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Graft copolymers for biomedical applications prepared by free radical polymerization of poly(L-lactide) macromonomers with vinyl and acrylic monomers

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Poly(L-lactide) macromonomers have been copolymerized with methyl methacrylate, methyl acrylate N,N'-dimethyl acrylamide (DMA) and N-vinyl pyrrolidone (VP) in order to obtain biodegradable–biocompatible comb-like copolymers with different hydrophilic characteristics. Comonomer reactivity ratios have been determined and compared with those obtained when the same comonomers are copolymerized with a model compound of the macromonomer. All results are in the range of values reported in the literature for the same comonomers in similar copolymerization processes. However, macromonomer reactivity differs from that of the model compound, depending on the comonomer considered. Thus, striking deviations are found when VP or DMA are concerned. It seems that compatibility between the growing chain and the macromonomer plays the main role in the copolymerization behaviour of the macromonomer. Miscibility studies of blends of poly(DL-lactate) (PDLA) with poly(methyl methacrylate), poly(N,N'-dimethyl acrylamide) (PDMA) and poly(N-vinyl pyrrolidone) (PVP) confirmed the repulsive interactions between PDLA and PVP and PDMA chains, which account for the deviations in the reactivity of the macromonomer when compared with that of the model compound.

(Keywords: macromonomers; graft copolymers; reactivity ratios)

INTRODUCTION

Since macromonomers were discovered by Bamford a number of years ago[1,2], the so-called 'macromonomer technique' has become the most effective method for producing well defined graft copolymers. This is not an unfounded statement as many reasons support it: the wide variety of macromonomers and comonomers available makes possible the synthesis of graft copolymers with properties that can be selected in advance. The length of their branches can be controlled since the molecular weight of the macromonomer and its distribution can also be preselected. Finally, once the reactivity ratios have been determined, the final molecular structure can be predicted as well.

Graft copolymers have many important applications in the polymer industry, mainly as surface modifiers for uses as coatings, adhesives and dispersants, as compatibilizing agents in polymer blends, but also for biomedical use. In this sense, polymers and copolymers prepared by the polymerization of poly(ethylene oxide) macromonomers with acrylic and vinyl comonomers have been extensively studied as semi-permeable membranes for biomedical applications, as well as support systems for the preparation of microcapsules and nanoparticles that are being used in drug delivery systems[3–5].

Graft copolymerization by free radical mechanism is an interesting way for the preparation of composite polymeric systems with specific properties, which can be modulated by the average composition of the copolymer, as well as by the chemical structure and the length of the graft segments. In this sense, the preparation of high molecular weight graft copolymers from macromonomers of biodegradable polymers is particularly attractive, because of the difficulties in the preparation of high molecular weight biodegradable polyesters by classical polycondensation reactions of the corresponding α-hydroxy acids[6–8]. These limitations can be eliminated by means of specific functionalization of the biodegradable blocks, and the preparation of high

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molecular weight block or graft copolymers with other vinyl and acrylic monomers.

This paper deals with the preparation of copolymers of poly(L-lactide) (PLLA) macromonomers and four monomers of different hydrophilic character: methyl acrylate (MA), methyl methacrylate (MMA), *N*,*N*′-dimethyl acrylamide (DMA) and *N*-vinyl pyrrolidone (VP). Depending on the comonomer used in the copolymerization process, graft copolymers can be designed for different applications as biomaterials. For example, the copolymerization with MA or MMA gives rise to, respectively, soft or stiff hydrophobic systems with good mechanical response, which can be applied to design useful devices in orthopaedic surgery. On the other hand, copolymers prepared by the polymerization of the macromonomer with DMA or VP are very hydrophilic, and they could be suitable for the preparation of support matrices for controlled drug delivery systems. Nevertheless, the main properties depend both on the average composition of the systems and the microstructural distribution of the comonomer sequences along the macromolecular backbone, which is determined by the reactivity ratios of the macromonomer and the corresponding comonomer in the free radical polymerization process. Thus, in this work the reactivity ratios will be determined and compared with those obtained when the same comonomers are copolymerized with a model compound of the macromonomer. The differences will be discussed and explained in terms of the main factors which affect the reactivity of macromonomers.

EXPERIMENTAL

Macromonomer synthesis

2-Oxyethylmethacrylate-terminated PLLA macromonomers (MC) were synthesized by ring-opening polymerization of L-lactide using 2-hydroxyethyl methacrylate functionalized aluminium alkoxides following the method previously described[9]. Molecular weights were determined by ^{1}H n.m.r. ($M_n = 4500$).

Copolymer synthesis

PLLA macromonomers were copolymerized with MA, MMA and VP in dioxane at 60°C with azobis(isobutyronitrile) (AIBN) as initiator, under a nitrogen atmosphere. Dioxane (99.5%) was refluxed over KOH and distilled just before use. MA and MMA (Aldrich) were purified by conventional methods and distilled before use; DMA (Sigma) and VP (Aldrich) were distilled before use. AIBN was recrystallized from methanol. Concentration of reagents: [Comonomers] = 1 mol l^{-1}; [AIBN] = 0.01 mol l^{-1}; [MC] = 0.025 g ml^{-1}.

Sample analysis

Samples were taken at different reaction times in order to determine the reagents' conversion. Thus, macromonomer conversion was determined by gel permeation chromatography (Waters Model 150-C ALC/GPC) (three columns; one 10^4 Å and two 500 Å), integrating the peak corresponding to the macromonomer; tetrahydrofuran (THF) was used as eluent (chloroform was used for the copolymers with VP) at a flow rate of 1 ml min^{-1}.

MA and MMA conversion was determined by gas chromatography; measuring the corresponding areas in relation to that of the chlorobenzene which had been included in the reaction medium (75% by weight related to the monomer) as an internal reference.

DMA and VP conversion had to be determined by ^{1}H n.m.r. as reproducible results were not attainable by g.c. Thus, the area of the protons of the double bond ($\delta = 6.7$ ppm for DMA and $\delta = 7.0$ ppm for VP) was measured in relation to that corresponding to known amounts of hydroquinone ($\delta = 6.5$ ppm), added to the n.m.r. tube.

Blend preparation

Blends of low molecular weight poly(DL-lactide) (LMWPDLA) or high molecular weight (poly(DL-lactide) (HMWPDLA) with poly(methyl acrylate) (PMA), poly(methyl methacrylate) (PMMA), poly(*N*,*N*′-dimethyl acrylamide) (PDMA) and poly(*N*-vinyl pyrrolidone) (PVP) were prepared by solution/precipitation (dioxane/hexane). The blends were thermally characterized by differential scanning calorimetry (Perkin Elmer DSC-2C) at a scan rate of 20°C min^{-1}.

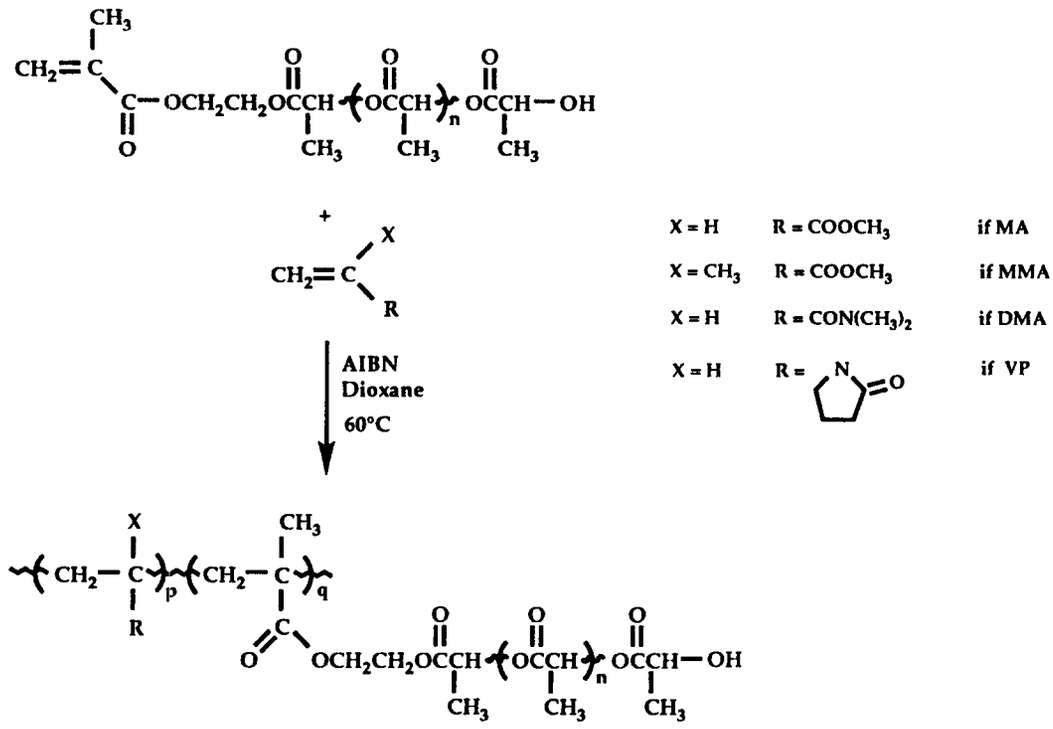
Both PDLAs were synthesized by ring-opening polymerization of *rac*-DL-lactide: HMWPDLA (M_n = 110 000) was obtained in bulk with stannous 2-ethylhexanoate as catalyst[10] and LMWPDLA ($M_n = 6400$) was obtained in toluene solution using aluminium isopropoxide as initiator[11]. PMA and PVP (M_w = 40 000) were purchased from Aldrich, and PMMA ($M_n = 480\,000$) from Polymer Laboratories. PDMA was synthesized by free radical polymerization of DMA in dioxane at 60°C, using AIBN as initiator.

RESULTS

In order to obtain biocompatible and partially biodegradable polymeric systems for biomedical applications with good mechanical response and controlled biodegradation, we designed the synthesis of PLLA macromonomers (M_n in the range 4000–5000), bearing an acrylic function at one of their ends, and their free radical copolymerization with acrylic and vinyl monomers. The polymerization reaction gives rise to the formation of graft copolymers which have a chemical structure that is represented in *Scheme 1*.

Kinetic parameters of the free radical copolymerization of PLLA macromonomers

All the methods developed so far to determine the relative reactivity ratios in addition copolymerization of single monomers can be, in principle, applied to the study of the reactivity of macromonomers. However, their high molecular weight compared with that of the comonomers, and the low molar concentration of macromonomer used in these copolymerization reactions, makes very difficult the application of the classical treatments based on the linearization of the copolymerization equation of Mayo and Lewis[12] or the non-linear least-squares approach suggested by Tidwell and Mortimer[13]. The application of these treatments requires working with high macromonomer concentrations (i.e. feed compositions higher than 20–30 mol% of macromonomer), which are not always attainable due to its restricted solubility. In addition, such high concentrations lead to extremely viscous media, and as a result the



Scheme 1 Chemical structure of graft copolymers

reactivity of the macromonomer might be influenced by the physical characteristics of the medium rather than by the chemical structure itself. However, Jaacks[14], in the 1970s, suggested a simplified method to determine reactivity ratios of monomers when a large excess of one of the comonomers is used in the experiments. This method does not depend on the conversion degree since, for a large excess of one of the comonomers, $[M_i] \gg [M_j]$, the composition of the reaction medium does not change appreciably with the conversion degree, particularly if the reactivity ratios of both monomers are close to one. According to the treatment suggested by Jaacks[14], it can be assumed that the propagation of active growing radicals ending in a macromonomer M_1 unit with another molecule of macromonomer can be neglected since its molar concentration is very low. Therefore, it is necessary to consider only two effective propagation reactions, which lead to equation (1) or its integrated form, equation (2):

$$\frac{d[M_2]}{d[M_1]} = r_2 \frac{[M_2]}{[M_1]} \tag{1}$$

$$\log \frac{[M_2]_t}{[M_2]_0} = r_2 \log \frac{[M_1]_t}{[M_1]_0} \tag{2}$$

where $[M_i]_t$ and $[M_i]_0$, $(i = 1,2)$ are the concentrations of macromonomer M_1 and the comonomer M_2 at a reaction time t, and in the initial feed ($t = 0$), respectively. This equation is valid provided that $r_2[M_2]/[M_1] \gg 1$ and $r_1[M_1]/[M_2] \ll 1$. If the comonomer and macromonomer concentrations are measured at different reaction times, a plot of $-\log([M_2]_t/[M_2]_0)$ vs. $-\log([M_1]_t/[M_1]_0)$ should result in a straight line with a slope that equals r_2 (the reactivity ratio of the comonomer).

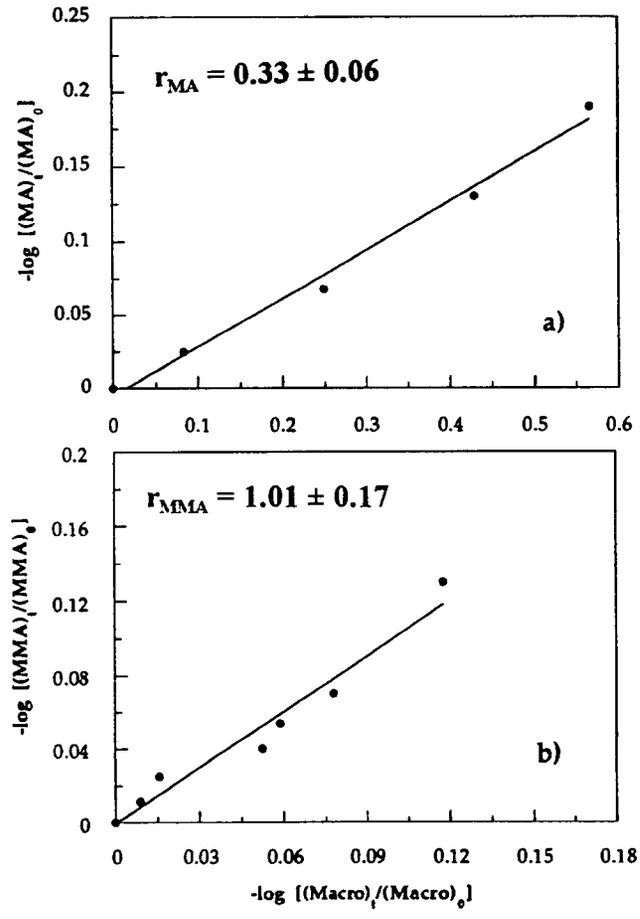


Figure 1 Application of Jaacks' treatment to the copolymerization systems (a) MA–MC and (b) MMA–MC

Before discussing our results, it should be pointed out that the relative reactivity in the copolymerization of a macromonomer is frequently expressed as $1/r_i$. This quantity is equal to k_{ij}/k_{ii}, the ratio of rate constants for the cross-addition of the propagating polymer chain (most commonly ending in M_i) to the macromonomer active end and the rate constant for the homo-addition process of M_i species. The higher the value of r_i, the less reactive the macromonomer will be. In this paper we will focus on the changes in the reactivity of the comonomers instead of discussing the reactivity of the macromonomer. The reason is as follows: the low molar concentration of macromonomer determines that the kinetic scheme for the copolymerization of a macromonomer involves essentially only the comonomer radical[15]. Accordingly, the macromonomer radical reactivity should have a small influence on the copolymerization kinetics. Several factors, which will be discussed later on, can modify the kinetics of these polymerizations. However, taking into account the small influence of the macromonomer reactivity on the copolymerization kinetics, the decreased macromonomer reactivity observed would probably not be due to a decrease in the macromonomer reactivity in itself, but rather to an enhanced reactivity of the comonomer radical in the growing polymer chain with its own monomer.

Figures 1a and *1b* show the diagrams obtained after the application of equation (2) to the experimental data for the copolymerization of MA and MMA with the end functionalized macromonomer MC, respectively. A linear relationship can be approximated with a good fitting of experimental points. *Figures 2a* and *2b* represent the diagrams obtained for the copolymerization of the hydrophilic acrylic monomer DMA and the polar vinyl monomer VP with the macromonomer MC. The fitting of the experimental data to equation (2) is relatively good for the copolymerization of DMA, but more noticeable deviations are obtained for the system with VP. The reactivity ratio of VP reported in *Figure 2b* has been determined taking only into consideration the first three experimental points in addition to the origin, since this is the only way to find a linear relationship as a first approximation.

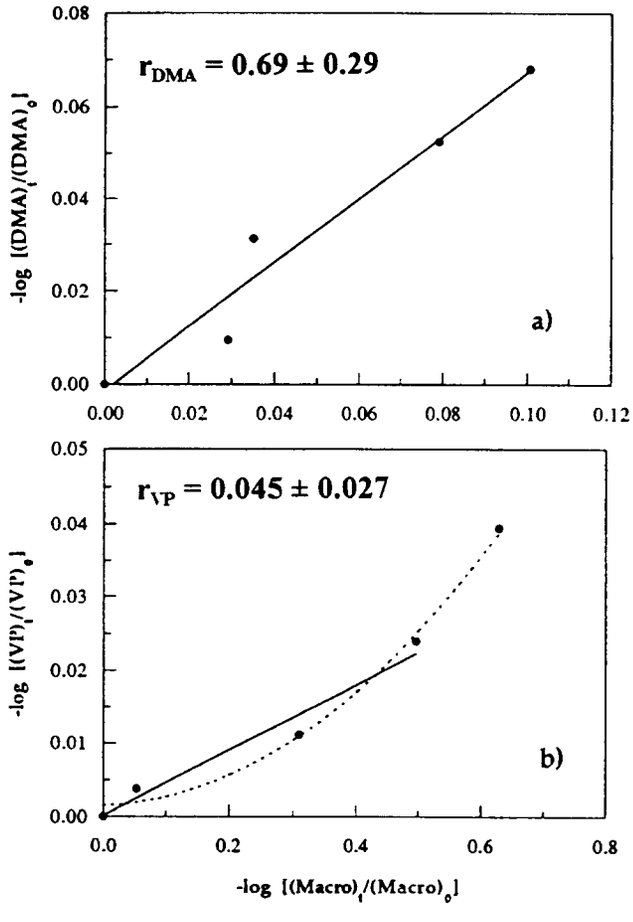


Figure 2 Application of Jaacks' treatment to the copolymerization systems (a) DMA–MC and (b) VP–MC

The reactivity ratios are in the range of the values reported in the literature for free radical copolymerization of single monomers with rather similar structure.

Characteristics of the copolymerization of the model compound 2-acetoxyethyl methacrylate (ML) in comparison with those of the PLLA macromonomers

In order to verify if the presence of a bulky group (as the polylactide chain is) pending from the methacrylic unit modifies the copolymerization behaviour of the small comonomers when they are copolymerized with the macromonomer, we also studied the copolymerization of the same comonomers with a low molecular weight homologue of the macromonomer, which reproduces the chemical structure of its end functionalization, i.e. 2-acetoxyethyl methacrylate (ML)[16]. The reactivity ratios were determined in the same experimental conditions used in the reactions with the macromonomer but at lower conversions (< 5%). Thus, the reactivity ratios obtained for the copolymerization of MA with model compound ML were $r_{MA} = 0.31 \pm 0.01$ and $r_{ML} = 2.44 \pm 0.08$. The reactivity ratio for MA is very close to the value obtained when it was copolymerized with the macromonomer (see *Figure 1a*), which means that the poly(lactide) chain does not noticeably modify the kinetic parameters of the copolymerization.

The copolymerization of MMA with the macromonomer appears to show the same behaviour, since the value of the reactivity ratio obtained when it is copolymerized with the model compound ($r_{MMA} = 0.85 \pm 0.01$ and $r_{ML} = 1.00 \pm 0.02$) is very close to that obtained when it is copolymerized with the macromonomer ($r_{MMA} = 1.01$; *Figure 1b*). Assuming that the reactivity ratio of the macromonomer is similar to that of the model compound in this copolymerization system (the reliability of this assumption will be considered later on) this result means that the copolymerization of MMA with the macromonomer can be considered practically ideal, with an almost perfect random distribution of comonomer sequences along the macromolecular chains. This is also supported by the values of r_{MMA} reported for other copolymerization systems with a chemical structure close to the one studied in this work. For example, Grassie *et al.*[17] reported values of $r_{MMA} = 1.10$ and $r_{EMA} = 1.00$ for the copolymerization of MMA with ethyl methacrylate (EMA), or those reported by Otsu *et al.*[18], $r_{MMA} = 1.16$ and $r_{CIM} = 0.97$, for the radical copolymerization of MMA with 2-chloroethyl methacrylate (CIM).

Although systems based on DMA have been less studied, our data seem to be congruent with prior results[19] for the copolymerization of DMA with MMA

Table 1 Relative reactivity of comonomers *i* (MA, MMA, DMA and VP) and of the macromonomer MC or model compound ML in free radical copolymerization

Comonomer	$1/r_i$	$1/r_{ML}$	$1/r_i'$	k_{i-MC}/k_{i-ML}
MA	3.03	0.41	3.22	0.94
MMA	0.99	1.00	1.18	0.84
DMA	1.45	0.37	1.92	0.75
VP	22.73	0.30	90.91	0.25

$r_i' = k_{ii}/k_{i-ML}$
$r_i = k_{ii}/k_{i-MC}$
ML = model compound
MC = macromonomer

in rather similar experimental conditions to those of the present work. There is a slight difference in the value of the reactivity ratio of DMA in its copolymerization with ML ($r_{DMA} = 0.52 \pm 0.01$ and $r_{ML} = 2.69 \pm 0.07$)[16] in relation to that calculated according to *Figure 2a* ($r_{DMA} = 0.69 \pm 0.29$). In this case, the kinetic parameters for the copolymerization of DMA with the macromonomer MC may be rather different because of the strong polar character of DMA with respect to the macromonomer methacrylic ending ester.

Perhaps the most controversial system is VP/MC, because of the very different polarity of both compounds and the normally low reactivity of VP with respect to acrylic monomers with no severe steric hindrance. However, the approximation considered in *Figure 2b* gives a value of $r_{VP} = 0.044 \pm 0.027$, which is in the range of the reactivity ratios determined for the copolymerization of VP with the comonomer ML at low conversion[16], i.e. $r_{VP} = 0.011 \pm 0.001$ and $r_{ML} = 3.34 \pm 0.08$. As in the case of DMA, the behaviour of the methacrylic derivative is not affected noticeably by the chemical structure or the length of its side group as demonstrated by the values reported for the copolymerization of VP with 2-bromoethyl methacrylate (BrM) ($r_{VP} = 0.020$ and $r_{BrM} = 3.92$)[20], or even the copolymerization of VP with furfuryl methacrylate (FM) ($r_{VP} = 0.004$ and $r_{FM} = 3.92$)[21].

As has been indicated above, the inverse ratio $1/r_i = k_{ij}/k_{ii}$ gives a clear idea of the relative reactivity of a growing radical ending in an *i* unit towards the addition of monomer *j*, in comparison to the tendency for the homopropagation or the addition of a monomer *i* of the same nature. The second and fourth columns of *Table 1* record the values of the relative reactivity of growing radicals ending in MA, MMA, DMA and VP units towards the end-functionalized poly(lactide) macromonomer MC ($1/r_i$) as well as towards the homologous acrylic compound ML ($1/r_i'$). As can be seen, rather similar values are obtained for the addition of MA or MMA ending radicals to the macromonomer MC or the homologous model compound ML. These results demonstrate that the reactivity of the growing free radicals is practically not affected by the length of the side poly(lactide) chains in the case of the relatively low polar species derived from MA or MMA monomers. It is interesting to stress that the reactivity of MA ending radicals towards both the macromonomer MC and model compound ML is approximately three times that of the reactivity towards its own monomer MA. However, in the case of MMA, no preference is detected in the addition reaction; this is not the case with the propagation reactions for DMA and VP growing radicals, which present higher reactivity towards the model compound ML than that of the macromonomer MC.

In relation to the reactivity of growing radicals ending in the model acrylic monomer ML, it is clear from the data recorded in the third column of *Table 1* that it is not strongly affected by the polarity of the vinyl or acrylic comonomer MA, MMA, DMA or VP.

If we consider that, under the experimental conditions of this work, the homopropagation rate constant k_{ii} of monomers MA, MMA, DMA or VP is the same for both the copolymerization reactions with the macromonomer MC and the homologous ML compound, then, according to the definition of the reactivity ratio, the following expression can be considered a good approximation:

$$[r_i'/r_i] = [k_{i-MC}/k_{i-ML}] \quad (3)$$

This means that the ratio of the kinetic parameters of copolymerization directly provides the ratio of the cross-propagation rate constants for the addition of active growing radicals to the macromonomer MC or the homologous model compound ML. The data obtained are recorded in the fifth column of *Table 1*, and indicate that cross-propagation is not affected by the length of the lactide side chains in the case of the copolymerization with MA and MMA, but decreases noticeably in the case of the polar monomers DMA and VP, with respect to the homologous ML.

Compatibility of components according to the miscibility of the corresponding homopolymers

There is no agreement in the literature on the factors that can influence the reactivities of monomers in this kind of copolymerization. As pointed out in a recent published review[22], there is a complex interplay of factors that govern the reactivities in copolymerizations involving macromonomers. When different comonomers are copolymerized with the same macromonomer, it seems that the degree of interpenetration between the macromonomer and the propagating copolymer backbone plays the major role in the measured reactivities. The degree of intertwining will be determined by the compatibility between both counterparts.

In order to elucidate if the compatibility of PLLA macromonomer with the different growing backbones is responsible for the results summarized in *Table 1*, the miscibility of poly(lactic acid) with PMA, PMMA, PDMA and PVP was studied. Two amorphous poly(lactic acid)s were used—low and high molecular weight PDLAs. We chose the amorphous poly(lactide) to study the miscibility of the corresponding blends in order to prevent the crystallization of poly(lactide). It is known that the capability of crystallization of one of the components in a polymer blend can be responsible for a phase separated morphology. When PLLA macromonomer is copolymerized, it is obviously in an amorphous state, and in such a situation only the repulsions or attractions arising purely from the chemical nature of both structures can be regarded as responsible for compatibility or incompatibility. Accordingly, the study of the blends with the amorphous poly(lactide) instead of PLLA macromonomer itself is, for us, a more real comparison.

Figure 3 shows the values of T_g (°C) (second runs) vs.

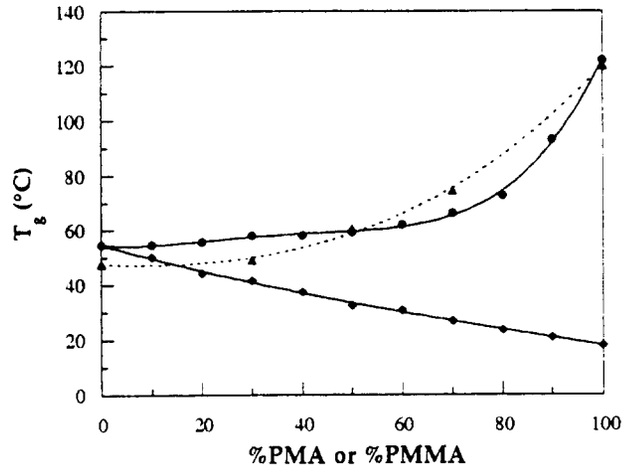


Figure 3 T_g vs. composition for physical blends of poly(DL-lactic acid) and acrylic polymers: (●) blend of PMMA with HMWPDLA; (▲) blend of PMMA with LMWPDLA; (◆) blend of PMA with HMWPDLA

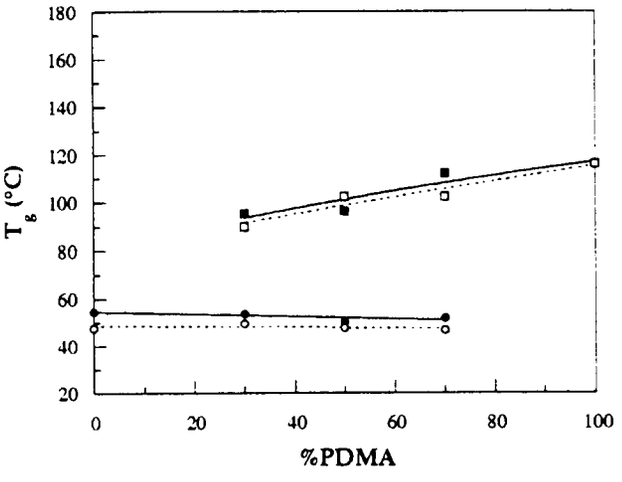


Figure 4 T_g vs. composition for physical blends of poly(DL-lactic acid) with PDMA: (●, ■) blends with HMWPDLA; (○, □) blends with LMWPDLA

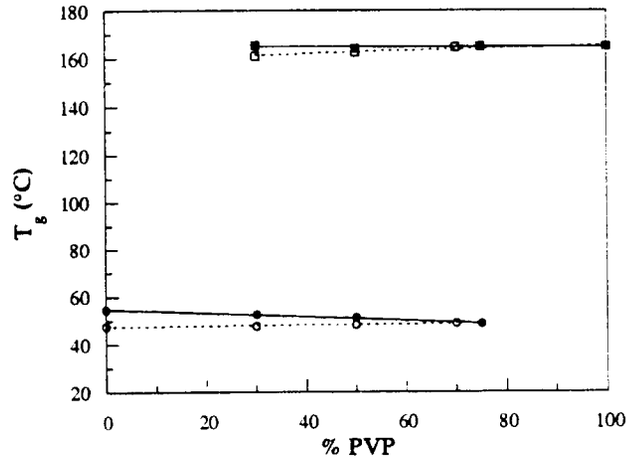


Figure 5 T_g vs. composition for physical blends of poly(DL-lactic acid) with PVP: (●, ■) blends with HMWPDLA; (○, □) blends with LMWPDLA

composition of blends of PDLA with PMA and PMMA homopolymers. According to the miscibility criterion of a unique glass transition temperature, it can be said that the PDLA/PMA system is a miscible blend, showing intermediate T_gs which change with blend composition. PDLA/PMMA blends are also apparently miscible, but it must be stressed that they seem to separate into phases when allowed to stand at room temperature (this is under study and will be the subject of a forthcoming paper).

The behaviour of blends of PDLA with PDMA and PVP is different as shown in *Figures 4* and *5*, respectively. Two T_gs with slight displacements from the values of the corresponding homopolymers in the case of the PDLA/PDMA blend, and little or no shifts in the PDLA/PVP blend, are clearly observed. Therefore, it can be concluded that both blend systems are immisicble.

The results seem to be scarcely affected by the molecular weight of the PDLA used in the experiments, especially for the incompatible blend with PDMA and PVP, where even a plasticizer effect produced by the low molecular weight species can be neglected.

DISCUSSION

The results of the miscibility study are in good agreement with the changes observed in reactivities. We have moved from a blend undoubtedly miscible (PDLA/PMA) to a system unequivocally immiscible (PDLA/PVP). The degree of compatibility between chains of different chemical nature is likely to be reflected when PLLA macromonomer is copolymerized with the corresponding comonomers. As a result of these differences, an increasing deviation in the reactivity of the comonomers is observed, and, in this way, we can explain why MA is only slightly more reactive towards the model compound than towards the macromonomer; however, when VP is the comonomer, a four-fold enhancement in the reactivity is observed.

In relation to the plot corresponding to the copolymerization of the macromonomer with VP (*Figure 2b*), it must be considered that the last point of this representation has not been taken into account for the calculation of the reactivity of VP. When all the experimental data are considered, the points are better fitted to a curve rather than a straight line, which means that the value of r_2 seems to increase with conversion. If experimental errors are neglected, two possible reasons could explain this behaviour. The first one would be the failure of the Jaacks' method under some experimental conditions. In order to verify if the conditions established for the application of this treatment ($r_2[M_2]/[M_1] \gg 1$ and $r_1[M_1]/[M_2] \ll 1$) are fulfilled, these values were calculated for the last points of each plot, giving in all cases values higher than 10. Therefore, all of them comply with the conditions, which means that this hypothesis can be rejected. The second possible reason refers to the effect of the solvent on the copolymerization: there are several examples in the literature where the role of the solvent on the copolymerization is shown. Ito *et al.*[23] copolymerized vinylbenzyloxy-terminated poly(ethylene oxide) macromonomers with styrene in methyl isobutyl ketone (MIBK), THF and benzene. They found that the reactivity of the macromonomer was higher in MIBK, which was the solvent where the intrinsic viscosity of the macromonomer was the lowest. Kennedy and Lo[24] studied the copolymerization of vinylbenzyl-terminated polyisobutylene macromonomers with MMA in four different solvents. They found that the reactivity ratios did not differ when ethylbenzene, toluene or ethyl caproate were used as copolymerization solvents.

However, with n-heptane as solvent (n-heptane is a good solvent for poly(isobutylene), but not for PMMA, although at very low conversions, the reactivity ratio r_2 was similar to that obtained with the first solvents; at higher conversions the reactivity of MMA dramatically dropped and milky solutions were observed, indicating that microphase separation had taken place.

The formation of phase separated domains can be a consequence of either a rather low compatibility of the backbone of the graft copolymer and the macromonomer and/or a large difference in the swelling behaviour of both in the same solvent. Dioxane, the solvent used in our study, is a good solvent for PLLA macromonomer but not for PVP. In fact, PVP is insoluble in dioxane at room temperature. It solubilizes on heating, leading to unstable solutions that precipitate on cooling. When the copolymerization of the macromonomer with VP is carried out at moderate conversions, considering the fast disappearance of the macromonomer, a copolymer richer in VP is likely to be formed. In a poor solvent this backbone is expected to be more coiled and compact than in a good one. According to the kinetic excluded volume effect, first proposed by Morawetz and co-workers[25,26], the lowered rate of chemical reaction between polymers is due to the shielding of the reactive centres within polymer coils. The swelling of a growing macromolecule would produce a decrease in the reaction rate with the other macromolecule (in our case the macromonomer) as the active centre is expected to migrate a longer distance until encountering the polymerizable group of the macromonomer. If we consider the poor compatibility between PVP and PLLA, as demonstrated by the miscibility tests, it is reasonable to think that a more compact, rich-in-VP growing chain will have difficulty encountering the double bond of the macromonomer. At low conversions, the repulsive forces between segments of PLLA and PVP are partially counteracted by the emulsifying effect of a rich-in-macromonomer growing backbone. At moderate or high conversions the miscibilization effect disappears as the backbone composition becomes richer in VP. The growing chains are now more coiled as a consequence of the poor interaction with the solvent, and this enhances even more the repulsive interactions between the macromonomer and the growing backbone. This results in a drastic decrease in the reactivity of VP towards the macromonomer, as shown in *Table 1*.

As has been stated above, the kinetic scheme of the macromonomer copolymerization is expected to involve essentially the comonomer radical due to the low concentration of macromonomer used. Thus, the parameter r_{MC} becomes of little practical importance since, unless r_i (i = MA, MMA or DMA) is especially large, the probability of a growing chain ending in a macromonomer unit on adding another molecule of macromonomer is really small[22]. In addition, r_{MC} is a parameter difficult to determine with sufficient accuracy[27]. However, the reactivity of the model compound (ML) of the macromonomer might be used, as a first approximation, to study the behaviour of the macromonomer. In order to verify the validity of this assumption the theoretical instantaneous copolymer compositions as a function of the feed were calculated for each pair of reactivities found. *Figure 6* shows the composition diagram for the copolymer systems prepared with MA and MMA as comonomers. In both cases, two series of data have been represented: the first one corresponds to the composition data obtained from reactivity ratios of these acrylic monomers with model compound ML. The second one corresponds to

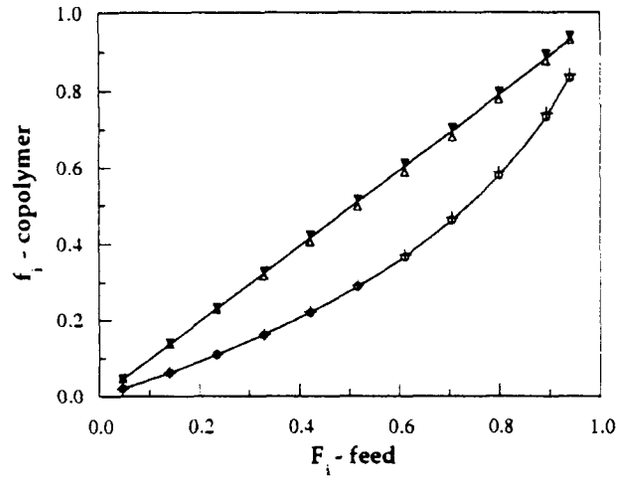


Figure 6 Composition diagrams for the copolymerization of the macromonomer MC and the homologous model ML with acrylic monomers: (+) ML/MA; (○) MC/MA; (▼) ML/MMA; (△) MC/MMA

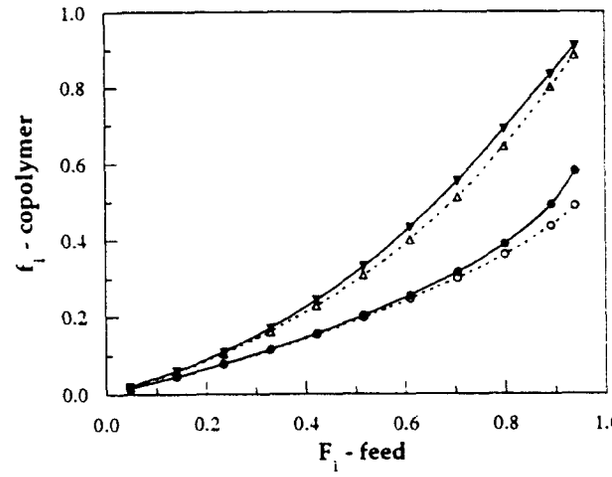


Figure 7 Composition diagrams for the copolymerization of the macromonomer MC and the homologous model ML with polar monomers: (▼) ML/DMA; (△) MC/DMA; (●) ML/VP; (○) MC/VP

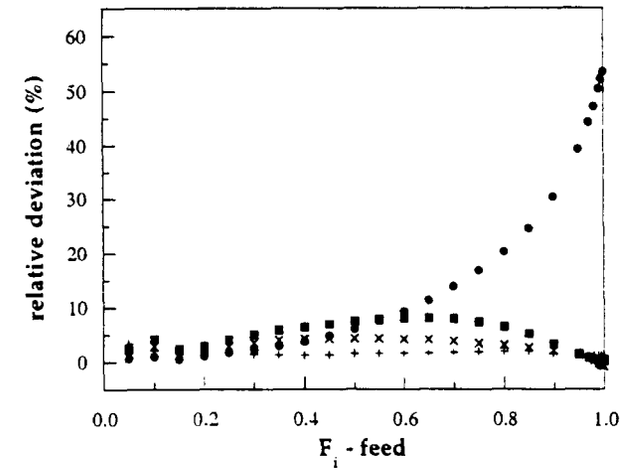


Figure 8 Relative deviation vs. feed composition: (+) copolymerization with MA; (×) copolymerization with MMA; (■) copolymerization with DMA; (●) copolymerization with VP

composition data, assuming that the reactivity of the macromonomer MC is similar to that of the model compound ML. In both cases the composition data adequately fit the same diagram. *Figure 7* shows the composition diagrams obtained for the systems prepared with the polar monomers DMA and VP. Only in the case of copolymerization systems with VP are noticeable deviations of the composition diagrams observed. This is better seen in the diagrams drawn in *Figure 8* which present the relative deviation of data for the four systems studied in this work. In all cases the deviation of composition, considering the reactivities of the macromonomer MC with respect to model compound ML, are lower than 5%, with the exception of the system with VP, particularly for feed compositions rich in this vinyl monomer. In this latter case the deviation is significant at a molar fraction of VP as low as 0.3, and can reach values about 50% for feeds which are very rich in VP.

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