Mechanical Properties and Porosity of Polylactide for Biomedical Applications

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ABSTRACT: In this study, the strength, ductility, and porosity of polylactide films prepared by immersion precipitation and film casting in air were investigated. To induce extra porosity in the films, dodecane was added to the polymer casting solution. The structure, porosity, and mechanical properties of the films were evaluated. The ultimate strength and elastic modulus of neat poly(L-lactide) prepared by film casting were at least twice those of the same film prepared in methanol, whereas the ductility of these films was considerably higher than that for air. The porosity, size of pores, and interconnectivity of pores increased gradually with increasing dodecane concentration. This dodecane-induced porosity (as high as 80%), progressively reduced the ultimate strength and modulus of practically all films but remarkably improved the ductility of films prepared in air, and this can be related to a decrease in the crystallization temperature. For films prepared in water or poly(D,L-lactide) films in general, the ultimate strength, modulus, and ductility of films prepared in water were significantly lower than those of air-cast poly(L-lactide) films. In summary, the results obtained in this research show that it is possible to tailor the properties of films for various biomedical applications through the use of the polymer type, preparation method, and dodecane-induced porosity as tools. © 2007 Wiley Periodicals, Inc. J Appl Polym Sci 107: 82–93, 2008

Key words: polyactide; mechanical properties; porosity; structure; biomedical applications

INTRODUCTION

Biodegradable polymers have received considerable attention in the past decades because of their widespread applications in pharmaceutical, biomedical, and environmental fields.[1,2] Typical examples of these polymers are aliphatic polyesters such as poly(butylene succinate), poly[(butylene succinate)-*co*-adipate], poly(3-hydroxybutyrate), poly(ε-caprolactone), and polylactide (PLA).[3–6] PLA is highly hydrolyzable in the human body and has good mechanical strength, thermal plasticity, fabricability, biodegradability, and biocompatibility;[7,8] that is why PLA has become one of the most popular biodegradable materials in biomedicine. It has been used for sutures, bone screws, bone plates, tissue repair, and regeneration and also for controlled delivery devices (e.g., microparticles or implants for drugs).[1,9–16] Also, for applications outside the medical field, recent developments in processing technology have made PLA more economically viable as an environmentally friendly substitute for conventional synthetic packaging materials.[2]

For many applications, the degradation and mechanical properties of PLA are important. The degradation behavior of PLA plays a big role in its *in vivo* performance and may influence many processes, that is, tissue regeneration, cell growth, and host response.[17,18] Degradation of PLA mostly occurs by hydrolytic attack of the ester bonds in the polymer, after which lactic acid monomers are formed and eventually removed via normal metabolic processes in the body.[19,20] There are many factors that can affect the degradation rate of PLA, including polymer material properties such as crystallinity, molecular weight, and monomer hydrophobicity.[19] Moreover, some researchers have reported that additives can also speed up or delay the degradation process of PLA.[21–23]

Beside the degradation behavior, which is beyond the scope of this article, the mechanical properties of PLA are of great importance also, and in this respect some improvement of the brittle nature, lack of toughness, and low deformation at break, for example, is desirable.[24–26] One solution lies within the polymer itself; it is well known that the physical properties of PLA, such as the melting point, mechanical strength, and crystallinity, can be influenced considerably by the stereoisomeric length/diameter ratio of the lactide units.[3,5] For instance, poly(L-lactide) (PLLA), which consists of pure L-lactide, is an isotactic and crystallizable polymer that gives

strength to structures.[3,27] In contrast, poly(D,L-lactide) (PDLLA), produced from racemic mixtures of L-lactide and D-lactide, is atactic and completely amorphous, resulting in more brittle structures.[3,27] Also, several other techniques to enhance flexibility and toughness have been reported, such as copolymerization or blending with other substances such as polymers,[3,6,28] plasticizers,[24–26,29] or fillers.[4,30]

Each application will have its own requirements; therefore, it is obvious that control over the mechanical properties of PLA is of great importance. However, structure-related properties should not be disregarded because they will influence the mechanical properties; at the same time, they may be required for a specific application (e.g., porosity for controlled-release purposes). Part of the solution can be found within the polymer itself, but obviously the production method will also play a role. Various production processes have been reported for PLA, such as injection molding, extrusion, film blowing, fiber spinning, film casting, and immersion precipitation.[2,5,9,13,24,30,31] In the last process, for instance, a dope consisting of a polymer, a solvent, and additives is immersed in a coagulation bath filled with a nonsolvent, and because of the subsequent exchange of the solvent and nonsolvent, phase separation takes place, and solidification of the polymeric product occurs.[31] Depending on the composition of the coagulation bath, completely different structures may be formed, ranging from dense films to highly porous structures. It can be expected that depending on the structures formed, different mechanical behaviors will be found, therewith codetermining the field of application.[9,32] Therefore, it is not strange that immersion precipitation has been proposed in very different fields, including the preparation of polymeric membranes and also the preparation of biodegradable scaffolds for blood vessels, drug delivery devices, microparticles, implants, fibers, and films.[13,16,31,33]

In this study, we systematically investigated PLA films (PLLA, PDLLA, and mixtures thereof) to correlate the structure formation with the mechanical behavior. The films were fabricated via two processes, film casting and immersion precipitation. In the first method, the film was cast and then exposed to the air, whereas in the last one, the film was immersed into different nonsolvents (instead of air), which are known to influence the film structure considerably. Besides that, dodecane was also used as an immiscible additive to the polymer solution that was used to prepare the films to induce porosity in the films away from the porosity generated by regular phase-separation processes. (The use of high alkanes, such as dodecane, has been described in literature for, among other things, the production of hollow polymeric particles.[33]) In this way, we hoped to combine structure-related requirements, such as

porosity, with mechanical strength. The results are summarized in an application graph that links (film) production conditions, mechanical properties, and methods with application fields.

EXPERIMENTAL

Materials

Two types of PLA were used in this study, PLLA and PDLLA (50/50), with intrinsic viscosities of 1.21 and 0.49 dL/g, respectively, and both were obtained from PURAC Biochem B.V. (Gorinchem, The Netherlands). Dichloromethane (DCM; high-performance liquid chromatography gradient grade) was purchased from Merck (Amsterdam, The Netherlands) and used as the solvent for the polymer. Dodecane (≥99%) was supplied by Sigma–Aldrich (Zwijndrecht, The Netherlands) and used as an additive. Methanol (high-performance liquid chromatography gradient grade, ≥99.9%; Aldrich) was used with Milli-Q water as a nonsolvent. All chemicals were used as received.

Methods

Film preparation

To form PLA films, solutions with weight ratios of 10 : 0 : 90, 10 : 5 : 85, 10 : 10 : 80, 10 : 15 : 75, and 10 : 20 : 70 (w/w) PLLA/dodecane/DCM, 10 : 0 : 90, and 10 : 5 : 85 (w/w) PDLLA/dodecane/DCM, and 10 : 5 : 85 (w/w) PLA mixture (1 : 1 PLLA/PDLLA)/dodecane/DCM were prepared. In the case of the films with 10% PDLLA, only one dodecane concentration was used because at higher concentrations, no films could be formed with PDLLA. The polymer was first dissolved in DCM, and if needed, dodecane was subsequently added. The solution was kept under stirring for 1–2 days. The films were formed with two procedures:

1. Film casting: the polymer solution was cast onto a mold and left in a fume hood for evaporation of the solvent under ambient conditions.
2. Immersion precipitation: the polymer solution was cast onto a mold and then immersed into a coagulation bath filled with nonsolvent and kept there for around 40 min. As nonsolvents, 100 : 0, 60 : 40, 30 : 70, and 0 : 100 (w/w) methanol/water mixtures were used in this study. The initial thickness of the cast layer was always 100 μm.

Mechanical properties

All films were left in the fume hood under ambient conditions for 1 day before use to ensure complete evaporation of the solvent. Out of films prepared by either film casting or immersion precipitation, sam-

ples with a dog-bone-like shape were cut. The total length of each sample was 37 mm, the gauge length of the samples was about 15 mm (±1), and the width was 13 mm at the top and 7.2 mm (narrowest) at the middle of the sample to induce the fracture in the middle of the sample. Tensile testing of the films was performed with the Texture Analyzer T2 (Stable Micro Systems, Ltd., Surrey, United Kingdom). The tensile tests were carried out at a constant crosshead speed of 0.1 mm/s until break. Stress–strain curves were calculated from load–elongation curves measured for 2–10 samples from films that were each separately produced under the various conditions described earlier. The tensile strength, elongation at break, and Young's modulus were calculated from the stress–strain curves.

Differential scanning calorimetry (DSC)

The thermal properties of the films were measured with a PerkinElmer (Boston, MA) DSC-7 differential scanning calorimeter with a TAC 7/DX thermal analysis controller. Scans of samples (ca. 8–10 mg) were run from 0 to 250°C at a heating rate of 10°C/min. The glass-transition temperature, crystallization temperature, melting temperature, and enthalpies of crystallization and melting were determined.

Scanning electron microscopy (SEM)

Structures of the films before and after tensile testing (with special interest for the fracture surfaces) were investigated by SEM (JSM-5600 LV, JEOL, Tokyo, Japan). Cross sections of the samples were cut, dried, and fractured in liquid nitrogen. Before observation with SEM, the cross sections were coated with a thin platinum layer ($\sim$ 5 nm) with a sputter coater (JFC-1300, JEOL).

Porosity and density of the films

The porosity of the films was estimated by the measurement of the mass and dimensions of the films as reported by Hu and coworkers and others.[16,34,35] The porosity (ε) was defined as follows:

$$\varepsilon = 1 - \rho_{film}/\rho_{polymer} \qquad (1)$$

where ρ_{film} and $\rho_{polymer}$ are the (bulk) densities of the film and polymer, respectively. The densities of the films were measured by the calculation of the mass/volume ratio for three samples of each film. The film prepared without dodecane [Fig. 1(a)] showed a porosity of zero, and therefore the density of this film was taken as the polymer density.[16,36]

For the theoretical description of the bulk density of the films (ρ_f) and, therefore, of the porosity as a function of the dodecane concentration, eq. (2) was used:

$$\rho_f = \frac{X_{polymer}}{(X_{polymer}/\rho_{polymer}) + (X_{dodecane}/\rho_{dodecane})} \qquad (2)$$

where $X_{polymer}$ and $X_{dodecane}$ are the mass fractions of the polymer and dodecane, respectively, and $\rho_{polymer}$ and $\rho_{dodecane}$ are the densities of the polymer and dodecane, respectively. It was assumed that the total volume fraction of the voids (porosity) in the film was equivalent to the volume fraction of the dodecane added to the film. This implies that the volume loss of the air-cast film was caused by evaporation, and the weight of the film was equivalent to the initial weight of the polymer in the cast. These assumptions were true only for air-cast films in Figure 1, as the porosity was mainly caused by dodecane, whereas for immersion-precipitation films, these assumptions did not hold because part of the porosity in the films was generated by the phase-inversion process.

RESULTS AND DISCUSSION

Film characterization

Morphology air casting

The morphologies of the cross sections of PLLA films prepared by air casting were investigated by SEM. In Figure 1, the results for different dodecane concentrations are shown. When no dodecane was present in the casting solution, a solid, dense, and nonporous film was obtained [Fig. 1(a)]. When the film was exposed to air, only evaporation of the solvent DCM occurred because air could hardly diffuse into the polymer solution; no demixing took place, and therefore a nonporous structure was observed.

When dodecane was added, the structures were entirely different; they became porous, and porosity increased with increasing dodecane concentration (this is described in more detail in the Film Porosity and Density section). For 5% dodecane, an asymmetric morphology consisting of a thin, dense top layer and a porous sublayer with a fairly uniform closed cellular structure was obtained [Fig. 1(b)]. With increasing dodecane concentration (i.e., >10% w/w), symmetric structures with more open morphologies were observed [Fig. 1(c–e)]. The overall pore fraction, size of the pores, and interconnectivity of the pores gradually increased with increasing dodecane concentration. On the basis of these findings, one can say that the addition of dodecane is a novel and easy approach to the production of porous structures by the film-casting method.

The influence of dodecane on the structure can be explained as follows: when a film containing dode-
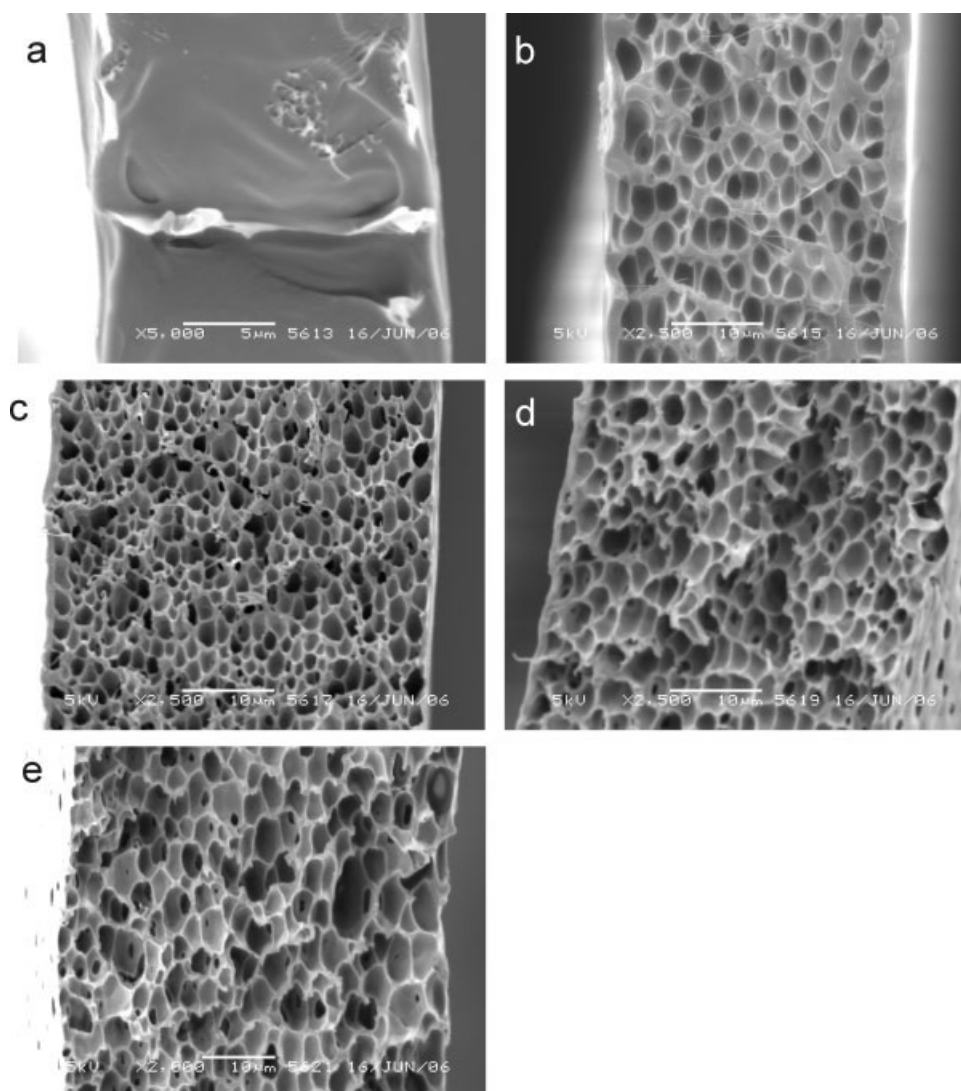
Figure 1 SEM images of cross sections of PLLA films prepared in air and with different dodecane concentrations (w/w) in casting solutions: (a) 0, (b) 5, (c) 10, (d) 15, and (e) 20%. The initial polymer concentration in all films was 10% (w/w).

cane is exposed to the air, the solvent DCM will start to evaporate, and consequently, the dodecane concentration in the film will increase. Because dodecane is a poor solvent for PLA, one expects that when dodecane reaches a certain concentration, demixing will start to occur in the film by nucleation and growth of the polymer.[32] The dodecane droplets are the precursors of the pores that were observed by SEM. The amount of these droplets is expected to increase when more dodecane is added to the polymer solution. Thus, the incidence of coalescence will become higher, and this will eventually result in a structure with more and larger pores. This is in line with the SEM observations. The resulting structure is expected to be solidified by crystallization of the polymer. How this influences the mechanical properties is discussed in a later section.

Morphology immersion precipitation

The structures in air-cast films are now compared with those obtained by immersion precipitation in various nonsolvents (see Fig. 2). With methanol, the structures were to a certain extent similar to the ones obtained with air. When water/methanol mixtures were used, the porosity, size of the pores, and interconnectivity of the pores increased with increasing water concentration.

During immersion precipitation, the phase-separation process is different and more complex than that for air casting. Contacting the polymer solution with the nonsolvent will lead to out-diffusion of the solvent into the nonsolvent (instead of air) and in-diffusion of the nonsolvent into the polymer solution. When the polymer solution becomes saturated with the nonsolvent, phase separation will take place. In a previous study,
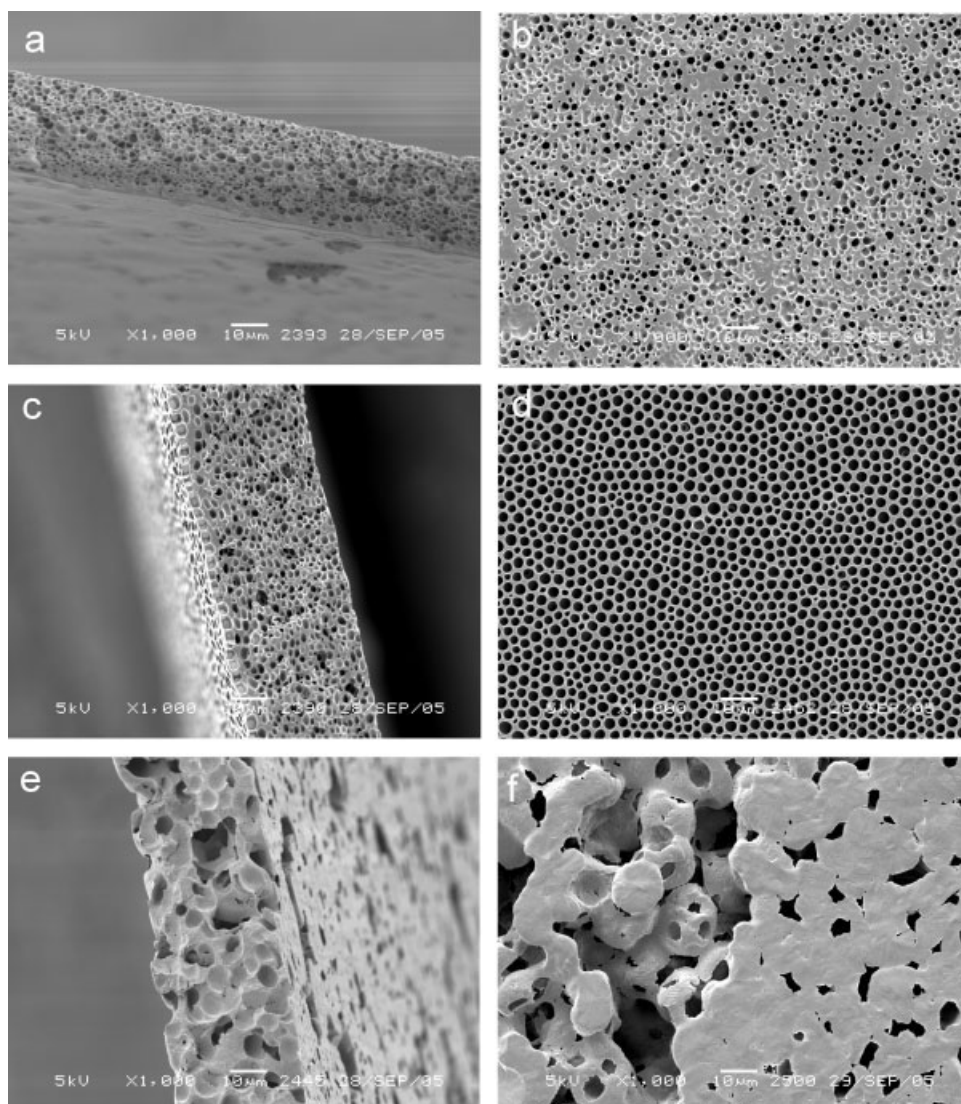
Figure 2 SEM images of cross sections of films prepared from 10:05:85 (w/w) PLLA/dodecane/DCM with different nonsolvents: (a) methanol, (b) methanol (surface), (c) 60 : 40 (w/w) methanol/water, (d) 60 : 40 (w/w) methanol/water (surface), (e) water, and (f) water (surface).

we found that PLLA films are solidified by crystallization of the polymer, and depending on the nonsolvent used, crystallization will set in early (methanol) or later (water), therewith allowing more or less time for solidification of the structure and/or structural rearrangements.[32] Furthermore, dodecane speeds up phase separation and induces faster crystallization in the films, depending on the nonsolvent used. Even when we used PDLLA in combination with dodecane, the films did not collapse, and porous structures were obtained.[32] Thus, crystallization is not necessity for solidification in the film. For a more complete description of the effects involved, we refer readers to previous work.[32]

Film porosity and density

Figure 3 shows the porosity and density of films prepared in air as a function of the dodecane concentra-

tion. The results were in line with the SEM observations; the higher the dodecane concentration was, the higher the porosity was in the films. With increasing porosity, obviously the bulk density of the films decreased [see Fig. 3(a)]. Figure 3(a) shows that the theoretical model always overestimates the measured porosity, which points to partial collapse of the structure. This effect is, perhaps surprisingly, more pronounced at low dodecane concentrations [see Fig. 3(b)]. It is thought to be caused by the time-scale of solidification in these films, which was slow in comparison with high dodecane concentrations, which solidify quickly.[32] This is expected to lead to better preservation of the structure. Although part of the porosity that is induced by dodecane collapses, it is important to note that the largest part of this porosity remains, and more so at higher concentrations
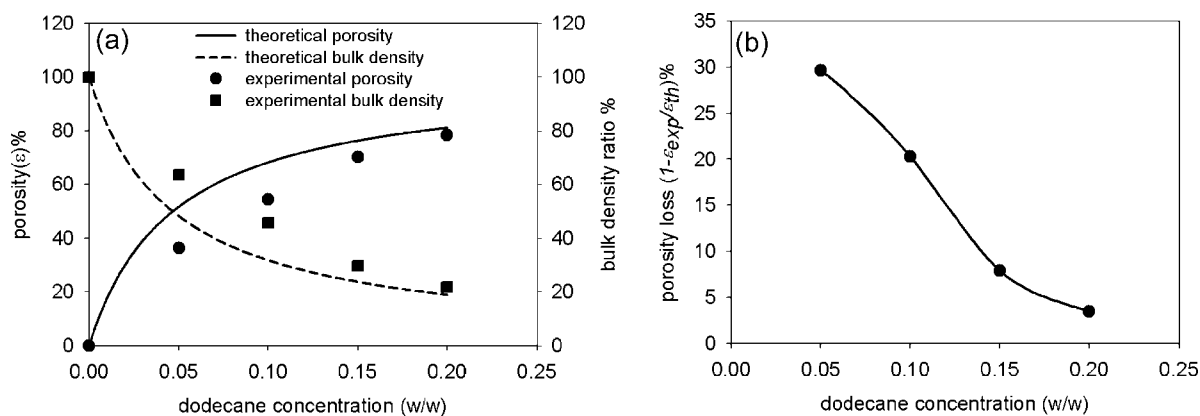
Figure 3 Influence of the dodecane concentration on the porosity and bulk density of PLLA films prepared in air. The theoretical porosity and bulk density of the films were calculated with eqs. (1) and (2). The initial polymer concentration in all films was 10% (w/w).

of dodecane [Fig. 3(b)]. This is true not only for air-cast films but also for films prepared by immersion precipitation.[32] This indicates an additional way of inducing porosity in a film away from pores generated by regular phase separation. Whether this also leads to mechanically more interesting structures is discussed in the next section.

Mechanical properties

The ultimate tensile strength, elasticity modulus, and elongation at break were measured for all films described in the Experimental section. The effects of the dodecane, preparation method, and type of PLA on the mechanical properties of the films were investigated.

Ultimate tensile strength and elastic modulus

In Figure 4, the effect of dodecane on the ultimate tensile strength [Fig. 4(a)] and elasticity modulus [Fig. 4(b)] of PLLA films prepared by either air casting or immersion precipitation with methanol or water is shown. The film without dodecane prepared by air casting showed a maximum tensile strength of approximately 70 MPa and an elasticity modulus of approximately 2.4 GPa, which are, in fact, similar to those reported elsewhere for neat PLLA.[5,37] When the same film was prepared by immersion into methanol, the tensile modulus and strength dropped to around half of the original values (see Fig. 4), and we think that the presence of pores (less than if dodecane were added) caused these effects. This conclusion is in line with the fact that dodecane-induced porosity leads to significant decreases in the ultimate strength and elasticity modulus. Please note that these latter porosities can be as high as 80% (Fig. 3).

When comparing films with dodecane prepared in air and methanol, we found it remarkable that the

films showed approximately the same ultimate strength, whereas the elasticity moduli of films prepared in air were higher than those in methanol [Fig. 4(b)]. When comparing with films prepared in water, we found that both the ultimate strength and elasticity were considerably less than for methanol and air. This was investigated in more detail; with increasing water concentration in water/methanol mixtures, the films became gradually more fragile and weak [Fig. 4(c)]. This can be attributed to the formation of large pores, which are known to occur in films with dodecane cast in water [see Fig. 2(e,f)] and which are generally considered weak spots within the structure.[35] In air-cast films and films submerged in methanol, these large pores were not present [see Figs. 1(b–e) and 2(a,b)].

The results for crystalline PLLA are compared to those for amorphous PDLLA and 1 : 1 mixtures of both polymers. As expected, the higher the PLLA concentration was in the films, the higher the strength and modulus were (see Fig. 5). This is ascribed to the high load-bearing capacity of the crystalline domains in PLLA.[27,38]

On the basis of these results, one can conclude that the mechanical properties of the films are dependent not only on the polymer type but even more so on their structure; the tensile strength and elasticity modulus decrease with increasing porosity, pore size, and interconnectivity. This is reasonable if we keep in mind that fracture in films originates from local concentrations of stress at flaws, scratches, or notches[39] and propagates by nucleation and growth of cracks or crazes inside structures. These cracks can easily propagate and grow in regions containing voids, and they become even easier to grow from larger pores or macrovoids within films. Furthermore, it is expected that the cross-sectional area of the load-bearing polymer will decrease with increasing porosity in the film, which will reduce the
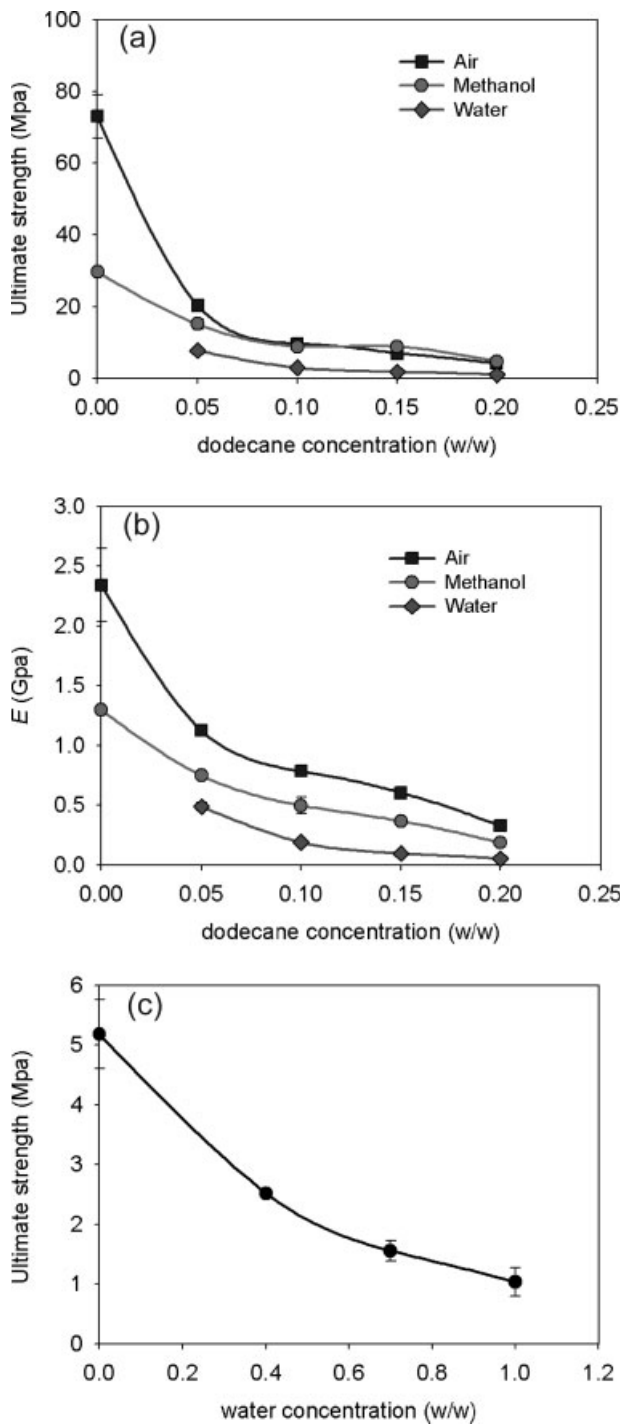
Figure 4 Influence of the dodecane concentration and preparation method (air, methanol, and water) of 10% polymer films on (a) the ultimate strength and (b) elastic modulus (E) of PLLA films and (c) the ultimate strength of 10 : 20 : 70 PLLA/dodecane/DCM films as a function of the water concentration in the nonsolvent.

tensile modulus and ultimate strength.[11] A first attempt to quantify these effects is given in the next section.

The reduction in strength and elasticity modulus with increasing porosity was also observed in other

studies,[35,36,40] and for highly porous materials such as foams, a power-law relation between the porosity (ε) and elasticity modulus (E) was given:[36,40]

$$E = E_0(1 - \varepsilon)^n \qquad (3)$$

where E_0 is the modulus of the nonporous film and n is a constant. For E_0, the E value of a film prepared without dodecane was taken, and the model was fitted to our experimental data for films prepared in air with the least sum of squares. For a value of n of 1.326, the data points are described adequately (see Fig. 6). The theoretical value of n for completely open cell foams has been reported to be 2, whereas for closed cells, this value is around 1.[40] Our value is between these extremes, indicating partially open cells (see Fig. 1).

The same model was explored to describe the ultimate tensile strength (σ) of the films as a function of the porosity (ε) and ultimate strength of the film prepared without dodecane (σ_0):
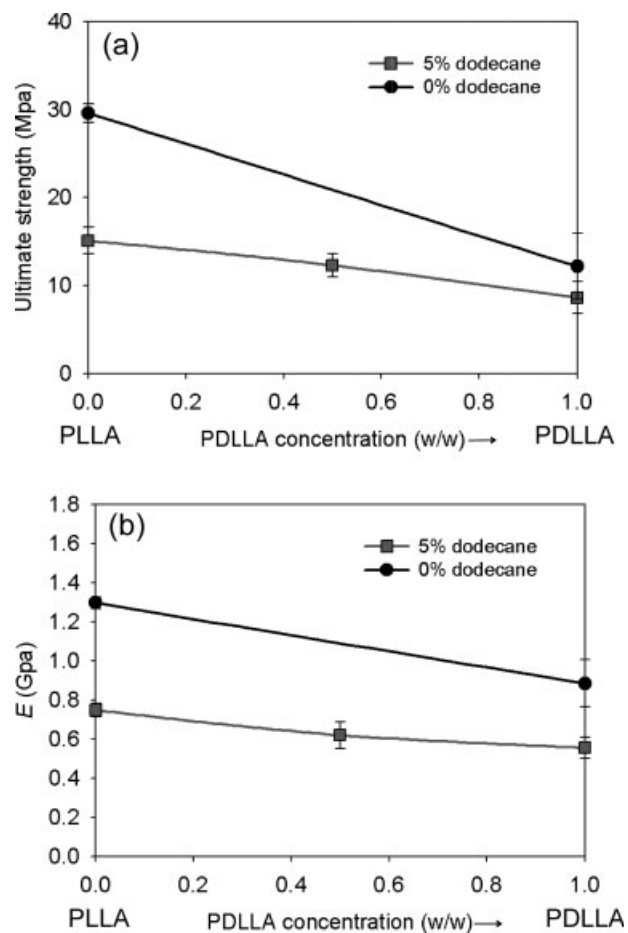

Figure 5 Influence of the PLA type (PLLA or PDLLA) on (a) the ultimate strength and (b) elastic modulus (E) of PLA films prepared in methanol and with different dodecane concentrations. The initial polymer concentration in all films was 10% (w/w).
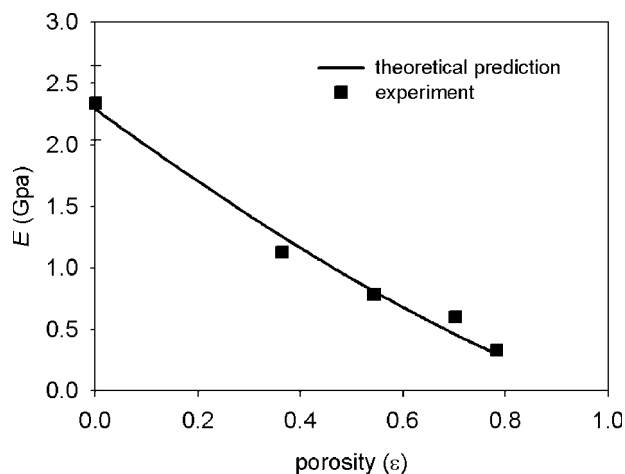
Figure 6 Influence of the porosity on the elastic modulus (E) of PLLA films prepared in air with different dodecane concentrations. The initial polymer concentration in all films was 10% (w/w).

$$\sigma = \sigma_0(1 - \varepsilon)^n \qquad (4)$$

Again, the data were fitted with the least sum of squares method, and for $n = 2.596$, the fit is reasonable (see Fig. 7).

Elongation at break

Besides the elasticity modulus and ultimate strength, the elongation at break is also an important feature of a film. In Figure 8, results are shown for films prepared by air casting and immersion precipitation (with or without added dodecane). When no dodecane was added, the film formed in air showed typical stiff behavior of neat PLLA with a total elonga-
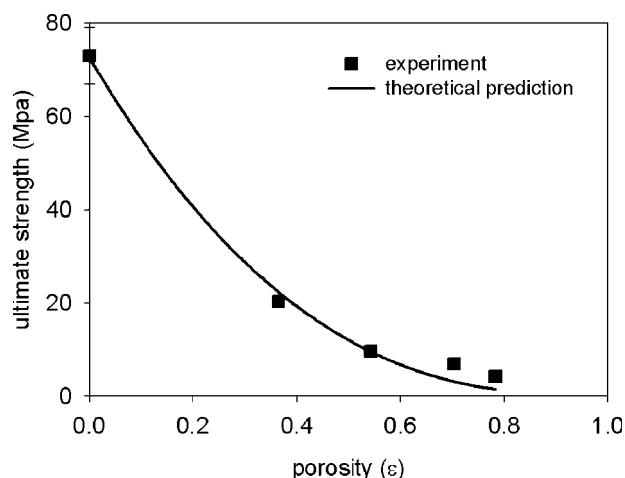
tion of 8%, which is close to values stated in other studies.[26] Remarkably, with methanol, the flexibility of the film was significantly enhanced, and an elongation at break of up to 35% was recorded. This may be due to the higher degree of deformation that a regular cell structure permits during elongation.

The effect of dodecane depends on the preparation method used. A remarkable improvement in ductility was observed for the films prepared in air (although the strength and modulus decreased considerably; see Fig. 8). For example, the elongation of the film with 5% (w/w) dodecane was 3 times that of a neat PLLA film; that of a film with 10% (w/w) dodecane was 8 times that of a neat PLLA film. This can be related to the structure of the films; in air-cast films with dodecane, we observed the formation of fairly large but uniform pores (Fig. 1), which can deform during elongation and hence allow for a much larger maximum elongation at break. This was investigated in more detail with DSC, and the results are shown in that section.

The effect of dodecane on the ductility of films prepared with methanol was different from the effect on those prepared with air. At 5% (w/w) dodecane, the elongation at break of the films was slightly enhanced in comparison with neat PLLA, but when higher concentrations of dodecane were used, a progressive reduction in the elongation at break was observed, as shown in Figure 8. At 5%, the films still contained many small pores [Fig. 2(a)], but at higher dodecane concentrations, these films had many large pores with thin, fragile lamellae between them[32] and were, therefore, more susceptible to break at less elongation.

For films produced by precipitation in water, a low ductility was found; dodecane did not show any influence on the elongation of the films (see Fig. 8). These findings are in line with the effects on the
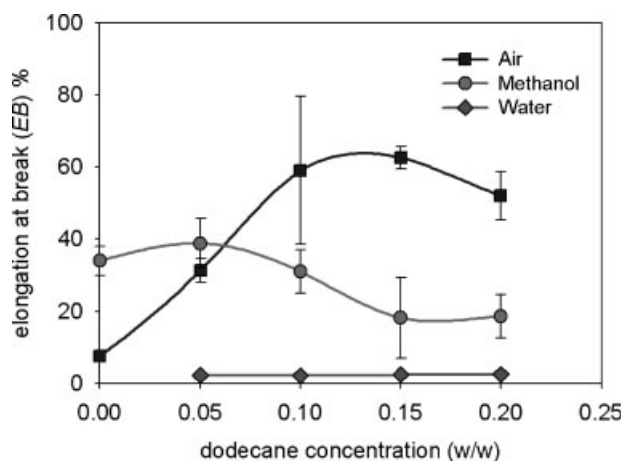

Figure 7 Influence of the porosity on the ultimate strength of PLLA films prepared in air with different dodecane concentrations. The initial polymer concentration in all films was 10% (w/w).

Figure 8 Influence of the dodecane concentration and preparation method (air, methanol, and water) on the elongation at break of PLLA films. The initial polymer concentration in all films was 10% (w/w).
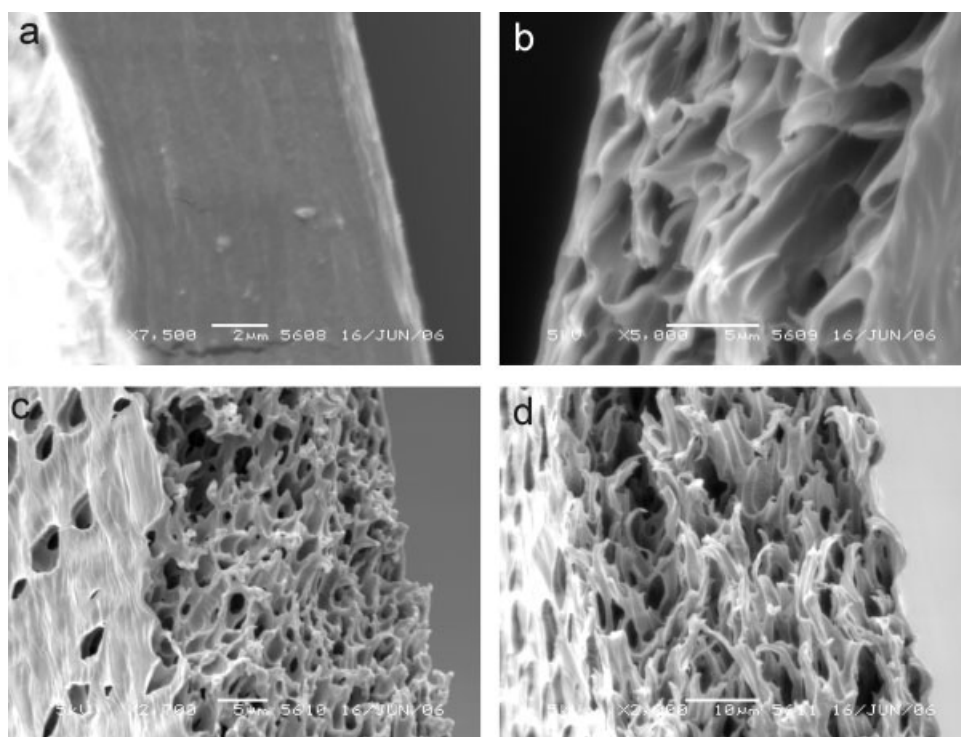
Figure 9 SEM images of cross sections of fracture surfaces of films prepared in air and with different dodecane concentrations in casting solutions: (a) 0, (b) 5, (c) 10, and (d) 15%. The initial polymer concentration in all films was 10% (w/w).

strength and elasticity modulus; films produced in water remained weak, and we think that this is caused by the small contact areas between crystalline spherulites or domains [Figs. 2(e,f)]. When water/methanol mixtures were used as the nonsolvent, the elongation at break of these films was close to that of water (5.5% elongation for 60 : 40 methanol/water and 3.9% elongation for 30 : 70 methanol/water).

The elongation at break for the PDLLA films was less than 2%, which was very low in comparison with PLLA films (32%). Also, the addition of dodecane did not increase the ductility ($\sim$ 2.2%). This was due to the low flexibility and deformability of the amorphous domains in the PDLLA structure in comparison with the crystalline ones in PLLA. Elongation of the PDLLA films was significantly enhanced through blending with PLLA; for a 1 : 1 mixture, the elongation at break was approximately 18%.

In the previous sections, we have shown structures in relation to observed mechanical behavior. In summary, porous films with controlled pore size and distribution (i.e., PLLA films with dodecane prepared in air and those of methanol with a low dodecane concentration) are more flexible under tension than nonporous films (neat PLLA films prepared in air).

These effects are visualized in the morphology of the fracture surfaces of the films. SEM images of cross sections of PLLA films prepared in air and with different dodecane concentrations, taken directly below

the fracture surface, are shown in Figure 9. Typical brittle fracture was observed for the films without dodecane [see Fig. 9(a)], and this is in line with findings in other studies.[29] The micrographs of the films prepared with dodecane [see Fig. 9(b–d)] show a large amount of plastically deformed materials. Figure 9(b–d) shows the typical morphology of a crazed material consisting of two phases; the continuous phase consists of fibrils, and the dispersed phase consists of
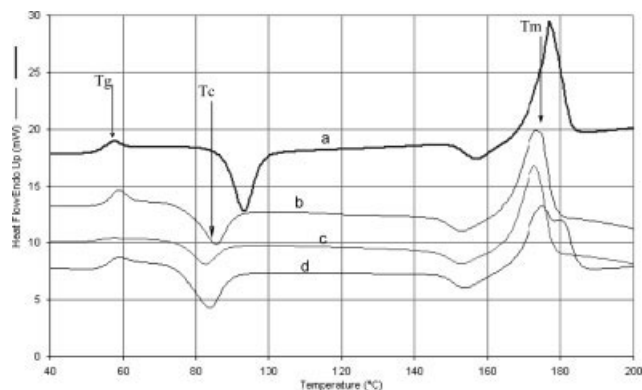

Figure 10 DSC curves (first scan) of PLLA films prepared in air with different dodecane concentrations in casting solutions: (a) 0, (b) 5, (c) 10, and (d) 15%. The initial polymer concentration in all films was 10% (w/w). T_m is the melting temperature, T_g is the glass-transition temperature, and T_c is the crystallization temperature.

TABLE I
Strength, Ductility, and Porosity of PLA Films Prepared by Immersion Precipitation and Film Casting and with Different Dodecane Concentrations for Different Possible Applications in Biomedicine

Parameter	Film specifications				
	• PLLA • No dodecane • Film casting	First set • PLLA • No dodecane • Precipitation in methanol Second set • PLLA • Low dodecane • Precipitation in methanol and film casting Third set • 1:1 PLLA/PDLLA • Low dodecane • Precipitation in methanol and film casting	• PLLA • High dodecane • Film casting	• PDLLA • Precipitation in methanol and film casting	• PLLA • With dodecane • Precipitation in water
Strength (+ = strong)	+++ (70 MPa)	++ (20–30 MPa)	+ (4–10 MPa)	+ (10–15 MPa)	− (<4 MPa)
Ductility (+ = ductile)	− (7% elongation)	+ (20–40% elongation)	++ (40–70% elongation)	−− (<4% elongation)	−− (<4% elongation)
Porosity (+ = porous)	−− (nonporous)	+ (<30%)	++ (>60%)	− (<10%)	++ (>60%)
Potential application	• Sutures[1] • Buttress for prevention of air leaks after stapled pulmonary resection[10] • Fracture fixation plates and rods	• Tissue engineering[16] • Drug delivery devices[13] • Cell culture[9] • Nerve regeneration	• Tissue engineering and repair[16] • Drug delivery devices[13] • Heart tissue engineering[16] • Cartilage tissue engineering[15] • Bone tissue regeneration • Cell scaffolding and culture[9]	• Guided tissue regeneration[9] • Sutures[1]	• Drug delivery devices[13] • Ultrasound contrast agents

microvoids. During deformation, the material can absorb more energy because of the extension of the fibrils across the microvoids; dissipation of the energy can occur by deformation or friction of the fibrils as they pull out from the bulk of the material.[39,41] In the literature,[29] similar fracture structures have been reported in plasticized PLLA, which is more deformable than neat PLLA.

DSC

Besides the structure itself, the aggregation state (crystalline or amorphous) also will influence the mechanical behavior. In particular, the effect of dodecane needs further elucidation (Fig. 8); therefore, the thermal characteristics of PLLA films prepared in air were investigated with DSC. Figure 10 shows DSC thermographs of PLLA samples prepared with different dodecane concentrations. The results indicate glass-transition temperatures of approximately 53°C and melting temperatures ranging from 172 to 177°C, which did not differ significantly between the samples. A significant decrease in the crystallization temperature of up to 10°C (from 93 to 83°C) was observed when neat PLLA films and films with dodecane were compared independently of the dodecane concentration used. For plasticized PLLA, a reduction in the crystallization temperature was reported by other researchers,[26,29] and they attributed this effect to an increase in chain mobility. When relating these finding to our DSC results, one may conclude that dodecane phenomenologically slightly acts as a plasticizer.

Options for biomedical applications

For the application of PLA products in biomedicine, specific requirements depending on the application will come into play, and these will always be a combination of structural and mechanical properties. For instance, in some applications such as guided tissue regeneration, isolation of the wounded area during the healing process is required. Therefore, devices with dense structures are preferred over porous ones, as the polymer implant will function as a barrier to allow the growth of specific tissue and to obstruct the migration of other tissues that disturb the healing process.[9,14] For some other applications, devices with porous structures are preferred. One may think here of, for example, cell scaffolding; for transport of nutrients and oxygen to the cells, pores are required.[9]

The findings in this study show how certain structures with specific properties can be produced through the use of the process conditions (e.g., air casting versus immersion precipitation, choice of polymer, addition of dodecane, and nonsolvent) as

variables. In principle, this enables us to tailor for various biomedical applications by adjusting the aforementioned process conditions. In Table I, a summary of our films is presented, with some suggestions for potential applications in biomedicine based on their strength, ductility. and porosity.

CONCLUSIONS

A variety of PLA films were prepared with film-casting and immersion-precipitation methods. The results show that the mechanical properties, morphology, and porosity of PLA films can be fine-tuned by the preparation procedure, nonsolvent quality, dodecane concentration, and PLA crystallinity.

Neat PLLA films prepared by air casting showed the hard and brittle nature of the polymer, whereas films prepared by immersion precipitation in methanol showed less hardness and improved ductility. The addition of dodecane was found to be an effective and straightforward method to generate porous films with a highly regular pore structure. The addition of dodecane reduced the tensile strength and elastic modulus of films but remarkably improved the ductility of the films prepared in air. The films prepared in water were fragile and much weaker than those prepared in methanol and air. PDLLA films had less tensile strength, lower modulus, and considerably lower ductility than PLLA films.

The diversity in the properties of the films obtained in this study opens the way for a wide range of potential applications in the field of biomaterials.

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