

PLGA/PEO 블렌드의 수용성 및 기계적 특성에 미치는 사슬간 수소결합의 영향

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(2020년 1월 29일 접수, 2020년 3월 3일 수정, 2020년 3월 18일 채택)

Effect of Interchain Hydrogen Bond on the Water Solubility and Mechanical Properties of PLGA/PEO Blend

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(Received January 29, 2020; Revised March 3, 2020; Accepted March 18, 2020)

Abstract: Polyethylene oxide (PEO) possesses poor mechanical properties, which limits its application. For the purpose of improving the mechanical properties of water-soluble films, blend of polylactic glycolic acid (PLGA) with PEO was prepared by melt blending. The hydrogen bonding between PEO and PLGA was investigated by Fourier transform infrared spectrometer. The crystallization behavior, water solubility, and mechanical properties were evaluated. The results showed that there was a hydrogen bonding force between PLGA and PEO, and this force can improve the mechanical strength and water absorption of the film. When the PLGA content reached 20 wt%, the tensile strength and the elongation at break achieved a maximum 26.1 MPa and 771.2%, respectively. Compared to neat PEO, blend with 10 wt% of PLGA had considerably higher water absorption capacity. When the PLGA content was 40 wt%, the film would not disperse in water.

Keywords: polylactic glycolic acid, polyethylene oxide, crystallization, water solubility, mechanical properties.

Introduction

Polyethylene oxide (PEO) is a degradable biocompatible polymer material. It is soluble in water and most organic solvents. It can be absorbed by the body and does not produce any toxic side effects.¹ Therefore, PEO can be applied to biomedical area, such as preventing protein adhesion (biological contamination), controlling drug delivery, tissue scaffolds and hydrogel nanocomposites.² But, PEO has poor thermal stability and poor mechanical strength, so it needs to be modified. Modification methods mainly include blending, copolymerization, branching and interpenetrating polymer network structure.³⁻⁷ Among them, blending is the most economical and simple modification method. However, most studies focus on modifying PEO with small molecules.³⁻⁷ This paper attempted

to modify it with degradable polylactic glycolic acid (PLGA) via melt blending.

PLGA is also an important biodegradable material produced by the copolymerization of lactic acid and glycolic acid. It has good biocompatibility and non-toxicity. It can be decomposed normally in the human body, so it is also widely used in medical materials, drug delivery and so on.^{8,9} The main methods for synthesizing PLGA include ring-opening polymerization and melt polymerization. Compared with ring-opening polymerization, melt polymerization is simpler, more cost-effective and less toxic.¹⁰⁻¹³ Studies have shown that the higher the glycolic acid content of PLGA, the faster the degradation rate of PLGA. But there is a special case when the molar ratio of lactic acid to glycolic acid reaches 1 : 1, the degradation rate of PLGA is faster, which only is two months.¹⁴ And the water absorption of PEO can make PLGA more easily degraded in humid environment. So, PLGA/PEO will be a better biodegradable material.

It has been reported that two macromolecules can form

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hydrogen bonding complexes through hydrogen bonding interactions between polymer chains.^{15,16} The formation of hydrogen bonds will change the aggregated structure of the material, enhance the mechanical properties of the material, improve the compatibility between different components of the material, and give the material special properties such as shape memory and self-healing properties.¹⁷⁻¹⁹ Therefore, it can improve the properties of materials by regulating the hydrogen bonding between end groups in PLGA and ether bonds in PEO.

PLGA/PEO materials have high application value in the medical field. Most of previous studies focus on the effects of PLGA/PEO on biological activity of microencapsulated proteins.²⁰ In this paper, The modification effect of PLGA to PEO has been discussed in terms of crystallization behavior, water solubility and mechanical properties.

Experimental

Materials. Polyethylene oxide (Mw=3000000) was supplied by Shanghai Liansheng Company (Shanghai, China). Glycolic acid was supplied by Jiangsu Taixing Water Chemical Co., Ltd (Shanghai, China). Toluene-4-sulfonic acid was purchased from Acme Biochemical Co., Ltd (Shanghai, China). Lactic acid and tin chloride were both purchased from Shanghai Aladdin Biochemical Technology Co., Ltd (Shanghai, China).

Synthesis of PLGA. Lactic acid and glycolic acid (166 g in total) were weighed at a molar ratio of 1 : 1 and added to a 250 mL three-necked flask, which was heated in an oil bath with magnetic stirring. Firstly, the mixture was heated at 100 °C to remove water for 1 h, then heated at 120 °C for 2 h. Secondly, it was mixed with catalyst stannous chloride (0.5 g) and catalyst toluene-4-sulfonic acid (0.5 g), heated at 140 °C for 2 h with an absolute pressure of 400 Pa. Finally, it was heated at 175 °C for 7 h with an absolute pressure of 100 Pa.

Preparation of PLGA/PEO Blend. The PLGA and PEO were added to a KCCK XSS-300 rheometer equipped with a 60-mL mixing chamber (KCCK, China) at a mass ratio of 10:90 (5 g/45 g), 20:80 (10 g/40 g), 30:70 (15 g/35 g), and 40:60 (20 g/30 g) for 6 min. The three sections of the mixing chamber are all 130 °C, the rotor speed is 100 r/min. Then, the blends were moulded via hot-press into a 0.5-mm-thick film at 130 °C for 10 min, followed by water cooling for 1 min to 25 °C with a pressure of 10 MPa.

Measurements. Gel Permeation Chromatograph (GPC): Determination of sample molecular weight were examined by gel permeation chromatograph (GPC, 1515, USA), and rinse

speed is 1.0 mL/min with polystyrene as standard at 35 °C. The solvent is THF.

Fourier Transform Infrared Spectroscopy (FTIR): To determine the functional group of a sample, the Nicolet 6700 spectrometer (Thermo Fisher, USA) were used to perform the FTIR spectra of blends. The measurement range is 4000~600 cm⁻¹, the resolution is 4 cm⁻¹, and the number of scans is 32.

Nuclear Magnetic Resonance Spectrometer (NMR): Nuclear magnetic resonance spectrometer (NMR, AVANCE 500, Germany) was used to measure the structure of the samples at 600 MHz with CDCl₃ as solvent, using tetramethylsilane (TMS) as an internal standard, chemical shifts (δ) were given in ppm.

Differential Scanning Calorimetry (DSC): To test the thermal properties of the sample and analyze the crystallinity, differential scanning calorimetry (DSC) measurements were recorded on a modulated DSC 2910 (TA Instruments, USA). The pan contained 10 mg sample, and a blank aluminum pan was used as the reference. All the samples were heated from 25 to 140 °C, hold at 140 °C for 5 min, cooled to -20 °C, hold at -20 °C for 5 min, and heated to 140 °C. Heating and cooling rates were always 10 °C/min. The crystallinity is calculated using the following formula:

$$x_c = \frac{\Delta H_m}{\Delta H_m^\circ \times W} \times 100\% \quad (1)$$

ΔH_m : melting enthalpy. ΔH_m° : enthalpy change when PEO is completely crystallized (213.7 J/g).²¹ W : mass fraction of PEO in blend.

Weight Change in Water: The water absorption and water solubility of the sample were reflected by weight change in water, and tested by using a constant temperature water bath instrument. The dried film was cut into a size of 2 × 2 cm², immersed in 50 mL of distilled water and taken out at regular intervals. The surface water was dried slightly by filter paper, and the weight of the films was measured. The water absorption (WS) is calculated using the following formula:²²

$$WS = \frac{(W_1 - W_0)}{W_0} \times 100\% \quad (2)$$

where W_1 is the weight of PLGA/PEO composite film when it absorbs water (g); W_0 is the dried weight of PLGA/PEO composite film (g).

Results and Discussion

PLGA Structure Analysis. Figure 1 is the infrared spectrum of PLGA. There is a strong absorption peak at 1751.11 cm^{-1} , which corresponds to the stretching vibration of the C=O bond. The absorption peaks at 2997.47 cm^{-1} and 2952.25 cm^{-1} are the C-H bonds correspond to stretching vibrations. The absorption peaks at 1423.99 and 1394.87 cm^{-1} correspond to the bending vibrations of the C-H bond. The broad absorption peaks at 1176.54 and 1095.01 cm^{-1} corresponding to the bending vibration of the C-O-C bond, indicate the presence of an ester group. The absorption peak at 3514.84 cm^{-1} is the stretching vibration of the hydroxyl group.

Figure 2 is the ^1H NMR spectrum of PLGA. The peak 1 ($\delta=5.24$) is the proton resonance peak of the methine group of the lactic acid unit, and the peak 2 ($\delta=4.84$) is a proton resonance peak of the methine group of the glycolic acid unit.

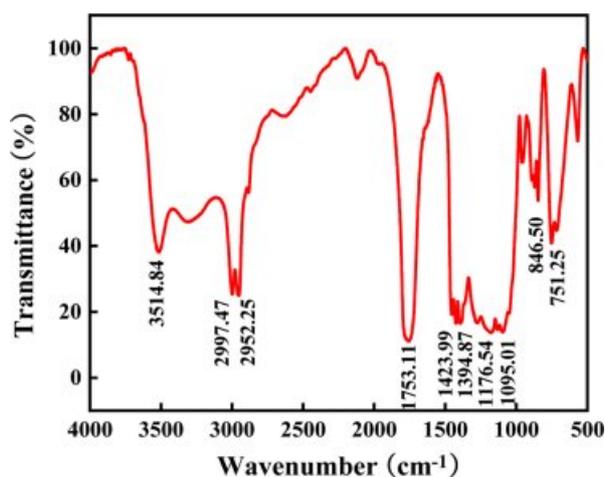


Figure 1. FTIR spectra of PLGA.

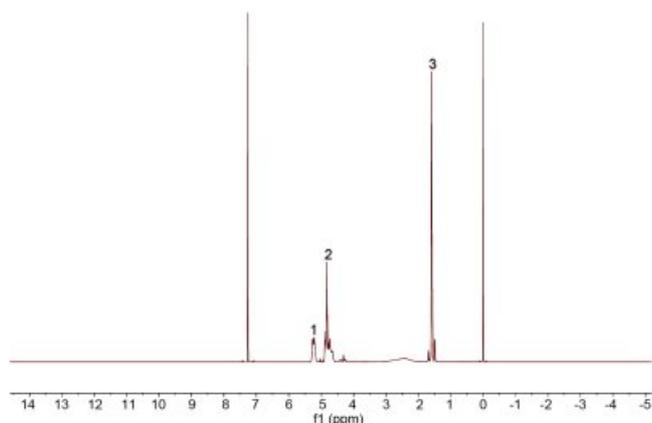


Figure 2. ^1H NMR spectrum of PLGA.

The peak 3 ($\delta=1.49$) is the methylene peaks of the lactic acid unit.

Figure 3 is a molecular weight distribution diagram of PLGA. The polydispersity index is 1.31. It can be considered that the molecular weight distribution is narrow and concentrate in the high molecular weight region. The relative molecular weight (Mw) of the polymer obtained by GPC was 5269.

Hydrogen Bond Analysis. Infrared spectroscopy was used to study the hydrogen bonding in PLGA and PEO. As shown in Figure 4. The absorption peak of the ether-oxygen bond stretching vibration of pure PEO is 1118.35 cm^{-1} . Ozaki *et al.* analyzed the main components and found that the carbonyl characteristic peaks were broken down into 4 parts: 1686, 1705, 1723, and 1745 cm^{-1} .²³ The components at 1705 and 1745 cm^{-1} may be assigned to C=O stretching modes of the

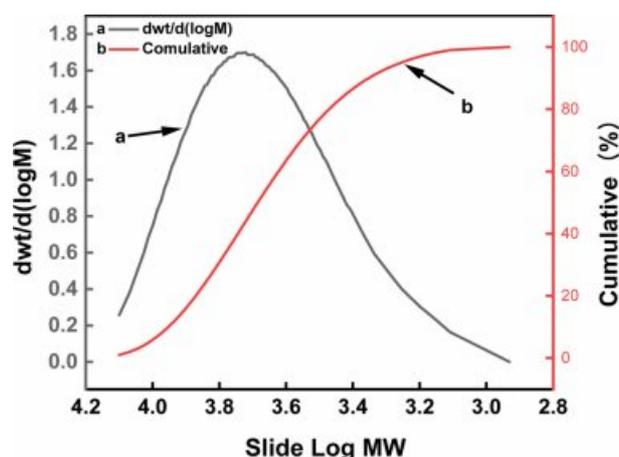


Figure 3. Distribution of molecular weight of PLGA.

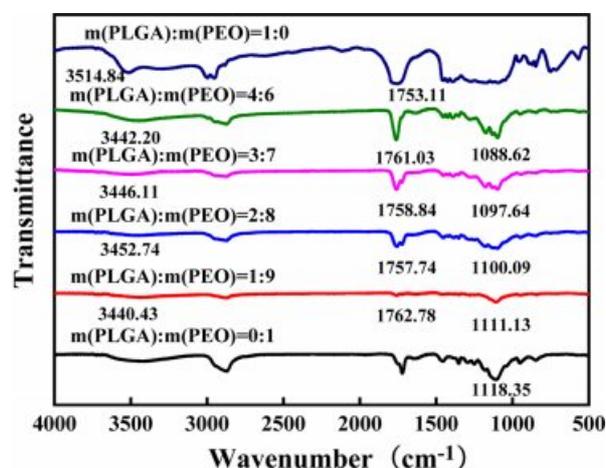


Figure 4. FTIR spectra of PLGA/PEO blends with different mass ratios.

cyclic hydrogen-bonded COOH group in dimeric form and free (non-hydrogen bonded)-COOH group, respectively. 1686 cm^{-1} is attributed to the carbonyl stretching vibration of the oligomer. 1723 cm^{-1} is attributed to the terminal carboxyl group of the oligomer group. As shown in Figure 1, in the PLGA body, the stretching vibration absorption peak of the carbonyl group is broad and asymmetric, with the peak position at 1751.11 cm^{-1} ; the stretching vibration absorption peak of the hydroxyl group is at the position of 3354.84 cm^{-1} .

When PLGA and PEO form a hydrogen bonding complex, hydrogen bonds between carboxyl groups, especially hydrogen bonds between ring-forming carboxyl groups, will dissociate.^{24,25} When -OH of the -COOH in PLGA forms hydrogen bonds with C-O-C in PEO, C=O in COOH will be released. So, the number of free C=O will increase. Therefore, as shown in Figure 4, compared with pure PLGA, the carbonyl peak of PLGA in the blend shifts to a high wavenumber, and the hydroxyl peak of PLGA and the ether-oxygen bond of PEO move to a low wavenumber. Because the number of ether oxygen bonds in PEO is much larger than the number of carboxyl groups and hydroxyl groups in PLGA. Carboxyl groups and hydroxyl groups of PLGA will fully form hydrogen bonds

with ether oxygen bonds. Therefore, with the increase of PLGA content, the positions of hydroxyl peak and carboxyl peak do not change much. However, with the increase of PLGA, the number of ether-oxygen bonds forming hydrogen bonds also increase, and the peaks of ether-oxygen bonds gradually shift to lower wavenumbers.

Crystallinity. DSC is a very good thermal analysis method. Figure 5 shows the second heating curve (a) and cooling curve (b) of PLGA/PEO blends with different mass ratios. Table 1 shows the results obtained by DSC. As the PLGA content in blend increases, both the melting enthalpy (ΔH_m) and the crystallization enthalpy (ΔH_c) gradually decrease, because PLGA is a random copolymer and amorphous. But the crystallinity of PEO does not change much, and it is always maintained at about 50%. It shows that the hydrogen bonding between PLGA and PEO has little effect on the crystallinity of PEO. With the increase of PLGA content, the melting point (T_m) and crystallization temperature (T_c) of the blend decrease. It shows that PLGA and PEO have good compatibility. PLGA can enhance the mobility of PEO molecular chains. So, T_m shifted to a low temperature with the addition of PLGA. In addition, PEO crystallized at lower temperatures due to the improved

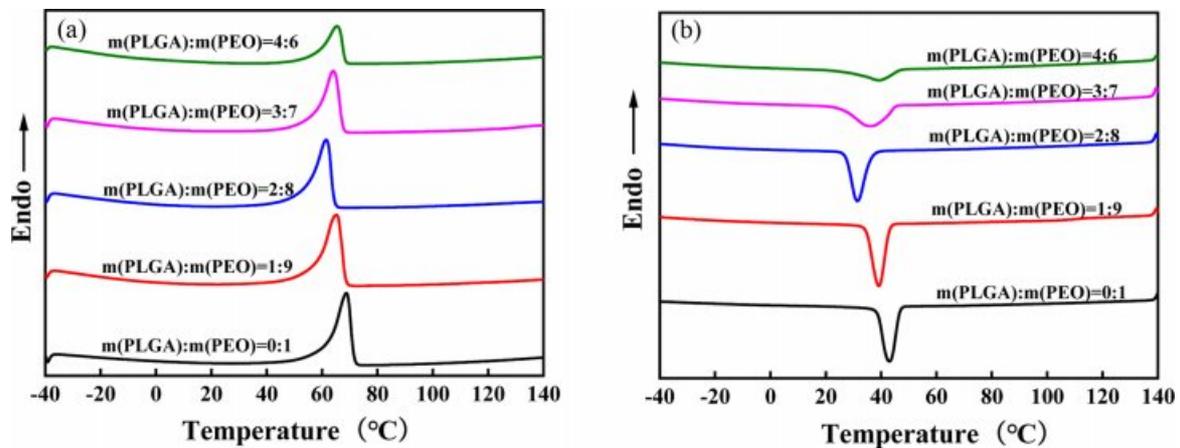


Figure 5. Second heating curves (a); cooling curves (b) of PLGA/PEO blends with different mass ratios.

Table 1. Crystallization Ability of PLGA/PEO Blends with Different Mass Ratios

Sample	T_c (°C)	T_m (°C)	ΔH_m (J·g ⁻¹)	ΔH_c (J·g ⁻¹)	X_c (%)
PEO	43.00	68.82	108.99	106.77	51.00
m(PLGA):m(PEO)=1:9	39.15	65.20	99.88	97.79	51.92
m(PLGA):m(PEO)=2:8	31.41	61.48	85.08	84.60	49.76
m(PLGA):m(PEO)=3:7	36.06	64.07	75.62	80.35	50.56
m(PLGA):m(PEO)=4:6	39.25	65.39	60.95	55.89	47.53

chain mobility. When the content is higher than 20%, the T_m and T_c begin to increase. But they are always lower than T_m and T_c of neat PEO. It shows that PLGA and PEO appear phase separation. T_m starts back to original T_m of neat PEO.

Weight Change in Water. The solubility of polymer materials is a slow process. First, they must absorb water to swell, and then dissolve. When the rate of water absorption is fast than the rate of solubility, the weight will increase. Otherwise it will decrease. PLGA is an insoluble substance, and PLGA/PEO films will not completely dissolve. When the PLGA content is low, PEO is the matrix and the dispersed phase is PLGA. When PEO is completely dissolved, PLGA will disperse and become particles dispersed in water. It can be known from Table 2 that as the PLGA content increases, dissolution time also increases. When the PLGA content reaches 40%, the PLGA has been transformed from a dispersed phase to a continuous phase and will not disperse when placed in water. Besides, it can be seen from Figure 6 that the addition of PLGA can significantly improve the water absorption of the material. Because end groups in PLGA and ether bond in PEO

Table 2. Water Solubility of PLGA/PEO Blends with Different Mass Ratios

Content of PLGA (%)	Water absorption (%)	Dissolution time (h)
0	222.68	9
10	596.62	18
20	455.35	35
30	431.07	46
40	403.19	-

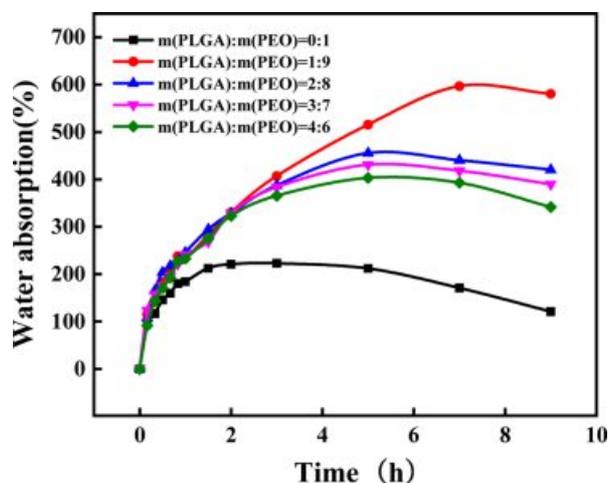


Figure 6. Weight change of PLGA/PEO blends with different mass ratios in water.

produce hydrogen bonding to form a cyclic structure, making it difficult for PEO to dissolve out of the material, but water is locked in the cyclic structure. It enhances the water retention of the film and increases the water absorption of the material. But when the PLGA content is more than 10%, water absorption begins to decrease. Because as the PLGA content increases, hydrogen bonding between PLGA and PEO increase. It makes PEO hard to absorb water and swell.

Mechanical Properties. As shown in Figure 7, the mechanical strength of neat PEO is poor, because the molecular weight of PEO is as high as three million. Although the larger the molecular weight, the mechanical strength will be increased, after reaching the limit, the strength of the material will decrease as the molecular weight increases. Because as the molecular weight of the polymer increases, the intermolecular forces also increase, which increases the high-temperature flow viscosity of the polymer, resulting in molecular agglomeration, and the product contains a lot of bubbles and voids. The molecular weight of PLGA is not high. The insertion of PLGA can well reduce the force between PEO molecules, thereby reducing the viscosity of the polymer and improving the toughness of the material. It can be seen from Figure 8, when the content of PLGA is 20%, the tensile strength reaches 26.1 MPa and the elongation at break reaches 771.2%. The hydrogen bonding between PLGA and PEO can improve the mechanical strength of the film. However, when the content of PLGA exceeds 20%, the mechanical properties of the film gradually decrease. Because PLGA and PEO appear phase separation. As shown in Figure 7, as the degree of orientation increases, the intermolecular forces increase. When the deformation of the film reaches about 500%, the tensile strength

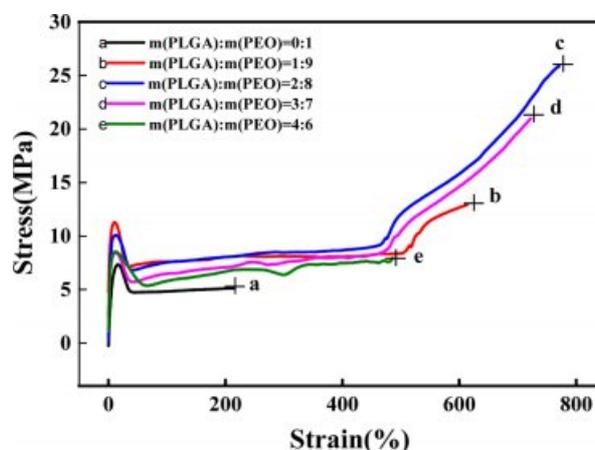


Figure 7. Stress-strain curve of PLGA/PEO blends with different mass ratios.

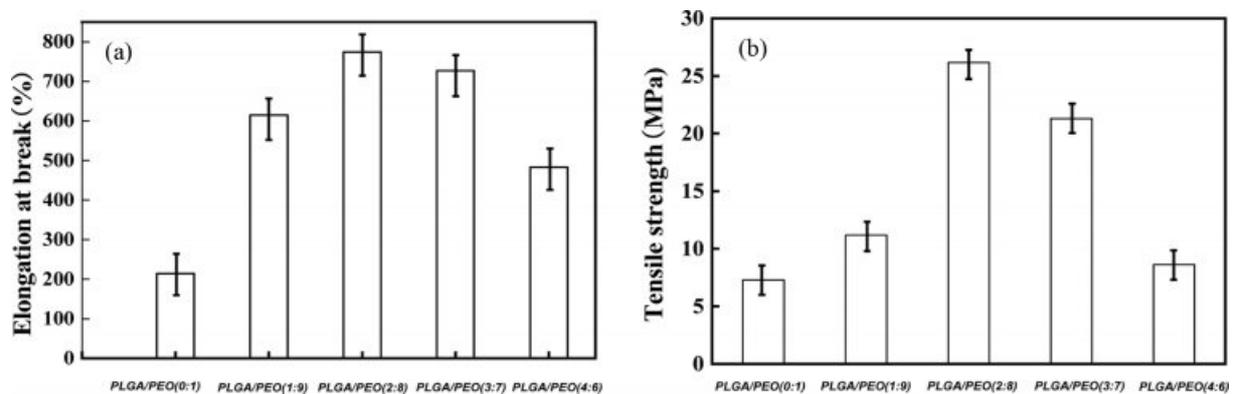


Figure 8. Tensile properties of PLGA/PEO blends with different mass ratios: (a) elongation at break; (b) tensile strength.

increases sharply. The longer the molecular chain, the easier the molecule is oriented to harden. However, because the molecular chain of PLGA is not long, the orientation is difficult. So, the elongation at break and tensile strength decrease.

Conclusions

In this paper, PLGA was prepared by melt polymerization. Then PLGA and PEO were blended in different proportions. It is found that there is a hydrogen bonding force between PLGA and PEO, and this force can improve the mechanical strength and water absorption of the film. When the PLGA content reached 20 wt%, the tensile strength and the elongation at break achieved maximum 26.1 MPa and 771.2%. Compared to neat PEO, blend with 10 wt% of PLGA had considerably higher water absorption capacity. So, it can be used as a good water-absorbing material. When the PLGA content was 40 wt%, the film would not disperse in water. So, it would also be a good insoluble biomaterial. There is no doubt that the application prospect of PLGA/PEO materials will be more promising and broader.

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