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A model for biodegradation of composite materials made of polyesters and tricalcium phosphates

Jingzhe Pan [a,*], Xiaoxiao Han [a], Wenjuan Niu [a,b], Ruth E Cameron [c]

[a] Department of Engineering, University of Leicester, Leicester LE1 7RH, UK
[b] Department of Materials Science and Engineering, Chong-Qing University, China
[c] Department of Materials Science and Metallurgy, University of Cambridge, Pembroke Street, Cambridge CB2 3QZ, UK

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ABSTRACT

A saturation behaviour has been observed when incorporating tricalcium phosphate (TCP) in various polyesters to control the degradation rate. This paper presents an understanding of this behaviour using a mathematical model. The coupled process of hydrolysis reaction of the ester bonds, acid dissociation of the carboxylic end groups, dissolution of the calcium phosphates and buffering reactions by the dissolved phosphate ions is modelled together using a set of differential equations. Two non-dimensional groups of the material and chemical parameters are indentified which control the degradation rate of the composites. An effectiveness map is established to show the conditions under which incorporating TCP into polyesters is effective, saturated or ineffective. Comparisons are made between the model predictions and existing experimental data in the literature. The map provides a useful tool to guide the design of polyester/TCP composites for tissue engineering and orthopaedic fixation applications.

1. Introduction

An intensive effort is being made worldwide to develop composite materials between biodegradable polyesters and calcium phosphates and use these materials to make internal fixation devices for orthopaedic surgery, implants for bone reconstruction and scaffolds for tissue engineering. Typical examples of the calcium phosphates include hydroxyapatite (HA) and tricalcium phosphate (TCP). Examples of the polyesters are polyglycolic acid (PGA), polylactic acid (PLA) and their copolymers (PLGA). The polyesters are well established biomaterials for a wide range of applications such as internal fixation screws, surgical sutures, drug delivery carriers and scaffolds for tissue engineering. The pure polyesters, however, generate an acidic environment during degradation which can induce inflammatory tissue response, result in osteolytic reactions and delay bone healing or fusion. A fixation screw made of the polyesters can also leave a hole in the bone after full degradation. On the other hand calcium phosphates are ideal materials for healing bone defects because of their biocompatibility and osteoconductivity. TCPs in porous form are suitable for implants used in bone reconstruction or as bone substitutes. They have been used for many years to replace or complement autologous bone in bone grafts. TCPs are however very brittle and poor in mechanical strength, which limit them to low stress bearing applications. The idea of combining the polyesters with the calcium phosphates is that the composites have good bone-bonding properties due to the osteoconductivity of the calcium phosphates. Furthermore the dissolved phosphate ions buffer the acidity of the carboxylic end groups (produced by the polyester chain cleavage) while the polyester provides the composites with the appropriate mechanical properties. Consequently the composites degrade more slowly and maintained their shape longer than the pure polymer. The pH of the surrounding media remains stable for longer periods of time for the composites than for the pure polyesters. However different researchers have observed very different buffering effects in their experimental studies. Heidemann et al. [1] introduced 76% (molar) tricalcium phosphate (TCP) particles of about 2.2 μm in diameter in a poly(D,L)lactide (PDLLA) with D/L ratio of 50:50 and weight averaged molecular weight of 220,000 g/mol. They tested rod and cube samples in rats for 72 weeks and observed that the average molecular weight of the PDLLA reduces much more slowly in the TCP/PDLLA composite than in the pure PDLLA. It was unclear whether α- or β-TCP particles were used. Niemela [2] introduced 20wt% β-TCP particles of 50–125 μm in diameter in a PDLLA with D/L ratio of 4:96 and tested rod samples of 2.7 mm in diameter in phosphate buffered saline solution (PBS) at 37 °C for up to 104 weeks. They also observed that the average molecular weight of the PDLLA reduces more slowly in the composite than in the pure

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* Corresponding author. Tel.: +44 116 223 1092; fax: +44 116 252 2525.
E-mail address: jp165@le.ac.uk (J. Pan).

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Nomenclature

A_{cp}	surface area of a calcium phosphate particle
A_d	dissolution rate constant of calcium phosphate
$C_{Ca^{2+}}$	mole concentration of calcium ions
$C_{cp,solid}$	molar concentration of calcium phosphate in solid state
C_e	mole concentration of ester bonds of polymer chains
C_{e0}	initial value of C_e
C_{ol}	mole concentration of ester bonds of oligomers
C_{end}	mole concentration of polymer chain ends
C_{end0}	initial value of C_{end}
C_{H^+}	mole concentration of H^+
J	dissolution flux of calcium phosphate
K_1, K_2, K_3	equilibrium constants for buffering reactions
K_a	equilibrium constant of PLA
K_s	solubility of calcium phosphate
k_1	reaction rate constant for non-catalyzed chain scission
k_2	reaction rate constant for auto-catalyzed chain scission
M_n	number average molecular weight
M_{unit}	molecular weight of a repeating unit of polymer chains
m	average degree of polymerization of oligomers
n	dissolution rate exponent of calcium phosphate
R	radius of a representative unit
R_s	total number of chain scissions.
r	radius of calcium phosphate particle in a representative unit.
r_0	initial radius of calcium phosphate particle in a representative unit.
S_{cp}	relative rate of calcium phosphate dissolution to auto-catalytic hydrolysis
$V_{polyester}$	volume of polyester in the representative unit
w_{cp0}	initial weight fraction of calcium phosphate
α, β	parameters in the relation between chain scission and oligomer production
σ	relative undersaturation of calcium phosphate in the polymer matrix
ρ_{cp}	density of calcium phosphate
ρ_{poly}	density of polyesters
t	degradation time

PDLLA. Ehrenfried et al. [3] fabricated β-TCP/PDLLA composites by infiltrating and in-situ polymerization of PDLLA respectively in continuous foams of TCP with 75% of porosity. They tested their samples in phosphate buffered saline solution (PBS) at 42 °C for up to 80 days and observed that the average molecular weight of the PDLLA reduces more slowly in the composite than in the pure PDLLA although the effect is much more significant in the infiltrated samples. Ehrenfried et al. [4] and Yang et al. [5] compared the change in the pH of the dissolution media (PBS) as a function of time between pure poly(D,L-lactide-co-glycolide) (PLGA) and PLGA/α-TCP composites of different weight percentages of TCP [4] and different TCP particle sizes [5]. They observed that the incorporation of α-TCP delays the onset of pH reduction and leads to a higher pH in the solution at the end of the degradation. However their data suggest that there exists an upper limit of the TCP weight percentage (about 30%) above which further improvements in the buffering effect are small [4]. The data also show that for the same weight percentage of TCP, changing the particles from micron-sized to nano-sized does not improve the buffering effect in a major way [5]. On the other hand Ignatius et al. [6] and Jin et al. [7] compared the average molecular weight as the function of the degradation time between pure PDLLA and PDLLA/β-TCP composites, and between pure PLGA and PLGA/β-TCP composites. They observed no significant change in the degradation rate of the polyesters when incorporated with β-TCP of different weight fractions.

The purpose of this paper is to present a mathematical model for the degradation of polyester/TCP composites and to present an understanding of the saturation behaviour using a mathematical model. The coupled process of the hydrolysis reaction of the ester bonds, the acid dissociation of the −COOH end groups, the dissolution of the calcium phosphates, and the buffering reactions by the dissolved phosphate ions is modelled together using the set of differential equations. Comparisons are made between the model prediction and existing experimental data in the literature. Two non-dimensional groups of the physical and chemical parameters are indentified which control the degradation behaviour of the composites. A TCP effectiveness map is established using the model to show the conditions under which incorporating calcium phosphates into polyesters is effective, saturated or ineffective in terms of changing the degradation rate.

2. Governing equations for polyester degradation buffered by calcium phosphate

Fig. 1 shows an example of the bioresorbable devices considered in this paper. TCP particles are embedded in the polyester matrix. We consider a spherical representative unit of the composite material which contains only one particle and its surrounding polymer matrix. The first step of the biodegradation is the diffusion of water into the device. Although water absorption often continues to increase during the entire process of the device degradation, the water content reaches an abundant level in a few days and further absorption of water has little effect on the degradation rate [8]. It is therefore reasonable to assume that water is always abundant when modelling biodegradation. The hydrolysis reaction between the ester bonds and water is responsible for the chain cleavage of the polyester [9,10]. The reaction is catalyzed by H^+ [11,12] and produces hydroxyl alcohol and carboxylic acid end groups, which can be schematically described as:

$$\mathrm{PLA/PGA} + \mathrm{H_2O} \xrightarrow{\mathrm{H^+}} \mathrm{R{-}COOH} + \mathrm{R{-}OH} \tag{1}$$

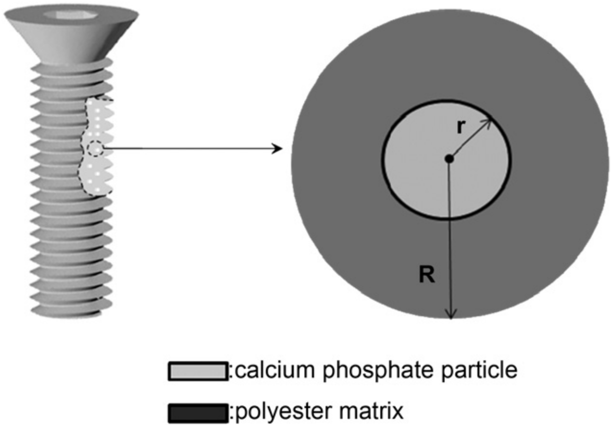

Fig. 1. A representative unit of a fixation device made of polyester/tricalcium phosphate composite considered in the mathematic model.