molecular weight and polydispersity index) of the as-synthesized samples used in this work. Table 1 shows also that the experimental TMC weight percentages are in full agreement with the theoretical values (denoted by *z* in the abbreviated polymer nomenclature).

2.3. Sample preparation for degradation studies

Films of all samples were produced by compression molding of 0.5 g of the as-synthesized copolymers at temperatures between 160 °C and 220 °C, according to their corresponding melting temperatures, and using a pressure of 5 bar for 5 min. The samples were then slowly cooled at controlled rates of 4 °C/min, well below their melt crystallization temperatures to obtain semicrystalline specimens. The molded films were finally cut into parallelepiped samples (20 × 5 × 0.2 mm³) and immersed in the degradation medium.

2.4. Hydrolytic degradation

In vitro hydrolytic degradation assays were carried out in a phosphate buffer (pH 7.4) at 37 °C. Samples were kept under orbital shaking in bottles filled with 50 mL of the degradation medium and sodium azide (0.03 wt-%) to prevent microbial growth for selected exposure times. The samples were then thoroughly rinsed with distilled water, dried to constant weight under vacuum and stored over P₄O₁₀ before analysis. Weight retention, molecular weight, changes in NMR and IR spectra as well as calorimetric and tensile properties were then evaluated. Degradation studies were

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