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Forensic engineering of advanced polymeric materials – Part II: The effect of the solvent-free non-woven fabrics formation method on the release rate of lactic and glycolic acids from the tin-free poly(lactide-*co*-glycolide) nonwovens

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ABSTRACT

We report the forensic engineering study on the non-woven fabrics made from poly(lactide-*co*-glycolide), PLGA, with low toxicity. The comprehensive degradation investigations were conducted under abiotic conditions. The extent of degradation was monitored by weight loss, composition and molar mass changes of the copolymer and by macro- and microscopic observations of the sample surfaces. The structure of the degradation products was evaluated at the molecular level by electrospray ionization mass spectrometry and high-performance liquid chromatography analysis. The degradation process takes place predominantly by the bulk erosion mechanism and rate of release of lactic and glycolic acids from the non-woven fabrics is dependent on their formation method. Described solvent-free formation method of nonwovens from the tin-free PLGA results in biomaterials with higher biocompatibility, what is particularly important for their applications. Moreover, the continuous release of lactic and glycolic acids from the PLGA biomaterials studied allows their gradual removal *via* biochemical processes and prevents local acidification of the body.

1. Introduction

Forensic engineering of advanced polymeric materials (FEAPM) deals with the evaluation and understanding of the relationships between their structure, properties and behavior before, during and after practical applications. It is of particular importance in the case of nano materials and their nano-safety, biodegradable polymeric materials as well as nanocomposites. Classical forensic engineering is considered to be the investigation of materials, products, structures or components that fail or do not function as intended [1]. Despite of the fact, that such information are needed, there are also opinions indicating the need to detect problems before they arise [2,3]. Therefore, both the *ex-ante* investigations as well as the *ex-post* studies are needed in the area of FEAPM in order to increase efficiency and to define and minimize the potential failure of novel polymer products before and after specific applications. In the studies on forensic engineering of biodegradable polymeric materials (FEBPM) testing in simulated environments is needed before they are rolled out. Due to the wide spectrum of their potential applications e.g.,: in medicine, in the field of compostable polymer packages (especially of long-shelf life products such as cosmetics or household chemicals), as well as in agrichemical formulations, the FEBPM can provide basic knowledge and a valuable service by increasing understanding and helping prevent future problems. Such novel approach may help to design

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novel polymeric materials and to avoid the failures of medical devices.

Among the commercially available aliphatic polyesters most attention for medical applications is focused on poly(α-hydroxyacids) derived from lactic and glycolic acids as well as their copolymers. Many practical applications of these materials in medicine arise from their degradability by simple hydrolysis of the ester backbone in aqueous environments such as body fluids, to products that are ultimately metabolized *in vivo* to the non-toxic components carbon dioxide and water [4]. Devices prepared from poly(α-hydroxyacids) can be divided into three major categories: wound closure in the form of sutures, surgical clips, surgical staples and adhesives; tissue repair and regeneration (scaffold) and drug delivery [5]. Among the bioresorbable and biocompatible aliphatic copolyesters, poly(lactide-*co*-glycolide) with various lactide/glycolide ratios has been used in drug delivery systems, wound dressings, sutures, orthopedic devices and guided tissue engineering (membrane or scaffolds). The incorporation of glycolide monomer units into the polylactide chain enhances the hydrophilicity of the material and, therefore, results in faster degradation of the copolymer sample [6–12]. Additionally, biocompatible PGA, PLA and their copolymer, PLGA have gained FDA (US Food and Drug Administration) approval for clinical use [13]. Poly(lactide-*co*-glycolide) is in a glassy state during degradation process because its glass-transition temperature (T_g) is above 37 °C, which accounts for its low water absorption and slow drug release [14]. To modify the biological and mechanical properties of PLGA, composites with carbon fibers and hydroxyapatite were prepared [15–18]. The membranes or nanofibers and the PLGA-based nanocomposities for applications such as scaffolds in cardiac tissue engineering or bone regeneration were obtained using an electrospinning method [19–23].

The synthesis of poly(lactide-*co*-glycolide) with low toxicity, using zirconium acetylacetonate, Zr(Acac)$_4$, was previously reported by some of us [24,25]. Recently, the hydrolytic degradation of electrospun nanofibrous scaffolds prepared from this tin-free PLGA and loaded with bioactive molecules, has been studied [26]. However, most of the electrospinning methods used to date require the use of solvents. Only newly the solvent-free laser melt process, far safer than the conventional electrospinning process, has been reported [27]. However, despite of the electrospinning technology, the electrospun nanofibrous biomaterials are valuable candidates for tissue engineering. On the other hand, the non-woven fabrics are appropriate material for implants in terms of dimensions and consistency. Furthermore, *via* solvent-free methodology it is possible to manufacture biodegradable non-woven fabrics with good wettability without the use of chemicals during the formation process [28]. Additionally, the solvent-free method provides the opportunity to obtain materials with higher biocompatibility.

Herein, we report the FEBPM studies of tin-free PLGA non-woven fabrics degraded under abiotic conditions at 37 °C. The main purpose of this study was to determine the effect of the solvent-free non-woven fabrics formation method on the hydrolytic degradation and release rate of lactic acid (LA) and glycolic acid (GA) from the studied PLGA copolymer.

2. Experimental section

2.1. Materials

The fiber-forming copolymer of L-lactide (Purac) with glycolide (Purac), PLGA was obtained on a large laboratory scale using the low toxicity initiator zirconium(IV) acetylacetonate, Zr(Acac)$_4$ (Aldrich Corp.). The synthesis was conducted in bulk with a molar ratio of initiator to the total amount of the comonomers (I/M) of 1:4000 [24]. Because of the specific mechanism occurring at the initiation stage of the copolymerization [25], no other co-initiators or catalysts were used. Additionally, the application of a zirconium initiator with a relatively high chemical stability allowed for the use of both L-lactide and glycolide without purification. To obtain the maximum yield of the reaction (99%) and minimize the impact of thermal degradation of the product, the synthesis was carried out using two slightly different temperature cycles (first cycle of 36 h at 140 °C and the second cycle of 36 h at 110 °C). Because of the known low toxicity of zirconium compounds and the high efficiency of the copolymerization reaction, technologically cumbersome purification process of obtained PLGA copolymer was eliminated. The total amount of unreacted monomers and the content of zirconium did not exceed 1.2 weight % of the product. PLGA was then melt-spun into multifilament fibers, that were cut into staple fibers and needle punched into non-woven fabrics (denoted as NWMs). Non-woven fabrics were produced by carding process from staple fibers with length 60 mm and linear mass 6.02 dtex. Obtained fleeces were bonded by needle punching method, with needle no. 15 × 18 × 40 × 3 ½ RB. Number of needle punching was 240 cm^{-2}, needle punching depth was 15 mm. Surface mass of obtained non-woven fabric was at the level of 560 g/m^2. Produced non-woven fabric was cut onto 5 parts, each of them additionally bonded using thermal bonding method, with different technological parameters specified in Table 1.

2.2. Abiotic hydrolytic degradation under the laboratory conditions

The polymeric fabrics were incubated in water at 37 °C over a period of 180 days. Two series, each containing five rectangle-shaped samples of approximately 20 mm × 10 mm, were prepared. The samples were inserted into 30-ml screw-capped vials, each containing 25 ml of distilled water, and placed in a laboratory oven at 37 °C. The pH of the solutions before and after the specified incubation period was measured. After 90 and 180 days of incubation the samples were removed from the vials and cleaned by washing in distilled water, drained on blotting paper and then dried to a constant weight under vacuum at a temperature of 30 °C. The progress of materials hydrolysis at 37 °C was estimated by sample weight loss, macro- and microscopic observations of the polymer surfaces and molar masses and composition changes of the samples during the performed experiments. The structure of the water soluble degradation products of the studied samples was determined at molecular level by electrospray ionization mass spectrometry and high performance liquid chromatography (ESI-MS and HPLC-DAD).

2.3. Methods

2.3.1. Weight measurements

The weight of degraded samples was determined using a RADWAG WAS 160/X electronic balance with a precision of 0.1 mg. The

Table 1
Properties and parameters of the PLGA non-woven fabrics thermal bonding process.

Sample name	Process temp. [°C]	Pressing time [s]	Surface mass [g m^{-2}]	Thickness [mm]	Apparent density [kg m^{-3}]
NWM 1	RT	0	560.44	2.85	196.6456
NWM 2	60	120	888.57	1.48	600.3851
NWM 3	60	60	832.44	1.78	467.6629
NWM 4	60	60[a]	894.22	1.70	526.0118
NWM 5	RT	0[b]	532.44	1.63	326.6503

[a] With additional stress of 100 Ba.

[b] Cold rolled at 12 Ba.