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Poly (D,L-lactic acid)/poly (ε-caprolactone) blend membranes: preparation and morphological characterisation

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With the aim of exploring possible application of the concept of blend compatibilisation into the field of biodegradable membranes, a study of the influence of random copolymer poly(D,L-lactide-co-ε-caprolactone) on the properties of corresponding homopolymer blends has been conducted. Blends of plain homopolymers and blends containing 5 and 10 wt% of a copolymer of suitable composition have been prepared in the melt and characterised for their molecular interactions using thermal, dynamic-mechanical, mechanical (tensile tests) and morphological analyses. The blends are characterised by a good dispersion of the poly-ε-caprolactone (PCL) minor phase into the poly(D,L-lactic acid) (PDLLA) matrix and better mechanical properties compared to plain PDLLA, and such characteristics further improve when adding the copolymer. Microporous blend membranes consisting of PDLLA and PCL were then prepared by a phase inversion method and characterised by scanning electron microscopy. The addition of compatibilising agent led to a highly homogeneous structure, while in absence of compatibiliser a clear phase separation occurred. © *2000 Kluwer Academic Publishers*

1. Introduction

Biocompatible and biodegradable polymers have great interest as supports for tissue repair and reconstruction [1–3] Potential of use of various biological and synthetic materials as supports for the regeneration of several tissues, as liver [4], pancreas [5], cartilage [6] and bone [7] has been explored. A polymeric support for tissue growth must meet, depending upon the application and together with biocompatibility and biodegradability, several other requirements, as high porous structure, interconnected pore network, and good mechanical strength and flexibility.

One field of application of such principles is guided tissue regeneration (GTR) [8, 9] used for the treatment of periodontal diseases. The first membranes used in this technique were non-resorbable (GORE-TEX) [10, 11] and had the evident disadvantage of a second surgical operation for its removal. Recently, membranes based on resorbable materials have been developed, as collagen [12], vicryl [13] and polylactic acid (PLA) [14–16]. Such materials have also the advantage to accelerate the regeneration of soft connective tissue and cementogenesis [17], as they act as a support on which the cells of the damaged tissues can grow.

Polylactic acids are an important class of biodegradable and biocompatible polymers approved for human clinical use, as other aliphatic polyesters. They are currently used as materials for surgical suture and controlled drug release, or as pins and screws in orthopaedics, but their physical and mechanical properties were found to be poorly adapted for applications as membranes. In cases like this, solutions may be sought in polymer chemistry through co-polymerisation or blending.

In the literature, examples of membranes obtained using polymer blends are reported [18], but they are limited to few pairs of miscible polymers. Dense and anisotropic membranes with dense skin can be produced from a homogeneous blend of different polymers [19, 20]. Membranes obtained from such

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blends exhibit an enhancement of permselectivity with respect to that of membranes composed of the parents polymers, as demonstrated in the case of poly(dimethylphenyleneoxide)/polystyrene blend [21]. Anyway, homogeneity with respect to some desired properties, as mass-transport, can be achieved also with compatible blends, in which a microphase separation between components occurs. In fact, mass transport in polymer matrices is directly influenced by morphology. If the membrane has a microphase structure with domains of dimension well below the effective membrane thickness, the polymer blend acts as a homogeneous material.

In the present study, microporous membranes made by mixing high molecular weight racemic polylactic acid (PDLLA) and poly(ε-caprolactone) (PCL) have been prepared by a phase-inversion technique. The addition of the soft, ductile PCL should in principle improve the mechanical and physical characteristics of membranes compared to those obtained by plain PDLLA. Unfortunately, it is reported that the two polymers are immiscible, then some compatibilisation is needed.

While an extended literature has been produced on the use of block or graft copolymers to emulsify immiscible blends in the bulk [22–25], the authors have not found literature examples that the same principles could hold in the field of blend membranes, when the requirements to get homogeneous material and useful morphologies are more stringent.

In our case, a (D,L-lactide-co-ε-caprolactone) copolymer of suitable composition has been added in two different percentages, to improve the level of compatibility of the components. A preliminary study on the influence of such copolymer on the morphology and on thermal, dynamic-mechanical and mechanical characteristics of blends obtained by melt-mixing is also reported. The membranes have been characterised by scanning electron microscopy and thermal analysis.

2. Experimental

2.1. Materials

Poly(DL-lactide) (PDLLA) (Resomer TM-R, pm $\cong$ 100,000) has been kindly supplied by Boehringer Ingheleim. Poly(ε-caprolactone) (PCL) is a commercial Solvay product (CAPA 650, pm = 50,000). D,L-Lactide (Boehringer-Ingheleim) has been purified by recrystallisation from ethyl acetate. ε-Caprolactone (Aldrich) has been dried over molecular sieves. Stannous (II)-2-ethylexanoate (Sigma) has been used as received.

2.2. Thermal analysis

Analysis by differential scanning calorimetry (DSC) was performed on a Mettler T.A.-3000 apparatus, equipped with a control and programming unit for the elaboration of data, and with a calorimetric cell (DSC-30), which allows scans from −170 to 600°C. All the experiments were run in N_2 atmosphere at an heating rate of 20°C min^{-1}.

2.3. Dynamic-mechanical analysis

Dynamic-mechanical measurements were performed at 1 Hz in tensile mode using a Polymer Laboratories dynamic mechanical thermal analyser (DMTA) MKIII apparatus. Tests were carried out at an heating rate of 4°C min^{-1} in dry nitrogen. Rectangular specimens 6 mm wide and 8 mm long were used.

2.4. Tensile testing

Tensile tests of plain PDLLA and of blends were performed by using an Instron machine (4301 model) equipped with a 100 N cell. Specimens of 1.8 mm of thickness were obtained in form of dumbbells (according to 53504 T.S3A standard dimension) from sheets compression-molded in a heated press at 110°C for 5 min at a load of 4.5 tonnes. The samples were tested at room temperature (about 25°C) at a deformation rate of 10 mm/min.

2.5. Morphological analysis

Scanning electron microscopy (SEM, Philips mod.XL20) was performed on liquid N_2 fracture surfaces both of compression-molded bars of the blends and of membranes as obtained from phase inversion method. Samples were coated with AuPd alloy.

2.6. Preparation of Poly(D,L-Lactide-co-ε-caprolactone)

Poly(D,L-Lactide-co-ε-caprolactone), Poly(DL-co-CL), has been prepared in bulk by ring-opening copolymerization at 120°C for 24 hours [26]. Stannous(II)-2-ethylexanoate was used as catalyst. Details of the synthesis and the characterisation of such copolymers are going to be published elsewhere.

2.7. Blends preparation

3.60 g of PDLLA and 0.40 g of PCL (90/10 wt/wt) are heated at 160°C under a nitrogen atmosphere and then mixed for 10 minutes at a rotor speed of 40 rpm in a home-made mixer (see Results and Discussion). After this time, the obtained blend is allowed to rapidly cool until room temperature, then finely grounded.

In the case of compatibilised blends, 0.20 or 0.40 g of copolymer are added to the batch to obtain blends with a content of 5% or 10% by wt., respectively, of compatibilizer. The blends are coded PDLLAPCL, PDLLAPCL5 and PDLLAPCL10, respectively.

2.8. Membranes preparation

Membranes have been prepared by a phase-inversion process largely employed to prepare membranes used in microfiltration, dialysis, reverse-osmosis, and gas-separation techniques.

For the preparation of a PDLLAPCL membrane, 1.35 g of PDLLA and 0.15 g of PCL are dissolved in 10^{-5} m^3 of acetone (15% wt solution). The solution is poured into a glass Petri-dish and the dish is then rapidly immersed in a bath containing a large excess (about 20 : 1 by volume) of a non solvent (methanol, water, etc., see Results and Discussion). The membrane forms rapidly. After one hour, the membrane is recovered, repeatedly washed with water and finally dried under vacuum at room temperature over night.

In the case of the PDLLAPCL5 membrane, 0.075 g of copolymer are added to the starting solution.

3. Results and discussion

3.1. Characterisation of blends

Blends have been prepared in a home-made static mixer, consisting of a glass vial equipped with an inlet for nitrogen and a stainless steel rotating screw, which allows an efficient mixing of small amounts of material (4–6 g) in a short time. The glass vial is immersed in a thermostatic oil bath with an accurate control of the temperature. The control of the process for a possible degradation of either PDLLA or PCL during the melt-mixing was made by means of thermogravimetric analysis performed on the single components both in dynamic and isothermal mode. According to these analyses the degradation of the components during melt-mixing was not significant.

The binary PDLLA/PCL blend and two ternary blends containing different amounts of compatibilizer (5% and 10% b.w) have been prepared. Such blend compositions have been chosen so that the amount of PCL would be high enough to soften the rigid PDLLA but not so high to destroy the structural stability of the membrane. The used compatibilizer is a poly(DL-co-CL) copolymer, of composition 82/18 mol/mol (amorphous, $T_g = 35°C$). with a random block structure [27]. Studies of ^{13}C-NMR spectroscopy permitted to determine the average length of DL-lactide and caprolactone blocks, which for the chosen composition resulted to be 8 and 3, respectively. The molecular weight, M_w, as determined from GPC measurements, was of 132000.

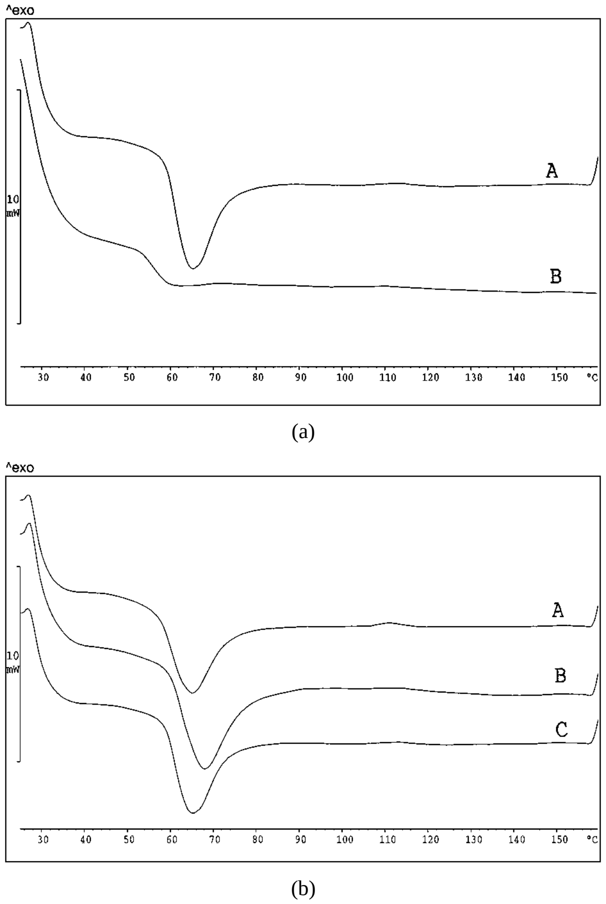
The use of random block copolymers as compatibilizing agents in blends of the two corresponding homopolymers is already reported in literature [28] and they are shown to be effective in promoting interfacial adhesion, being a good alternative to the more usual diblock copolymers, whose synthesis is normally more complicated.

3.1.1. *Thermal analysis*

A DSC trace relative to a PDLLAPCL sample is reported in Fig.1a as example. Both the T_g of PDLLA (55–57°C) and the melting endotherm of PCL ($T_m = 58$–$61°C$) are evident, and their superimposition makes it impossible to calculate the enthalpy of melting of PCL phase. The T_m of PCL and the T_g of PDLLA are not significantly influenced by the presence of the other component; this is an indication of a substantial immiscibility of the two polyesters, at least as far as PDLLA is concerned.

In second run, after slow cooling, the peak of fusion of PCL is not present, but it does reappear after several days (see Fig. 1b), thus indicating that the kinetics of crystallisation of PCL inside the PDLLA matrix are very slow. Further investigation on crystallisation of the PCL phase by optical microscopy is in progress.

No significant variations are found in the presence of compatibilizer, neither in the blends or in the membranes. This is not unexpected, as it is known that while a compatibilizer strongly influences the interfacial properties of a blend, it has no or scarce influence on the bulk properties of the blend components.



(a)

(b)

Figure 1 (a) DSC trace of PDLLAPCL sample; A): I run; B): II run. (b) DSC traces of PDLLAPCL (A), PDLLAPCL5 (B) and PDLLAPCL10 (C) blends.

3.1.2. *Dynamic-mechanical analysis*

As the DSC analysis is not an useful technique to detect the T_g of the PCL phase, DMTA measurements have been performed on samples of blends and, for comparison, of plain homopolymers, to study the behaviour of T_gs in the presence of the other component. The T_g values, calculated as the temperature of the maximum of tan δ, are reported in Table I. Taking into account that the low amount of PCL in the blends renders somehow uncertain a precise location of its T_g, the T_g of PCL seems to slightly increase in the blends, as a consequence of good compatibility with PDLLA. The T_g of PDLLA does not change in blends, with and without copolymer added, thus confirming the DSC data. As a matter of fact, the T_g of the PDLLA cannot be detected in the PDLLAPCL10 blend, as the sample loses its mechanical stability above 50°C.

3.1.3. *Mechanical analysis*

The Young's elastic modulus (E) and the tensile strength at the yielding point (σ_y) of plain PDLLA and of blends are reported in Table II. It must be pointed out

TABLE I Glass transitions temperatures (°C) of blends and of single components obtained by DMTA measurements

Sample	$T_{g\,PDLLA}$	$T_{g\,PCL}$
PDLLA	62	—
PDLLAPCL	61	~ -35
PDLLAPCL5	61	~ -38
PDLLAPCL10	not determind	~ -37
PCL	—	~ -39

TABLE II Numerical values of Young's modulus (E) and tensile strength at yielding point (σ_y) of plain PDLLA and of blends

Sample	E (MPa) (±3%)	σ_y (MPa) (±1%)
PDLLA	3200	31
PDLLAPCL	2800	30
PDLLAPCL5	2600	29
PDLLAPCL10	2500	22

that the mechanical parameters at high deformations, as elongation and strength at break, are not reported as the available small number of specimens showed large scattering in the results. Therefore, the discussion is limited to the results obtained at low elongation.

It can be noted that the addition of PCL causes a decrease in the elastic modulus and, less pronounced, in the yield strength. The addition of the copolymer (PDLLAPCL5 and PDLLAPCL10 blends) further reduces the modulus and the σ_y, as the copolymer causes higher interpenetration between the two phases. In particular, the diminution of σ_y is worthy of note in the PDLLAPCL10 blend (35% less respect to plain PDLLA). It was felt that the values of the mechanical parameters of this blend are too low for its use as a membrane, so we concentrate on the PDLLAPCL5 blend.

3.1.4. Morphological analysis

Fracture surfaces of the PDLLA/PCL blends obtained by fracturing molded bars in liquid N_2 have been investigated by SEM. Fig. 2 reports the surface of the PDLLAPCL blend. The dispersed phase forms spherical domains well distributed inside the matrix, of average dimensions of 1 μm. The addition of the compatibilizer further reduces the size of the domains (about 0.2 μm, see Figs 3 and 4). As a matter of fact, the dispersed phase is barely visible in the PDLLAPCL10 blend.

Although the fracture has been done, for all the blends, at temperatures well below the T_g of the material, nevertheless the appearance of the surfaces of compatibilized blends is more rough, with well evident fracture lines, thus suggesting that these blends are tougher.

3.2. Characterisation of membranes

Membranes of blends of PDLLA and PCL, alone and in the presence of 5 wt% of copolymer, have been prepared starting from a solution obtained by dissolving together the single components in a common solvent ("solution blending"), via phase inversion method, using a glass Petri-dish as a casting surface.

The acetone solution of the components became optically clear after mild heating (40°C) and then kept its transparency also at room temperature. The solution showed neither separation into two layers nor any precipitation even after several days. A 15 wt% clear solution was cast on a Petri dish and then immersed in a coagulation bath containing a non-solvent miscible with the solvent. Water is the common coagulant used in this technique; anyway, we also used different non-solvents, namely methanol, propanol and hexanol, to examine the dependence of the morphology of the

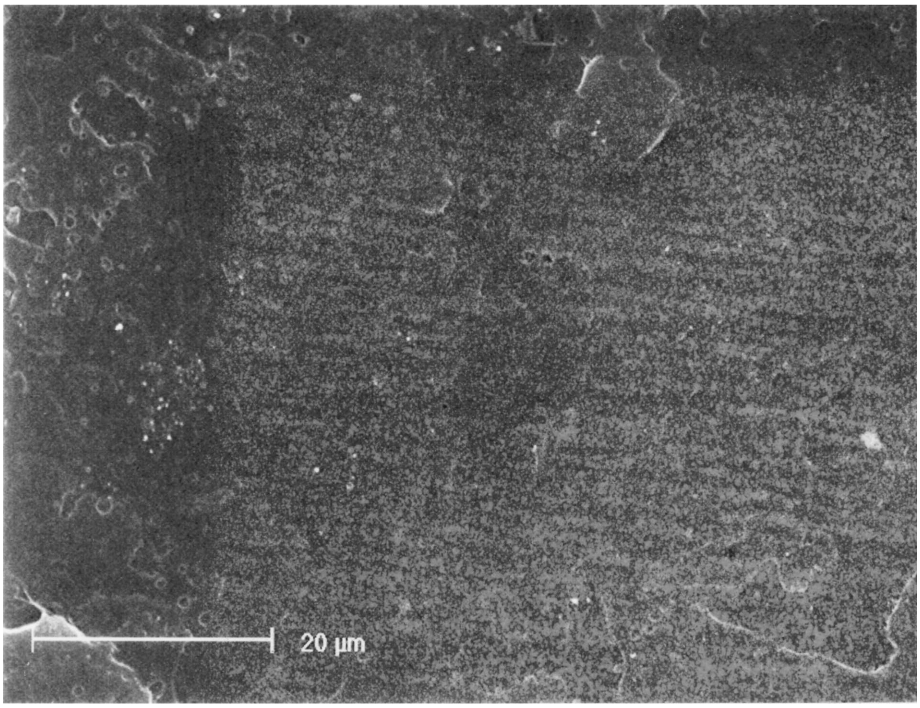


Figure 2 SEM micrograph of liquid N_2 fracture surface of PDLLAPCL blend.

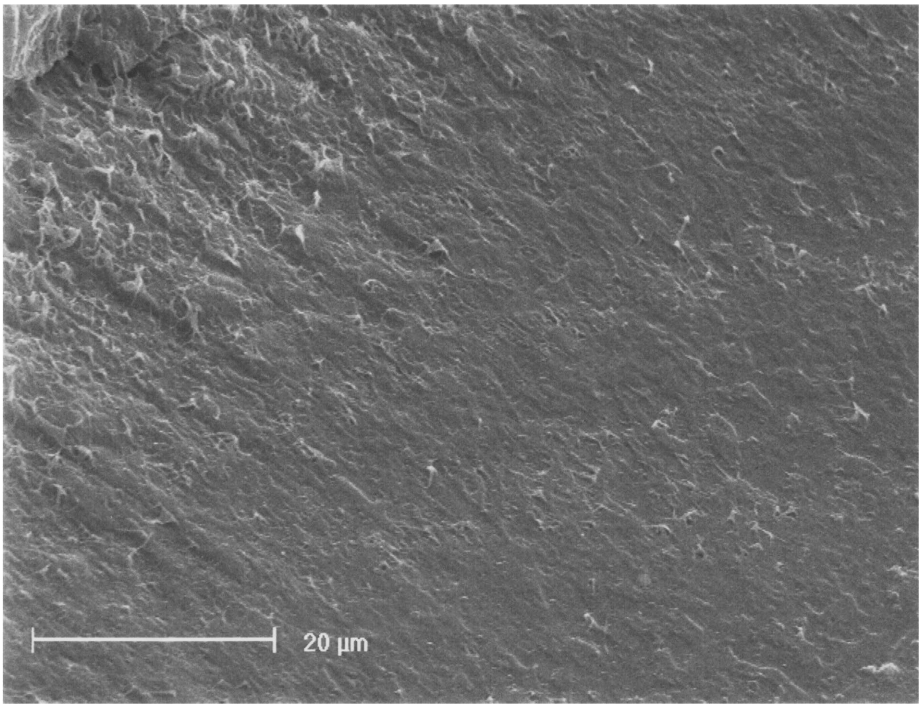


Figure 3 SEM micrograph of liquid N_2 fracture surface of PDLLAPCL5 blend.

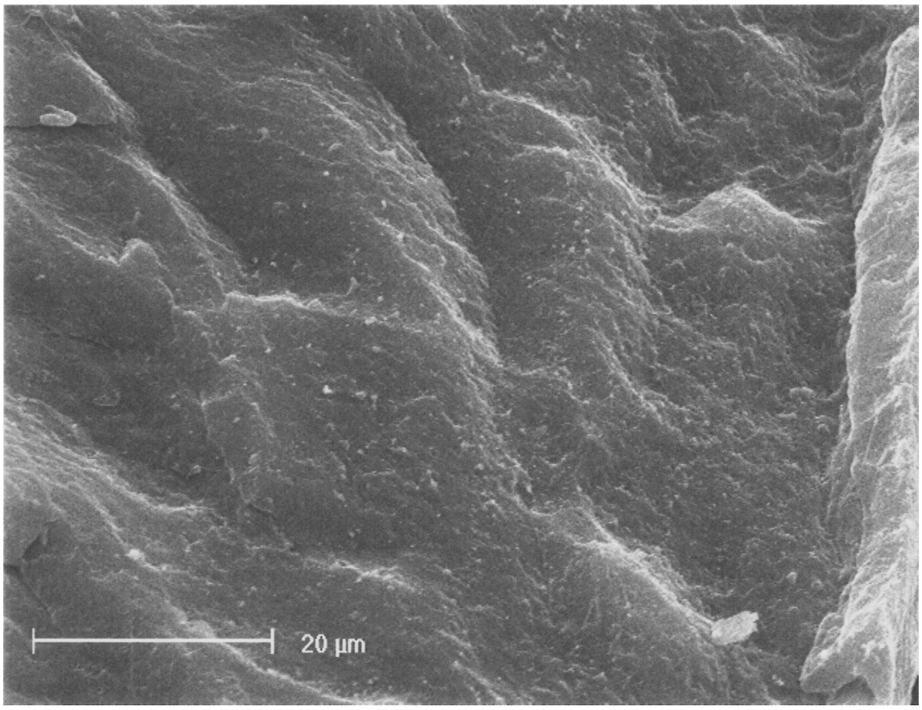


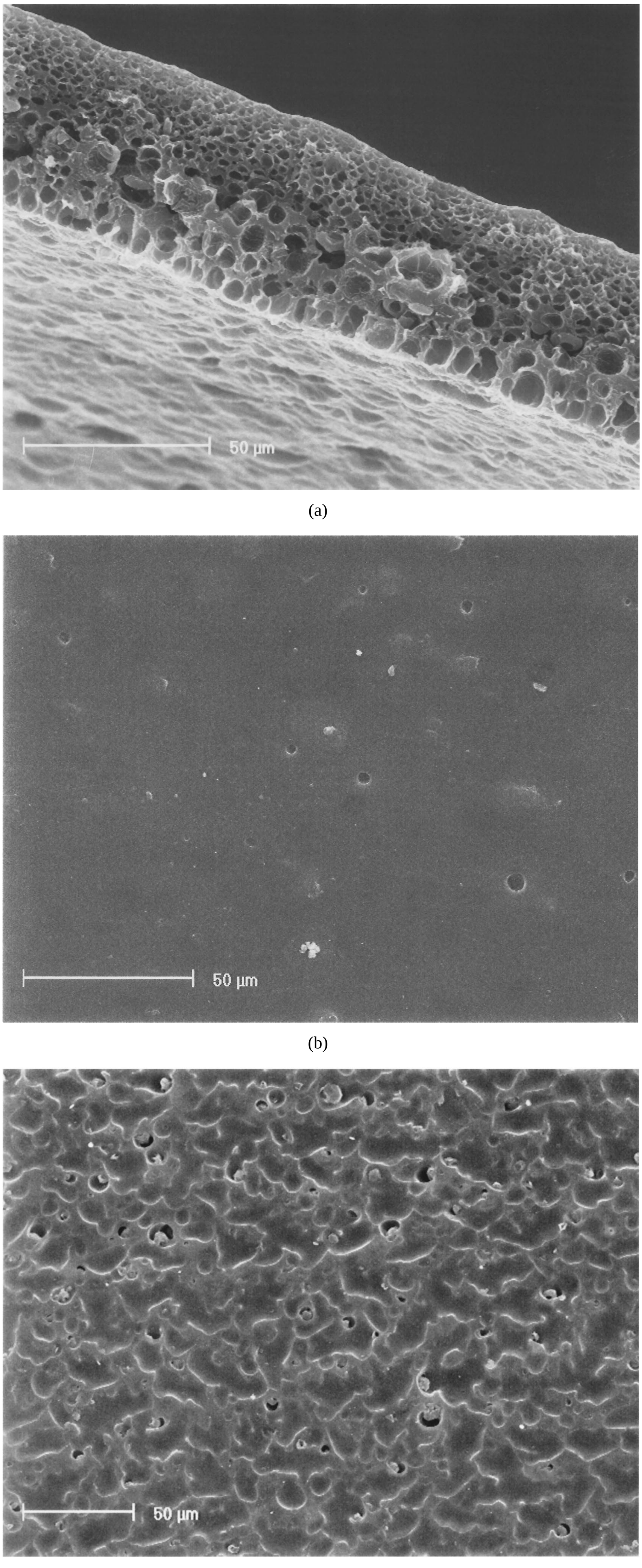
Figure 4 SEM micrograph of liquid N_2 fracture surface of PDLLAPCL10 blend.

membrane on the nature of the non-solvent (polarity and density).

3.2.1. Morphological analysis

Generally speaking, membranes coagulating in a non solvent bath precipitate rapidly, as the concentration gradient of the permeating coagulant is steep, and an anisotropic porous membrane forms. Such membranes are said to be skinned, as a dense skin of polymer is formed on the surface which interfaces with the coagulant. The microporous structure of an anisotropic membrane gradually forms from the surface skin, below which an assembly of macrovoids (pore radius $>10\,\mu$m) is often present. The bottom surface is usually an extension of the highly porous internal structure; as a consequence, it displays the same porous morphology. The morphology of the bottom surface varies with the chemical nature of the casting surface (e.g., glass, Teflon, Mylar), as it is influenced by the degree of adherence of the polymers to it.

Fig. 5a shows a water coagulating PDLLAPCL5 membrane after fracturing in liquid N_2, as example. The anisotropic morphology above described is clearly



(a)

(b)

(c)

Figure 5 SEM micrograph of a water-coagulated PDLLAPCL5 membrane: a) = liquid N_2 fracture surface, b) = surface skin, c) = bottom surface.

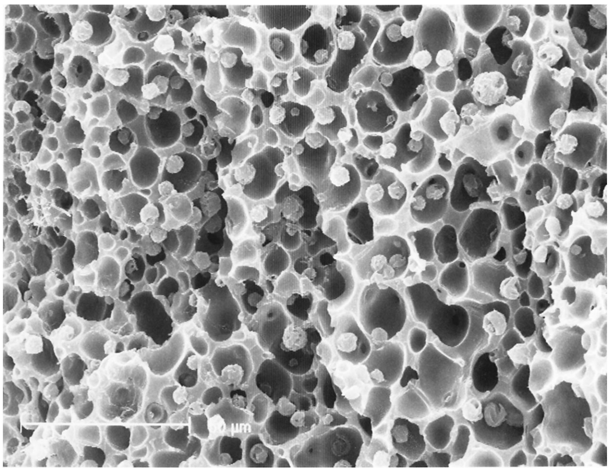


Figure 6 SEM micrograph of a methanol-coagulated PDLLAPCL membrane.

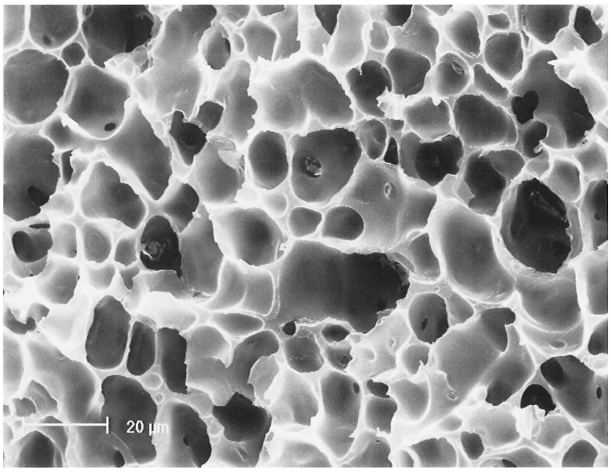


Figure 7 SEM micrograph of a methanol-coagulated PDLLAPCL5 membrane.

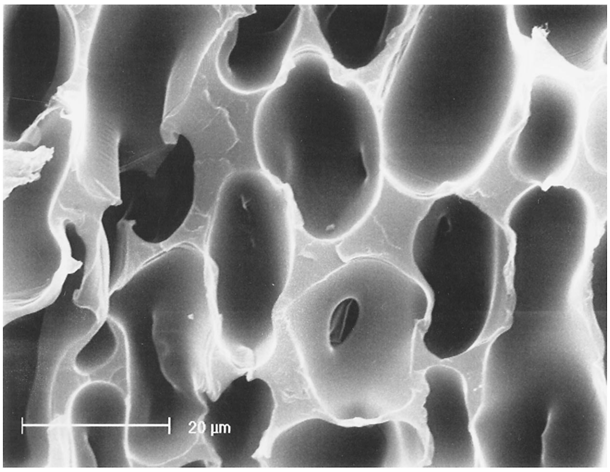


Figure 8 SEM micrograph of a methanol-coagulated PDLLA membrane.

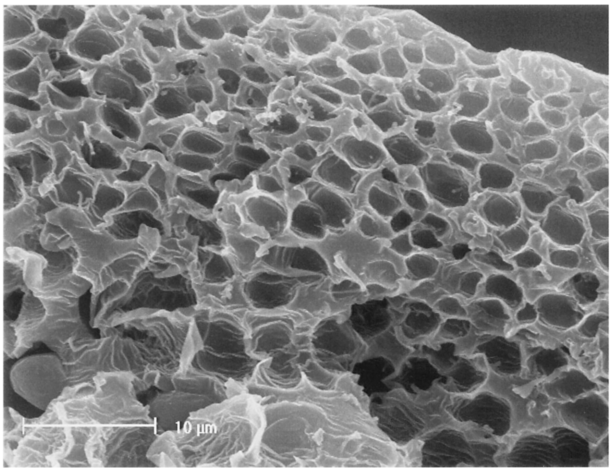


Figure 9 SEM micrograph of a water-coagulated PDLLAPCL5 membrane.

visible. The surface skin (Fig. 5b) is very tight; the bottom surface (Fig. 5c) is porous, as expected, with a structure similar to the internal microporous one.

To study the efficiency of the compatibilizer in the solution blending method, the morphology of membranes coagulating in methanol of PDLLAPCL and PDLLAPCL5 blends have been investigated and compared. Micrographs of the microporous membranes after fracturing in liquid N_2 are shown in Figs 6–10. The PDLLAPCL blend (Fig. 6) shows a clear phase separation with PCL domains of size of 5–8 μm located inside the pores. Such heterogeneous morphology would definitely hamper any possible application of this membrane in tissue repair. The PCL domain dimension is larger than in the case of melt blends as a consequence of swelling. The addition of as much as 5% of the block copolymer has a dramatic influence on membrane homogeneity; in fact separated domains are absent in the PDLLAPCL5 blend (Fig. 7.), thus indicating that the copolymer is able to perform its compatibilizing effect also in solution; as a consequence, upon fast coagulation (few seconds) the PCL phase remains well dispersed, trapped into the wall of micropores and hardly visible, giving rise to a highly homogeneous network. The pores have an average diameter of 10 μm, and are not interconnected. As the diameter of the pores in a microporous material to be used as substrate in the guided tissue regeneration must be in the range 10–100 μm [1], the PDLLAPCL5 membrane could really be interesting as a support material in such applications.

A comparison with a plain PDLLA membrane, prepared in the same conditions evidences that the blends membranes have pores of reduced dimensions and thinner walls (Fig. 8). Moreover, the blends membranes appear to be less brittle and with a moderate flexibility, when deformed by blending, as a consequence of the presence of PCL. These characteristics render them easier to be handled.

A preliminary investigation on the influence of polarity of coagulating bath has been also carried out. Figs 9 and 10 show the PDLLAPCL5 membranes coagulated in water and in isopropanol, respectively. The structure of the material is very regular in the first case, the size of the pores is small (4–5 μm) and more uniform. In the case of propanol, the membrane is more dense, with pores of larger dimensions (10–15 μm), more irregular and with bulky walls; PCL domains of submicronic dimensions are visible in the dense zones. This suggests that a less polar nonsolvent is not suitable in this technique, at least in our case; in fact, membranes coagulating in hexanol are very dense, with few and very irregular pores.

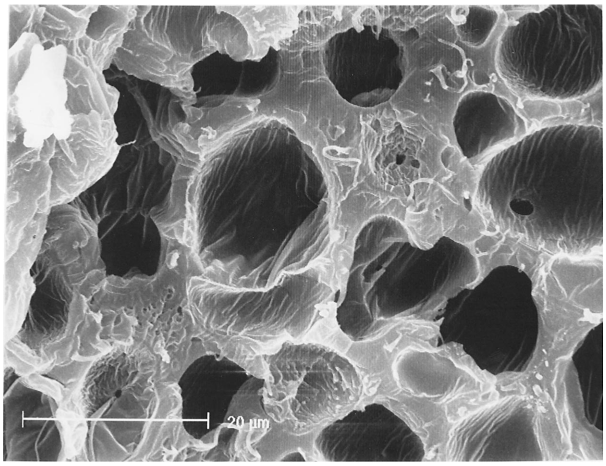


Figure 10 SEM micrograph of an isopropanol-coagulated PDLLAPCL5 membrane.

4. Conclusions

In order to obtain membranes based on Polylactic acid with better mechanical characteristics (flexibility and strength), blends of PDLLA with 10% b.w. of PCL have been prepared and characterised. The melt-mixed blend shows a reasonable compatibility of components although immiscible, giving rise to a morphology characterised by PCL domains well distributed into the matrix. The addition of a PDLLA-co-PCL copolymer as compatibiliser further reduces, as expected, the average size of PCL domains. Mechanical tests have shown that the addition of PCL reduces the elastic modulus of PDLLA while keeping the tensile yield strength. Such behaviour too further improves when adding 5% by weight of copolymer. The thermal and dynamic-mechanical characteristics of PDLLA are, instead, only slightly influenced by the presence of the other component.

Microporous membranes have been obtained by a phase inversion method. The membranes show a clear phase separation in the absence of compatibilizer, while the addition of 5% of copolymer gives rise to a highly homogeneous pore network. The structure of the membranes is highly porous, with very regular pores of small dimensions (5–15 μm) and thin walls. This result is quite interesting, as homogeneous membranes have been, so far, reported only for blends of miscible polymers, and open a new area of interest, as it will be possible to produce continuous alteration of membrane properties as a function of blend composition also with immiscible polymer pairs.

More work is in progress on the possibility to obtain blend membranes with different methods, in order to modulate the porosity degree and the pores dimension. Studies on mass-transport characteristics and tests on biodegradation in vitro of such membranes will be reported in a future paper.

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