Synthesis of the Amino Acid-based Polyesteramide for Hydrophilic Modification of Polycaprolactone

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Abstract. To solve the problem that the strong hydrophobicity of Polycaprolactone (PCL) was not conducive to cell adhesion and spreading in artificial blood vessels, the amino acid-based polyesteramides (AA-PEAs) material was synthesized using L-phenylalanine, 1,3-propylene glycol and sebacyl chloride for hydrophilic modification of PCL. The chemical structure, water contact angles, and thermal performance, were characterized by ^{1}H NMR, Water contact Angle tester, Thermogravimetric Analyzer, and Differential Scanning Calorimeter. The hydrophilicity of PCL fiber membranes was significantly improved by adding the AA-PEAs. The glass transition temperature (T_g) of the PCL fiber membrane was 34.1℃, which was lower than the human body temperature with the 30% content of AA-PEAs. The melting temperature (T_m) was 55.0℃, which was higher than the human body temperature. It is conducive to maintaining good flexibility under the impact and pressure of blood flow in the body.

Keywords: Polycaprolactone (PCL); Amino Acid-based Polyesteramides (AA-PEAs); Hydrophilic Modification; Water Contact Angle.

1. Introduction

Polycaprolactone (PCL) is a semi-crystalline biodegradable polyester with a low melting point of 60℃, produced by ring-opening polymerization of ε-caprolactone, and possessing good biocompatibility and permeability [1-2]. The drawbacks of PCL, such as hydrophobic nature and long degradation time, can be overcome by combining it with other polymeric materials; such polymers have been widely used in the field of biomedical engineering[3]. Amino acid-based polyesteramides (AA-PEAs) are another widely used class of polymeric materials. AA-PEAs not only have a chemical structure similar to that of proteins, but can also participate in normal physiological metabolism as pseudo-proteins [4]. After simple hydrolysis or enzymatic degradation, the natural amino acids will be released into the circulation and absorbed [5]. Due to the structural diversity, especially the multiple stereospecific information on different functional groups and amino acids, AA-PEA becomes a promising biomaterial, and some preliminary studies on its structure-property relationships have been conducted [6].

In this paper, the AA-PEAs material was synthesized using L-phenylalanine, 1,3-propanediol and sebacyl chloride as the main raw materials. By blending the AA-PEAs and PCL, the fiber membranes were prepared via electrospinning technology. The influence of AA-PEAs on the hydrophilic properties of electrostatic fiber membranes was emphatically studied, as well as the thermal performance.

2. Experiment

2.1 Materials

Polycaprolactone (PCL, Mn=80,000Da), 1,3- Propylene glycol, and Sebacyl chloride were provided by Shanghai Maclean Biochemical Technology Co., L-phenylalanine was supplied by Shanghai Aladdin Biochemical Technology Co., P-methylbenzenesulfonic acid monohydrate was supplied by Alfaesah (China) Chemical Co., Ultra-dry Dichloromethane was supported by Sigma

Aldrich (Shanghai) Trading Co., Ethyl Acetate and Anhydrous sodium carbonate were provided by Tianjin Yongda Chemical Reagent Co..

2.2 Synthesis of amino acid-based polyesteramides (AA-PEAs)

The L-phenylalanine, p-toluenesulfonic acid monohydrate and 1,3-propylene glycol were esterified in a molar ratio of 2:2:1 to synthesize phenylalanine propylene diester (Phe). Next, the crude amino acid-based polyesteramides (AA-PEAs) was obtained through interfacial reaction at a molar ratio of 1:1 between phenylalanine propylene diester and sebacyl chloride. After washing with a sufficient amount of deionized water, it was purified through a tetrahydrofuran/ethyl acetate solvent system. Finally, the AA-PEAs were obtained after vacuum drying for later use. Its synthesis path was shown in Figure. 1.

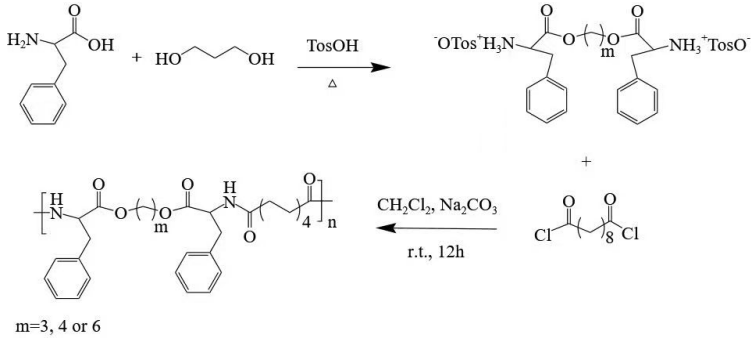

Figure 1. The synthetic pathway of polyesteramides.

2.3 Fabrication of PCL/AA-PEAs Electrostatic Fiber Membranes

The different ratios of PCL/AA-PEAs were completely dissolved in the mixed solvent of chloroform/dimethyl sulfoxide ($CHCl_3$/DMSO, v/v=4/1), obtaining a spinning solution concentration of 130-150 mg/mL. In this study, the addition amounts of the AA-PEAs were 20%, 30% and 40% respectively. The liquid supply speed was 1.2 mL/h and the receiving distance was 18 cm at a voltage of 18-20 KV. The obtained electrospun fiber membranes were vacuum-dried at room temperature in 48 hours for performance testing.

2.4 Characterization

The chemical structure of the AA-PEAs was recorded at room temperature using BRUKER Spectrometer operating at 400 MHz for ^{1}H NMR spectrum with the deuterated dimethyl sulfoxide as the solvent. The water contact angles on the surface of the fiber membranes were measured using an optical contact Angle tester. The 3 μL droplet was placed on the membrane surface, and the static images of the droplets at different times were recorded. The thermal stability was determined using a TGA-Q50 thermogravimetric analyzer under the following conditions: nitrogen atmosphere, heating rate: 20℃/min, and test range: 30-700℃. The T_g was determined by using a DSC214 differential thermal scanning calorimeter under the following conditions: nitrogen atmosphere, heating rate: 20℃/min, and test range: -80-100℃.

3. Results and Discussion

3.1 ^{1}H NMR Analysis

The chemical structure of the obtained AA-PEAs was characterized by ^{1}H NMR. As shown in Figure. 2 (a), the proton peak of δ=7.26-7.10 ppm was the characteristic peak of H on the benzene ring, the chemical shift δ=7.51-7.41 ppm was the characteristic peak of H on the TosoH benzene ring, and the chemical shift δ=2.28 ppm was the characteristic peak of the methyl group on TosoH. At around 1.30 ppm and 3.95 ppm, The characteristic peaks of H on different methylene groups in 1,3-

propanediol appeared, implying the successful synthesis of phenylalanine propylene ester. As shown in Figure. 2 (b), the characteristic peaks of ToSOH benzene ring and the H on methyl group at chemical shifts δ=7.51-7.41 ppm and 2.28 ppm had disappeared, indicating that the ToSOH protecting group has been completely removed. In addition, a methylene characteristic peak near the amide bond in the decanoyl chloride monomer appeared at around 2.03 ppm, indicating the successful synthesis of AA-PEAs.

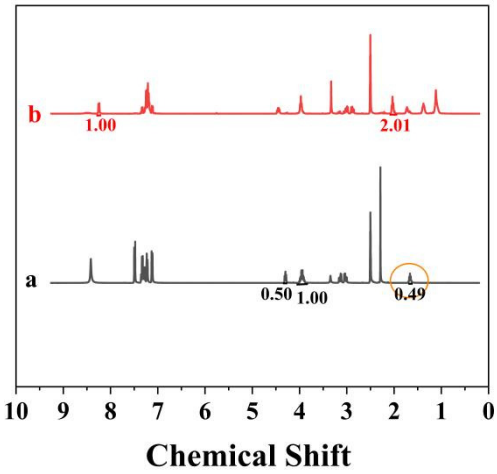

Figure 2. The ^{1}H NMR spectra of the polyesteramides.

3.2 Water Contact Angle Analysis

The wettability of the PCL/AA-PEAs fiber membranes was presented in Figure. 3. As shown in Figure. 3 (a), the PCL had a static contact angle of 152°, indicating a certain degree of hydrophobicity. With the increase content of AA-PEAs, the static contact angle of PCL fiber membrane gradually decreased, enhancing its hydrophilicity in Figure. 3. When the addition amounts of the AA-PEAs were 20% (b), 30% (c) and 40% (d), the contact angles of PCL/AA-PEAs fiber membranes were 97.4°, 47.5° and 44.9°, respectively. In addition, Figure. 4. recorded the changes of the droplet in the fiber membranes over time. When the addition amount of AA-PEA was 20%, the contact angle gradually decreased after the droplet was added. However, when the addition amounts of AA-PEA were 30% and 40%, the contact angles rapidly reduced to 53.4°-55.3° within 30s. These results indicated that the addition of AA-PEAs effectively improved the hydrophilicity of PCL.

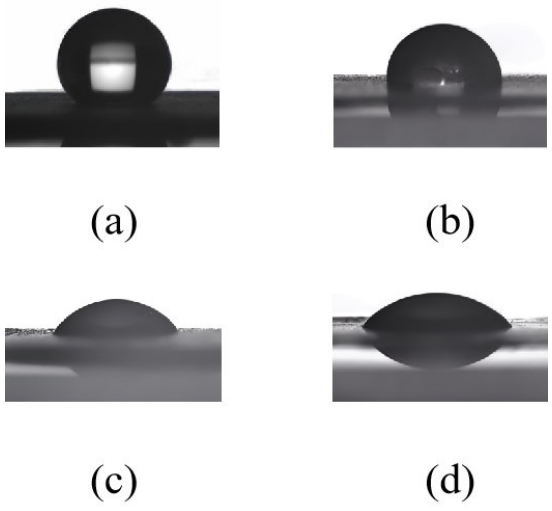

Figure 3. The water contact angles of PCL fiber membranes with different AA-PEAs contents.

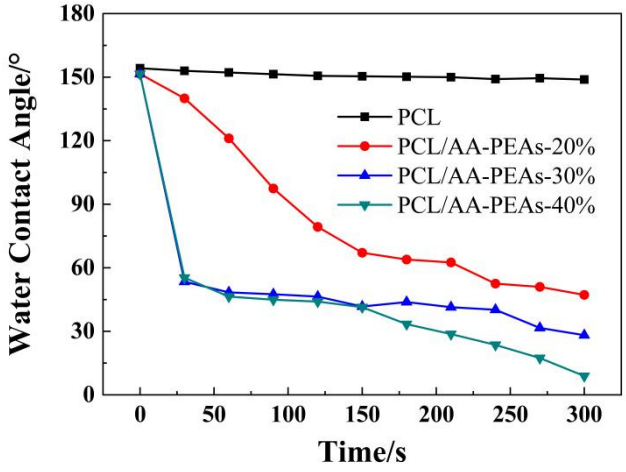

Figure 4. The changes of water contact angles over time.

3.3 Thermal Performances Analysis

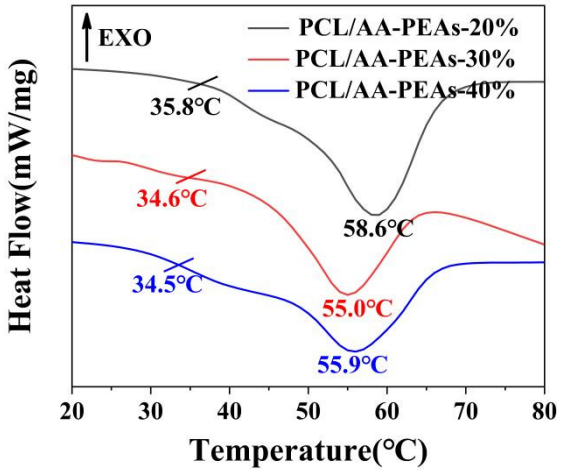

Figure 5. DSC curves of PCL/AA-PEAs fiber membranes.

Table 1. The thermal performances of PCL/AA-PEAs fiber membranes.

Sample	T_g/°C	T_m/°C	$T_{d5\%}$/°C	$T_{d10\%}$/°C
PCL	-53.0	56.6	335.12	352.03
PCL/AA-PEAs-20%	35.8	58.6	322.55	344.74
PCL/AA-PEAs-30%	34.6	55.0	320.33	337.34
PCL/AA-PEAs-40%	34.5	55.9	298.89	341.78

The relevant thermal performances were presented in Figure. 5 and Table 1. As shown in Figure. 5, the T_g of the PCL/AA-PEAs fiber membranes gradually decreased as the addition amounts of AA-PEAs. The trend of T_m change was irregular. The values of T_g for the PCL/AA-PEAs fiber membranes were 35.8°C (20% AA-PEAs), 34.6°C (30% AA-PEAs) and 34.5°C (40% AA-PEAs), respectively, which were lower than the human body temperature (37°C). The values of T_m were 58.6°C (20% AA-PEAs), 55.0°C (30% AA-PEAs) and 55.9°C (40% AA-PEAs), respectively, which were higher than that of the human body. This was suitable for artificial blood vessel materials. It could also be seen

from Table 1 that the thermal decomposition temperatures of 5% and 10% of pure PCL fiber membranes were 335.12℃ and 352.03℃, respectively. The thermal decomposition temperatures of both 5% and 10% of PCL/AA-PEAs fiber membranes decreased as the adding amount of AA-PEAs, but the thermal decomposition temperature of 5% remained above 298℃, maintaining good thermal stability.

4. Conclusion

The amino acid-based polyesteramides were successfully synthesized using L-phenylalanine, 1,3-propanediol and sebacyl chloride. The hydrophilicity of the PCL fiber membranes was significantly improved after adding the AA-PEAs. With the increase content of AA-PEAs, the static contact Angle of the PCL fiber membrane gradually decreased. When the amounts of AA-PEA were 20%, 30% and 40%, the water contact angles of the PCL/AA-PEAs fiber membranes were 64.7°, 57.5° and 44°, respectively. The values of T_g for the PCL fiber membrane were in the range of 34℃-35.8℃, which were lower than the human body temperature (37℃). The thermal decomposition temperatures of both 5% and 10% of PCL/AA-PEAs fiber membranes decreased as the adding amount of AA-PEAs, but the thermal decomposition temperature of 5% remained above 298℃, maintaining good thermal stability.

Acknowledgments

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