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Poly(ethylene oxide)/poly(butylene terephthalate) segmented block copolymers: the effect of copolymer composition on physical properties and degradation behavior

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Abstract

In this study, the influence of copolymer composition on the physical properties and the degradation behavior of thermoplastic elastomers based on poly(ethylene oxide) (PEO) and poly(butylene terephthalate) (PBT) segments is investigated. These materials are intended to be used in medical applications where degradability of the implant is desired. PEOT/PBT copolymers are microphase separated and up to four thermal transitions are measured by differential scanning calorimetry. Phase separation in the system is enhanced by increasing the molecular weight of starting poly(ethylene glycol) (PEG) or by increasing the PBT content. The mechanical properties, swelling characteristics and degradation rates of the copolymers are influenced by the phase separation. By changing the PEOT/PBT composition, tensile strengths vary from 8 to 23 MPa and elongations at break from 500 to 1300%. Water uptake ranges from 4 to 210%. The in vitro degradation of PEOT/PBT copolymers occurs via hydrolysis and oxidation. In both cases, degradation is more rapid for copolymers with high contents of PEO. Deterioration of copolymer films takes place when the films are exposed to light in the absence of antioxidant. In preventing oxidation under daylight conditions, Irganox 1330 turned out to be a more efficient antioxidant for the copolymers than vitamin E.

Keywords: Poly(ether ester); Phase separation; Degradation

1. Introduction

Polymers to be used as implant materials should be biocompatible and their mechanical properties, water absorption and rates of degradation have to be optimal for a particular application. Poly(ethylene oxide) (PEO) and poly(ethylene glycol) (PEG) are hydrophilic, semi-crystalline polyethers with a glass transition temperature below room temperature. They are biocompatible, non-toxic, non-antigenic and non-immunogenic [1]. Therefore, PEG has been frequently used to modify the surface of a variety of polymers in order to decrease protein adsorption and to improve their biocompatibility [2–5]. Materials combining these properties with in vivo degradability have been prepared by copolymerization of lactones and PEG [6–8]. Such block copolymers have been investigated for use as drug delivery systems [9,10] and scaffolds in tissue engineering [11,12]. First developed for textile applications [13], PEOT/PBT block copoly(ether ester)s (Fig. 1) have shown to possess interesting physical properties for medical use as well [14]. In vitro, epidermal keratinocytes, dermal fibroblasts [15], skeletal muscle cells and chondrocytes [16] showed good adhesion and proliferation on PEOT/PBT copolymer films. In vivo no adverse tissue reactions were observed after subcutaneous implantation in rats [17,18].

Recently, effective release of proteins from PEOT/PBT microspheres has been demonstrated [19,20] and the potential use of these polymers for tissue engineering of bone has been shown [21]. Degradation of PEOT/PBT segmented copolymers in vivo has also been reported [18]. In vivo two degradation pathways of these copolymers are expected to take place. The first route involves hydrolysis of ester bonds in the PBT part or of ester bonds connecting PEO segments and terephthalate units. Besides hydrolysis, oxidation reactions may play a role in the degradation of PEO segments. Implantation of medical devices provokes a foreign body response, during which specific activated cells such as macrophages release enzymes and superoxide anion radicals, which can combine with protons to form

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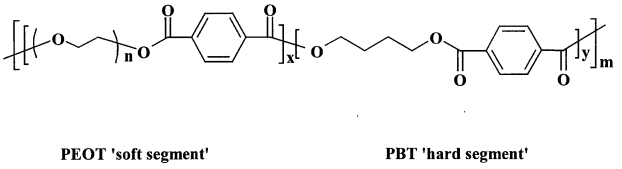


Fig. 1. Chemical structure of PEOT/PBT segmented block copolymers.

hydroperoxide radicals [22]. It has been suggested that in vivo degradation of poly(ether urethane) elastomers, and in particular, the aliphatic ether groups in these polymers, involves phagocyte-derived oxidants [23]. Several in vitro studies confirm the oxidative degradation of PEO by a radical mechanism initiated at random along the chain [22,24–26].

The aim of this study is to establish the effects of copolymer composition and phase separation on the physical properties and the degradation behavior of segmented PEOT/PBT block copolymers with relatively high soft segment contents. The variation of the mechanical properties of PEOT/PBT copolymers as a function of molecular weight in the dry and swollen state has been investigated. In vitro hydrolysis and oxidation of PEOT/PBT block copolymers have been evaluated. The degradation of the copolymers under different storage conditions has been studied.

2. Materials and methods

2.1. Polymerizations

PEOT/PBT multiblock copolymers were prepared by a two-step polycondensation in the presence of titanium tetrabutoxide (Merck) as catalyst (0.1 wt%) and Irganox 1330 (Ciba-Geigy) as antioxidant (1 wt%). The transesterification of PEG, dimethyl terephthalate (DMT) and 1,4-butanediol was carried out under a nitrogen atmosphere at 180°C. After 2 h, the pressure was slowly decreased from 1000 to 0.1 mbar to allow polycondensation. Simultaneously, the temperature was increased from 180 to 240°C. PEG 300, PEG 1000, PEG 2000 and PEG 4000 from Fluka, DMT from Merck and 1,4-butanediol from Acros were used without further purification. Copolymers of different molecular weights were prepared by varying the reaction times.

With the exception of the materials used in the DSC and water-uptake experiments, the copolymers were purified and the antioxidant was removed by dissolution in chloroform and precipitation into excess of ethanol.

The composition of the block copolymers is indicated as *a b*/*c*, in which *a* is the starting PEG molecular weight, *b*, the weight percentage of PEOT soft segments and *c*, the weight percentage of PBT hard segments (Fig. 1). It has to be noted that terephthalic ester units are present in both the soft and the hard segments. Therefore, the notation PEOT (T for terephthalate) is used to refer to the soft part. The weight contribution of PEO and terephthalic ester units in the soft part is determined by the starting PEG molecular weight. At constant soft to hard segment ratio, the total PEO content in the copolymer increases with the molecular weight of the used PEG (Table 1).

Table 1
PEO content (wt%) of PEOT/PBT copolymers synthesized with PEG of different molecular weights at given soft to hard segment ratios

	Soft/hard segment ratio (wt/wt)					
	100/0	70/30	60/40	55/45	30/70	0/100
PEG 300	100	49	42	38	21	0
PEG 1000	100	62	53	49	26	0
PEG 4000	100	68	58	53	29	0

2.2. Polymer characterization

The intrinsic viscosity $[\eta]$ of the copolymers in chloroform (solution of approximately 0.3 g/dl) was determined by single point measurements [27,28] at 25°C using an Ubbelohde OC viscometer. The intrinsic viscosity is related to the molecular weight by the Mark–Houwink equation:

$$[\eta] = K \times M_v^a \qquad (1)$$

where M_v is the viscosity average molecular weight, K and a depend on the polymer, the solvent and the temperature. For polymer 1000 70/30 in chloroform at 25°C, K and a values have been estimated at 1.522×10^{-3} dl/g and 0.545, respectively. The Mark–Houwink constants are not known for other copolymer compositions, therefore values of $[\eta]$ are used for comparison.

The polymer composition was determined by proton nuclear magnetic resonance spectroscopy (^{1}H-NMR). 300 MHz ^{1}H-NMR (Varian Inova 300 MHz) spectra were recorded using polymer solutions in deuterated chloroform (Sigma). In the case of copolymers insoluble in $CHCl_3$, small amounts of trifluoroacetic acid were added.

The thermal properties of copolymers containing antioxidant were evaluated by differential scanning calorimetry (DSC) with a Perkin Elmer DSC 7. A heating rate of 10°C/min was applied, and stainless steel pans were used. The copolymer samples (8–15 mg) were heated from −80 to 250°C. The samples were then quenched rapidly (300°C/min) until −80°C and after 5 min, a second scan was recorded. The data presented are from the second heating scan. The glass transition temperatures were taken as the midpoint of the heat capacity change, the melting temperatures were determined from the maximum in the melting endotherm. Indium and gallium were used as standards for temperature calibration.

The equilibrium water uptake in demineralized water was defined as the weight gain of the unpurified polymer sample after conditioning at 37°C according to Eq. (2):

$$\text{Water uptake (wt\%)} = \frac{m - m_0}{m_0} \times 100 \qquad (2)$$

where m_0 is the initial specimen weight (approximately 0.5 g) and m the weight of the specimen after conditioning to equilibrium.

2.3. Mechanical properties

Tensile testing was performed on dry and swollen PEOT/PBT block copolymer films. Specimens were cast from chloroform solution (50–100 μm thick) and were cut according to ASTM D882-91 specifications ($100 \times 5\ \mathrm{mm}^2$). Tensile tests in duplicate or triplicate were carried out at room temperature on a Zwick Z020 universal tensile testing machine operated at a crosshead speed of 50 mm/min using a 0.01 N pre-load and a grip-to-grip separation of 50 mm. The specimen elongation was derived from the grip-to-grip separation, and therefore, the presented values of the *E*-modulus give only an indication of the stiffness of the different polymers. The specimens were tested at ambient conditions. The error is less than 5% for the *E*-modulus and the maximum stress determination and is up to 20% for the elongation at break. The data presented in figures and tables are representative of the copolymer properties.

2.4. Degradation

In vitro hydrolysis experiments with 50–100 μm thick solution cast films were carried out in duplicate at 37°C using phosphate buffer saline (PBS) containing sodium azide (Sigma) as antibacterial agent (0.02 wt%). The PBS solution was refreshed every two weeks. Hydrolyzed samples were analyzed at predetermined times in terms of their intrinsic viscosity, chemical composition and mechanical properties.

Solution cast films were oxidatively degraded at 37°C in 10% H_2O_2 solution (prepared by diluting 30% H_2O_2 from Merck) containing 0.1 M $CoCl_2$ (Aldrich). $CoCl_2$ catalyzes the formation of hydroxyl radicals from the hydrogen peroxide through a Haber–Weiss reaction [29]. Oxidized samples were analyzed in duplicate in terms of their intrinsic viscosity, chemical composition and mechanical properties.

The adequacy of Irganox 1330 and vitamin E (α-tocopherol) as antioxidants during sample storage was studied with 1000 70/30 films. Beforehand, the polymer was purified in order to remove the Irganox 1330 used during the synthesis. Polymer films with and without antioxidant were prepared by casting solutions containing 0, 0.5, 1 and 2 wt% of Irganox 1330 or vitamin E (Aldrich). The presence of antioxidant in the films did not influence the initial mechanical properties of the polymers. The films were kept under three different conditions: in the light at ambient conditions, in the dark at ambient conditions and in the dark at −21°C. Degradation of the samples was evaluated in triplicate by following the change of the mechanical properties in time.

3. Results and discussion

3.1. Physical properties

PEOT/PBT segmented block copolymers are thermoplastic elastomers built up of hard segments (PBT) and soft segments (PEOT). The PBT hard segments have a glass transition temperature above body temperature and are able to crystallize, which gives strength to the material. The hydrophilic PEOT segments have a glass transition below room temperature, providing flexibility and hydrophilicity to the system.

The variation in hard and soft segment contents and in the molecular weight of the PEG used during the synthesis has an effect on the phase separation of the system. The miscibility of polymeric systems is controlled by the factor χN, where χ is the Flory–Huggins interaction parameter and N, the number of repeat units in the polymer chain. In polymer blends the χ-parameter is usually positive and large, and as a rule, polymers phase separate. In the case of block copolymers where the different macromolecules are covalently linked, macrophase separation is impeded, however, microphase separation can still occur. In (multi)block copolymers, an increase in molecular weight of the blocks favors phase separation [30]. Therefore, an increase in PEOT length and in PBT average sequence length will lead to enhanced phase separation in PEOT/PBT multiblock copolymers. Upon cooling, crystallization of one of the components is an additional driving force for phase separation.

Fakirov and coworkers studied the structure of PEOT/PBT copolymers with high PBT contents by DSC [31,32] and small angle X-ray scattering (SAXS) [33,34]. As was the case in their work, DSC experiments with PEOT/PBT copolymers containing higher amounts of PEO also show several amorphous and crystalline phases. Fig. 2 gives DSC spectra of PEOT/PBT of various compositions where the starting PEG molecular weight is kept constant (1000) and the soft to hard segment ratio is changed, or where the ratio

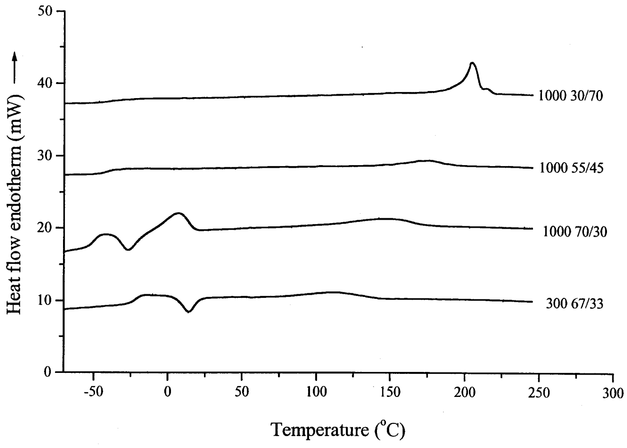


Fig. 2. DSC spectra of PEOT/PBT block copolymers of different compositions.

Table 2
Thermal properties of PEOT/PBT block copolymers with high molecular weight ([η] ranging from 0.7 to 1.6 dl/g). The weight fraction, mole fraction and number average sequence length ($\bar{L}_n$) of the PBT component were calculated from ^{1}H-NMR

Composition	PEOT-segment			PBT-segment							
	T_g (°C)	T_m (°C)	ΔH (J/g)	Weight fraction	Mole fraction	$\bar{L}_n$ [a]	T_g (°C)	T_m (°C)	ΔH (J/g)	w_c [b] (%)	$w_{c(n)}$ [c] (%)
300 67/33	−23	– [d]	–	0.33	0.49	2.0	–	114	13.4	9.2	27.9
300 56/44	−23	–	–	0.44	0.57	2.3	26	145	20.9	14.5	35.4
300 50/50	−17	–	–	0.50	0.66	2.6	46	159	25.3	17.5	35.0
300 27/73	−11	–	–	0.73	0.84	6.2	58	197	34.0	23.5	32.2
1000 70/30	−50	6	15.8	0.30	0.69	3.2	–	149	11.5	8.0	26.7
1000 61/39	−50	−1	3.1	0.39	0.77	4.3	–	166	13.0	9.0	23.1
1000 55/45	−41	–	–	0.45	0.81	5.3	–	176	15.0	10.4	23.1
1000 41/59	−40	–	–	0.59	0.88	8.3	–	182	21.6	15.0	25.4
1000 30/70	−38	–	–	0.70	0.92	12.5	40	204	30.1	20.8	29.7
2000 29/71	−52	5	0.4	0.71	0.96	25.0	–	215	28.6	19.8	27.9
4000 81/19	–	47	68.8	0.19	0.81	5.3	–	173	6.4	4.5	23.7
4000 71/29	–	39	45.8	0.29	0.88	8.3	–	192	9.5	6.6	22.8
4000 55/45	–	34	39.8	0.45	0.94	16.7	–	210	22.2	15.4	34.2
4000 20/80	–	32	12.7	0.80	0.99	100.0	–	223	34.8	24.1	30.1
10000 81/19	–	57	80.7	0.19	0.91	11.1	–	224	7.0	4.8	25.3
PBT	–	–	–	1	1	$\propto$	54	226	43.4	27.2	27.2
PEG 300	−48	−16	78.2	–	–	–	–	–	–	–	–
PEG 1000	–	39	150.2	–	–	–	–	–	–	–	–
PEG 2000	–	57	160.8	–	–	–	–	–	–	–	–
PEG 4000	–	60	178.7	–	–	–	–	–	–	–	–

[a] $\bar{L}_n = 1/(1 - x_{PBT})$, x_{PBT} = mole fraction of PBT.
[b] $w_c = \Delta H/\Delta H^0 \times 100$.
[c] $w_{c(n)} = w_c$/weight fraction$_{PBT}$.
[d] (–) not observed.

is kept constant (70/30) and the PEG molecular weight is changed from 1000 to 300. These examples are representative of the copolymers studied and, depending on the composition, up to four transitions can be observed. All PEOT/PBT block copolymers investigated are semi-crystalline at room temperature. A T_m corresponding to crystalline PBT ranging from 114 to 224°C was detected (the T_m of PBT homopolymer is 226°C). This T_m is relatively broad (about 25°C) due to the random condensation process during the synthesis, which leads to the formation of chains with a distribution of PBT sequence lengths. Recrystallization of the PEOT fraction could be detected between −30 and 31°C in case of high PEO contents. The degree of crystallinity (w_c) of a polymer can be estimated from the heat of fusion by the expression:

$$w_c = \frac{\Delta H}{\Delta H^0} \tag{3}$$

ΔH is correlated to the total weight of the polymer. The heat of fusion of 100% crystalline PBT (ΔH^0) is reported to be 144.5 J/g [35]. w_c gives an indication of the crystallinity of the PEOT/PBT multiblock copolymers (Table 2). To be able to compare the crystallinity with the PBT homopolymer, these values were also normalized to the PBT content of the block copolymer. It then appears that the normalized degree of crystallinity is similar for all copolymers and close to the degree of crystallinity of the PBT homopolymer.

The average sequence length ($\bar{L}_n$) of the PBT segments was calculated from the PBT mole fraction (x_{PBT}) in the copolymer assuming random copolymerization of the components:

$$\bar{L}_n = \frac{1}{1 - x_{PBT}} \tag{4}$$

The melting point of the hard segments depends strongly on the average sequence length. An increase in PBT weight fraction results in higher melting temperatures and in an increase in the heat of fusion of the PBT.

The phase separation between the distinct blocks also depends strongly on the starting PEG length. At a constant soft to hard segment ratio, an increase in the molecular weight of the used PEG enhances phase separation. This is illustrated by the appearance of high PEO and PBT melting points. Simultaneously, no T_g was detected anymore. Lower PEG molecular weights result in lower PBT average sequence lengths. A T_g corresponding to the presence of amorphous PBT domains is then observed, indicating a decreased phase separation between soft and hard segments. This is also confirmed by the depression in the melting point of the PBT segments and in the increase of the T_g of PEOT (Table 2).

In case of semi-crystalline polyesters, hydrolysis occurs preferentially in the amorphous phase [36,37]. An increase in crystallinity reduces the water permeability of the polymer

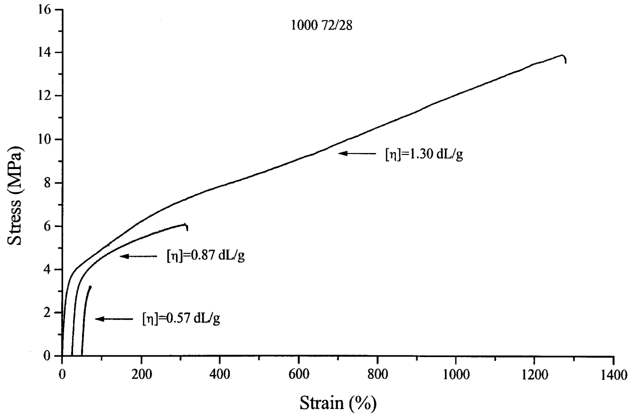


Fig. 3. Typical stress–strain diagrams of 1000 72/28 with different intrinsic viscosities. Stress–strain curves are offset for clarity. Measurements performed on dry samples.

and the accessibility of hydrolyzable bonds. During long term degradation experiments on poly(L-lactide), highly crystalline debris resistant to hydrolysis could be found, possibly causing an inflammatory response [38]. Therefore, in the case of implants made from PEOT/PBT copolymers, the use of material containing minimal amounts of PBT is recommended.

Phase separation is a main factor influencing the mechanical properties of PEOT/PBT block copolymers. To be able to compare the different copolymers, it is necessary to have polymers of a sufficiently high molecular weight since many physical properties depend considerably on it [39]. The mechanical characteristics of PEOT/PBT copolymers improve significantly with increasing molecular weight. Fig. 3 shows the stress–strain behavior of 1000 72/28 with three different intrinsic viscosities. For this copolymer, the *E*-modulus increases from 36 to 39 MPa when a polymer with an intrinsic viscosity higher than 0.87 dl/g is tested. The change in intrinsic viscosity has a more pronounced effect on the elongation at break and the tensile stress. At an intrinsic viscosity of 0.57 dl/g, the elongation at break is relatively low (22%), whereas a very high deformation of 1300% is reached for 1000 72/28 with an intrinsic viscosity of 1.3 dl/g. The values of the maximum tensile stress also increase significantly (from 3.2 to 13.9 MPa) with the intrinsic viscosity. Fig. 4 shows that a similar behavior is observed for PEOT/PBT copolymers of other compositions. For these copolymers, a limiting intrinsic viscosity value of approximately 0.4–0.6 dl/g can be established below which tensile strength and elongation at break are minimal. No upper plateau of the mechanical properties was observed for our system. The two-step polycondensation method used in this study to synthesize PEOT/PBT block copolymers yielded copolymers with intrinsic viscosities ranging from 0.40 to 1.62 dl/g. However, even better mechanical properties would be obtained if the polymer molecular weight could be increased further.

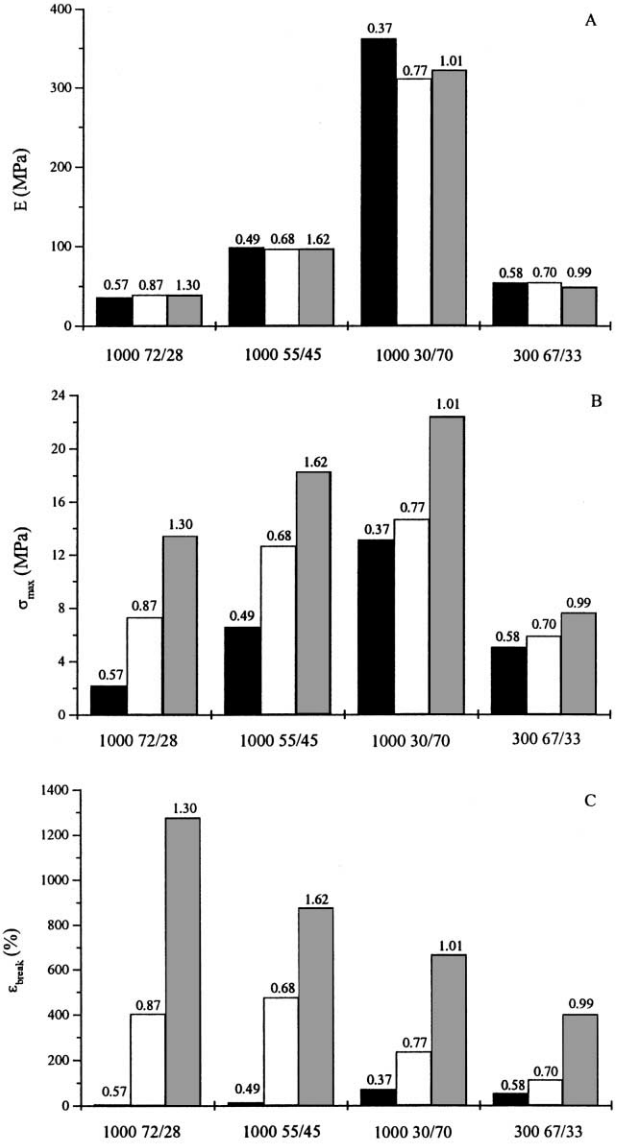


Fig. 4. Mechanical properties of different PEOT/PBT block copolymers as a function of composition and intrinsic viscosity. (A) *E*-modulus (*E*), (B) maximum tensile strength (σ_{max}), (C) elongation at break ($\varepsilon_{\mathrm{break}}$). The numbers above the bars represent the intrinsic viscosity of the polymer. Measurements performed on dry samples.

Fig. 5 shows the tensile behavior of four different copolymer compositions with high intrinsic viscosities (ranging from 0.99 to 1.62 dl/g). In comparing the stress–strain curves, it can be seen that the soft PEOT and the hard PBT segment ratios of polymers prepared with PEG 1000 as well as the effect of starting PEG molecular weight at constant soft to hard segment ratio (approximately 70/30) are of influence. As was also seen for PEOT/PBT copolymers with high PBT contents [31,32], keeping the PEG used in the synthesis at a constant molecular weight of 1000, an increase in soft segment content causes a decrease in *E*-modulus and in maximum stress. The *E*-modulus is reduced from over 300 MPa for 1000 30/70 to only 40 MPa for 1000 72/28 and the maximum stress from 23.2 to 13.9 MPa. At

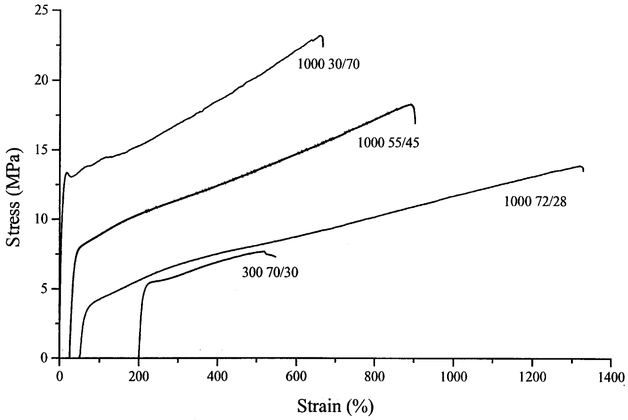


Fig. 5. Typical stress–strain diagrams of PEOT/PBT block copolymers of different compositions. Stress–strain curves are offset for clarity. Measurements performed on dry specimens.

Table 3
Water uptake and tensile properties (*E*-modulus, maximum stress and elongation at break) for dry and swollen PEOT/PBT segmented copolymers

Composition		1000 72/28	1000 30/70	300 70/30
Water uptake (wt%)		62	26	4
E (MPa)	Dry	39	322	49
	Swollen	25	274	44
σ_{max} (MPa)	Dry	13.4	19.0	7.7
	Swollen	11.4	17.9	6.9
$\varepsilon_{\text{break}}$ (%)	Dry	1278	667	402
	Swollen	1013	529	318

the same time, the elongation at break increases from 600 to 1300%. By increasing the soft segment content, the number of domains that contribute to the strength decrease and a more flexible material is obtained.

In the case of constant soft to hard segment ratios, the *E*-modulus decreases only slightly (from 49 to 39 MPa) when PEG 1000 is used instead of PEG 300. The elongation at break and the maximum stress increase significantly from 490 to 1300% and from 7.7 to 13.9 MPa, respectively. In case of a constant soft to hard segment ratio, the mechanical properties are considerably enhanced by a more pronounced phase separation between the soft and hard segments for the polymer prepared with the higher PEG molecular weight.

PEOT/PBT multiblock copolymers absorb water due to the presence of the hydrophilic PEO in the PEOT segments of the copolymers. Two parameters influence the uptake of water by PEOT/PBT copolymers: the PEG molecular weight via the phase separation in the copolymers and the PEO content. As stated earlier, at a constant soft to hard segment ratio, phase separation decreases when a shorter PEG is used in the copolymerization. The presence of hydrophobic PBT segments in the soft domains diminishes the uptake of water (Fig. 6). For a given soft to hard segment ratio, the use of a lower PEG molecular weight also means a lower content of PEO in the copolymer (Table 1).

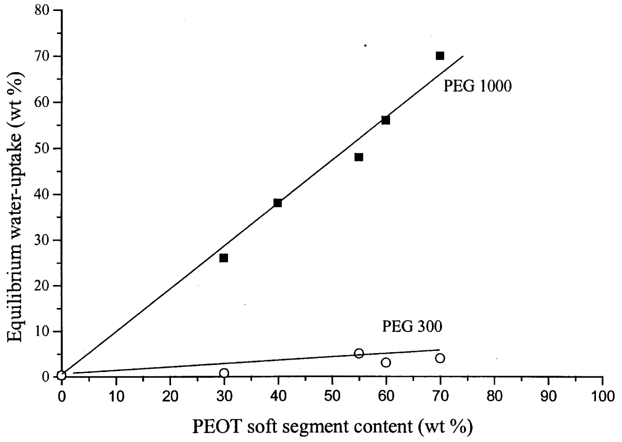


Fig. 6. Equilibrium water uptake (wt%) as a function of PEOT soft segment content (wt%) for PEOT/PBT copolymers synthesized from (■) PEG 1000 and (○) PEG 300.

When used as an implant in the body, the material will absorb body fluids and will swell. Consequently, the mechanical properties of PEOT/PBT copolymers need to be evaluated in the swollen state as well. *E*-modulus, maximum tensile strength and elongation at break in the dry and in the swollen state for several copolymer compositions are reported in Table 3. For all copolymers, the mechanical properties, especially the *E*-modulus, decrease in the swollen state. 1000 70/30 is the most hydrophilic of these copolymers and is the most affected by the uptake of water. Although the stiffness decreases during water uptake, all swollen materials can be handled with ease and are applicable in non-load-bearing situations such as in soft tissue applications and tissue engineering.

3.2. Degradation

PEOT/PBT block copolymers contain two types of potentially degradable chemical bonds in the polymer chain: ester bonds can be hydrolyzed and ether bonds can be oxidized. Both mechanisms are normally occurring in vivo.

The hydrolysis of PEOT/PBT copolymers in PBS was investigated. Three copolymers, 300 69/31, 1000 69/31 and 1000 61/39 were chosen with identical starting PEG molecular weight (PEG 1000) or with identical soft to hard segment ratio (69/31). The intrinsic viscosity and the mechanical properties during degradation are shown in Table 4 and Figs. 7 and 8.

No significant change in intrinsic viscosity, mechanical properties or chemical composition is observed for 300 69/31, which does not seem to degrade in PBS during a period of 24 weeks.

Polymers 1000 69/31 and 1000 61/39 show a decrease in intrinsic viscosity and in mechanical properties. The intrinsic viscosity of 1000 69/31 is initially 0.88 dl/g and ends at 0.05 dl/g after 24 weeks. Simultaneously, its mechanical properties are lowered (Table 4). After only three weeks

Table 4
Change in intrinsic viscosity, *E*-modulus, maximum stress and elongation at break during degradation of PEOT/PBT copolymers in PBS. The mechanical properties of swollen samples were measured

Property	Degradation time (weeks)	300 69/31	1000 69/31	1000 61/39
$[\eta]$ (dl/g)	0	0.99	0.88	1.20
	1	0.94	0.93	1.27
	2	0.97	0.80	0.89
	3	–	0.51	0.86
	6	–	0.54	0.83
	12	0.98	0.13	0.51
	24	0.92	0.05	0.18
E (MPa)	0	52	27	41
	1	46	28	38
	2	43	25	36
	3	50	21	38
	6	50	–[a]	36
	12	48	–	33
	24	54	–	–[a]
σ_{max} (MPa)	0	6.9	6.0	9.1
	1	6.6	5.7	8.3
	2	6.9	4.5	7.2
	3	7.1	1.1	6.4
	6	6.8	–[a]	4.9
	12	6.7	–	3.0
	24	7.7	–	–[a]
ε_{break} (%)	0	318	657	712
	1	199	107	509
	2	361	95	185
	3	365	6	147
	6	307	–[a]	42
	12	242	–	10
	24	337	–	–[a]

[a] Tensile testing not possible.

in PBS, σ_{max} falls from 5.7 to 1.1 MPa and ε_{break} from 657 to only 6% (Fig. 8 and Table 4). Moreover, after 24 weeks of degradation, dissolution of 1000 69/31 in chloroform is difficult, due to a change in the copolymer composition as shown by ^{1}H-NMR. It appeared that after 12 weeks in PBS the soft segment content has decreased from 69 to 60 wt% and only 52 wt% remains after 24 weeks. This corresponds to a decrease in PEO content from 62 to 42 wt%.

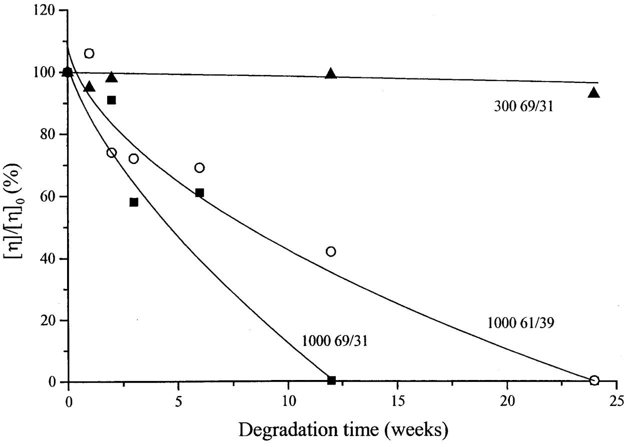


Fig. 7. Relative intrinsic viscosity ($[\eta]/[\eta]_0$) as a function of degradation time in PBS at 37°C for (▲) 300 69/31, (■) 1000 69/31 and (○) 1000 61/39.

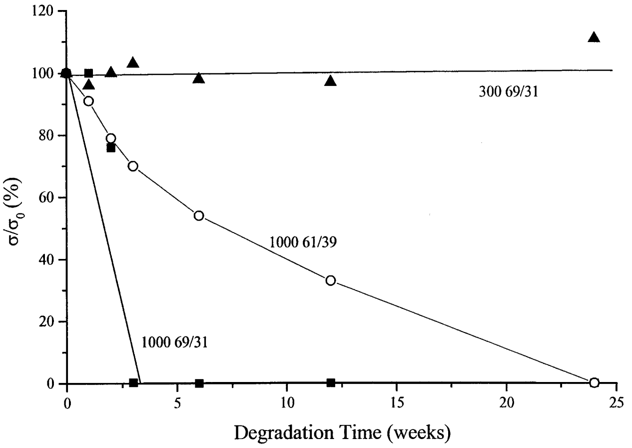


Fig. 8. Relative maximum stress (σ/σ_0) as a function of degradation time in PBS at 37°C for (▲) 300 69/31, (■) 1000 69/31 and (○) 1000 61/39.

Polymer 1000 61/39 follows the same trend as 1000 69/31, but its degradation is slower. Over 24 weeks, the intrinsic viscosity drops from 1.2 to 0.18 dl/g (Table 4). After six weeks, σ_{max} decreases from 9.1 to 4.9 MPa and ε_{break} from 712 to 42%. After 12 weeks, the mechanical properties have strongly deteriorated, but the samples can still be tested, which is not possible after 24 weeks (Fig. 7 and Table 4). After 24 weeks, no change in composition is detected by ^{1}H-NMR yet.

Besides the soft to hard segment ratio, the results show that the used PEG molecular weight is of large influence on the hydrolytic degradation of PEOT/PBT block copolymers. This can be related to the actual PEO content in the copolymer and the better phase separation in 1000 69/31 than in 300 69/31. In 1000 69/31, the hydrophilic PEOT domains are more accessible to water than in 300 69/31, water uptake is higher and the possibility to hydrolyze the ester bonds in these PEOT domains increases. The loss in PEO found for 1000 69/31 during hydrolytic degradation may also indicate that the ester bond connecting the PEO and the terephthalate unit (Fig. 1) is the most sensitive for hydrolysis. At long degradation periods, such preferential degradation of ester bonds can result in the appearance of residues with high PBT contents. In the case of copolymers with a high PBT content (large $\bar{L}_n$) these residues will probably be highly crystalline and even more resistant to hydrolysis.

The maximum tensile strength in the swollen state as a function of the intrinsic viscosity for samples 1000 69/31 degraded for different times in PBS and synthesized samples of 1000 71/29 with different intrinsic viscosities is shown in Fig. 9. Such comparable behavior suggests random chain scission and allows the estimation of molecular weights of PEOT/PBT copolymers during degradation by evaluating their mechanical properties if no compositional change

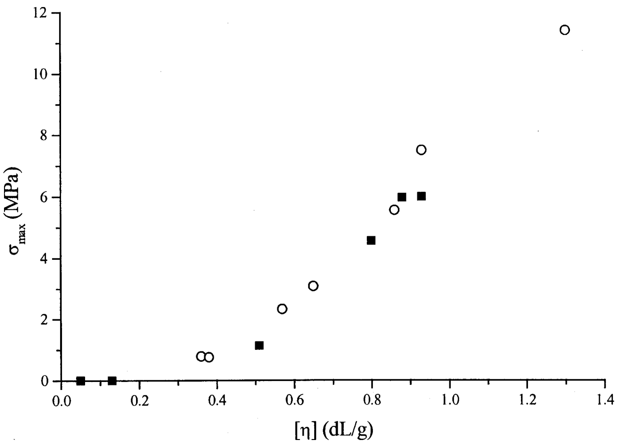


Fig. 9. Maximum stress (σ_{max}) of swollen samples as a function of intrinsic viscosity ($[\eta]$) of 1000 69/31 during degradation in PBS (■) and for 1000 71/29 of different initial molecular weights (○).

has occurred. Again, an intrinsic viscosity of 0.4 dl/g seems to be a limiting value below which the mechanical properties are negligible.

Besides hydrolysis, a second possible degradation pathway is the oxidation of ether bonds in the PEO part. Copolymers 1000 70/30 and 300 70/30 were subjected to oxidative degradation. The changes in composition, intrinsic viscosity and mechanical properties are presented in Table 5. Degradation in $H_2O_2/CoCl_2$ solution has a drastic effect on the polymer properties. Regardless of the initial polymer composition and molecular weight, the tensile strengths and elongations at break significantly decrease after only one day in the medium.

For the PEOT/PBT copolymers with the lowest initial intrinsic viscosity, a notable change in composition is observed. NMR spectroscopy shows that the initial composition of 1000 70/30, 70 wt% soft segment and 62 wt% PEO, has decreased to 59 wt% PEOT soft segment and 50 wt% PEO after one day in the oxidative medium. After two days, this sample is not soluble in chloroform anymore, due to polymer chains with high contents of PBT. High molecular weight 1000 69/31, with $[\eta]$ of 1.3 dl/g, undergoes only a very slight decrease in PEO content, and is still soluble in chloroform after two days.

Polymer 300 70/30, which is relatively stable during hydrolytic degradation, now shows a large decrease in intrinsic viscosity during oxidative degradation. Especially, the lowest molecular weight polymer, of which the PEO content has decreased from 49 to 45 wt% after one day and to 37 wt% after two days, is rapidly degrading. The initial polymer molecular weight seems an important parameter not only in obtaining good initial mechanical properties, but also in maintaining suitable material properties during degradation.

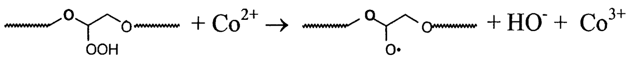
The results illustrate the sensitivity of PEOT/PBT copolymers to oxidation, especially for the copolymers with high PEG molecular weight and high PEOT contents. The loss in PEO can be explained by oxidative reactions of ether bonds in the presence of radicals. The thermo-oxidative [26,40,41], photo-oxidative [42–44] and γ-radiation [45] degradation reactions of PEO and PEO-containing polymers occur via free-radical reactions, leading to scission of the chain.

In H_2O_2 solutions containing $CoCl_2$, hydroxyl radicals (HO) are formed through a Haber–Weiss reaction [29]:

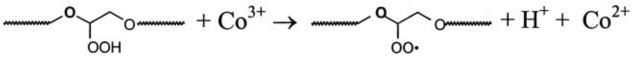
$$Co^{2+} + H_2O_2 \rightarrow Co^{3+} + HO^- + HO^{\cdot} \quad (5)$$

The reaction with PEO involves H-abstraction by $HO^{\cdot}$ from the α-carbon atom leading to the formation of a macrochain radical. The macrochain radical can then react either with another hydroxy radical or with oxygen as shown in Scheme 1 [46,47]. The chain scission subsequently occurs by hydrolysis.

In addition, cobalt ions act as a catalyst in the generation of macrochain radicals through reactions of the hydroperoxide that has previously been formed [46,48]:



(6)



(7)

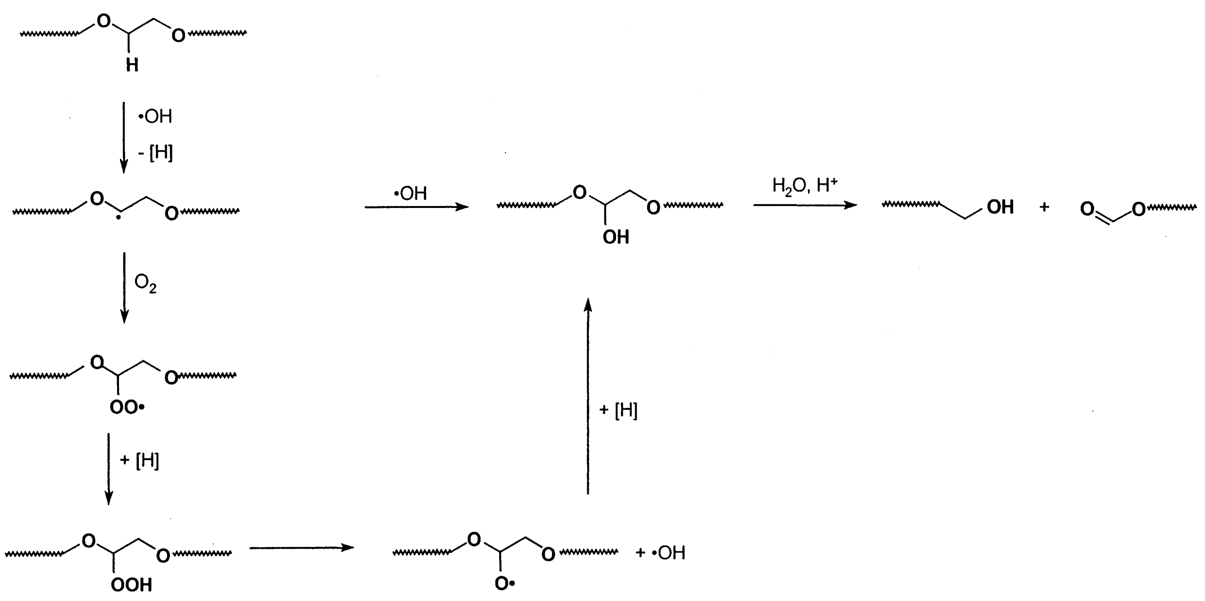
Together, these reactions lead to solubilization of PEO-containing segments and a change in composition of PEOT/PBT copolymers.

Table 5

Composition, intrinsic viscosity ($[\eta]$), maximum stress (σ_{max}) and elongation at break (ε_{break}) of 1000 70/30 and 300 70/30 with different initial molecular weights after one day (t_1) in $H_2O_2/CoCl_2$ 10%. The mechanical properties of swollen samples were measured

Composition		$[\eta]$ (dl/g)		σ_{max} (MPa)		ε_{break} (%)	
t_0	t_1	t_0	t_1	t_0	t_1	t_0	t_1
1000 69/31	1000 69/31	1.30	0.55	7.2	4.0	852	141
1000 70/30	1000 59/41	0.88	–[a]	6.0	2.1	657	13
300 69/31	300 69/31	0.99	0.60	6.9	5.7	318	40
300 70/30	300 64/36	0.70	0.21	5.2	4.0	75	12

[a] Sample insoluble in chloroform.



Scheme 1. Possible reaction pathways in the oxidative chain scission of PEO [46,47].

Oxidation can also play an important role in the stability of the copolymers during storage due to the formation of radicals by the action of light. Therefore, the influence of the amount of antioxidant on 1000 70/30 degradation under different storage conditions has been evaluated. Irganox 1330 and vitamin E were used as antioxidants. In industry, Irganox 1330 is a commonly used antioxidant, whereas vitamin E is a natural antioxidant that may be preferred in biomedical applications. To assess the extent of polymer degradation, the mechanical properties of films with and without antioxidant were evaluated.

When stored for eight months in the dark at room temperature or at −21°C, 1000 70/30 films were stable even without the addition of Irganox 1330 or vitamin E as antioxidant: no loss in mechanical properties or visual changes of the films could be observed.

When exposed to daylight at room temperature during the same time period, 1000 70/30 films containing 0.5 to 2 wt% of Irganox 1330 were stable as well. However, in the absence of antioxidant or when vitamin E is used an antioxidant, significant decreases in mechanical properties are observed during storage under ambient daylight conditions. Fig. 10 shows the decrease in time of the maximum tensile stress of the films containing different amounts of vitamin E. The elongation at break shows similar behavior, while the *E*-modulus is much less affected. As shown previously, this loss in mechanical properties can be related to a decrease in intrinsic viscosity and molecular weight of the polymer. Fig. 10 shows that without vitamin E the mechanical properties start deteriorating after a short induction period of approximately six weeks. The mechanical properties are negligible after 4.5 months. Adding vitamin E in different amounts significantly increases the onset time after which the films start loosing their strength. Furthermore, it seems that the rate at which the 1000 70/30 films loose their mechanical properties is dependent on the vitamin E content. The higher the amount of vitamin E added, the more stable are the films are and the slower is the degradation.

As this decay in properties is only observed during storage in the light, oxidation reactions involving radicals are likely involved. Irganox 1330 and vitamin E are both hindered phenol derivatives (Fig. 11) and are able to scavenge radicals [48,49]. Per gram of antioxidant, Irganox 1330 contains 1.7 times as many phenol groups than vitamin

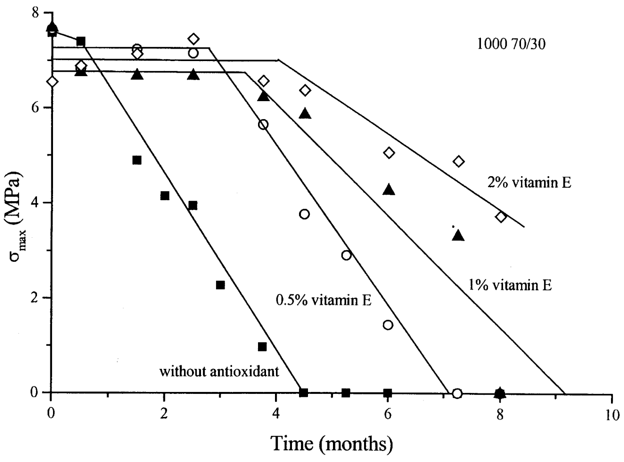


Fig. 10. Maximum stress ($\sigma_{\max}$) during storage under ambient daylight conditions as a function of time for 1000 70/30 films without antioxidant (■) containing 0.5 wt% (○), 1 wt% (▲) and 2 wt% (◇) of vitamin E.

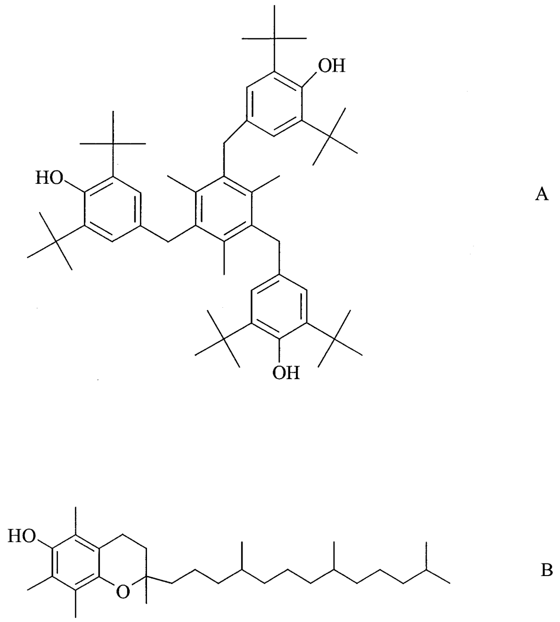


Fig. 11. Chemical structures of Irganox 1330 (A) (M = 774 g/mol) and vitamin E (B) (M = 431 g/mol).

E. Films containing 0.5 wt% vitamin E start loosing their mechanical properties after three months. The observation that after eight months films containing 0.5 wt% Irganox 1330 still show no signs of degradation, indicates that Irganox 1330 is more efficient in preventing oxidation of 1000 70/30. In experiments simulating melt processing, previous work has shown a higher efficiency of vitamin E in comparison with synthetic hindered phenols. This contradictory result can be due to the different experimental settings, as these researchers suggested [50].

In the late stage of the degradation experiments, yellowing of 1000 70/30 films without antioxidant or films containing vitamin E was observed. This yellowing of PBT-containing poly(ether ester)s exposed to UV light can be attributed to the formation of mono- and di-hydroxy substituted aromatic compounds [51]. Films stabilized with Irganox 1330 did not become yellow during these storage experiments.

4. Conclusions

Segmented PEOT/PBT block copolymers are phase-separated. The extent of phase separation varies with copolymer composition. Phase separation is more pronounced for polymers with high hard segment contents and polymers containing high molecular weight PEG.

The physical properties of these copolymers depend strongly on the molecular weight, the soft to hard segment ratio and the starting PEG molecular weight. By changing the copolymer composition, the mechanical properties and the swelling characteristics of PEOT/PBT copolymers can be tuned and adjusted to the requirements for medical application.

PEOT/PBT copolymers are degraded in vitro by hydrolysis and oxidation. In both situations, a decrease in intrinsic viscosity, PEO content and mechanical properties has been observed. The degradation is more severe in the case of polymers with a high PEOT content prepared from a high molecular weight PEG.

Oxidation of PEOT/PBT also takes place during exposure of the polymers to light at ambient conditions. Under these conditions, Irganox 1330 is a more efficient antioxidant for PEOT/PBT polymers than vitamin E.

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