Synthesis and Characterization of Poly(ethylene glycol) Methyl Ether Endcapped Poly(ethylene terephthalate)

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Summary: Linear and branched poly(ethylene terephthalate) (PET) copolymers with poly(ethylene glycol) (PEG) methyl ether (700 or 2000 g/mol) end groups were synthesized using conventional melt polymerization. DSC analysis demonstrated that low levels of PEG end groups accelerated PET crystallization. The incorporated PEG end groups also decreased the crystallization temperature of PET dramatically, and copolymers with a high content of PEG (>17.6 wt%) were able to crystallize at room temperature. Rheological analysis demonstrated that the presence of PEG end groups effectively decreased the melt viscosities and facilitated melt processing. XPS and ATR-FTIR revealed that the PEG end groups tended to aggregate on the surface, and the surface of compression molded films containing 34.0 wt% PEG were PEG rich (85 wt% PEG). PEG end-capped PET (34.0 wt% PEG) and PET films were immersed into a fibrinogen solution (0.7 mg/mL BSA) for 72 h to investigate the propensity for protein adhesion. XPS demonstrated that the concentration of nitrogen (1.05 %) on the surface of PEG endcapped PET film was statistically lower than PET (7.67%). SEM analysis was consistent with XPS results, and revealed the presence of adsorbed protein on the surface of PET films.

Keywords: biocompatibility, crystallization rate, melt polymerization, poly(ethylene glycol) (PEG), poly(ethylene terephthalate) (PET)

Introduction

Poly(ethylene terephthalate) (PET) is an important polyester composition for a myriad of applications such as textile fibers, packaging materials, films, and container products.[1] However, PET has not emerged as a preferred engineering material or adhesive in many applications due to a low crystallization rate and poor compatibility with other substrates,

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fillers and polymers.[2-3] To improve the performance of PET, several methodologies were developed.[2-8] For example, inorganic nucleating agents such as talc were used to accelerate the crystallization rate.[2] However, heterogeneous particles often act as stress concentrators that decrease impact strength, and glass fibers are required to reinforce the nucleated PET.[2] Thus, the development of novel compositions that exhibit a high crystallization rate will promote the utility of PET as an engineering material.

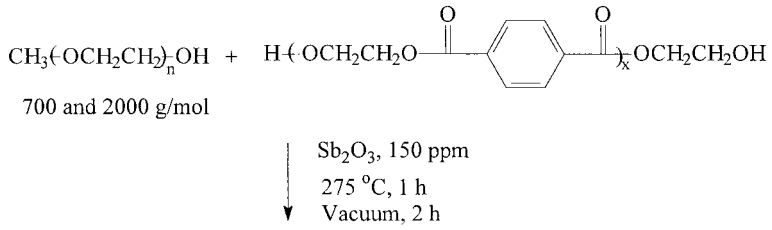
Recently, Xue and coworkers demonstrated that the crystallization rate of PET was improved via precipitating PET from a PEG solution at a low temperature.[9-11] In addition, PET segmented block copolymers prepared from difunctional aliphatic polyethers, such as PEG and PTMO, have been extensively studied.[12] However, the random incorporation of aliphatic polyether segments decreased the chain regularity and resulted in soft multiphase elastomers with a low level of crystallinity.[12-15] Earlier research has demonstrated that the incorporation of functional groups as end groups did not disrupt the regularity of the polymer backbone.[3] In order to eliminate the disruptive effect of random incorporation of PEG, mono-functional PEG was used to synthesize semicrystalline PET with PEG end groups. In addition, PET has been widely used in biomedical applications such as non-resorbable structures, tendons, ligaments, and facial implants.[16] PEG has also been used as an effective surface modifier to prepare biomaterials with low levels of protein adsorption and cell adhesion.[16-19] The incorporation of PEG end groups provides a novel methodology for the surface modification of semicrystalline PET.

In this manuscript, the synthesis of PEG end-capped linear and branched PET copolymers is reported. Low levels of incorporated PEG effectively accelerated the crystallization rate. Moreover, a high level of incorporated PEG resulted in a PEG rich layer on the film surface. This hydrophilic surface improved the biocompatibility and decreased protein adsorption on film surfaces.

Experimental

Synthesis of linear PEG endcapped PETs. Linear PEG endcapped PET copolymers were prepared via the melt polymerization of a PET oligomer with various levels of PEG endcapping reagents. Antimony oxide (150 ppm) was added to facilitate polycondensation.

The reactor consisted of a 250 mL round-bottomed flask equipped with an overhead mechanical stirrer, nitrogen inlet, and condenser. The reactor containing the monomers and catalysts was degassed using vacuum and nitrogen three times, and subsequently heated to 275 °C. The reaction was maintained at 275 °C for 1 h, and vacuum was gradually applied to 0.5 mm Hg and polycondensation continued for 2 h at 275 °C. The copolymers were termed PET-x-y, for example PET-700-1.5, wherein x denotes the molecular weight of PEG end-capper, and y denotes the molar percentage of endcapping reagent versus PET repeating units.

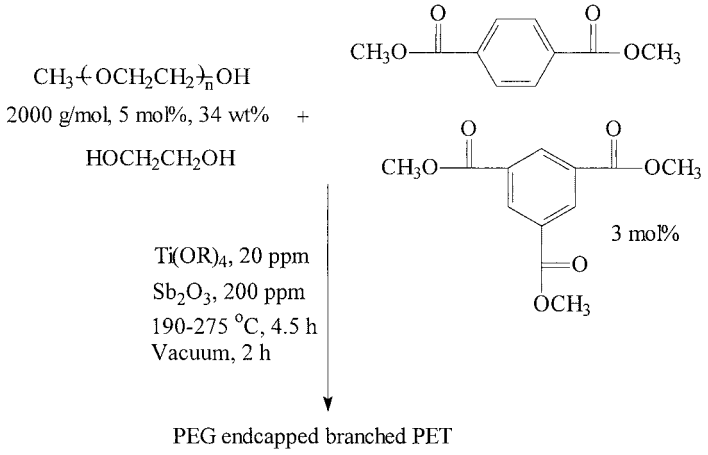


Scheme 1. Synthesis of linear PEG endcapped PETs via melt polycondensation.

Synthesis of PEG endcapped and branched PET. PEG end-capped branched PET was prepared via the melt condensation of dimethylterephthalate (DMT), ethylene glycol (EG) and 3 mol% branching agent (trimethyl 1, 3, 5-benzenetricarboxylate) (Scheme 2). Both titanium tetra(isopropoxide) (20 ppm) and antimony oxide (150 ppm) were added to facilitate ester exchange and subsequent polycondensation. The reactor consisted of a 250 mL round-bottomed flask equipped with an overhead mechanical stirrer, nitrogen inlet, and condenser. The reaction was maintained at 190 °C for 2 h, and the temperature was increased to 275 °C over 2 h. The reaction was allowed to proceed for 30 min at 275 °C. Vacuum was gradually applied to 0.5 mm Hg and polycondensation continued for 2 h at 275 °C. The product is termed BPET-2000-5, where B signifies a branched PET composition.

Protein Adhesion. Fibrinogen (50.0 mg) was dissolved in 100 mL PBS solution (pH = 7.4), and was filtered using a syringe filter. The relative concentration of protein was measured using a "Lowry protein assay". BSA standard tubes containing 0, 10, 20, 40, 70, 100 μg BSA

(Sigma) in a total volume of 100 μL were prepared. Standard agent was prepared as follows: 0.20 mL of 4.00% K Na tartrate and 0.20 ml of 1.28% $CuSO_4$ were mixed together, and then 10.0 mL of 3.00% Na_2CO_3 dissolved in 0.10 N NaOH was added. A standard agent (0.10 mL) and 0.10 mL phenol agent (Sigma) were added into each BSA tube. The absorbance of solutions at 750 nm was measured to generate a standard curve. The concentration of fibrinogen was measured using similar procedures, which was approximately 0.72 mg/mL BSA. PET and BPET-2000-5 films were initially immersed in a PBS solution for 2 h at 37 °C, and then a fibrinogen solution for different times (24, 48 and 72 h) at 37 °C. The films were rinsed using PBS solution for 20 seconds to remove weakly adsorbed fibrinogen, and dried at room temperature for 72 h for further analysis.



Scheme 2. Synthesis of PEG endcapped and branched PET, BPET-2000-5

Characterization. The inherent viscosities of the samples were measured at 25 °C in a capillary viscometer using a 0.5 g/dL solution in a 60/40 w/w mixture of phenol and tetrachloroethane. ^1H NMR spectra were recorded on a Varian 400 MHz spectrometer. Trifluoroactetic acid–d was suitable as a NMR solvent. Thermal transitions were determined on a Perkin-Elmer DSC Pyris 1 under N_2 purge. Thermogravimetric analysis (TGA) was performed on a Perkin-Elmer TGA 7 under a nitrogen atmosphere at a heating rate of 10 °C/min. Contact angle measurements were conducted using the static drop method with a

Rame-Hart NRL contact angle goniometer. Angular dependent X-ray photoelectronic spectroscopy (XPS) was performed on a Perkin-Elmer physical electronic model 5400 with a hemisphere analyzer and a position sensitive detector. The rheological analyses were performed using a TA Instruments AR 1000 melt rheometer. SEM was performed on a (JEOL-JSM 5800), and samples were coated with Au prior to the analysis.

Results and Discussion

Synthesis. Our previous research demonstrated that residual catalysts exerted a pronounced effect on crystallization rate.[3] To minimize the effect of residual catalysts, the linear PEG endcapped PETs were synthesized using PET oligomers in the absence of transesterification catalysts (Scheme 1). In addition, a low level of antimony oxide (150 ppm) was used to facilitate polycondensation. Elemental analysis demonstrated that the actual level of residual catalyst agreed well with the charged amounts (Ti: ±1.0 ppm; Sb: ± 10 ppm).

A major limitation of endcapping methodologies is decreased molecular weight with an increase in the level of endcapping reagent; however, the simultaneous incorporation of a low level of branching agent will increase the number of end groups and permit higher weight average molecular weights. Thus, trimethyl 1, 3, 5-benzenetricarboxylate was used as a branching agent for the preparation of high molecular weigh PET with a high concentration of PEG end groups. This telechelic polyester was synthesized using a one step polymerization of DMT, excess EG, PEG endcapper (5 mol%), and branching reagent (3 mol%) (Scheme 2).

Table 1. ^{1}H NMR analysis and inherent viscosity of PEG end-capped PETs.

Sample	Charged PEG (mol%)	Charged PEG (wt%)	Residual PEG (wt%)[b]	$\eta_{inherent}$ (dl/g)[a]
PET	0	0	0	0.47
PET-700-1.5	1.5	5.2	5.0	0.42
PET-2000-1	1.0	9.4	8.9	0.47
PET-2000-1.5	1.5	13.5	12.7	0.46
PET-2000-2	2.0	17.6	16.5	0.44
BPET-2000-5	5.0	34.0	31.2	0.81

[a]: Determined at 25 °C using a capillary viscometer in a 0.5 g/dL solution of 60/40 w/w mixture of phenol and tetrachloroethane. [b]: Determined using ^{1}H NMR spectroscopy.

The composition of poly(ethylene terephthalates) with PEG endcappers (700 and 2000 g/mol) were verified using ^{1}H NMR spectroscopy. To ensure the absence of unreacted PEG, the films were immersed in water for 2 h prior to the NMR experiment. The results of the ^{1}H NMR analysis (Table 1) demonstrated that the PEG endcapper was quantitatively incorporated into PET as end groups. Linear copolymers had solution viscosities ranging from 0.47 to 0.42 dL/g. As expected, the presence of PEG end groups slightly decreased the molecular weight of the polyester products, i.e. the molecular weight decreased as level of end capping reagent increased. If a perfect telechelic copolymer, PEG-PET-PEG, was achieved, the molecular weight can be estimated using the equation reported in a previous report.[3] In this manuscript, only a low level (< 3 mol%) of PEG endcapper was used, and the estimated number average molecular weight for a perfect PEG-PET-PEG copolymers was 22000 g/mol (0.80 dL/g). Without further solid state polymerization, high molecular weight products were not obtained. Thus, the products were not perfect triblock structures, but a mixture of copolymers with one or two PEG end groups. Furthermore, it was presumed that the perfect telechelic structure would not offer advantageous properties, and perfect triblock polymers with high molecular weights are not described in this manuscript.

Thermal transitions and rheological analysis. Thermogravimetric analysis (TGA) demonstrated that the presence of PEG end groups did not exert a pronounced effect on the thermal stability of the final products. The telechelic polyesters exhibited a similar weight loss profile versus temperature as PET homopolymers, and the onset of degradation was approximately 360 °C. In order to study the crystallization behavior of PEG endcapped PET, amorphous films were compression molded. The polymer film was quenched using ice water, and transparent amorphous films were obtained immediately after quenching. However, BPET-2000-5 film developed haze within several minutes after quenching. PET-2000-2 formed a soft film immediately upon quenching. This film became opaque and the modulus gradually increased in two weeks presumably due to slow crystallization at room temperature. DSC analysis of the opaque films (two weeks after quenching) demonstrated that only a melt transition associated with PET (240 °C) was observed, which indicated that these two

copolymers were able to crystallize at room temperature, and the crystallization rate increased with an increase in the level of PEG.

The thermal transitions of the transparent films were examined using DSC at a heating rate of 10 °C/min (Table 2). DSC results demonstrated that PEG endcapped PETs exhibited that the onset of crystallization was very close to the glass transition. As a result, it was difficult to measure the glass transition temperature accurately; however, the onset of the glass transition decreased with an increase in the PEG level (Table 1). Moreover, crystallization also occurred at lower temperatures compared to PET homopolymers at equivalent molecular weight, and both the onset of crystallization and the peak maximum of crystallization decreased with an increase in the PEG level. The heats of fusion for the copolymers were used to characterize the approximate levels of crystallinity (Table 2). PET copolymers and homo-PET had heats of fusion at 45 - 48 J/g (~35 – 40 % crystallinity based on 120.0 J/g for 100 % crystallinity)[1] (Table 2), and an increase in the level of crystallinity in blends of PET/PEG was not observed.[9-10] Isothermal crystallization of the transparent films was also performed at 85 °C. PET was obviously not able to crystallize at this temperature because it was just slightly higher than its glass transition temperature (78 °C). However, the PEG endcapped PET copolymers were able to crystallize at this temperature since the presence of PEG end groups improved polyester diffusion. The onset time (t_{onset}) and half time of crystallization ($t_{1/2}$) decreased with an increase in the PEG level, and isothermal crystallization data were analyzed using the Avrami equation,

$$\ln[-\ln(1-x_t)] = \ln K + n\ln t \qquad \text{(Eqn. 1)}$$

where x_t is the weight fraction of materials crystallized at time t, K is the kinetic growth constant, and n is the Avrami exponent. The values of n were determined to be in the range 2.0 -2.5 (the linear regression correlation coefficients were $r^2 = 0.98$), which were indicative of two dimensional crystal growth.

DSC analysis demonstrated that the incorporated PEG end groups effectively increased the PET crystallization rate. Melt rheological analysis was also performed to investigate PEG endgroup effects on viscosity. The results of the temperature sweep demonstrated that the copolymers exhibited lower melt viscosities than PET homopolymers with nearly equivalent

inherent viscosities, and the difference in melt viscosity increased with an increase in the PEG content (Figure 1).

Table 2. Thermal transitions and water contact angle of quenched films.

Sample	T_g[a] (°C)	T_{hc} (°C)	ΔH_{hc} (J/g)	T_m (°C)	ΔH_m (J/g)	ΔH_m[b] (J/g)*	Contact Angle (°)
PET	62	138.5	16.2	237.6	45.2	45.2	82
PET-700-1.5	50	111.1	28.11	240.0	44.1	46.2	73
PET-2000-1	45	106.4	27.1	240.1	43.0	47.5	46
PET-2000-1.5	35	100.5	25.7	239.7	42.2	48.8	35
PET-2000-2	20	90.6	18.4	236.5	38.3	46.4	23
BPET-2000-5	-10	-----	-----	239.4	28.1	42.6	----

[a]: T_g (onset); [b]: after weight fraction calibration

Table 3. Isothermal analysis of quenched films.

Sample	t_{onset} (minute)	$t_{1/2}$ (minute)	ΔH (J/g)	ΔH^a (J/g)	n
PET-700-1.5	1.61	6.78	25.1	26.5	2.50
PET-2000-1	0.68	3.21	21.9	24.2	2.33
PET-2000-1.5	0.38	1.10	19.4	22.4	2.22
PET-2000-2	0.21	0.42	19.0	23.1	2.29

[a]: after weight fraction calibration

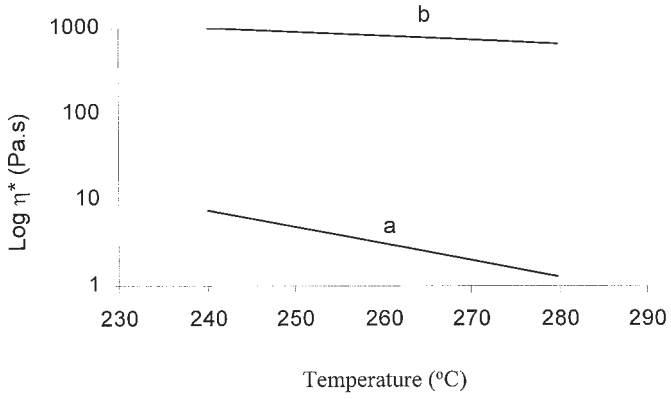
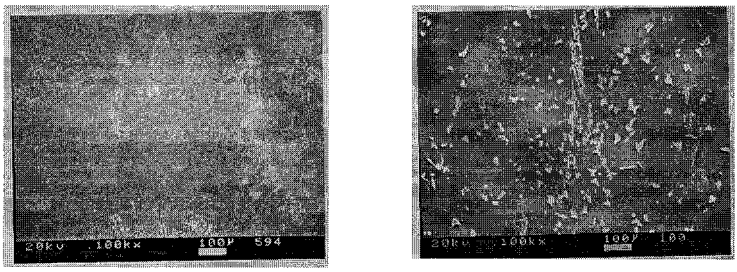


Fig. 1. Rheological analysis of BPET-2000-5 (a) and PET (b) with identical inherent solution viscosities (0.81 dL/g).

Surface analysis and biocompatibility. Water contact angles of PEG endcapped PET copolymers films are listed in Table 2, which showed a gradual change from a hydrophobic surface to a hydrophilic surface with an increase in PEG concentration. XPS revealed a clean PEG rich (85 wt%) layer on the surface of BPET-2000-5 (34 wt% charged PEG). To investigate potential biocompatibility, the PET and BPET-2000-5 films were immersed into a fibrinogen solution. The control PET and BPET-2000-5 films exhibited no signal related to the presence of nitrogen prior to immersion. However, the N_{1s} peak appeared in the XPS spectra of immersed films due to the presence of adsorbed protein on the surface (Table 4), which increased with an increase in time. Furthermore, the concentration of nitrogen on the surface of BPET-2000-5 films was much lower than PET homopolymer films with an identical time of immersion (Table 4). SEM micrographs revealed adsorbed protein on the surface of PET films immersed into fibrinogen solution for 72 h (Figure 2). However, adsorbed protein was not observed on the surface of BPET-2000-5 film under identical immersion conditions. These results confirmed that a PEG layer on the PET surface was able to improve the biocompatibility and decrease protein adsorption.

Table 4. Concentration of nitrogen (mol%) on the surface of films dipped into fibrinogen solutions for different times.

Sample	0 h	24 h	48 h	72 h
PET	0	5.48 %	6.89 %	7.37 %
BPET-2000-5	0	0.56 %	1.05 %	1.31 %



a b

Fig. 2. SEM analysis: (a): BPET-2000-5 immersed into a fibrinogen solution for 72 h; (b): PET immersed into a fibrinogen solution for 72 h.

Conclusions

PEG endcapped linear PETs were synthesized using PEG (700 and 2000 g/mol) and PET oligomer. High molecular weight PEG endcapped PET with a high level of PEG was prepared using a branching agent. DSC analysis demonstrated that low levels of incorporated PEG accelerated the crystallization of PET, and decreased the crystallization temperature dramatically. A PEG rich layer (85 wt%) on the surface of PEG endcapped branched PET (34 wt%) was revealed using XPS and ATR-FTIR. This hydrophilic surface improved the biocompatibility and decreased protein adsorption. XPS analysis indicated that the PEG endgroups effectively retarded the adsorption of fibrinogen on compressed films compared to conventional PET homopolymers. SEM analysis agreed well with the XPS results, and revealed adsorbed protein on the surface of PET films without PEG end groups, and significantly less protein adhesion for PEG modified PET.

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