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A non-linear viscoelastic model to describe the mechanical behavior's evolution of biodegradable polymers during hydrolytic degradation

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ABSTRACT

The biodegradable triblock copolymer PLA-*b*-PEG-*b*-PLA presents, in its initial state, a non-linear viscoelastic behavior. Its mechanical properties evolves during the *in vitro* degradation process. Tensile and relaxation tests are performed at 2%, 4% and 6% of load strain for different degradation steps. In order to describe the behavior of the polymer during degradation, an adaptive quasi-linear viscoelastic model is considered. In a first step, the model calibrated on the non-degraded state, perfectly fits the load and relaxation curves for every strain. Then, based on considerations about the preservation of the normalized relaxation curves over degradation time, the adaptive quasi-linear viscoelastic model is adapted to degradation. A degradation parameter that drives the mechanical degradation kinetics is deduced for every tested degradation states. A physically motivated model is finally used to describe the degradation parameter at every degradation step. The whole constitutive model is very accurate to fit the mechanical curves at every strain during degradation.

1. Introduction

Due to its large range of mechanical properties and degradation times, the biodegradable and biocompatible tribloc copolymer PLA-*b*-PEG-*b*-PLA is an excellent candidate for tissue engineering applications [1]. In this case, the polymer is used to be a physical temporary support for the tissular reconstruction called “scaffold”. The objective of this scaffold is to be a substitute to injured tissues during healing and to provide a three dimensional environment for tissue reconstruction. Moreover, in many cases, the scaffold has to temporarily replace the functions of the tissues, especially the mechanical support. Thus, it is necessary to have a detailed knowledge of the initial mechanical properties and their evolution due to degradation. Therefore, in order to design a polymeric architecture for scaffolds, the development of mechanical constitutive equations that are able to model the initial mechanical properties and that take into account the degradation is essential.

In their initial state, the PLA-based biodegradable materials can present some complex non-linear behaviors, especially non-linear viscoelasticity [2]. In order to model these properties, a large class of non-linear viscoelastic models used to describe the mechanical properties of polymeric biomaterials and living tissues is based on single integral models. These models are extensions of the linear viscoelastic model [3]. Pipkin and Rogers [4] developed a single integral model that can take into account the dependence on strain of stress relaxation modulus. By considering that strain and time variables can be separated, Fung [5] simplified the Pipkin and Rogers model. In his model, the strain of the linear single integral model is replaced by a non-linear function of strain called “instantaneous elastic response”. Nevertheless, the model does not take into account the strain dependence of the time-related response and can be difficult to calibrate [6]. In order to overcome these problems, Nekouzadeh et al. [7] developed an alternative approach called “adaptive quasi-linear viscoelastic” model that allows to simplify calibration and considers the strain non-linearity of the viscoelastic part.

The properties of PLA-based polymers are changing in use due to degradation. Their main degradation mechanism is the hydrolysis of ester links that breaks the polymeric bonds. It means that, in an

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aqueous media, a decrease of number average molecular weight, a mass loss and a material erosion can be observed [8]. Another important macroscopic effect of polymeric bonds cut is the lost of mechanical properties. Many studies show that Young's modulus and tensile strength decrease after a variably long latency period [9–11]. Thus, to predict the evolution of the mechanical properties of scaffolds, the constitutive equation must include hydrolytic damage. Two types of methods can be distinguished to model mechanical properties degradation. The first one consists in modelling the evolution of mechanical parameters such as Young's modulus or tensile strength by a micro-mechanical approach. The entropy spring theory [12] or the molecular dynamic approach [13] are used to model the Young's modulus evolution. By considering scissions as cavities in the polymeric matrix, Samami and Pan [14] modelled the polymer as a continuum solid containing randomly distributed cavities. Then, using existing theories for porous solids, they deduced a constitutive equation that predicts the evolution of Young's modulus and tensile strength. The second method consists in adapting classical hyperelastic [15], viscoelastic models [16] or viscoplastic model [17] to degradation by assuming that the model constitutive material parameters are dependent of a degradable variable [2]. These models are only calibrated on simple uniaxial load tensile tests. Breche et al. [18] performed uniaxial load-relaxation tests and shew that the normalized relaxation function can be considered as an invariant of the degradation. Thus, in the linear viscoelasticity formalism, they expressed the degradation variable as a function of a proportionality coefficient between the curves at different steps of degradation. Their model permits to describe the mechanical behavior for small deformation i.e. until 2%.

The objective of this paper is to establish a mechanical constitutive equation that is able to fit the PLA-*b*-PEG-*b*-PLA uniaxial behavior upon a strain of 2%. To achieve this, a non-linear viscoelastic adaptive quasi-linear viscoelastic (AQLV) model that takes into account the hydrolytic degradation is developed. First, after presenting materials and methods, experimental results of load-relaxation tests on PLA-*b*-PEG-*b*-PLA samples are presented. In a second part, the formalism of the AQLV model is introduced. Then, the calibration and the efficiency of the model to fit the experimental data are presented for the non-degraded material. In a last part, the AQLV model is adapted to take into account the hydrolytic degradation by a hydrolytic damage variable. The ability of this model to fit degraded experimental data is finally discussed.

2. Materials and methods

2.1. Material

The material used in this study is the same as the one used in a previous study [18]. The details about the elaboration of the material are related here. Poly(ethylene glycol) (average Mn 20 000 g/mol), tin(II) 2-ethylhexanoate (Sn(Oct)2, 95%), dichloromethane (DCM), diethyl ether and tetrahydrofuran (THF) were purchased from Sigma-Aldrich (St-Quentin Fallavier, France). D,L-lactide (D,L-LA) was purchased from Purac (Lyon, France).

PLA50-b-PEG-b-PLA50 triblock copolymer was synthesized following a procedure previously described by Leroy et al. [11]. Typically, predetermined amounts of D,L-LA and PEG were introduced in a flask. Sn(Oct)2 (0.1 M % with respect to LA units) was then added. After degassing, the flask was sealed under vacuum and polymerization was allowed to proceed at 110 °C. After 5 days, the copolymer was recovered by dissolution in DCM and precipitation in cold diethyl ether. Finally, the product was dried under reduced pressure to constant mass. The copolymer was obtained with a yield of 90%. Polymerization degree of each PLA block and molecular weight of the synthesized triblock copolymers were calculated using the following equations:

$$DP_{PLA}(\%) = \frac{1}{2} \times \frac{DP_{PEG}}{\frac{EG}{LA}} \quad (1)$$

$$M_{ntribloc}(\%) = 2 \times (DP_{PLA} \times 72) + M_{nPEG} \quad (2)$$

with EG/LA being the ratio of ethylene oxide and lactyl units calculated from Ref. ^{1} H NMR spectra. The polymer films have been manufactured by solvent evaporation. A predefined quantity of polymer was solubilized in acetone, spread in a small dish and placed during 36 h under an extractor hood for evaporation. Final solvent removal was obtained by further drying in *vacuo* under 1.10^{-3} mBar for 3 days. A 0.5 mm thick film was then obtained.

2.2. Methods for mechanical tests

Dogbone tensile specimens were cut in 0.5 mm thick films with a specific punch of 14 mm in length and 2 mm wide gauge length. They were then placed in 20 ml test tubes and submitted to two times of degradation, 1 and 3 weeks, in phosphate buffer solution (PBS) at 37°C within an agitator/incubator. The mechanical tests were realized in an aqueous media at a controlled temperature of 37°C via a steel hermetic bath adjustable on the mechanical test machine in order to be in conditions as closed as possible to *in vivo* ones.

Uniaxial tensile tests on dogbone specimens at three different strain levels (2%, 4% and 6%) with a strain rate during loading of 1% per second followed by a tensile relaxation test are performed. The latter were performed with a Gabo Eplexor mechanical test machine with a load cell of 10 N at 0, 1 and 3 weeks of degradation. The

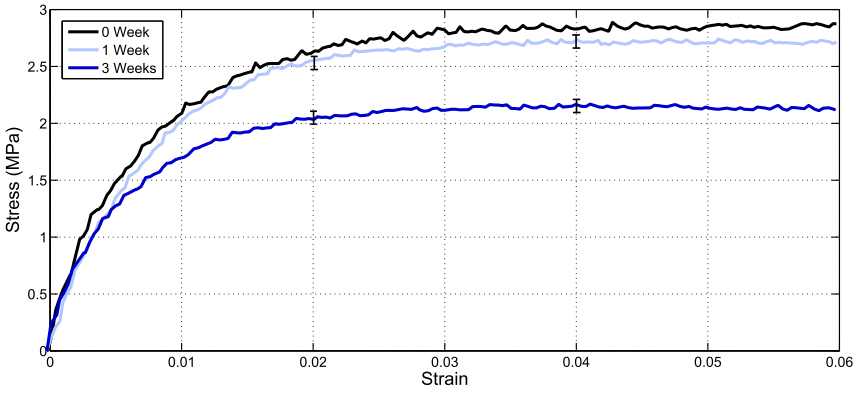

Fig. 1. Experimental load curves at 6% strain load at 0, 1, and 3 weeks of degradation.