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Analysis and characterization of resorbable DL-lactide–trimethylene carbonate copolyesters*

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Randomized copolyesters of DL-lactide (DLLA) and trimethylene carbonate (TMC) in a wide range of composition were synthesized, analysed and characterized with the aim of assessing their potential benefit in biomedical applications. The chemical composition was analysed using ^{1}H-nuclear magnetic resonance (NMR) spectroscopy. Sequence information was obtained by means of ^{13}C-NMR spectroscopy. From the occurrence of TMC–lactate–TMC triads it is concluded that synthesis by melt copolymerization at 190 °C is accompanied by transesterification. The copolymers were characterized by means of differential scanning calorimetry (DSC), tensile testing and accelerated hydrolysis tests at 80 °C. Their properties were compared with those of the parent polymers. It was found that all properties under investigation are strongly affected by the molar composition: with increasing TMC moieties the glass transition temperature (T_g) is depressed, the tensile strength reduced, the elasticity increased and the *in vitro* hydrolysis rate decelerated.

1. Introduction

Synthetic bioresorbable polymers have become interesting for a variety of biomedical applications. They have been evaluated or are already in clinical use as resorbable sutures, implants or microspheres for controlled drug release and as medical devices for bone fixation, such as plates, rods, screws and wires. Investigations of the suitability for further applications are in progress [1]. The properties and applications of these polymers have been widely reviewed in the literature [1–13].

The chemical structure of resorbable polymers includes polyesters, polyorthoesters [14], polyanhydrides [15], poly (ether esters) [16], poly (amino acids) [17, 18] and polydepsipeptides [19, 20]. Of the above, most attention has been paid to polyesters and copolyesters derived from lactic and glycolic acid, both acids normally occurring in the human body.

The homopolymers of this group, poly (L-lactide), poly (D-lactide) and poly (glycolide), are semicrystalline high-strength materials [11]. In copolymers the crystallinity depends on the monomer composition and sequence (random or block copolymers). Poly (DL-lactide) (P-DLLA), a random copolymer with 50% L- and 50% D-lactate units, is an amorphous material due to its stereo-irregular polymer chain [21]. All of the above polyesters, either crystalline or amorphous, are relatively rigid and brittle materials. In the amorphous copolymers the rigidity is attributed to their T_g being considerably above ambient temperature. Thus, at room or body temperature the materials are in their glassy state.

For certain medical applications, in particular soft tissue implants, stiff and brittle materials do not seem well suited, but a more ductile or even elastic mechanical response is desirable.

One approach to modifying the polymer characteristics in order to meet specific requirements for different applications is copolymerization of different monomers. Thus, a successful modification of polyglycolide was achieved by incorporation of TMC units into the glycolide chain. Due to its enhanced flexibility, this copolymer with a blockwise sequence is used for surgical monofilament sutures [22, 23]. In comparison with the glycolide homopolymer, this copolymer is more resistant to hydrolytic attack. Further TMC-modified copolymers of lactide or glycolide are mentioned in the open and patent literature: random copolymers from glycolide and TMC are suggested as coatings for surgical sutures [24]. Rosati and Casey synthesized block polymers with one block being poly(ethylene glycol) and the other comprising randomized glycolide and TMC units [25]. More recently randomized copolymers from L-lactide (LLA) and TMC with low lactide content along with various block polymers from LLA, DLLA and TMC were described [26, 27].

Homopolymeric TMC (P-TMC) has been known for a long time [28]. Its mechanical properties and hydrolytic degradation were recently reported in the literature [29]; except for low-molecular weight species, it represents an amorphous, rubbery polymer with low tensile strength. The *in vitro* degradation is reported to be very slow, whereas *in vivo* tests revealed

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a considerable decrease in molecular weight during a 6 month period [29].

This paper is directed at randomized copolymers of racemic DLLA and TMC (P-DLLA–TMC), with the aim of obtaining bioresorbable polymers with new characteristics in view of mechanical properties and hydrolysis kinetics. Since both parent polymers, P-DLLA and P-TMC, differ greatly in their properties, the characteristics of random copolymers of both components should be strongly affected by the molar composition.

For an initial assessment of their potential benefit in biomedical applications, copolyesters of DLLA and TMC covering a wide range of chemical compositions were synthesized, analysed and characterized by DSC measurements, tensile testing and *in vitro* hydrolysis tests. Their characteristics are compared with those of the parent polymers.

2. Experimental

2.1. Materials

TMC (1,3-dioxan-2-one) and DLLA (racemic mixture of RR-3,6-dimethyl-dioxan-2,5-dione and SS-enantiomer) were used in polymer grade from Boehringer (Ingelheim, FRG) without further purification. Analytical grade solvents were obtained from Merck (Darmstadt, FRG). Tin(II) ethylhexanoate was supplied by Bärlocher, FRG. The P-DLLA used for reference was a Resomer R206 from Boehringer (Ingelheim, FRG) with an inherent viscosity (IV) of 1.2 dl g^{-1}.

2.2. Polymer synthesis

A mixture of the monomers was charged into a glass ampoule and tin(II) ethylhexanoate, dissolved in toluene, was added. The tin content amounted to 100 p.p.m. relative to the monomer weight. The solvent was removed by evacuation several times. The ampoule was purged with dry nitrogen, sealed and immersed in an oil bath at 190 °C for 2.5 h. After the reaction the ampoule was quenched in an ice bath and the polymer was discharged. For removal of residual monomers, selected polymers were purified by re-precipitation from chloroform–petroleum ether and dried *in vacuo*. P-TMC was synthesized in the same way as the copolymers, but the reaction time was 2 h and tin content 50 p.p.m.

2.3. Analysis and characterization

The IV of all polymer samples was measured in a 0.1% chloroform solution at 25 °C, using an automated Ubbelohde viscometer.

^{1}H-NMR and ^{13}C-NMR spectra were recorded in $CDCl_3$, referenced to tetramethylsilane on a Bruker AM 250 spectrometer (250 and 63 MHz, respectively). For the carbon spectra a scan frequency of 2 s was employed. The chemical composition of the copolymers was determined by ^{1}H-NMR integrations and is given as percentage by weight, e.g. P-DLLA–TMC 70/30. ^{1}H-NMR data are reported in Table I.

The T_g were recorded by DSC at a heating rate of 5 K min^{-1}, using Setaram 111 equipment. In all cases the mean value of the onset and offset of the glass transition region is reported.

For stress–strain testing, sheets of thickness of about 2 mm were manufactured by melt-pressing at processing temperatures of between 50 and 120 °C. The sheets were cut into test specimens 180 mm × 15 mm. Control of the IV showed thermal processing at these temperatures did not affect the molecular weight of the polymers. Tensile testing was performed at room temperature on a Zwick 1485 machine at a crosshead speed of 200 mm min^{-1} (P-DLLA and P-DLLA–TMC 90/10 20 and 50 mm min^{-1}, respectively). The reported data are mean values for at least nine specimens (P-DLLA–TMC 90/10 only four specimens). Moduli were calculated from the initial slope of the stress–strain curves. The test specimens were manufactured and tested at the Institute of Plastics Processing, Aachen, FRG.

TABLE I ^{1}H-NMR chemical shifts for polymers and monomers

	Methyl	Methine	β-Methylene	α-Methylene
DLLA	1.64, 1.67	5.05, 5.08, 5.11, 5.13		
RS-lactide	1.70, 1.73	5.04, 5.07, 5.11, 5.13		
P-DLLA	1.54–1.59 (m)[a]	5.11–5.27 (m)		
P-DLLA–TMC 50/50	1.48–1.61 (m)	4.95–5.27 (m)	2.00–2.09 (m)	4.19–4.26 (m)
P-TMC			2.00, 2.03, 2.05, 2.08, 2.10	4.17, 4.21, 4.24
TMC			2.12, 2.14, 2.16, 2.18, 2.20	4.44, 4.46, 4.48

[a] (m) denotes multiplet.

For hydrolysis tests P-DLLA was compressed to tablets of 200 mg weight, 13 mm diameter and 1.3 mm thickness. From the rubbery P-DLLA–TMC, samples of weight 200 mg and approximately the same shape as the tablets were cut from the bulk. The specimens were incubated in 150 ml phosphate buffer of pH 6.1 at 80 °C with magnetic stirring. The specimens were periodically removed, vacuum-dried and subjected to IV measurement. For this analysis, parts of 100 mg weight were taken from the degraded samples.

3. Results and discussion

3.1. Synthesis and analysis

Syntheses of copolymers were performed by the ring-opening reaction of the dimeric DLLA and TMC under standard reaction conditions. Since these conditions gave satisfactory molecular weights, as indicated by the IV, no attempt was made to modify the catalyst, temperature or reaction time. The synthesis is illustrated in Fig. 1.

A series of copolymers ranging from 2 to 93% TMC moieties were synthesized. Selected samples from these were purified for the removal of residual monomers, and were subjected to analysis and further characterization. The copolymers synthesized and the analytical results are listed in Table II.

In all runs the conversion of DLLA was around 96%, whereas the TMC conversion strongly depended on the composition in the monomer feed (Table II). The higher conversion of TMC in reactions with a TMC-rich monomer feed indicates that the homopropagation of TMC is faster than its heteropropagation.

The content of non-converted monomers and the copolymer composition can be calculated from the ^{1}H-NMR integrations, since the methyl resonances of monomeric and polymeric DLLA as well as the α-methylene resonances of monomeric and polymeric TMC are separated. The ^{1}H-NMR shift values were given in Table I. In addition to monomeric DLLA, small amounts of mesolactide (RS-lactide) could be detected in the spectra of the crude polymers. The lines of this monomer were identified by comparison with the spectrum of an authentic sample of RS-lactide. As the methyl doublet of RS-lactide occurs with a slight downfield-shift to that of DLLA, detection of this side-product is possible, but without allowing for an accurate quantification. The overall monomeric lactide amount of around 4% (relative to polymeric DLLA) was near the accuracy level of NMR measurements.

The ^{1}H-NMR spectra, furthermore, allow a rough indication of the monomer distribution in the copolymers. In particular, the resonances of lactate units are sensitive to different monomer sequences. In Fig. 2 the methine portion of the ^{1}H-NMR spectrum of P-DLLA–TMC 50/50 is shown. It shows two major sets of peaks, labelled 1 ($\delta < 5.1$ p.p.m.) and 2 ($\delta > 5.1$ p.p.m.). Since set 1 is not found in the spectrum of P-DLLA and its intensity increases as the content of TMC moieties in the copolymer increases, assignment to methine protons linked to carbonate groups is suggested. This is in compliance with line assignments of poly(L-lactide-co-trimethylene carbonate) (P-LLA–TMC) [30]. However, as the several methine quartets overlap, reliable separated integration is not possible.

Since the monomer sequence may have a considerable influence on the polymer properties, a more detailed sequence analysis was done by means of ^{13}C-NMR spectroscopy. As illustrated in Fig. 3 for

TABLE II Copolymerizations of DLLA and TMC

Sample no.	TMC charged (wt %)	TMC conversion (wt %)	Polymer composition DLLA/TMC (wt %)	IV (dl g^{-1})
1	5	~ 25	~ 98/2	1.2[a]
2	10	55	94/6	1.4
3	13	65	90/10	1.3
4	20	84	83/17	1.1
5	31	92	70/30	1.0
6	40	95	59/41	0.9[a]
7	50	97	50/50	1.0
8	60	98	39/61	1.2[a]
9	69	98	30/70	1.0
10	70	98	28/72	1.1
11	87	98	12/88	1.2
12	88	98	10/90	1.2
13	90	98	7/93	1.5
14	100	98	0/100	1.7

[a] IV was determined on crude polymers.

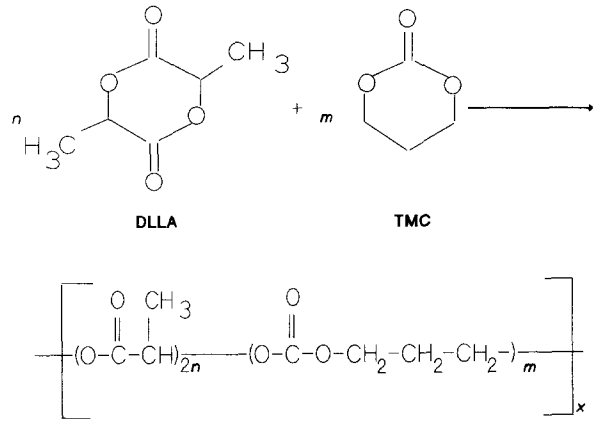

Figure 1 Synthesis of P-DLLA–TMC.

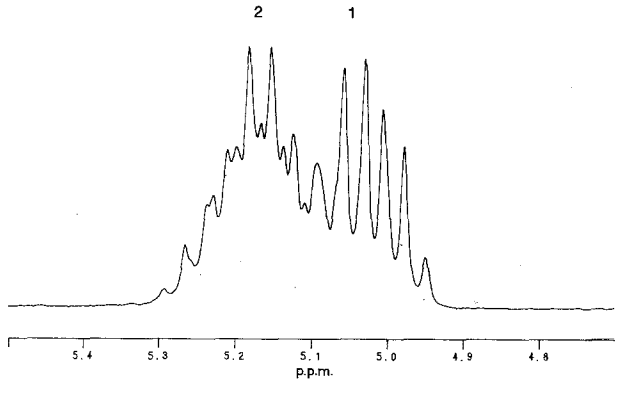

Figure 2 Methine portion of the ^{1}H-NMR spectrum of P-DLLA–TMC 50/50.

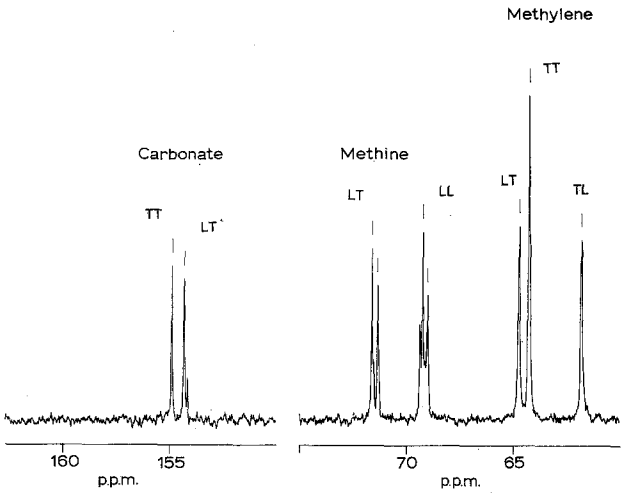

Figure 3 Selected regions of the ^{13}C-NMR spectrum of P-DLLA–TMC 50/50.

TABLE III ^{13}C-NMR signals for P-DLLA–TMC 50/50

Type	Shift (p.p.m.)	Structural fragment	Dyad label[a]
Carbonate	154.89[b]	–CH_2–O–$\underline{C}$O–O–CH_2–	TT
	154.33[b]	–CO–$CHCH_3$–O–$\underline{C}$O–O–CH_2–	LT
	154.17		
Methine	72.02	–CO–$\underline{C}HCH_3$–O–CO–O–CH_2–	LT
	71.64[b]		
	71.54		
	71.36[b]		
	69.39	–CO–$\underline{C}HCH_3$–O–CO–$CHCH_3$–	LL
	69.26[b]		
	69.20		
	69.02[b]		
Methylene	64.74[b]	–CO–$CHCH_3$–O–CO–O–$\underline{C}H_2$–	LT
	64.29[b]	–$\underline{C}H_2$–O–CO–O–$\underline{C}H_2$–	TT
	61.22[b]		
	61.82[b]	–$\underline{C}H_2$–O–CO–$CHCH_3$–	TL

[a] L, L- or D-lactate; T, TMC.
[b] These lines were also found in the spectrum of P-LLA-TMC 50/50.

P-DLLA–TMC 50/50, the carbon spectra are highly sensitive to particular monomer sequences, especially the shift values for the carbonyl, methine and α-methylene resonances. The signals of the carbonate, methine and α-methylene carbons each form distinctive sets of lines that can be separately integrated, whereas the lactate carbonyl portion displays a great number of lines that cannot be separately integrated. Detailed sequence assignments on a triad level of P-LLA–TMC, which does not contain D-lactate units, were recently achieved by various NMR techniques [30]. Compared with P-LLA–TMC, the spectra of P-DLLA–TMC are more complex, in particular the methine portions. The multitude of lines for one individual carbon not only reflects the chemical but also the sterical heterogeneity (D- and L-lactate units). In Table III the sets of lines for the carbonate, methine and α-methylene carbons are assigned at a chemical dyad level on the following basis: L- and D-lactate are treated as a whole, so that a dyad of both enantiomeric units is considered as a homodyad. The impact of different stereosequences on shift values is considered to be much less than the impact of different chemical sequences. Resonances of homodyads are directly assigned by comparison with the corresponding lines of P-DLLA and P-TMC. Heterodyads are assigned in compliance with the spectrum of a P-LLA–TMC 50/50 sample, which was prepared under identical polymerization conditions. Compared with the reported [30] sequence analysis of P-LLA–TMC on a triad level, this simplification to a chemical dyad level does not mean the loss of substantial information, since both levels allow for calculating average block lengths.

The number-average block lengths (L_L for L- or D-lactate and L_T for trimethylene carbonate) of both types of units can be calculated according to

$$L_L = (I_{LL}/I_{TL}) + 1 = (I_{LL}/I_{LT}) + 1 \quad (1)$$

$$L_T = (I_{TT}/I_{TL}) + 1 = (I_{TT}/I_{LT}) + 1 \quad (2)$$

respectively, where I represents the relative frequency of the corresponding dyad.

In Table IV the block lengths of selected copolymers are given. L_L was calculated from the methine peaks, L_T from the carbonate and methylene peaks of both the TL and LT dyads. For the sake of checking the correctness of the method used, the L_T/L_L ratio for each copolymer is compared with the molar ratio (T/L) obtained from the ^{1}H-NMR spectra.

The calculated L_T/L_L ratios match the observed molar ratios (T/L) from the proton spectra very well. The above data not only indicate an essentially random distribution of lactate and TMC units along the polymer chain. The average block lengths of lactate in P-DLLA–TMC 30/70 and 12/88 (both being < 2) furthermore demonstrate that lactate units connected to TMC on both sides (TLT triads) must be present. The occurrence of this sequence is of interest for mechanistic considerations because "dimeric" propagation by ring-opening of DLLA could never yield a TLT triad. Thus, under the reaction conditions described, polymerization must be accompanied by transesterification. Transesterification was also observed in the copolymerization of LLA and TMC under similar reaction conditions [30]. Although not mentioned in the paper, it becomes evident from the sequence data presented.

This conclusion is supported by the presence of monomeric RS-lactide in the reaction mixture after polymerization as determined by ^{1}H-NMR. Since

TABLE IV Block lengths of P-DLLA–TMC

Composition (% DLLA/TMC)	L_L	L_T			L_T/L_L	T/L molar ratio
		a	b	c	d	
90/10	14.86	1.16	1.17	1.23	0.080	0.079
70/30	4.50	1.36	1.37	1.41	0.31	0.30
50/50	2.36	1.73	1.74	1.72	0.73	0.71
30/70	1.58	2.53	2.54	2.53	1.60	1.66
12/88	1.10	5.64	5.64	5.53	5.09	5.17

(a) Calculated from methylene peaks, TL dyads; (b) calculated from methylene peaks, LT dyads; (c) calculated from carbonate peaks; and (d) calculated from the average values of columns a–c.

polymerization of lactide proceeds with retention in the chiral centres [31], the formation of RS-lactide can be explained only by transesterification either directly from the racemic monomer or from polymer units during the reaction. This is confirmed by the polymerization of LLA and TMC under the same reaction conditions, which does not yield RS-lactide in detectable amounts.

4. Polymer characterization

4.1. Glass transition and mechanical properties

Selected copolymers from Table I with different chemical compositions, and for reference P-DLLA and P-TMC, were subjected to DSC measurements and to tensile testing. The T_g and mechanical properties are reported in Table V.

As expected, in the DSC traces of all P-DLLA–TMC samples no evidence of crystallinity was shown. Only in the DSC curve of P-DLLA–TMC 94/6 can a slight endotherm superimposing the T_G be detected. This enthalpy relaxation can also be observed for the amorphous P-DLLA, depending on the thermal history of the sample [32].

The T_G in the different copolymers continuously decreased as the amount of TMC units in the polymer backbone increased. Although P-DLLA- and DLLA-rich copolymers are in their glassy state at ambient temperature, copolymers with more than about 30% TMC moieties show glass transitions at or below room temperature.

According to the thermal characteristics, a strong impact of the copolymer composition on the mechanical behaviour is obtained at room temperature. Typical stress–strain curves are presented in Fig. 4. Due to the wide stress and strain ranges they are plotted on logarithmic scales.

With an increase in the TMC moieties the tensile strength was reduced, along with an increased elasticity of the materials. For P-DLLA–TMC 70/30 and 50/50 no moduli were calculated as no initial linear region in the stress–strain curves were shown. An especially high elongation was found in copolymers with a medium TMC content.

The relatively high strength, high modulus and slight elongation of P-DLLA reflect the strong but stiff and brittle character of this glassy polymer. As represented by P-DLLA–TMC 90/10, the incorporation of TMC units in amounts too small to depress the T_g below room temperature results in a more ductile mechanical response than for P-DLLA. This is achieved with a moderate effect on the tensile strength.

The incorporation of higher amounts of TMC units depresses the T_g below room temperature and subsequently alters the mechanical response completely. Copolymers with a TMC content of about 30–50% are highly flexible materials that are still reasonably strong. The several-fold elongation in this medium range of composition is typically found for rubbery materials. With even higher amounts of TMC moieties the mechanical characteristics assimilate very close to P-TMC.

4.2. *In vitro* hydrolysis

In order to obtain test results quickly, the polymers were subjected to accelerated hydrolysis at elevated temperature. The test specimens were immersed in phosphate buffer of pH 6.1 at 80 °C with magnetic stirring. As an indication of changes in molecular weight, the IV of hydrolysed samples was measured as a function of time. For viscosity measurements, parts of 100 mg weight were taken, including material from the surface and the centre of the degraded specimens.

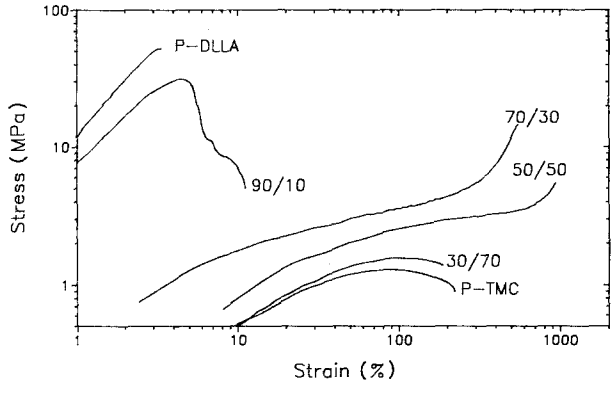

Figure 4 Stress–strain curves for P-DLLA–TMC.

TABLE V T_g and mechanical properties of P-DLLA–TMC[a]

Sample no.	Composition DLLA/TMC (wt %)	T_g (°C)	Tensile stress at maximum load (MPA)	Elongation at maximum load (%)	Modulus (MPA)
	100/0	+ 57	52	3.6	1900
2	94/6	+ 41			
3	90/10	+ 35	27	4.3	790
5	70/30	+ 23	14	519	
7	50/50	+ 9	5.2	963	
9	30/70	− 2	1.6	104	5
10	28/72	− 4			
12	10/90	− 13	1.2	84	5
13	7/93	− 15			
14	0/100	− 18	1.3	85	5

[a] The literature reported, for P-DLLA [21]: T_g 59 °C, tensile strength 48 MPa, elongation 8.7% and modulus 3200 MPa. For P-TMC [29]: T_g − 26 to − 15 °C, tensile strength 5 kg cm^{-2}, elongation at yield 20%, elongation at break 160% and modulus 30 kg cm^{-2}.

These pilot studies are used for an initial evaluation of the degradation kinetics. Several parameters that might play an important role in the complex mechanism of polyester hydrolysis in the solid state were not investigated: potential changes in polydispersity during degradation and changes in chemical composition, which are likely to occur towards the end of degradation, when weight loss of the samples starts. Although the test specimens were not mechanically degraded by magnetic stirring, the form stability of the polymers at 80 °C was low. Since recovery of hydrolysed samples with a desirable accuracy did not seem possible, the onset of weight loss was not determined. The viscosity data obtained reflect the average viscosity decrease and do not distinguish between surface and centre degradation. As was recently reported [33], the degradation of massive specimens of P-DLLA proceeds more rapidly in the centre then at the surface, resulting in bimodal size exclusion chromatography SEC curves. It was concluded [33] that this phenomenon can be attributed to a higher concentration of catalytic active carboxylic end-groups in the inner parts.

The degradation profile obtained in the accelerated tests was qualitatively similar for all copolymers, with an immediate onset of viscosity decrease. The IV decreased rapidly in the initial stage of hydrolysis, with smaller changes later. Disregarding the minor differences between the intrinsic viscosity and IV, the changes in IV during the degradation of P-DLLA–TMC were analysed according to a first-order kinetic model. This model was derived for the hydrolysis of polyesters in the solid state at 37 °C autocatalysed by generated carboxylic end-groups [34]

$$\ln \eta = \ln \eta^\circ - k't \quad (3)$$

$$k' = \alpha\,[\text{ester}]\,[H_2O]\,k \quad (4)$$

where η is the intrinsic viscosity, η° is the initial intrinsic viscosity, k' is the apparent rate constant for the decrease in η, t is the reaction time, α is the Mark–Houwink exponent, [ester] is the concentration of ester groups, $[H_2O]$ is the concentration of water and k is the rate constant.

Fig. 5 shows the corresponding semilogarithmic plots consistent with Equation 3. The full lines were generated by linear regression of log IV versus time. It is apparent from the figure and from the correlation coefficients (R, Table VI) that the first-order model for an autocatalysed hydrolysis is a good approximation to the experimental data, at least for lactide-rich polymers. This is found although the relatively simple model did not consider changes in the polydispersity and water uptake during degradation. Furthermore, the minor difference between the intrinsic viscosity and IV was disregarded and the experimental data did not differentiate between surface and centre of the specimens.

The half-life for the decrease in IV

$$t_{1/2} = (\ln 2)/k' \quad (5)$$

for the different polymers are given in Table VI. Calculation of k (Equation 4) from viscosity data was not possible, because α and $[H_2O]$ for the copolymers were not known. Furthermore, conversion of k' to k (Equation 4) will always be different for the different polymers, since [ester] varies to a large extent and α will not be the same.

Although the data obtained from the accelerated tests do not provide detailed information on the degradation of P-DLLA–TMC, these pilot studies allow for a comparison of the different polymers. The results clearly demonstrate the influence of chemical composition on the rate of degradation; hydrolysis is strongly decelerated with an increase in the TMC moieties.

For TMC-rich copolymers (samples 9 and 12) the autocatalytic model does not seem to correlate with the experimental results as well as for P-DLLA and DLLA-rich copolymers. The correlation coefficients

TABLE VI Hydrolysis kinetics of P-DLLA-TMC at 80 °C and pH 6.1

Sample	Composition (% DLLA/TMC)	Initial IV (dl g^{-1})	$t_{1/2}$ (h)	R
	100/0	1.1	8	0.994
3	90/10	1.5	12	0.996
5	70/30	1.1	20	0.996
7	50/50	1.1	33	0.996
9	30/70	1.1	61	0.981
12	10/90	1.2	209	0.983
14	0/100	1.0	(27 800)	0.889

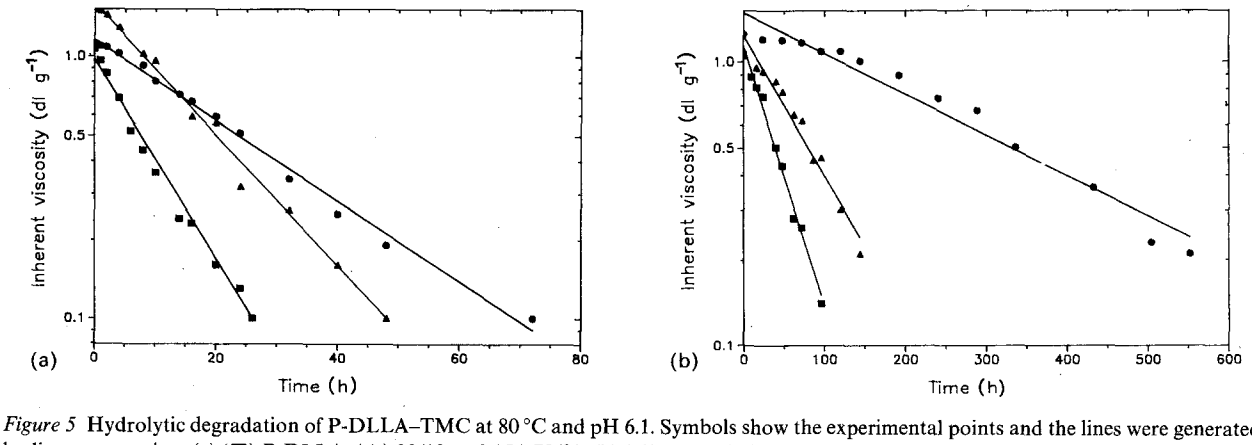

Figure 5 Hydrolytic degradation of P-DLLA–TMC at 80 °C and pH 6.1. Symbols show the experimental points and the lines were generated by linear regression. (a) (■) P-DLLA, (▲) 90/10 and (●) 70/30; (b) (■) 50/50, (▲) 30/70 and (●) 10/90.

(R, Table VI) for these polymers are poorer and the semilogarithmic plots show a deviation from a straight line, in particular the plot for sample 12 (10/90 in Fig. 5). The initial slope in this semilogarithmic plot represents an initial IV decrease from 1.2 to 1.0 dl g^{-1} during the first 144 h. The slope rises when degradation is more advanced. In the case of P-TMC the hydrolysis rate is extremely low. Over a period of 192 days a decrease in IV from 0.99 to only 0.93 dl g^{-1} is obtained. Thus, the data for this polymer in Table VI reflect only this small initial part of degradation. Since the hydrolysis of P-TMC has not yet been studied over a sufficient viscosity scale, it cannot be decided whether the poor correlation for P-TMC ($R = 0.889$, Table VI) is attributed to systematic deviation from the first-order model or to experimental error in measurement of the viscosity. For this reason the half-life for this particular polymer is given in parentheses. Following the results and discussions of Zhu *et al.* [29], who evaluated the hydrolysis of P-TMC at 37 °C, it can be concluded that the deceleration role of TMC units is due to a lower concentration of generated carboxylic end-groups in TMC-rich copolymers. Compared with carboxylic end-groups, the end-group generated by hydrolysis of carbonate bonds has no catalytic action, since the carbonic acid end-group is a weaker acid (pK 6.5 versus 3–5 for carboxylic acid) [29] and is unstable. As evidenced by comparative studies on the hydrolysis of P-TMC and poly(ε-caprolactone) [29], the extremely slow hydrolytic degradation of P-TMC cannot be explained by low hydrophilicity of P-TMC or by an intrinsically lower reactivity of carbonate groups compared with ester groups. It might be suggested that the low concentration of catalytic active end-groups also leads to deviations from the first-order kinetics in samples 9 and 12. The viscosity decrease of TMC-rich copolymers might be better analysed according to a rate law derived for uncatalysed hydrolysis [34]. However, this would require that the Mark–Houwink exponents (α) of these copolymers be known.

It should be noted that the results obtained from the accelerated *in vitro* tests do not permit precise calculation of the hydrolysis kinetics at physiological temperature, because the temperature dependence of hydrolysis may be different for the different polymers. Furthermore, the results can indicate only the contribution of random bulk hydrolysis to biodegradation. Although the *in vivo* degradation of glassy polylactones generally proceeds without a significant contribution of enzymatic attack, biodegradation of rubbery polylactones with low elastic moduli proceeds predominantly by enzymatic surface erosion [35]. As the *in vivo* degradation of P-TMC is reported to be considerably faster than that *in vitro* and is accompanied by a substantial increase in the polydispersity, it was concluded [29] that this rubbery polycarbonate is also subject to enzymatic chain scission under *in vivo* conditions. Thus, it would be expected that the contribution of enzymatic degradation of P-DLLA–TMC becomes increasingly important as the TMC content rises with increasing elasticity and decreasing susceptibility to random bulk hydrolysis. As a result, the large differences found in the degradation rates of P-DLLA–TMC in the *in vitro* tests are to some extent expected to be reduced under *in vivo* conditions.

5. Conclusions

Randomized copolymers of DLLA and TMC covering a wide composition range were synthesized, analysed and characterized with reference to the parent polymers, P-DLLA and P-TMC.

DSC measurements, tensile tests and accelerated hydrolysis tests showed that the molar composition strongly determines the characteristics of the copolymers. The T_g ranged from + 57 °C for D-PLLA to − 18 °C for P-TMC. The mechanical properties varied from strong, stiff and brittle (P-DLLA) and moderately strong and tough (copolymers with low TMC content) to rubbery, highly elastic (copolymers with high TMC content). TMC in small amounts acted as an impact modifier for the P-DLLA chain, and larger amounts as an internal plasticizer. The *in vitro* hydrolysis was strongly decelerated by increasing amounts of TMC moieties.

The properties of the copolymers described suggest their suitability as materials for resorbable soft tissue implants.

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