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Modelling the post treatment process of model implants prepared by in situ polymerized poly(ε-caprolactone) using a BF_3–glycerol catalyst system

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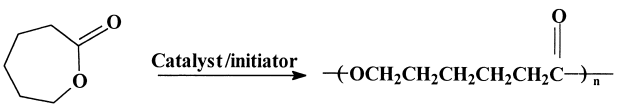
Abstract

The post treatment process of a poly(ε-caprolactone) (PCL) model implant prepared using a boron trifluoride (BF_3) catalyst and glycerol initiator by in situ polymerisation process for craniofacial and maxillofacial treatment is modelled using a 'moving-boundary' diffusion model. A numerical method was used to solve a system of diffusion equations of the model. The variable diffusion coefficient (D) was correlated with crystallinity (x_c) of the polymer which is a function of its molecular weight (M_w) and its degradation rate constant (k_d), $D = f(x_c(M_w, k_d))$. The post treatment time and the molecular weight retained after post treatment can be obtained using this model. The modelling results show that the process is potentially suitable for manufacturing thin model implants of complex shape.

Keywords: Poly(ε-caprolactone); Degradation; Modelling

1. Introduction

Poly(ε-caprolactone) (PCL) was recognised as a biodegradable polymer by the scientists at Union Carbide [1] as early as the 1970s. Since then, much research has been carried out both on its synthesis method and on its degradation behaviour due to the increasing demand for biodegradable polymers in applications such as medical implants.



ε-caprolactone can be polymerised by various catalysts through cationic, anionic, or coordination mechanisms with or without active hydrogen compounds. Brode [2] and Pitt [3] have written very good reviews on the synthesis of poly(ε-caprolactone) in 1970s and 1990s. In order to obtain high molecular weight PCL, the catalyst used often involves organometallic compounds such as those of tin, aluminium or zinc. Recently, the preparation methods have focussed on using rare-earth metal catalysts, which initiate living polymerisation of lactones yielding polymers with very narrow polydispersities [4].

The degradation rate for PCL prepared using the above routes has been found to be too slow [5] for biomedical applications involving bone reconstruction, such as in craniofacial and maxillofacial treatment. In these applications, the mechanical properties of the implant are often required to be retained for about six weeks after which the implant should begin to degrade and be absorbed into the body. In order to obtain desirable degradation rates, complex chemical procedures have been used to modify the behaviour of PCL. These methods usually include copolymerization of ε-caprolactone with other cyclic esters, such as L-lactide, γ-butyrolactone [5].

A catalysis approach involving boron trifluoride and glycerol was developed in this research group [6] to produce PCL as the matrix polymer of a totally degradable polymer composite for craniofacial and maxillofacial applications in order to overcome these problems. These catalysts are less water and air sensitive than the organometallic catalyst, and the polymer produced using this catalyst system degrades at an acceptable rate due to the existence of trace BF_3 after post treatment. The lack of water and air sensitivity makes much more feasible the in situ polymerisation around enforcement materials such as fibres, which is a desirable

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Nomenclature

a	thickness of diffusion sample
C_E	concentration of ethanol within specimen
C_E^0	concentration of ethanol at surface of specimen
C_F	concentration of fluoride ions within specimen
C_F^0	concentration of fluoride ion at surface of specimen
D	diffusion coefficient
K	proportional constant
k_d	degradation rate constant
L	sample thickness for film used to measure diffusion coefficients
M_n	number averaged molecular weight
M_n^0	initial value of number averaged molecular weight
M_w	weight averaged molecular weight
M_w^0	initial value of weight averaged molecular weight
R	radius of diffusion sample
r	position within cylindrical specimen
t	time
x	position within plate specimen
x_c	crystallinity
κ	normalised position of moving boundary
ρ	density of poly(ε-caprolactone)
ξ	position of moving boundary

production route for complex shapes. The material produced in this way has been shown in our cell culture experiments to promote more rapid cell growth and to have a more suitable degradation rate than current forms of PCL for craniofacial and maxillofacial treatment application [7].

Virgin PCL cannot be used as bone fracture fixation devices due to its low stiffness (the Young's modulus is about 0.45 GPa, while that of bone is in the range of 6–20 GPa). The stiffness can be improved by incorporation of high stiffness degradable glass fibre. The recent development of powerful medical imaging techniques such as computer aided tomography combined with prototyping technologies has allowed the rapid production of net shape, patient specific implant models directly from patient scan data [8]. This technique combined with a composite forming process similar to resin transfer moulding developed in this research group [9] allows the preparation of patient specific polymer composite implants of complex shape in a single stage. In this technique, the reaction mixture (monomer + catalyst) is injected into a mould containing a fibre preform so that in situ polymerisation takes place in it, and therefore various complex shapes can be made in a single stage according to the mould. This shape-forming technique combined with the new catalyst system provides the potential to manufacture totally biodegradable polymer composite implants for craniofacial and maxillofacial treatment that have complex shape and suitable degradation rates.

However, the BF_3 catalyst tends to catalyse the rapid hydrolysis of the polymer once it has been manufactured. For example, the molecular weight reduced to around 20% of its original value when the model implant was put into water for 2 days observed in our experiment [6]. Therefore, residual BF_3 must be removed from the polymer before it is of practical use. In this research, the BF_3 is removed by conversion to tetrafluoroborate salts by diffusing potassium fluoride into the model implant [6].

$$BF_3 + F^- \rightarrow BF_4^-$$

The carrier medium to bring potassium fluoride into the implant needs to be carefully chosen. Ethanol or an ethanol containing solvent is chosen rather than water because water has a much slower diffusion rate in PCL than ethanol. However, when the model implant is soaked in a fluoride ion in ethanol or an ethanol containing solution, the PCL undergoes degradation due to the transesterification reaction between ethanol and PCL. This alcoholysis reaction is rapid in the presence of BF_3. There is therefore a trade-off between the diffusion and degradation processes, requiring a model to enable the behaviour of these processes to be properly understood.

The work presented here focuses on two different shapes of implant prepared, a plane sheet and a cylinder. Mathematical models are presented in this paper which predict the effective post treatment time and the molecular weight remaining after effective post treatment for a PCL implant. The effective post treatment time is defined here as the time for which the sample must be soaked in fluoride ion solution in order to stop its rapid degradation. The model can also be applied to composite implants, but for such predictions, the diffusion coefficient needs to be modified to represent diffusion in a composite (e.g. in a well-bonded composite, the fibres will act as barriers to diffusion, decreasing the diffusion coefficient) [10,11].

2. Development of mathematical models

2.1. Fluoride ion diffusion into the sample

Since BF_3 is a very strong electrophilic agent, and there are many ester bonds in PCL, the BF_3 was considered to be immovable and evenly dispersed through the model implant. Therefore, the fluoride ions diffuse into the polymer and react with BF_3. Since this reaction was believed to be very quick, it was assumed that the fluoride ion reacted with BF_3 instantaneously to form BF_4^- and then precipitated in the polymer. As the fluoride ions advance to the centre of the implant, a 'boundary' of the fluoride ion or BF_3 will exist. Beyond this boundary, the BF_3 concentration

is equal to the initial BF_3 concentration and there is no fluoride ion. Before this boundary, all the BF_3 has been converted into BF_4^-. The boundary moves during the diffusion of fluoride ion into the implant until it reaches the centre of the implant. This process has all the characteristics of a 'moving boundary' problem [12] in the modelling of diffusion processes. A schematic diagram of the process is shown in Fig. 1.

2.1.1. Flat plate sample

In modelling the post-treatment process for a flat plate sample, diffusion from the edges was ignored, and it was assumed that diffusion normal to the plane was the only contribution to the concentration of fluoride ion in the sample. Therefore, the process was simplified as a diffusion in an infinite plane.

The moving boundary was defined as $x = \xi$, i.e. beyond this position, there was no fluoride ion, and before this position, there was no BF_3 remaining. Before the boundary, i.e. when $x < \xi$, Fick's second law is applicable,

$$\frac{\partial C_F}{\partial t} = \frac{\partial}{\partial x}\left(D\frac{\partial C_F}{\partial x}\right) \tag{1}$$

where C_F is the concentration of fluoride ions at time t and at a distance x into the sample normal to its surface, and D is the diffusion coefficient of fluoride ions in the sample. At the position $x = \xi$, when the boundary moves forward by a differential distance $d\xi$ in a differential time dt, the fluoride ion consumed equals to $C_F\, d\xi$. The diffusion of the fluoride ion through the unit area at position $x = \xi$ is equal to $-D(\partial C_F/\partial x)_\xi dt$. According to mass conservation:

$$C_F\frac{d\xi}{dt} = -D\left(\frac{\partial C_F}{\partial x}\right)_\xi \tag{2}$$

The above equation has the following boundary condition and initial value

$$C_F(0,t) = C_F^0, \qquad C_F(x,0) = 0 \tag{3}$$

where C_F^0 is the concentration of fluoride ions on PCL surface. C_F^0 is assumed to be the concentration of fluoride ions in the saturated solution since ethanol or ethanol/acetone mixture has a good wettability to PCL surface. This assumption was justified through comparison between modelling results and experimental observation.

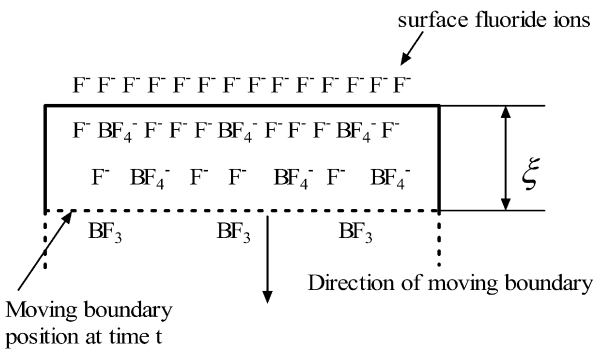


Fig. 1. A schematic diagram of fluoride ion diffusion into a PCL sample containing BF_3. ξ is the moving boundary position.

Crank [12] and Hermans [13] gave a solution for Eqs. (1)–(3) when the diffusion coefficient is a constant. Using our nomenclature, their solution is as follows:

$$\frac{C_{BF3}^0 - C_F^0}{g(k/2D^{1/2})} + C_{BF3}^0 = 0 \tag{4}$$

where

$$g(\kappa/2D^{1/2}) = \pi^{1/2}\frac{\kappa}{2D^{1/2}}\exp\left(\frac{\kappa^2}{4D}\right)\mathrm{erf}\left(\frac{\kappa}{2D^{1/2}}\right) \tag{5}$$

$\mathrm{erf}(z)$ is the error function, $\kappa = \xi t^{1/2}$, and C_{BF3}^0 is the initial BF_3 concentration in the sample.

When the boundary is halfway through the sample so that $\xi = a/2$, we can get an implicit expression of effective post treatment time t, sample thickness a, initial BF_3 concentration in the polymer C_{BF3}^0, fluoride ion concentration in post-treatment solution C_F^0 and a constant diffusion coefficient D in PCL:

$$\frac{C_F^0}{C_{BF3}^0} - 1 = \pi^{1/2}\frac{a}{4\sqrt{Dt}}\exp\left(\frac{a^2}{16Dt}\right)\int_0^{a/4\sqrt{Dt}}\exp(-\eta^2)d\eta \tag{6}$$

Since the diffusion coefficient D is variable during the post treatment process, it is necessary to use a numerical method to solve Eqs. (1)–(3) instead of using Eq. (6) to calculate the effective post treatment time for the plane shape model implant. Nevertheless, Eq. (6) provides a check of the stability of our numerical solution method.

2.1.2. Cylindrically shaped sample

For a cylindrical sample, the equations equivalent to Eqs. (1)–(3) for a flat sample are as follows:

$$\frac{\partial C_F}{\partial t} = \frac{1}{r}\frac{\partial}{\partial r}\left(rD\frac{\partial C_F}{\partial r}\right) \quad (r \geq R - \xi) \tag{7}$$

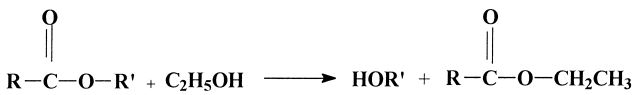
$$C_F\frac{d\xi}{dt} = -D\left(\frac{\partial C_F}{\partial r}\right)_\xi \quad (r = R - \xi) \tag{8}$$

$$C_F(0,t) = C_F^0, \qquad C_F(r,0) = 0 \tag{9}$$

where C_F is the concentration of fluoride ion at time t and at a distance r into the sample along its radial direction, R is the radius of the cylinder sample. Since there is no analytical solution for equation system (7)–(9), and also the diffusion coefficient is not constant, it is necessary to resort to a numerical method to solve them.

2.2. The molecular weight decrease of the sample

PCL can undergo a transesterification reaction with ethanol during post treatment, leading to a decrease in molecular weight of a PCL sample.



This reaction is significant when there is BF_3, since BF_3 is also a catalyst for the transesterification reaction. The rate of this reaction can be written as [14]:

$$\frac{dC_{HOR'}}{dt} = kC_{BF3}C_E C_{ester} \tag{10}$$

where $C_{HOR'}$ is the concentration of species HOR′, C_E is the concentration of ethanol in the sample, C_{BF3} is the concentration of BF_3 in the sample, and C_{ester} is the concentration of ester bonds in the sample, which can be considered a constant because it changes very little for the extent of degradation which occurs during post treatment. Thus, Eq. (10) becomes:

$$\frac{dC_{HOR'}}{dt} = k'C_{BF3}C_E \tag{11}$$

where $k' = kC_{ester}$. Since whenever a transesterification reaction occurs, a new HOR′ molecule appears during the degradation, the following equation should apply.

$$C_{HOR'} = \frac{\rho}{M_n} - \frac{\rho}{M_n^0} \tag{12}$$

where ρ is the density of PCL, M_n, and M_n^0 are the number averaged molecular weight at time t and initial number averaged molecular weight. During the numerical solution of Eqs. (1) and (2) or (7) and (8), the time step has to be made small enough to ensure that the numerical solution remains stable. In such a small time step δt, C_{BF3} and C_E in Eq. (11) were considered constant. Substitution of Eq. (12) into Eq. (11), yields:

$$\left(\frac{\rho}{M_n}\right)_{t+\delta t} - \left(\frac{\rho}{M_n^0}\right)_t = k'C_{BF3}C_E\delta t \tag{13}$$

In the process of post treatment, there was a small amount of loss of low molecular weight fraction produced by the transesterification reaction. This loss of low molecular weight fraction will influence M_n, but it has little influence on the weight averaged molecular weight M_w [15]. Furthermore, the molecular weight distribution did not change when there was not extensive degradation [16]. Thus, the rate of decrease of molecular weight can be written as:

$$\left(\frac{\rho}{M_w}\right)_{t+\delta t} - \left(\frac{\rho}{M_w}\right)_t = k_d C_{BF3}C_E\delta t \tag{14}$$

where k_d is a transesterification reaction rate constant when weight averaged molecular weight is used in the equation. The concentration of ethanol C_E in the sample during post treatment can also be expressed using Fick's second law for the plane sheet (Eqs. (15) and (16)) and for the cylinder sample (Eqs. (17) and (18))

$$\frac{\partial C_E}{\partial t} = \frac{\partial}{\partial x}\left(D\frac{\partial C_E}{\partial x}\right) \tag{15}$$

$$C_E(a,t) = C_E(0,t) = C_E^0, \quad C_E(x,0) = 0 \tag{16}$$

$$\frac{\partial C_E}{\partial t} = \frac{1}{r}\frac{\partial}{\partial r}\left(rD\frac{\partial C_E}{\partial r}\right) \tag{17}$$

$$C_E(0,t) = C_E^0, \quad C_E(r,0) = 0 \tag{18}$$

where C_E^0 is the concentration of ethanol on a sample surface, C_E is the concentration of ethanol and D is the diffusion coefficient of ethanol in PCL. Due to difficulties in accurately measuring the fluoride ion diffusion coefficient, to a first approximation it was assumed the same as that for the solvent.

The concentration of ethanol at each nodal point can be obtained by numerically solving Eqs. (15) and (16) in a plane sample or Eqs. (17) and (18) in a cylinder sample. The concentration of BF_3 at each node point is the difference of the initial BF_3 concentration C_{BF3}^0 and accumulated fluoride ion concentration that has diffused into this position. The final molecular weight after post treatment is the mean of the molecular weight at each node point in the last time step. During data processing, only the mean near to the centre of a sample was taken, for it was the molecular weight in the centre of the sample that was measured during the experiment.

3. Experimental

3.1. Sample preparation

The sample preparation and post treatment method has been reported elsewhere [6]. Two patterns of moulds were used: a set of four PTFE moulds with a rectangular cavity (30 mm × 80 mm × {2,4,6,8} mm) sealed with an O-ring and clamped between aluminium plates (which do not contact the reaction mixture), and a set of three PTFE tube moulds (ϕ{4,6,8} mm × 200 mm long). These moulds, together with the fittings for the mould ports, were cleaned carefully with toluene. They were then dried in a vacuum oven at 140 °C for at least 10 h after cleaning.

The monomer caprolactone (Solvay Interox) was distilled under vacuum from fresh calcium hydride (CaH_2) powder just before use. Boron trifluoride dimethylene etherate ($BF_3{\cdot}O(CH_3)_2$) (Aldrich, used as received) and glycerol (Aldrich, HPLC grade, used as received) were each added to the monomer. The reaction mixture was injected into the moulds; the entry and exit ports of the moulds were sealed and the moulds were put into an oven at 80 °C for a minimum of 32 h in order to have a complete conversion of the monomer.

3.2. Post treatment of the samples

After reaction, the moulds were taken out of 80 °C oven to cool down in ice while still clamped shut. The samples were then removed from the moulds, cut into several sections using a scalpel and put into KF saturated solution in ethanol or in an ethanol/acetone mixture at room temperature. The length and width of the sections cut from plane shape samples were at least four times their thickness; the length of the sections cut from cylindrical specimens were at least four times their diameter. This was to ensure that the changes at the centre of each sample were not due to diffusion from the ends or edges of the samples.

3.3. Determination of the post treatment time

At around the time predicted for post treatment of the samples, a section was taken out of the post treatment solution at several time intervals either side of the predicted post treatment time. The molecular weights of the samples were measured using gel permeation chromatography (GPC) (as detailed in Section 3.4) using material taken from a point on the specimen's centreline at least a diameter's (or thicknesses) length from the specimen's edges or ends. The section was then put into distilled water at 37 °C for degradation testing. After 5 days, the section was taken out of the degradation water bath and was cut apart along its centre to determine whether its centre had become soft like wax or had remained a tough polymer. If the centre position was still tough like the polymer just taken out of the mould, then the time when the section was taken out of the post treatment solution was considered longer than the effective post treatment time, and was considered as an effective post treatment. If the centre position had become soft, the post treatment was considered to have been ineffective and the time for effective post treatment was considered not to have been reached. The soft/tough condition was determined with a sharp instrument (i.e. a scalpel), and although some subjectivity was inevitable the distinction between undegraded (tough) and degraded (soft) polymer was obvious.

3.4. Measuring molecular weight of the sample

The molecular weight change of PCL before and after post treatment was monitored by GPC. The equipment used was a Polymer Labs GPC system with mixed D columns and a refractive index detector, and operated at 35 °C. Chloroform was used as the mobile phase at a flow rate of 1.0 cm^3/min. Calibration was accomplished directly against polystyrene standards in accordance with the manufacturer's recommendations.

3.5. Determination of the diffusion coefficient of KF/ethanol, KF/acetone/ethanol in PCL

The sorption experiment [12] was used to measure the diffusion coefficient of KF/ethanol or KF/acetone/ethanol mixture in PCL. The PCL sheets used to measure the diffusion coefficients were moulded from commercial PCL (Aldrich, used as received) understood to have been manufactured without the use of BF_3. The sheets had dimensions of approximately 30 mm × 30 mm × 0.4 mm, and their degree of crystallinity of the sheets was calculated from DSC measurement (as detailed in Section 3.7). The sheets were then immersed in the liquid to be measured. At each time point, the PCL sheets were removed from the liquid removing surface droplets quickly prior to weighing. The sheet was put back into the solution after the measurement.

Before doing the sorption experiment to measure the diffusion coefficient, about 5 cm^3 of the saturated solution was put into a weighing boat to measure the saturated concentration of KF using the evaporation method. The evaporation was carried out in an oven at 60 °C for 24 h.

3.6. Determination of the degradation constant of PCL in ethanol

A PCL pin was prepared using a mould of dimension of (20 mm × 20 mm × 84 mm). Several 0.05 mm PCL films were cut from the pin samples using a microtome. The BF_3 concentration in the films was calculated from its concentration in the reaction mixture, taking into account the density change from ε-caprolactone to PCL (ε-caprolactone: 1.08 g/cm^3, and PCL: 1.146 g/cm^3). Then $BF_3{\cdot}O(CH_3)_2$ ethanol solution of the same concentration was prepared and about 10 films were immersed in the solution. At each sampling point, one piece of film was taken out of the solution and the molecular weight of the sample was measured using GPC. Finally, ρ/M_w against degradation time was plotted and the degradation constant was determined using the slope of the line.

3.7. Determination of the relationship between molecular weight and crystallinity

A PCL pin of a diameter of 6 mm was prepared (without post treatment), and then cut into several sections. The sections were put into 37 °C water to degrade in several days. One section was taken out of the degradation bath at appropriate time intervals to get samples of different molecular weights. The molecular weight and the degree of crystallinity of the sample were measured by GPC and by differential scanning calorimetry (DSC) on a Perkin–Elmer Pyris 1. PCL samples of various molecular weights each weighing around 10 mg were run from 0 to 100 °C at a rate of 10 K/min, kept at 100 °C for 5 min. The temperature was then decreased from 100 to 0 °C at 10 K/min. The degree of

crystallinity was calculated from DSC endotherms ΔH_m in the second run from 0 to 100 °C in order that the heat history effect and solvent effect on the crystallinity were removed. The heat of fusion for a 100% crystalline polymer, ΔH_m^0, was taken as 142 J/g [17].

4. Results and discussion

4.1. Diffusion coefficient in amorphous phase

Using the sorption experiment procedure described in Section 3.5, the amount of material M_t (total mass of ethanol, acetone and potassium fluoride) absorbed by a sheet sample of thickness L at time t was measured and plotted against t/L^2. The average diffusion coefficient was calculated using Eq. (19) [12]:

$$\bar{D} = 0.049/(t/L^2)_{1/2} \tag{19}$$

where $(t/L^2)_{1/2}$ is the value of (t/L^2) when M_t/M_{eq} is 1/2, and where M_{eq} is the mass of absorbed material attained at equilibrium. An example of the uptake curves of KF in ethanol and in ethanol/acetone (volume ratio 4:1) solutions by PCL sheets are shown in Fig. 2. The value adopted in the mathematical model was the average from three separate experiments. $D = 0.0105 \pm 0.0010$ mm^2/h for KF/ethanol, and $D = 0.0196 \pm 0.0010$ mm^2/h for KF/ethanol/acetone.

The amorphous phase diffusion coefficient D_a was then obtained by Eq. (20) using the known crystallinity x_c of the polymer. Eq. (20) is a first approximation to the relationship between diffusion coefficient and the polymer crystallinity [18], making the assumption (justified in Ref. [18]) that diffusion occurs only in the amorphous part of the polymer and consequently crystalline regions obstruct the diffusion path.

$$D = D_a(1 - x_c) \tag{20}$$

x_c in this measurement was 0.51, therefore, $D_a = 0.214 \pm 0.0020$ mm^2/h for KF/ethanol, and $D_a = 0.0400 \pm 0.0020$ mm^2/h for KF/ethanol/acetone.

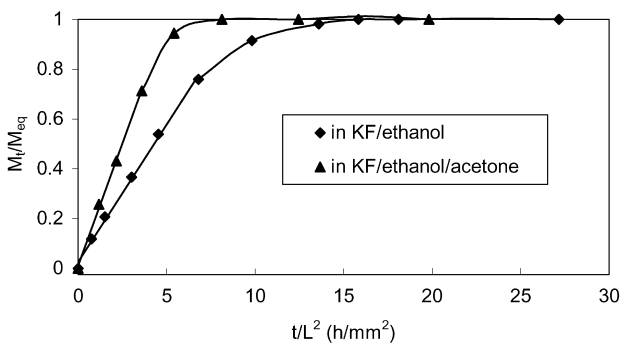


Fig. 2. Up-take curve of PCL sheet in the saturated solution of KF in ethanol and in acetone/ethanol (volume ratio 1:4). M_t represents weight gain of the sheet at time t; M_{eq} represents equilibrium weight gain of the sheet.

4.2. Degradation rate constant

Because the PCL sample is very thin in this experiment, the ethanol concentration in the sample was considered to reach its surface concentration C_E^0 rapidly. C_{BF3}^0 was also constant. The whole process of this experiment can be expressed as Eq. (21).

$$\frac{\rho}{M_w} - \frac{\rho}{M_w^0} = k_d C_{BF3}^0 C_E^0 t \tag{21}$$

Therefore, $k_d C_E^0$ can be determined using the slope of ρ/M_w against time t noting that the model requires the value of the product $k_d C_E^0$ (but not k_d and C_E^0 individually). Fig. 3 shows an example of a measured graph using this method. The value used in the model was the average from three separate experiments. The value obtained was $k_d C_E^0 = 0.045 \pm 0.005$/h.

4.3. The relationship between molecular weight and degree of crystallinity

During the post treatment of PCL implants in KF ethanol solution, ethanol also diffused into the implants containing BF_3. The BF_3 in the implant catalysed the transesterification between ethanol and PCL, leading to a decrease of molecular weight. Crystallinity of the samples was noted to increase, but there was no significant weight loss, hence the increase in crystallinity was not due to dissolution of the amorphous phase, but may be attributed to crystallization of tie segments made possible by the chain cleavage in the amorphous phase, facilitated by the low glass transition temperature of PCL (−60 °C) [19]. The increase in crystallinity leads to a decrease of the diffusion coefficient of the KF solution in PCL because crystals constitute obstacles for the transport of penetrants through the semi-crystalline polymer and cause an extension of the diffusion path [20].

Fig. 4 shows the relationship between crystallinity and molecular weight. The data points in Fig. 4 were fitted using

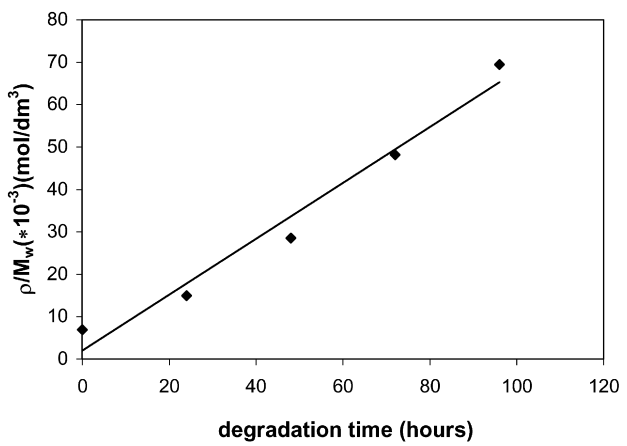


Fig. 3. The degradation of PCL in ethanol under the catalysis of BF_3. Degradation is at room temperature. BF_3 concentration is 0.015 mol/dm^3.

Eq. (22):

$$x_c = -0.083M_w + 63.8 \quad (22)$$

where x_c is the degree of crystallinity of PCL, and M_w is the weight averaged molecular weight.

4.4. Effective post treatment time and molecular weight remaining

4.4.1. The effect of BF_3 concentration on post treatment

The post treatment time and molecular weight remaining after post treatment are functions of sample thickness, initial BF_3 concentration, initial molecular weight, fluoride ion concentration in post treatment solution and diffusion coefficient. The diffusion coefficient is a function of the carrier medium used to transport fluoride ions.

The effective post treatment time of 2 mm thick plate samples with various BF_3 concentrations in KF/ethanol solution is shown in Fig. 5. The corresponding molecular weight remaining after post treatment is shown in Fig. 6.

It can be seen from Fig. 5 that the effective post treatment time increased slowly with the increase of BF_3 concentration in the samples, while the molecular weight remaining decreased rapidly with the increase of BF_3 concentration. This is a reasonable explanation as the more BF_3 was present in the sample, the more fluoride ions were needed to diffuse into the sample to react with it and thus a longer time was needed. In the range for BF_3 concentration which was explored experimentally (covering a range of approximately 0.01 to 0.025 mol/l), the effective post treatment time and BF_3 concentration have the following approximately linear relationship obtained by fitting to the data shown in Fig. 5:

$$t = 704.7C_{BF3} + 7.6 \quad (23)$$

where t is the effective post treatment time. The molecular weight remaining decreased rapidly with the increase of the BF_3 concentration in the sample. This was because the degradation rate was directly proportional to the product of BF_3 concentration and ethanol concentration in the sample. The BF_3 concentration in the centre kept its original value before fluoride ion reached the centre, while ethanol arrived at the centre much earlier, allowing degradation to occur

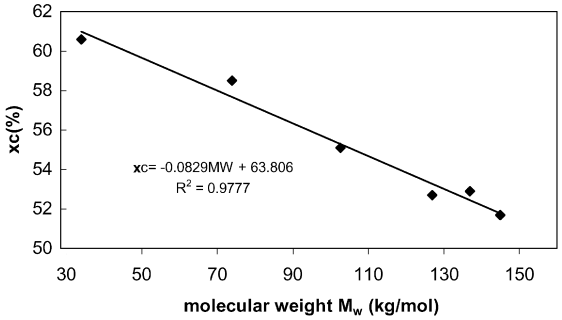


Fig. 4. The change of the degree of crystallinity of PCL (x_c) with its weight averaged molecular weight M_w.

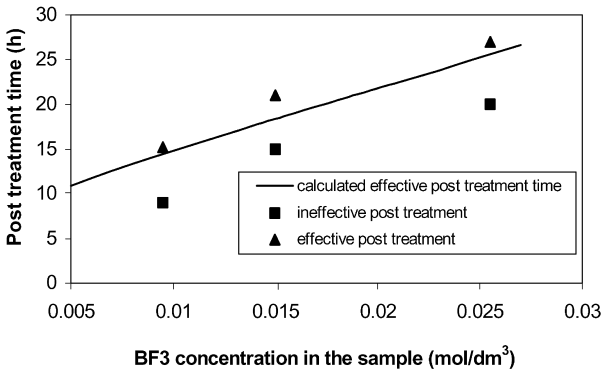


Fig. 5. A comparison between model prediction and experimental results of the post treatment time of a 2 mm thick plate sample in KF/ethanol saturated solution at room temperature.

until all the BF_3 was removed, at which point the effective post treatment was accomplished.

4.4.2. The effect of sample thickness on the post treatment

The effective post treatment time of plate samples of various thickness using KF/ethanol solution and KF/acetone /ethanol solution is shown in Fig. 7, and the corresponding molecular weight remaining is shown in Fig. 8. It can be seen that the effective post treatment time increased rapidly with increase of the sample thickness. From Eq. (6), the effective post treatment time should be directly proportional to the square of the sample thickness. In the post treatment process of PCL samples, however, the degree of crystallinity of PCL increased steadily with the decrease of molecular weight due to the transesterification reaction with ethanol, which would result in a decrease in the diffusion coefficient of KF in the sample. Therefore, it can be expected that the effective post treatment time was proportional to a power of greater than two of sample thickness. Power-law fitting to the curves relating effective post treatment time to thickness (for the KF/ethanol solution) showed that the power was around 2.3.

$$t = Ka^{2.3} \quad (24)$$

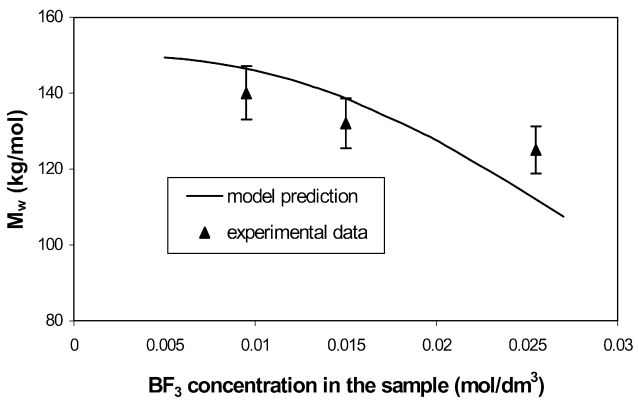


Fig. 6. Weight averaged molecular weight remaining after post treatment of a 2 mm thick plate sample in KF/ethanol solution at room temperature. Original weight averaged molecular weight was 150 kg/mol.

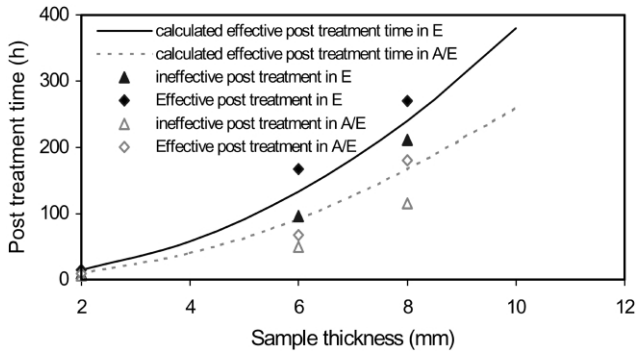


Fig. 7. A comparison between model prediction and experimental results of the post treatment time of plate samples of various thickness in KF/ethanol saturated solution (E) and in KF/acetone/ethanol saturated solution (A/E) at room temperature. The BF_3 concentration in the samples was 0.0095 mol/dm^3.

where t is the effective post treatment time, K is the proportional constant and a is the sample thickness. A similar calculation for the KF/ethanol/acetone solution gave a power of around 2.2.

It is seen in Fig. 8 that the molecular weight remaining after post treatment decreased rapidly with increase of the sample thickness. When the sample was over 6 mm thick, the centre of the sample became soft like wax due to extensive degradation during treatment with KF/ethanol solution. This was because the BF_3 concentration in the centre of the sample remained at its original value for several days before the fluoride ions diffused to the centre to convert the BF_3 and hinder further degradation. The molecular weight from an 8 mm thick sample surface towards its centre was calculated using the model and is shown in Fig. 9, illustrating the effect of continued degradation within the sample. The BF_3 concentration used in the calculation was 0.0095 mol/dm^3. If a higher BF_3 concentration were used during sample preparation, it would be expected that the centre of the sample would have degraded further and hence the thickness of the sample would have to be smaller if the sample was not expected to become soft in the centre after post treatment.

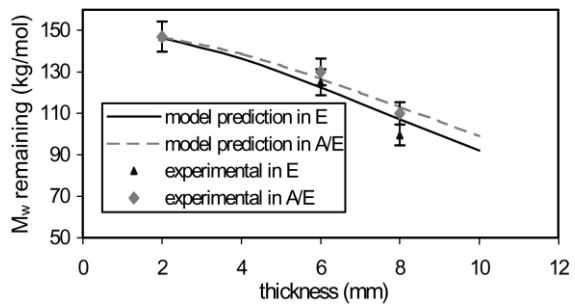


Fig. 8. Weight averaged molecular weight remaining after plate samples of various thickness were post treated in KF/ethanol solution (E) and in KF/acetone/ethanol solution (A/E) at room temperature. BF_3 concentration in the samples was 0.0095 mol/dm^3. Original molecular weights of the samples were 150 kg/mol. The points represent measured molecular weight remaining using GPC.

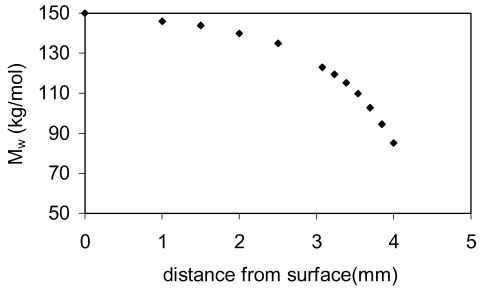


Fig. 9. Calculated results of the weight averaged molecular weight (M_w) from sample surface to the centre of an 8 mm thick plate after the post treatment in KF/ethanol solution was finished. Initial BF_3 concentration was 0.0095 mol/dm^3.

4.4.3. The effect of acetone as a swelling agent on post treatment

Acetone/ethanol mixtures were used to investigate the effect of acetone as a swelling agent to aid diffusion during post treatment. Various thickness of PCL plates containing an initial BF_3 concentration of 0.0095 mol/dm^3 were treated in KF/acetone/ethanol solution. The effective post treatment times are shown in Fig. 7, and their corresponding molecular weights remaining are shown in Fig. 8. It can be seen that the effective post treatment time was reduced while the molecular weight remaining was greater using KF/ethanol/acetone solution compared with that using KF/ethanol solution. The decrease of effective post treatment time was due to the increase of the diffusion coefficient, and the increase of the latter was due to the swelling effect of acetone on PCL. This effect was expected as acetone is a good solvent for PCL while ethanol is not. The incorporation of acetone caused the solubility of KF in ethanol to decrease. However, the negative effect of the decrease in solubility is compensated by the increase in the diffusion coefficient for KF into PCL.

The molecular weight of the samples after post treatment was greater when an acetone/ethanol mixture was used (in comparison to just ethanol) because of three interacting factors. The increase in diffusion coefficient leads to the rapid increase of ethanol concentration in the sample and thus rapid degradation, while it shortens the time for the degradation by ethanol under the catalysis of BF_3. The incorporation of acetone decreases the concentration of ethanol in the sample, which also leads to a slower degradation. The comprehensive result of the interaction of the three factors slows down the degradation rate according to the diffusion model and this was corroborated by experimental observations.

4.4.4. The effect of sample geometry on the post treatment

Two shapes of sample were made, plate and cylinder. The effective post treatment time for the cylindrical samples in KF/acetone/ethanol solution is shown in Fig. 10. The initial BF_3 concentration was the same as in Fig. 7. It can be seen by comparing these two graphs that the effective post treatment time for a cylindrical sample was nearly 70% of

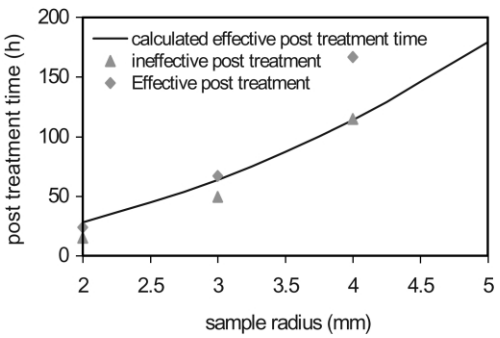


Fig. 10. A comparison between model prediction and experimental results of the post treatment time of various cylindrical samples in in KF/acetone/ethanol solution at room temperature. Initial BF_3 concentrations in the samples were 0.0095 mol/dm^3. Original weight averaged molecular weights of the samples were 150 kg/mol.

that for a plate sample when the diameter of the cylinder was the same as the thickness of the plate. Similar results were obtained by Allen [21] when solving heat transfer equation with change of state using a relaxational method and by Poots [22] when solving heat transfer equation with change of state using an integral method. The decrease was due to the surface area to volume ratio being greater for a cylinder.

5. Conclusion

From the comparison between experimental results and calculation results using the model established, the post treatment process is in good agreement with the moving boundary assumptions, i.e. the BF_3 is immovable in PCL bulk and F^- diffuses into the bulk to react with BF_3.

The rapid degradation of a model implant prepared by in situ polymerised poly(ε-caprolactone) using BF_3 catalyst can be stopped by diffusion of fluoride ions into it. The effective post treatment time of the model implant thus prepared depends on the sample thickness, initial BF_3 concentration, the carrier medium of KF into PCL, and the geometry of the sample.

The critical factors which determine the effective post treatment time are the sample thickness and diffusion coefficient. The effective post treatment time is approximately proportional to sample thickness raised to the power of 2.3, and inversely proportional to the diffusion coefficient of the transport medium in PCL.

Although the BF_3 concentration does not affect the effective post treatment time as much as sample thickness and diffusion coefficient, it determines the molecular weight remaining after post treatment. When the sample is thick enough, the ethanol diffusing into the sample can cause significant degradation of the centre of the sample before BF_3 in the sample is converted.

From this research, it was concluded that this synthetic route was more suitable for preparing thin implants, which is the case for craniofacial and maxillofacial applications, and it is preferable to prepare implants thinner than 6 mm in order to get a reasonable effective post treatment time.

Appendix A

Algorithm for solving Eqs. (1)–(3),(14)–(16),(20),(22) together

Simultaneously solving the above equations, the post treatment time and the molecular weight remaining after post treatment of a flat plate sample can be obtained. Similarly, the solutions for cylindrically shaped sample can be obtained. The adopted algorithm for the solution of fluoride ions diffusion was similar to that described by Croft and Lilley [23] in their numerical treatment of heat transfer involving phase change.

The finite difference equation for Eq. (1) is

$$\frac{C_{\mathrm{F}}^{i,j+1} - C_{\mathrm{F}}^{i,j}}{\delta t} = D\frac{C_{\mathrm{F}}^{i+1,j} - 2C_{\mathrm{F}}^{i,j} + C_{\mathrm{F}}^{i-1,j}}{(\delta x)^2} \tag{A1}$$

where C_{F} is the fluoride ion concentration in the sample (Fig. 11). The finite difference for Eq. (15) is

$$\frac{C_{\mathrm{E}}^{i,j+1} - C_{\mathrm{E}}^{i,j}}{\delta t} = D\frac{C_{\mathrm{E}}^{i+1,j} - 2C_{\mathrm{E}}^{i,j} + C_{\mathrm{E}}^{i-1,j}}{(\delta x)^2} \tag{A2}$$

where C_{E} is the ethanol concentration in the sample. According to the initial value and boundary condition, the value of ethanol concentration at any nodal point can be calculated as shown in Fig. 12. For the fluoride ion concentration, Eq. (2) was considered as follows. If the fluoride ion concentration does not exceed the initial BF_3 concentration at a spatial position (in the x direction), the fluoride ion concentration at this spatial position is taken as zero. Then the value calculated using the finite difference equations is accumulated with each time step. When the

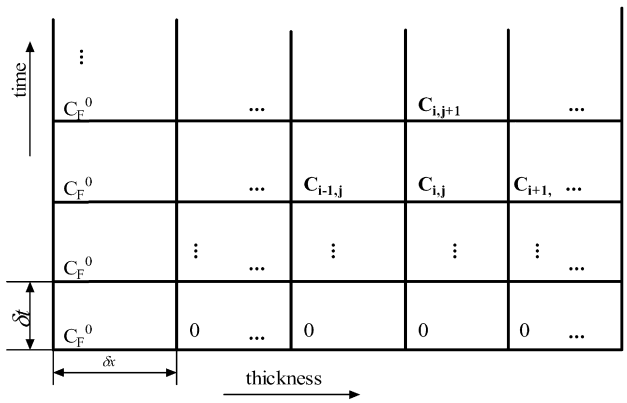


Fig. 11. Schematic graph of numerical solution of differential equations (1) and (15). The longitudinal steps represent the one-dimensional spatial discretisation of the model while the vertical steps represent the time increments of the time-marched solution. The numerical value on each node point is fluoride ion concentration.

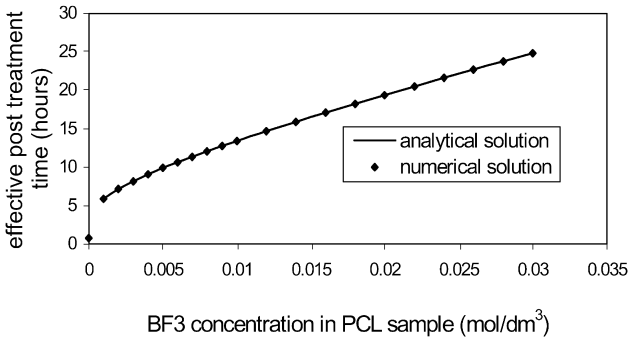


Fig. 12. A comparison between the numerical solution and analytical solution of the moving boundary diffusion in a plane sheet when initial BF_3 concentration = 0.0095 mol/dm^3. The analytical solution was calculated using Eq. (6).

cumulative concentration of fluoride ions at that position exceeds the initial BF_3 concentration, the fluoride ion concentration is taken as the value of the cumulative concentration of fluoride ion minus the BF_3 concentration. After subtraction of the BF_3 concentration, the concentration of fluoride ions at this spatial position should be allowed to increase in the normal manner according to Eq. (A1). The BF_3 concentration at each spatial position was taken as its initial value C^0_{BF3}. After the fluoride ions begin to diffuse, the BF_3 concentration is taken as its original value minus the concentration of the fluoride ions which have diffused into that spatial position, until its value becomes zero.

The molecular weight at each nodal point is calculated using Eq. (14). The BF_3 and ethanol concentration have been calculated in the above step. After the molecular weight is calculated, the degree of crystallinity is calculated using Eq. (22). After the degree of crystallinity is known, the diffusion coefficient is calculated using Eq. (20). Then in the next time step, r in Eq. (A3) is calculated using the newly calculated diffusion coefficient at this position and then the BF_3, fluoride ion and ethanol concentrations are calculated using the finite difference Eqs. (A1) and (A2).

$$r = D\delta t/(\delta x)^2 \tag{A3}$$

where δt and δx are time step and subdivision of the sample thickness, respectively. δx was taken as 1/100 of the sample thickness. During the computation process, the initial value of r was taken as 0.1 in order to get stable solutions [24]. The procedure was coded in Fortran and solved using a computer.

Fig. 12 is the comparison between the analytical solution and the numerical solution in linear diffusion using the above algorithm by adopting a constant diffusion coefficient of KF in ethanol solution. It can be seen that the numerical solution is in very good agreement with the analytical solution (Eq. (6)). The numerical method should therefore be reliable.

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