Available online at www.sciencedirect.com
ScienceDirect
Polymer Degradation and Stability 93 (2008) 811–817
Polymer Degradation and Stability
www.elsevier.com/locate/polydegstab

Biodegradation of poly(L-lactide-*co*-glycolide) tube stents in bile

Xiaoyi Xu [a,c], Tongjun Liu [b], Kai Zhang [b], Shaohui Liu [b], Zhen Shen [b], Yuxin Li [a], Xiabin Jing [c,*]

[a] *Research Center of Agriculture and Medicine Gene Engineering of Ministry of Education, Institute of Genetics and Cytology, Northeast Normal University, Changchun, Jilin 130024, China*
[b] *Department of General Surgery, First Hospital, Jilin University, Changchun 130021, China*
[c] *State Key Laboratory of Polymer Physics and Chemistry, Changchun Institute of Applied Chemistry, Chinese Academy of Sciences, Changchun 130022, China*

Received 11 November 2007; received in revised form 10 January 2008; accepted 13 January 2008
Available online 31 January 2008

Abstract

The objective of this study was to evaluate degradation behavior and the feasibility of biodegradable polymeric stents in common bile duct (CBD) repair and reconstruction. Various molar ratios of lactide (LA) and glycolide (GA) in poly(L-lactide-*co*-glycolide) (PLGA) were synthesized and processed into a circular tubing of ~10.0 mm outer diameter and a wall thickness of about 2.0 mm. This tubing was cut into 40.0 mm length to form CBD stents. The stents were placed into human bile to determine the degradation behavior in vitro. The morphology, configuration, mass loss, water uptake, molecular weight and composition changes were examined. The PLGA with LA/GA = 71/29 exhibited an acceptable degradation life and was chosen as an in vivo stent material. These PLGA stents were used in common bile duct exploration (CBDE) and primary suturing for rats. Degradation status of the stents was examined and comparison was made between those before and after surgical procedure. The results showed that the polymer stents exhibited the same biomedical functions as T tubes and spontaneously disappeared from CBD in 4–5 weeks. Therefore, the PLGA stents fits the requirements in repair and reconstruction of CBD, to support the duct, guide bile drainage and reduce T-tube-related complications.

Keywords: Bile; Biodegradable stent; Common bile duct; Poly(L-lactide-*co*-glycolide)

1. Introduction

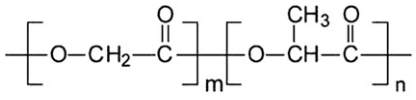
The injuries of common bile duct (CBD) are seen frequently in upper abdominal surgeries, i.e., common bile duct exploration (CBDE), cholecystectomies and hepatic operations. In order to ensure biliary decompression and create a track lined by granulation and fibrous tissue, "T tube" made of silicon rubber has been used in clinical practice since 100 years ago [1,2]. However, the use of T tube also can result in several complications, i.e., biliary leakage, CBD stenoses, and bile peritonitis [3,4]. Various types of new stents were used to reduce such complications, for example, metal, plastic or plastic-coated metal ones [5–8]. But they are usually non-biodegradable and thus have to be withdrawn by a second procedure.

Biodegradable aliphatic polyesters, such as poly(L-lactic acid) (PLLA), poly(glycolide) (PGA) and their copolymer poly(L-lactide-*co*-glycolide) (PLGA, Scheme 1), have been attracting much attention because they have excellent mechanical properties and are hydrolysable and can be used in important biomedical applications approved by FDA, such as surgical sutures, drug carriers, tissue-engineering scaffolds, implants for interior bone fixation and other temporary medical devices [9,10].

Degradation is one of the crucial properties in biomaterials design and selection. In this study, biodegradation behaviors of

* Corresponding author. Tel.: +86 431 85262775; fax: +86 431 85685653.
E-mail address: xbjing@ciac.jl.cn (X. Jing).

0141-3910/$ - see front matter © 2008 Elsevier Ltd. All rights reserved.
doi:10.1016/j.polymdegradstab.2008.01.022



Scheme 1. Structure of PLGA.

PLGA stents were investigated both in vitro and in vivo to explore the usefulness of biodegradable polymeric stents in human CBD repair and reconstruction.

2. Materials and methods

2.1. Materials and synthesis

L-lactide (LA) and glycolide (GA) were purchased from Purac, Holland. Stannous octoate ($Sn(Oct)_2$, 95%) was obtained from Aldrich. PLGA copolymers (with various copolymerization ratios of LA/GA, LA/GA = 88/12, 80/20, 71/29, 60/40, 50/50, respectively) were synthesized by bulk ring-opening copolymerization of LA and GA using $Sn(Oct)_2$ as catalyst.

2.2. Sample preparation

The PLGA was extruded into circular tubing with a Model XSS-300 extruder (screw diameter 20 mm and length-to-diameter ratio 25) at 155 °C. The tubing was cut into CBD stents. They had an outer diameter of 10.0 mm, an inner diameter of 6.0 mm, and a length of 40.0 mm.

2.3. In vitro degradation in bile

PLGA circular tubing stents with various molar ratios were placed in glass bottles filled with 20 ml fresh bile (collected and mixed from the T tube drained clinical patients) and the samples were incubated at 37 °C under oscillation of 70 r min^{-1}. The bile was changed everyday and the samples were withdrawn from the bile every 2 days. They were cleaned with distilled water and dried at room temperature under vacuum to a constant weight.

2.4. Measurements

Degradation of the specimens was monitored by determining morphological and dimensional changes, weight loss, water uptake, molecular weight and LA/GA changes. Morphological changes of surface and cross-section were observed by using scanning electron microscope (SEM, SS-550, Shimadzu) after gold-coating. The weight loss ($\Delta W_{weight\%}$) of the specimen was calculated according to Eq. (1).

$$\Delta W_{weight\%} = 100 \times (W_o - W_t)/W_o \quad (1)$$

where W_o and W_t stood for the specimen's original weight and dry weight after degradation, respectively.

The water absorption (ΔWwater%) was calculated by the following Eq. (2):

$$\Delta W_{water\%} = 100 \times (W_{wet} - W_o)/W_o \quad (2)$$

where W_{wet} meant wet weight of the specimen after degradation.

The molecular weight was evaluated by size exclusion chromatography (SEC). A Waters 410 high pressure liquid chromatograph (HPLC) pump combined with the columns of HT5, HT4 and HT3 in series was used for this purpose. The measurement was carried out at 25 °C using chloroform as a mobile phase at a flow rate of 1.0 ml min^{-1} and polystyrene as a standard. Since PLGA (LA/GA = 50/50) could not be dissolved in chloroform, its molecular weight was not measured.

Compositions of the PLGA samples before and after degradation were determined by ^1H NMR spectrometry using an AV 300M Bruker spectrometer with *d*-chloroform ($CDCl_3$) as solvent at room temperature.

2.5. In vivo test

The copolymer PLGA (LA/GA = 71/29) displayed acceptable duration and degradation behaviors. It was processed into CBD stents by the above method, which had an outer diameter of 0.98 ± 0.04 mm, an inner diameter of 0.66 mm, and a length of 5.50 ± 0.34 mm. The stents were sterilized with ^{60}Co radiation and used for CBD implantation in rats.

Adult male Wistar rats were obtained from Jilin University Research Resources Center. They had free access to rodent diet and tap water. The University Animal Care and Use Committee approved all animal procedures. Rats were anesthetized by intraperitoneal injection of ketamine (90 mg (kg body weight)$^{-1}$). After standard laparotomy, the CBD was liberated and a longitudinal incision was made on it under an operation microscope. One hundred and sixty rats were randomly divided into two groups. For the control group, the incision was directly sutured with 11-0 nylon suture with a 0.4–0.5 mm interval and 0.2–0.3 mm distance from the edge. For the experimental group, a PLGA stent was inserted into the lumen of CBD through the incision. Its position was properly adjusted to locate the incision in the middle of the stent. Then the incision was sutured as the control group (Fig. 1). Biliary leakage was examined via dissection at 3 days after operation. Five rats were sacrificed every week to examine degradation state of the stents with a 9 weeks period. Functions of biliary system were monitored by determination of serum levels of alkaline phosphatase (ALP). Body weight and outer diameter of CBD were measured when all rats were sacrificed in the ninth week.

3. Results

3.1. In vitro degradation of PLGA stent in bile

3.1.1. Morphological change

Biodegradable polymeric materials were developed rapidly in the late 20th century. The polymeric materials, such as PLLA, PGA and poly(ε-caprolactone) (PCL) have been widely used in medical practices, e.g., suture thread, inner-fixation of bone fractures, tissue engineering scaffolds, drug delivery and