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Synthesis and Characterization of New Unsaturated Degradable Poly(ether ester amide)s Containing Ethylene Oxide Moieties

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A series of novel biodegradable unsaturated poly(ether ester amide)s (PEEAs) have been successfully prepared through interfacial polycondensation of 1,6-hexanediamine and unsaturated diacylchlorides containing ethylene oxide moieties linked to maleic anhydride by ester. The structures of PEEAs are verified by FT-IR and NMR spectra. The DSC and TGA measurements demonstrate the obtained polymers are amorphous and stable up to 300°C under nitrogen. Synthesized PEEAs show good hydrophilicity and improved solubility. The rate of hydrolytic degradation performed in the phosphate buffer solution (pH = 7.2) at 37°C increases with increasing the number of ether linkages per repeat unit in polymers. The degradation results indicate that PEEAs are hydrolyzable in a rapid and steady way.

Keywords: degradable, interfacial polycondensation, unsaturated, synthesis; thermal

1 Introduction

Poly(ester amide)s (PEAs) have been widely studied for many years because they combine the favorable properties of polyesters and polyamides; that is, they possess not only good biodegradability, but also good mechanical and processing properties, such as thermal stability, tensile strength, and modulus. In fact, various poly(ester amide)s have been prepared by polycondensation of ester-containing diamine with dicarboxylic acids and their derivatives or by ring-opening polymerization of depsipeptide, and their degradability has been evaluated (1–11). The presence of hydrolytic readily cleavable ester bonds in the backbone and the lowering of the crystallinity thereby make PEAs promising materials for many different fields. The progress of PEAs in the field of biodegradable polymers was also reviewed recently (12, 13). Moreover, products of

BAK 1095 which correspond to a random poly(ester amide) derived from 1,4-butaediol, adipic acid and caprolactame by Bayer has recently been commercialized.

Most PEAs reported in the literature have saturated backbone structures and few active sites for further chemical modification; this means that they need to be modified before other functional groups can be grafted onto them or copolymerized with them. Therefore, PEAs with built-in functional groups that are ready to react with other chemicals will be better candidates for versatile applications. Chu et al. synthesized amino acid derived saturated PEAs with the availability of a pendant free –COOH group for the attachment of biological active agents like nitroxyl radicals (14, 15). Amino acid based unsaturated PEAs having inherent C=C double bonds along polymer backbone for photocrosslinking poly(ethylene glycol) diacrylate were also investigated (16, 17). These amino acid based PEAs have the advantages of biodegradability under certain enzymatically catalyzed conditions. On the other hand, non-amino acids derived functional poly(ester amide)s based on optically active aminoalcohols and maleic anhydride were reported. The radical additions of ethanethiol with the corresponding polymer proceeded smoothly with incorporation of thiols in the range of 65–98% (18). However, those non-amino acid based PEAs would degrade via the hydrolysis of their

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ester linkages while their amide blocks remained stable, and the response to water degradation under mild conditions was still too weak for many potential applications.

Insertion of a hydrophilic segment, usually poly(ethylene glycol) (PEG) in the main chain of a PEA is known to be an efficient means to increase the hydrodegradability of the polymer (19–20). The reason may be that the ether linkages can form hydrogen bonds with water, which *a priori* should improve their water uptake, thus enhancing hydrodegradability. On this basis, the aim of this work was to combine C=C double bonds as functional groups and short ethylene oxide chains as flexible spacer into non-amino acid based PEAs backbone. Thus, poly(ether ester amide)s (PEEAs) would have ether bonds incorporated in addition to the ester and amide linkages common to other PEAs. Tailoring of the properties of such polymers can be achieved by a variation of the length of the hydrophilic blocks, which results in polymer systems with a wide range of properties.

In this article, PEEAs were synthesized by interfacial polycondensation of unsaturated diacylchloride containing ethylene oxide moieties and 1,6-hexanediamine. To the best of our knowledge, this type of PEEAs has not been reported. The effects of the number of oxygen linkages on the thermal properties, solubility, water sorption and degradability of the PEEAs were explored. Also, with the availability of the inherent and reactive C=C double bonds in the backbone, it is anticipated that synthesized PEEAs can be functionalized or modified for further applications.

2 Experimental

2.1 Materials

1,6-hexanediamine was purchased from Guangzhou Chem. Co. (China) and purified by vacuum sublimation. Maleic anhydride (Guangzhou Chem. Co. China) was recrystallized from chloroform. Ethylene glycol, diethylene glycol, triethylene glycol and tetraethylene glycol were purchased from Aldrich. All diols were dried at 80°C for 24 h under vacuum before use. Thionyl chloride was distilled under vacuum before use. Chloroform (Guangzhou Chem. Co. China) was refluxed for 24 h at 65°C from calcium hydride, and then distilled before use. Pyridine (Guangzhou Chem. Co. China) was refluxed for 24 h at 120°C from KOH, and then distilled before use. All other reagents were commercially available from Guangzhou Chem. Co. (China) and used as received.

2.2 Syntheses

2.2.1. Preparation of dicarboxylic acid monomers containing ethylene oxide units (Ia)

Maleic anhydride (0.06 mol), ethylene glycol (0.025 mol) and anhydrous Na₂CO₃ in 200 mL acetone were placed in a flask equipped with a Dean-Stark apparatus, a CaCl₂ dry-

ing tube, and a magnetic stirrer. Then the reaction mixture was heated to reflux for 2 h. The solution was cooled and concentrated to dryness under vacuum. The crude product was recrystallized from acetone three times. 5.81 g of white crystalline **Ia** was obtained (yield: 90.0%).

Ia: IR cm⁻¹ (KBr): 3416 [-OH], 1707 [-C(O)-], 1266 (-O-), 1174(-CH₂-O-CH₂-), 3054, 1615, 859(-CH=CH-). ¹H-NMR (D₂O, 300M Hz, ppm): δ = 6.25 (4H, -CH=), 4.67 (4H, -C(O)OCH₂).

2.2.2. Preparation of dicarboxylic acid monomers containing ethylene oxide units (Ib–Id)

Diethylene glycol (0.025 mol) was dissolved in dry chloroform (100 mL). Maleic anhydride (0.1 mol) and dry pyridine (0.05 mol) were added, and the reaction mixture was kept at 60°C for 12 h. The solution was cooled and concentrated to dryness under vacuum. The crude product was extracted with ethyl ether three times, dried with anhydrous Na₂SO₄ and then the solvents were removed under vacuum. 8.84 g of brown oil **Ib** was obtained (yield: 88.0%). Monomers of **Ic** (9.47 g, yield: 85%) and **Id** (10.04 g, yield: 82%) were synthesized with the same procedures except diethylene glycol was replaced with triethylene glycol and tetraethylene glycol, respectively.

Ib: IR cm⁻¹ (KBr): 3426 [-OH], 1720 [-C(O)-], 1262 (-O-), 1172(-CH₂-O-CH₂-), 3069, 1637, 968 (-CH=CH-). ¹H-NMR (D₂O, 300M Hz, ppm): δ = 6.21 (4H, -CH=), 4.57 (4H, -C(O)OCH₂-), 3.62 (4H, -C(O)OCH₂CH₂-).

Ic: IR cm⁻¹ (KBr): 3428 [-OH], 1717 [-C(O)-], 1265 [-O-], 1169 [-CH₂-O-CH₂-], 3072, 1641, 971 [-CH=CH-]. ¹H NMR (D₂O, 300M Hz, ppm): δ = 6.18 (4H, -CH=), 4.47 (4H, -C(O)OCH₂-), 3.58 (4H, -C(O)OCH₂CH₂-), 3.48 (4H, -C(O)O(CH₂)₂-O-CH₂-).

Id: IR cm⁻¹ (KBr): 3429 [-OH], 1723 [-C(O)-], 1261 (-O-), 1175(-CH₂-O-CH₂-), 3065, 1635, 967 (-CH=CH-). ¹H NMR (D₂O, 300M Hz, ppm): δ = 6.24 (4H, -CH=), 4.61 (4H, -C(O)OCH₂-), 3.56 (4H, -C(O)OCH₂CH₂-), 3.38 (8H, -C(O)O(CH₂)₂-O-CH₂-CH₂-).

2.2.3. Preparation of diacylchloride (IIa–IId)

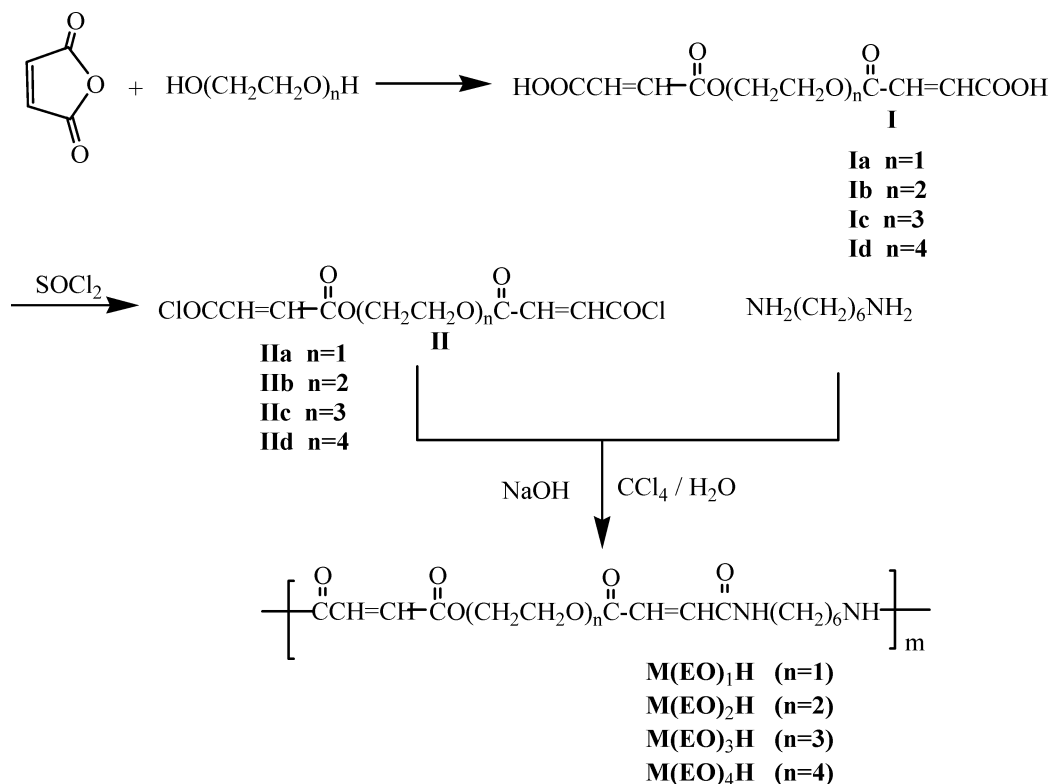
Diacylchlorides were prepared by refluxing dicarboxylic acid (**Ia–Id** 0.25 mol) in thionyl chloride (1.60 mol) for 6 h, respectively. The excess thionyl chloride was removed, and diacylchlorides (**IIa–IId**) were distilled under vacuum, respectively.

IIa: IR cm⁻¹ (KBr): 1745 [-C(O)-], 3071, 1638, 969 (-CH=CH-).

IIb: IR cm⁻¹ (KBr): 1741 [-C(O)-], 3074, 1636, 967 (-CH=CH-).

IIc: IR cm⁻¹ (KBr): 1743 [-C(O)-], 3069, 1637, 969 (-CH=CH-).

IIId: IR cm⁻¹ (KBr): 1739 [-C(O)-], 3069, 1639, 971 (-CH=CH-).



Sch. 1. Synthesis of unsaturated PEEAs containing ethylene oxide moieties.

2.2.4. Polymerization

PEEAs were prepared by interfacial polycondensation of diacylchlorides (**II**) with 1,6-hexanediamine. Their name designations are shown in Scheme 1.

A typical procedure for preparing PEEAs is described as follows (shown in Scheme 1). Diacylchloride (15 mmol) was dissolved in 150 mL of carbon tetrachloride. Under vigorous stirring, the solution was rapidly poured into a 150 mL of blender containing an aqueous solution of 1,6-hexanediamine, 1.74 g (15 mmol), and sodium hydroxide, 1.2 g (30 mmol). The precipitated polymer was washed with water (300 mL), carbon tetrachloride (300 mL), acetone (300 mL) and diethyl ether (300 mL), respectively, and finally dried at 80°C in vacuum overnight.

2.3 Analytical Techniques

For Fourier transform infrared (FTIR) characterization, samples were ground into powder and mixed with KBr at a sample/KBr ratio of 1:10 w/w. FTIR spectra were then obtained from a Perkin-Elmer 1600 spectrometer. A Varian Unity 300 MHz spectrometer was used for ¹H-NMR and ¹³C-NMR investigations at room temperature using tetramethylsilane (TMS) as internal standard.

Thermal properties of synthesized polymers were characterized by a Perkin-Elmer DSC-PYRIS1 (USA). The measurement was carried out from 0 to 300°C at a scanning

rate of 10°C/min and nitrogen gas flow rate of 25 mL/min. TA Universal Analysis software was used for thermal data analysis, such as the determination of the glass transition temperature. Thermogravimetric analysis (TGA) was carried out with Perkin-Elmer TGA-6 under nitrogen atmosphere at a heating rate of 10°C/min. Wide-angle X-ray scattering patterns were obtained from films on a Philips X-ray PW 1130 diffractometer with Cu K α radiation.

The PEEA films were cast from a 10%(w/v) chloroform solution on smooth Teflon Petri dishes, and the solvent was allowed to evaporate completely at room temperature. The films were further dried *in vacuo* at room temperature overnight and finally punched into small disc shaped pieces for various tests.

The inherent viscosity (η_{inh}) of the polymers synthesized was determined with a Cannon-Ubbelohde microviscometer at a temperature of 25°C; dichloroacetic acid was used as a solvent. The surface hydrophilicity of the PEEA films was determined using a contact angle meter (Kr \acute{e} ss DSA-10). Distilled water was used as the spreading liquid, the contact angles of five randomly chosen surface areas of each PEEA film were measured. Water sorption measurements were determined gravimetrically at room temperature. Dried powdered polymer samples (0.3–0.4 g) were placed in a closed desiccator containing a saturated aqueous solution of NaNO₂, which provided a relative humidity of 65%. The samples were frequently weighted during 15 h and then were allowed to humidify for 5 more days until

they had equilibrated with their surroundings, as denoted by no weight change. Water sorption (*S*) was estimated from the weight change of samples based on the following equation:

$$S(\%) = \left[\frac{W_w - W_d}{W_d} \right] \times 100 \quad (1)$$

Where W_d is the original weight of the dried PEEAs, and W_w is the weight of wet PEEAs until no weight change after equilibration. The data of water sorption average of the three specimens was recorded.

A degradation test of PEEAs was carried out in a small vial containing a dry PEEA disc film (diameter 12.5 mm) and 10 mL of pure PBS buffer (pH 7.2, 0.1 M). The vial was then incubated at 37°C with constant reciprocal shaking (100 rpm). At predetermined intervals, the retrieved samples were thoroughly rinsed with water, dried to constant weight in vacuum at 80°C for 24 h, and stored over CaCl_2 before analysis. The degree of biodegradation (*W*) was estimated from the weight loss of the PEEA film sample based on the following equation:

$$W(\%) = \left[\frac{W_o - W_t}{W_o} \right] \times 100 \quad (2)$$

Where W_o is the original weight of the dry PEEA film sample before immersion, and W_t is the dry PEEA film sample weight after incubation for a predetermined time. The weight loss average of the three specimens was recorded.

The solubility of poly(ester amide)s in common organic solvents was estimated according to the method of Braun (21).

3 Results and Discussion

3.1 Synthesis of PEEAs

The route of synthesis leading to PEEAs is depicted in Scheme 1. The general procedure includes three steps: the preparation of unsaturated dicarboxylic acids containing ethylene oxide units (**Ia–Id**), the preparation of corresponding diacylchlorides (**IIa–IId**), and the polycondensation of diacylchlorides with 1,6-hexanediamine.

Excess maleic anhydride reacts with ethylene glycol or oligoethylene glycol (OEG) so that both the ends of each resulting compounds are carboxyl groups. There are four different types of unsaturated dicarboxylic acids containing one and four ether linkage (**Ia–Id**) used as precursors to provide the carboxylic ester groups of PEEAs in this work. The structures of dicarboxylic acids (**Ia–Id**) were all confirmed by FTIR and $^1\text{H-NMR}$ data, as detailed in the Experimental section. The FTIR spectra were shown in Figure 1, and their main absorption bands such as ester groups (1707 to 1723 cm^{-1}) and unsaturated H-C= bonds (~ 3060 , ~ 1615 , ~ 970 cm^{-1}) were assigned. The strong absorption bands around 1170 cm^{-1} were attributed to the

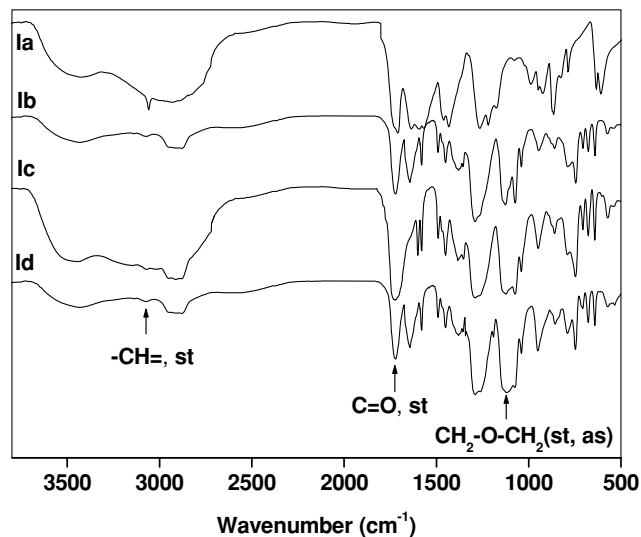


Fig. 1. FTIR spectra of dicarboxylic acids monomer (**Ia–Id**) (st: stretching vibration and as: asymmetry vibration).

stretching vibration of the ether group. The broad absorption around 3420 cm^{-1} could be attributed to the stretching vibration of carboxylic hydroxyl groups. The $^1\text{H NMR}$ data of **Ia–Id** also showed characteristic signals of $-\text{CH}_2-\text{O}-\text{CH}_2-$ (~ 3.50 ppm) and $-\text{C}(\text{O})\text{OCH}_2-$ (~ 4.60 ppm), indicating ethylene oxide units have incorporated into monomer. All monomers were obtained with good yields.

In order to improve the reactivity of dicarboxylic acid, the dicarboxylic acid monomer is reacted with excess thionyl chloride to convert all the carboxyl ends into acylchloride ends, which is confirmed by FT-IR data, as detailed in the Experimental section. The broad band at about 3420 cm^{-1} assigned to O-H stretching band disappears, showing all the carboxyl ends have been converted into acylchloride ends. Moreover, the carbonyl stretching band is observed at about 1745 cm^{-1} due to the presence of electron-withdrawing acylchloride groups. In this study, PEEAs were produced through interfacial polycondensation of 1,6-hexanediamine in the aqueous phase containing NaOH and unsaturated diacylchlorides in the CCl_4 . Table 1 summarizes the results of the polycondensation and the properties of the obtained PEEAs. All four PEEAs were obtained in moderate yields (63 to $\sim 69\%$), with η_{inh} ranging from 0.62 to 0.85 dL/g. The unsaturated PEEAs could not dissolve in THF, which was the designated eluent for the central GPC facility available to us. This was similar with observations reported by Guo et al. (23).

3.2 FTIR Analysis

The structures of these PEEAs were confirmed by both FT-IR and NMR spectra. The infrared spectra of the polymers were fully consistent with the anticipated chemical constitution, as shown in Figure 2. It showed the

Table 1. Fundamental properties of PEEAs^a

Sample	Yield (%)	η_{inh} (dL/g)	T_g (°C)	$T_{d,onset}$ (°C)	Contact angle (°)	Water Sorption (%)
M(EO) ₁ H	69.3	0.62	89	351	65.4 ± 5.2	9.8 ± 1.2
M(EO) ₂ H	68.6	0.73	76	345	59.3 ± 6.3	10.5 ± 1.5
M(EO) ₃ H	63.2	0.85	65	331	53.6 ± 4.2	11.6 ± 1.6
M(EO) ₄ H	65.8	0.76	52	324	48.3 ± 6.8	12.7 ± 1.4

^aIntrinsic viscosities measured in dichloroacetic acid at 25°C, contact angle determined by Krüss DSA-10.

characteristic absorptions bands corresponding to the amide (~3303, ~3052, ~1629, ~1548 cm⁻¹) and unsaturated H-C=C bonds (~3030, ~958 cm⁻¹). The intense C=O stretch at about 1711 cm⁻¹ confirmed the formation of ester bonds. This was similar with the reported results for other poly(ester amide)s (22). The characteristic ethylene oxide stretching bands at about 1135 cm⁻¹ could also be observed as well. The broad absorption around 2900 cm⁻¹ could be assigned to the aliphatic hydrocarbon structure existing in the polymers.

3.3 ¹H-NMR and ¹³C-NMR Analyses

More detailed elucidation of the structure of the polymers can be obtained from NMR spectrum. The representative ¹H-NMR spectrum of M(EO)₁H is shown in Figure 3. The peak at 4.41 ppm could be assigned to -COOCH₂-methylene protons, indicating that the ethylene oxide moieties were present in PEEAs. The resonances at 3.16 ppm belonged to methylene protons of -NHCH₂- unit, while the peaks at 1.45 and 1.28 ppm were assigned to remaining methylene protons of 1,6-hexanediamine units. The single

peak at 9.07 ppm and multiple peaks at 6.23, 6.40 ppm were attributed to proton of -NHCO-unit and protons of unsaturated C=C double bonds, respectively.

¹³C-NMR spectrum of M(EO)₁H is much more definitive, as shown in Figure 4. The signals for carbonyl carbon could be observed at 70.6 and 169.5 ppm. The peaks at 138.1 and 137.0 ppm were attributed to the carbon atoms of unsaturated double bonds. The peak at 65.3 ppm corresponded to methylene carbon atoms linked to ester bond, further confirming ethylene oxide unit had incorporated the PEEAs chain. The chemical shift of the aminomethylene carbon (-NHCH₂-) atom appeared at 38.2 ppm, whereas the peaks at 34.6 and 32.1 ppm were assigned to remaining methylene carbon atoms of 1,6-hexanediamine units. Therefore, both characteristic absorptions bands from FTIR spectrum and well defined assignment of hydrogen and carbon atoms from NMR spectra confirmed that anticipated PEEAs had been successfully obtained.

3.4 Thermal Properties Analysis

The thermal properties are analyzed by differential scanning calorimetry (DSC). It is found that only a well-defined

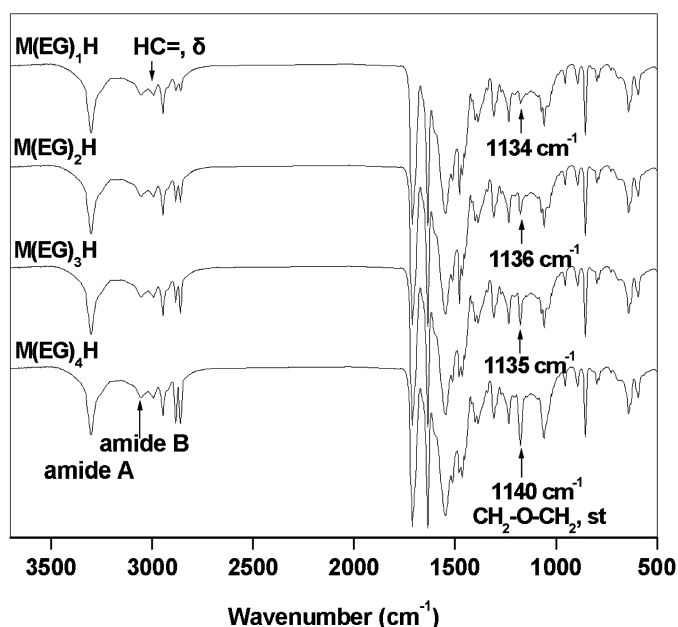


Fig. 2. Infrared spectra of PEEAs (st: stretching vibration).

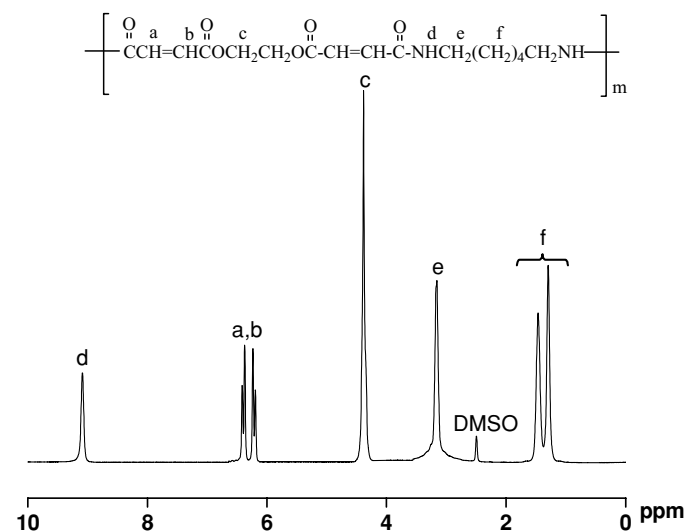


Fig. 3. ¹H-NMR spectrum of M(EO)₁H.

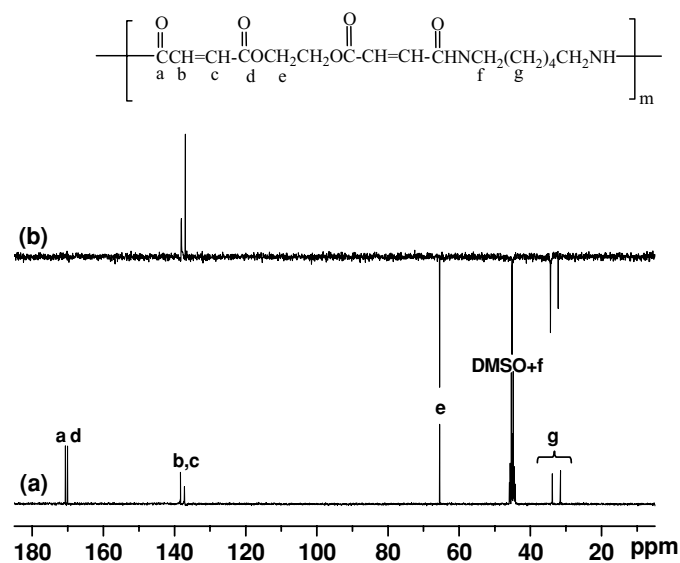


Fig. 4. ^{13}C -NMR (a) and dept- ^{135}C -NMR (b) spectra of $\text{M}(\text{EO})_1\text{H}$.

slope change is observed and no crystal melting peaks are found for all of the polymers. The T_g 's data of PEEAs were listed in Table 1. It was found that the separation of the amide groups by lengthening the flexible ethylene oxide sequences brought about an effective decrease of the hydrogen bond density, thus lowering of T_g 's. For example, their T_g values decreased from 89°C ($\text{M}(\text{EO})_1\text{H}$ with one ether bond per repeating unit) to 76°C ($\text{M}(\text{EO})_2\text{H}$ with two ether bonds per repeating unit) and 65°C ($\text{M}(\text{EO})_3\text{H}$ with three ether bonds per repeating unit) and 52°C ($\text{M}(\text{EO})_4\text{H}$ with four ether bonds per repeating unit). The same trend was observed for polymer containing ether linkages (23, 24). The lower T_g of PEEAs was attributed to the presence of one or more ether bonds in the repeating units of the PEEA macromolecules. It is well-known that the ether bond is a quite flexible bond for free rotation (i.e., increasing the polymer chain flexibility and promoting the chain segmental movement and hence, a lower T_g value) and the energy required for the rotation of a single bond is weaker if ethylene glycol spacers are longer (25, 26).

The wide-angle X-ray diffraction (WAXD) patterns of PEEAs were recorded. All PEEAs of this work showed a typical X-ray halo with no diffraction signals, as shown in Figure 5. Considering analysis of DSC and WAXD, it indicated that PEEAs were amorphous.

Thermal stability of these PEEAs is studied by thermogravimetric analysis (TGA), and the results are summarized in Table 1. With the onset decomposition temperature ($T_{d,\text{onset}}$) as a criterion of thermal stability, PEEAs displayed decomposition temperatures higher than 300°C , for which an inverse relationship between both of $T_{d,\text{onset}}$ and the number of ether bond per repeating unit was observed.

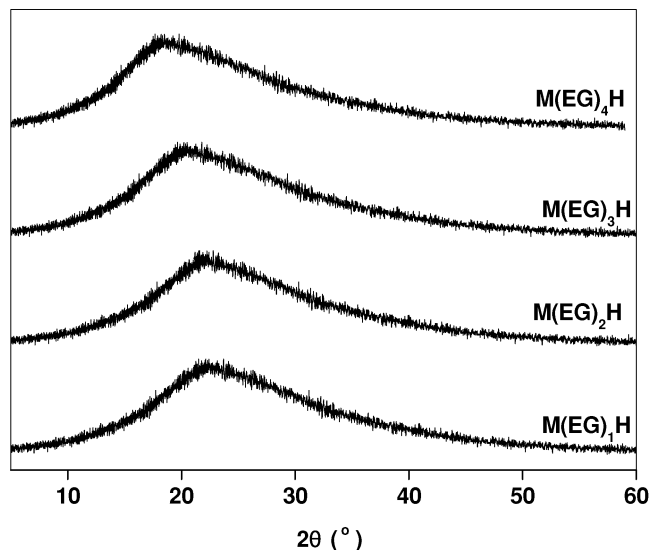


Fig. 5. WAXD curves for synthesized PEEAs.

That is, an increase in the number of oxygen linkages per repeating unit led to a slight reduction in $T_{d,\text{onset}}$.

3.5 Water Sorption and Contact Angle

The isothermal water sorption for the synthesized PEEAs is given in Table 1. It was found PEEAs having increasing ether linkages per repeating unit exhibited a more water sorption, ranging from 9.8% for $\text{M}(\text{EO})_1\text{H}$ up to 12.7% water sorption for $\text{M}(\text{EO})_4\text{H}$. This seemed to confirm the number of ether linkages of the repeat unit played an important role in water sorption. Increasing the ethylene oxide units increased the percentage of available groups to interact with water and consequently increasing the overall water uptake.

In addition, as shown in Table 1, the data of contact angle ranged from 65.4° to 48.1° and showed a decrease as increasing hydrophilic ether linkages per repeating unit in the PEEAs chains. The possible reason is that since ether linkages is hydrophilic, the presence of ethylene oxide units in poly(ester amide)s will improve hydrophilicity of corresponding polymer. From $\text{M}(\text{EO})_1\text{H}$ to $\text{M}(\text{EO})_4\text{H}$, the increase of density of ethylene oxide enhanced hydrophilicity of PEEAs, thus decreasing contact angle. From investigations of both water sorption and contact angle, it indicated that obtained PEEAs possessed good and controllable hydrophilicity by changing numbers of ethylene oxide units in polymer chain.

3.6 Solubility

As shown in Table 2, the solubility of PEEAs in common organic solvents was evaluated. All PEEAs were completely soluble in *m*-cresol, CHCl_3 , and strong aprotic solvents such as DMSO, DMF and formic acid, which

Table 2. Solubility of PEEA at room temperature^a

Sample	DMF	DMSO	Formic Acid	CHCl ₃	THF	Ethyl Acetate	Acetone	Ethyl ether	H ₂ O
M(EO) ₁ H	+	+	+	+	–	–	–	–	–
M(EO) ₂ H	+	+	+	+	–	–	–	–	–
M(EO) ₃ H	+	+	+	+	–	–	–	–	–
M(EO) ₄ H	+	+	+	+	–	–	–	–	–

^a+: soluble; –: insoluble.

showed improved solubility than that of reported poly(ester amide)s without incorporation ethylene oxide moieties previously (18). However, they could not dissolve in water, ethyl acetate, acetone, THF and ethyl ether, which may be the conjugation effect of C=C double bonds and carbonyl groups in both the diester and the diamide parts.

3.7 Hydrolytic Degradation

Hydrolytic degradation under simulated physiological conditions (37°C and pH 7.4) is studied for PEEAs. The degradation results are presented in Figure 6 where weight loss of the samples is plotted against hydrolysis time. It is found more hydrophilic PEEAs exhibited a faster weight loss, ranging from 16.8% for M(EO)₁H up to 50.2% weight loss for M(EO)₄H after a degradation time of 56 days. It is obvious that the increased hydrophilicity of the polymers caused by introducing OEG segments resulted in the increase of degradation rate. Most likely, degradation of the PEEAs takes place by hydrolysis of the ester bonds (19, 27). Because it can be expected that the ester bond in polymer main chain is the most labile bond, an increase in OEG length probably results in an increase in degradation rate. In addition, incorporation of hydrophilic OEG segments in PEEAs facilitates the solubilization of larger polymer frag-

ments, leading to an increase in the rate of weight loss with increasing OEG length. The presence of OEG increases the accessibility of the polymers for water and consequently ensures degradation in the bulk of the matrices.

Degradation *in vivo* of the PEEA copolymers might be faster than was observed *in vitro*. Several reports describe that the degradation of poly(ester amide)s is enhanced in the presence of enzymes (28, 29). In addition, oxidative cleavage of the OEG segments may contribute to the degradation pathway, as has been demonstrated for poly(ether urethane)s, for which *in vivo* degradation takes place essentially at the ether linkage of the soft segment (30).

4 Conclusions

A series of novel degradable PEEAs containing ethylene oxide moieties and C=C double bonds in every repeat unit of the polymer backbone were successfully synthesized by interfacial polycondensation from unsaturated diacylchloride and 1,6-hexanediamine. The properties of PEEAs, such as T_g, water-uptake, and rate of degradation, can be modulated by variation of the ether bonds in repeated units. Due to the presence of ether bonds in the polymer chains, PEEAs showed good and controllable hydrophilicity as well as improved solubility in organic solvents. Results of hydrolytic degradation indicated that PEEAs degraded in a steady way.

Acknowledgements

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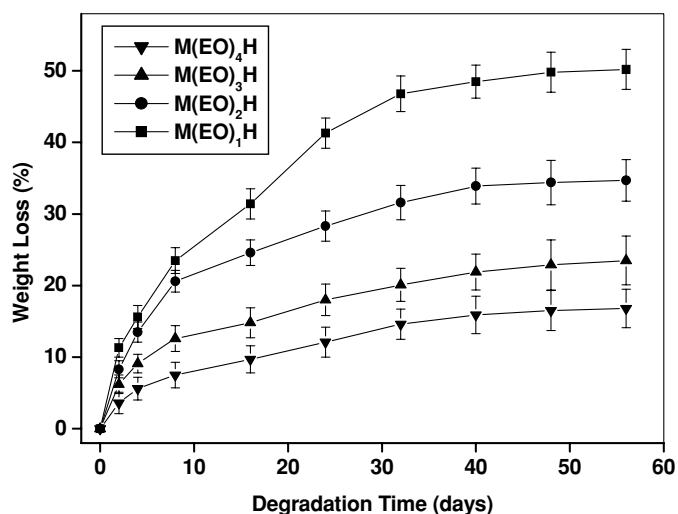


Fig. 6. Weight changes of PEEA samples during *in vitro* hydrolytic degradation (n = 3).

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