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The influence of basic filler materials on the degradation of amorphous D- and L-lactide copolymer

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Composite films made of poly L/D copolymer and hydroxylapatite (HA) as filler material were made in two different volume percentages. As references pure copolymer films and composite films with magnesium oxide (MgO) were prepared to serve as strongly basic model filler material. All these materials were immersed in phosphate buffered saline to study the effect of filler materials on the degradation rate of the copolymer. Filled films showed less molecular weight decrease than the unfilled films, while lactate release was higher for the filled films than for the unfilled films. This effect implies that the filler materials influence the degradation mechanism by preventing the occurrence of the autocatalytic effect of the acidic endgroups, resulting from hydrolysis of the polymer chains. The polymer chains at the surface of the material are less protected by the filler materials, which causes a more rapid degradation of these chains and a higher lactate release. At the same time composites seem to show an erosion type of degradation rather than bulk degradation in unfilled materials.

1. Introduction

Amorphous poly-DL-lactides have been tested as biomaterials and showed good compatibility and resorbability [1, 2]. The use of this material as a bone repair material is not feasible because of the limited load-bearing possibilities and the relatively fast degradation. High-strength crystalline poly-L-lactide (PLLA) does not degrade as fast as poly-DL-lactide, but its use has become controversial because of the noxious crystalline residuals which remain unresorbed for very long periods [3, 4], resulting in long-term foreign body responses.

In our laboratory, the possibilities of strengthening amorphous polylactide by incorporation of resorbable hydroxylapatite (HA), which has bone bonding abilities, have been tested. This study focuses on the effect of HA filler particles on the degradation rate of composites with polylactic acid copolymer.

The hydrolytic degradation of polylactides is (auto) catalysed by the increasing concentration of acidic polymer endgroups [5]. Therefore the hypothesis is put forward that the presence of basic filler materials, such as HA, might retard the degradation by neutralizing and/or absorption of acidic endgroups. The ability of HA to bind carboxylic groups is well documented [6], but, to further test the hypothesis, a strongly basic filler material, MgO, was also studied on its effect on the degradation rate.

2. Materials and methods

Polymer films (0.3–0.5 mm in thickness) were made of a copolymer of L- and D- lactic acid, with an L/D ratio of 85/15 (Purac Biochem bv.), by dissolving the polymer in chloroform, decanting the solution in a teflon mould and slowly evaporating the chloroform. Composite films were cast by mixing 30% or 50% (w/w) of filler material into the polymer solution in chloroform and stirring carefully until a homogeneous mixture was achieved. As filler material, sintered hydroxylapatite (HA) was used, milled and sieved to a powder, with a particle size range of 1–45 μm. Also, composite films were made with 30% MgO (Merck, Darmstadt, as received) to serve as a strongly basic model filler material. The films were cut in three parts, weighed and immersed, in triplo, in 11 ml phosphate buffered saline (PBS) pH 7.2 at 37 °C in a shaking waterbath for 1, 2 and 4 days and for 1, 2, 4, 8 and 12 weeks without changing the PBS. As reference a film was made of each material without immersing it in PBS ($t = 0$).

At the end of the immersion times the films were taken out of the PBS, dried between filter paper and the weight changes were determined. Then the films were dried, first in vacuum for 48 h at room temperature and next for 1 h in vacuum at 50 °C. The samples were sealed in plastic and stored in a freezer at −20 °C prior to further characterization. The residual PBS

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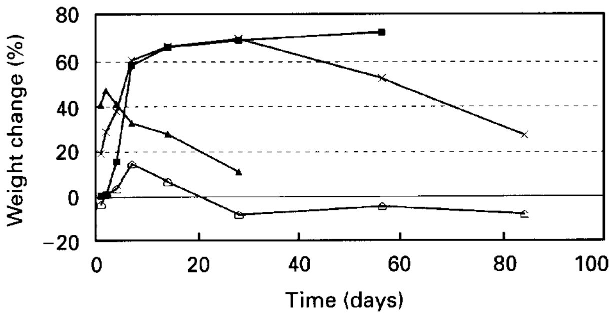

Figure 1 Weight change as a percentage of initial weight, mean of triplo measurements. ■ 0% HA; × 30% HA; ⌂ 50% HA; ▲ 30% MgO.

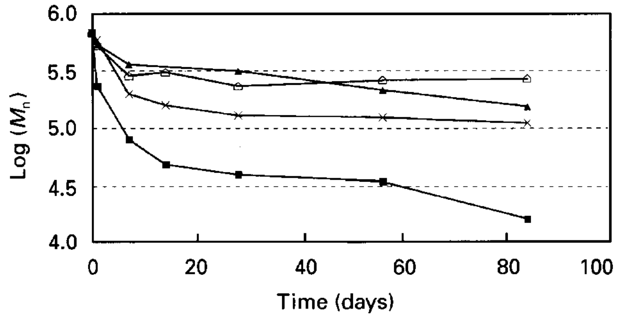

Figure 2 Results of GPC measurements: the average molecular weight (M_n) of the residual film, mean of triplo measurements. ■ 0% HA; × 30% HA; ⌂ 50% HA; ▲ 30% MgO.

was stored at 4 °C. Molecular weight changes due to degradation were measured by gel permeation chromatography (GPC) with chloroform as solvent. As references the starting material and the non-immersed film ($t = 0$) were measured. Polystyrene standards were used for calibration.

Thermal analysis of the residual films was done by differential scanning calorimetry (DSC, DuPont 910) by equilibrating at 10 °C and heating at 10 °C per minute to 250 °C.

The lactate release in the residual PBS was measured by a discrete clinical analyser (ACA IV DuPont, at 340 and 383 nm) after enzymatical oxidation into pyruvate. Also the pH-changes of the PBS were checked.

3. Results

The weight change pattern of the films indicated water uptake in the first days of immersion, followed by weight loss (Fig. 1). Saturation with water takes place for each material after different periods of time. This water uptake masks the weight loss effects of degradation. After 2 days the film with 30% MgO, for instance, showed a rapid decrease in weight, comparable with the 50% HA film after 7 days. With 0% HA and 30% HA films water uptake dominates over longer periods. Due to disintegration, the MgO films could not be weighed after 8 weeks of immersion; the weight of 0% HA films could not be measured at an immersion time of 12 weeks. The films filled with 30% and 50% HA retained integrity during the whole experiment.

The average molecular weight (M_n) of the copolymer changed rapidly for the 0% HA films (Fig. 2); the decrease of M_n was less rapid for the 30% HA films. Both the 50% HA and the 30% MgO films showed the slowest decrease in average molecular weights.

DSC proved that there were no crystallinity peaks in either the HA-filled or the unfilled materials. Only MgO-containing films showed, after 12 weeks of immersion, a broad endothermal peak at 124 °C of 158 J/g composite (Fig. 3).

After 1 day, the lactate release in PBS was very high for MgO-containing films (Fig. 4), almost 50% of the total lactate present in the material being released after 12 weeks. The rest of the samples gradually released about equal amounts of lactate in time. The

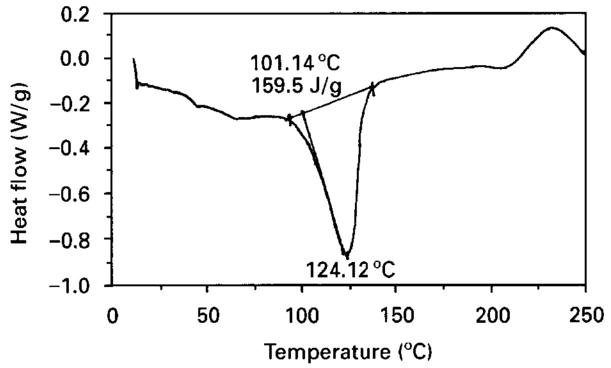

Figure 3 Thermal analysis: a DSC graph of a MgO-filled film after 12 weeks of immersion in PBS.

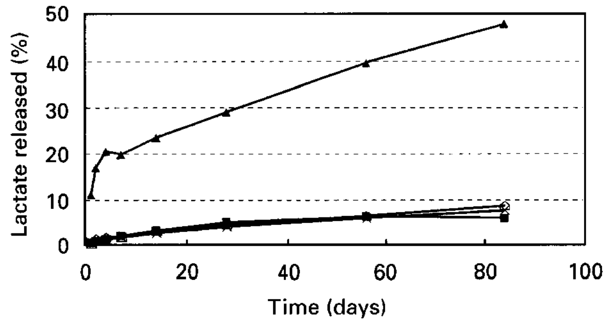

Figure 4 Lactate release after immersing the materials in PBS, mean of triplo measurements. ■ 0% HA; × 30% HA; ⌂ 50% HA; ▲ 30% MgO.

PBS-buffer pH changes rapidly (Fig. 5) during the first 2 days, but then the pH stabilizes at a different pH for each material.

4. Discussion

The two main parameters describing the process of lactide degradation are the release of lactate (monomer) and the average molecular weight (M_n) of the remaining polymer in the composite films. The amount of soluble lactate molecules present in PBS reflects hydrolysis of endgroups, although degradation by hydrolysis will attack the polymer at randomly distributed sites.

The results show that polymer films without filler material and films filled with HA release lactate at the lowest rates, while MgO-filled films release lactate

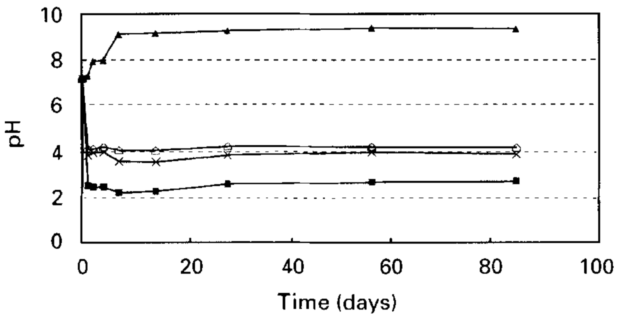

Figure 5 pH-changes in PBS due to degradation of poly L/D copolymer, mean of triplo measurements. ■ 0% HA; × 30% HA; ○ 50% HA; ▲ 30% MgO.

very rapidly. The unfilled films show the fastest decrease in average molecular weight. The composite films show lower rates of molecular weight decrease, the effect being more pronounced when more filler material is present and when the filler is more basic, as with MgO-filled films. After 4 weeks the average molecular weight of MgO films seems to decrease faster than at the beginning of the test. This can be explained by the increase of specific composite surface due to disintegration, so the shielding effect of the basic filler material is decreased.

The weight loss patterns also show different effects to some extent although water uptake partly compensates the loss of weight due to lactate going into solution.

The observed effects can be explained by assuming that the basic filler particles are indeed effective in neutralizing or immobilizing the acidic endgroups, especially in the bulk of the films. At the surface of these films, due to the presence of the surrounding solution, the shielding effect of the basic filler materials is less pronounced and the degradation processes can be accelerated by acidic endgroups. In the case of unfilled films, degradation takes place throughout the bulk of the film resulting in rapid decrease in average molecular weight.

Although the lactate release in unfilled films is very low, the pH of the PBS is lower than for the composite materials. This can be explained if lactate has been released, at least partly, in the form of Ca or Mg salts. The higher lactate release in combination with larger weight change effect and the small change in average molecular weight of the remaining polymer for 30% MgO shows a more pronounced erosion-type degradation for MgO-filled materials and might partly be caused by better solubility by Mg lactates than HA-bonded lactates. The film with 50% HA shows a rapid loss of weight and a small M_n change, comparable with MgO-filled films.

Apparently the presence of the filler material slows down the degradation rate and leads to a more erosion-based type of degradation at the surface of the films.

Over the experimental period of time none of the HA-filled or unfilled films showed development of crystallinity [5]. Crystallinity was found only at the 12 weeks stages of MgO model films. The ΔH value of 160 J/g composite films, 205 J/g polymer, indicates that the crystalline products are of low molecular weight type, presumably Mg salts of oligo-lactates.

5. Conclusions

The effect of the filler materials on the degradation rate is significant and corroborates our hypothesis considering the order of effectivity: 30% HA has less effect on the degradation than 50% HA, the latter being about equal to 30% MgO in the beginning, but 30% MgO films disintegrate in 8 weeks, while the HA filled films remain in good condition. Moreover, the faster weight loss of composites combined with less molecular weight change as compared to unfilled materials indicates an erosion type of degradation in the former and bulk degradation in the latter composites.

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