RESEARCH ARTICLE | FEBRUARY 05 2019

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AIP Conf. Proc. 2065, 040003 (2019)
https://doi.org/10.1063/1.5088323

Preparation and properties of biocompatible PCL-PEG-PCL(PCEC)

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Abstract. In this work, the ring-opening polymerization of ε -caprolactone was performed, and the structure and properties of the copolymer were characterized. Copolymerization of PEG into PCL is expected to improve the hydrophilicity and degradation properties of PCL. In our study. We have studied the effect of various factors on the block polymer of PCL-PEG-PCL by changing the reaction time, reaction concentration and the ratio of CL/PEG, then provided a basis for the controllable preparation of PCEC with a certain molecular weight. Experiments show that with the increase of reaction concentration, reaction time and the CL/PEG ratio, the molecular weight of the PCEC increases; in addition, the effect of different molecular weight PEG macroinitiators on the molecular weight of PCEC is also studied. The results show that with the PEG molecular weight increases, the molecular weight of PCEC also shows an increasing trend.

Keywords: PCL-PEG-PCL; biocompatible; ring-opening polymerization
PACS: G04 376

INTRODUCTION

PCL as a kind of biodegradable and biocompatible polyester, has already attracted great attention in drug delivery and tissue engineering due to its nontoxicity and great penetrability. However, PCL has some shortcomings, such as slow degradation rate due to its hydrophobicity and relatively high crystallinity. Coincidentally, polyethylene glycol (PEG) has a unique biological compatibility as we all know, such as hydrophilic, non-toxic and non-antigenic. Researchers generally choose PEG to incorporated with PCL. The polyether chain introduced by PEG can not only improve the biohydrophilicity of the copolymer, but also reduce the crystallinity. However, according to studies, the molecular weight of PCL is one of the key to its degradation rate and biocompatibility. In recent years, people have synthesized a large amount of PEG-induced PCEC block copolymers with ring-opening polymerization. .Stannous octoate ($Sn(oct)_2$), as a good initiator of coordination ring-opening polymerization, has advantages of low toxicity, high efficiency, etc. It has been widely used in the synthesis of biodegradable polyester. Therefore, our team uses different molecular PEG and stannous octoate as macroinitiators to initiate the ring-opening polymerization of caprolactone. In addition, we also studied the effect of various factors on the block polymer of PCL-PEG-PCL by changing the reaction time, reaction concentration and the ratio of CL/PEG, then provided a basis for the controllable preparation of PCEC with a certain molecular weight. Our work may can provide some reference for the degradation and biocompatible performance of PCEC.

EXPERIMENTAL SECTION

Materials

$Sn(Oct)_2$; Poly(ethylene glycol) (PEG, Mn = 200, 400, 800), Calcium hydride(CaH) and Caprolactone (CL) were obtained from Aladdin Company (China). Toluene was purchased from Hangzhou Shuanglin Chemical Reagent Co., Ltd. Hydrochloric acid (HCl) was obtained from Hangzhou Shuanglin Chemical Reagent Co., Ltd. Ethanol was purchased from Zhejiang Hannuo Chemical Technology Co., Ltd..

Proceedings of PPS-34
AIP Conf. Proc. 2065, 040003-1–040003-5; https://doi.org/10.1063/1.5088323
Published by AIP Publishing. 978-0-7354-1793-9/$30.00

Synthesis of PCEC Triblock Copolymers

Biodegradable polyetherester copolymer (PCL/PEG/PCL, PCEC) was synthesized by ring-opening polymerization of caprolactone initiated by poly(ethylene glycol) (PEG). All reagents and solvents were pretreated with CaH_2 to remove water before the reaction, and N_2 protection was necessary during the reaction. PCEC block polymer were prepared by the following procedure. In brief, a certain amount of PEG and stannous octoate (PEG/stannous octoate = 1/2 molar ratio) were dispersed in toluene and then reacted at room temperature for 15 minutes to prepare a macroinitiator(PEG-M). To prepare PCEC, caprolactone was subsequently dissolved in the mixture at 90°C for a certain hours until the viscosity of the mixture was significantly increased. Finally, the reaction was terminated by adding an alcohol/HCl mixture(the content of HCl does not exceed 5%), and then dry the product at room temperature under vacuum.

In this study, the molecular weight of PCEC was controlled by changing molecular of PEG (respectively Mn=200,400,800), reaction time (respectively 12h,24h,36h), reaction concentration (respectively 2mol/L, 3mol/L, 3mol/L) and the ratio of CL/PEG (respectively CL/PEG=25/1,50/1,100/1).

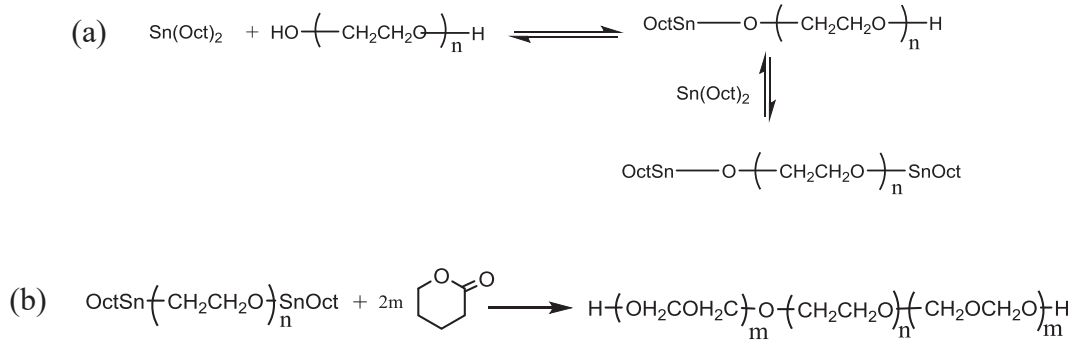

FIGURE 1. The Synthesis of PCEC. (a)The synthesis of macroinitiator (PEG-M), (b)ring-opening polymerization of CL

Instrumentation and Measurements

Nuclear Magnetic Resonance (NMR) was performed using a AVANCE Ⅲ 500MHz instrument(Bruker company), solvent is deuterochloroform. gel permeation chromatography (GPC) were measured on a Waters 1525 (USA) with tetrahydrofuran as a mobile phase using polystyrene (PS) samples as standard tabs, respectively, The flow rate is 1.0 mL/min.

RESULTS AND DISCUSSION

Characterization of $PCEC_{200}$

Figure 2 shows the ^{1}H-NMR of $PCEC_{200}$ (Mn_{PEG}=200) and the relationship between reaction concentration and the molecular weight of $PCEC_{200}$. From (a-c) we can see that chemical shifts of 4.07 and 3.7 correspond to the associated hydrogen in the CL unit and the PEG unit, and according to it, the molecular weight of PCEC can be calculated by calculating the ratio of this two peak areas. (d) shows the molecular weight increases as the reaction concentration increases.

GPC data loses accuracy due to the molecular is too small, so the results are not put here.

Characterization of $PCEC_{400}$

From Table 1(number 1,2,3) we can conclude that as the reaction time increases, the NMR results increase first and then decrease, while the GPC results gradually increase. The two conclusions are somewhat biased. This may be because in the NMR test, when the reaction time was 36 hours, the polymer molecular weight was large, and the PEG segments in the PCEC polymer could not be fully stretched, thus affecting its calculation of the integral area at chemical shift 3.7. Figure 3(a) is the GPC results of $PCEC_{400}$. we can find that while reaction time increases, the molecular weight of PCEC is also increases.

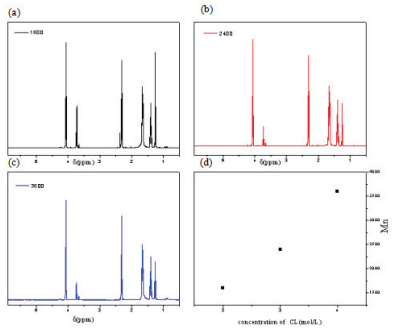

FIGURE 2. (a-c)The ^{1}H-NMR of $PCEC_{200}$ (Mn=1600,2400,3600,molecular weight calculated by ^{1}H-NMR), (d)the relationship between reaction concentration and the molecular weight of $PCEC_{200}$

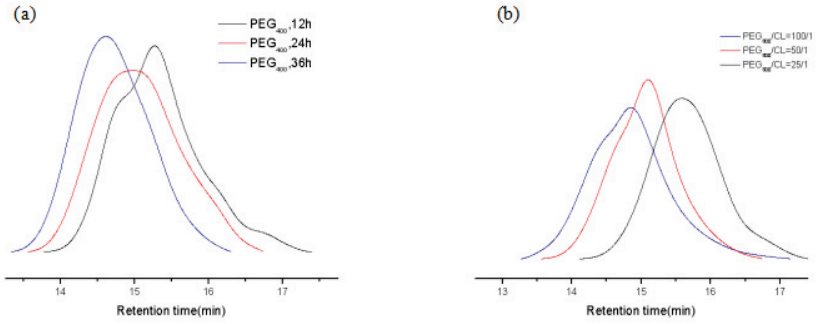

FIGURE 3. The GPC of PCEC. (a)$PCEC_{400}$ (respectively 12h,24h,36h), (b)$PCEC_{800}$ (respectively CL/PEG=25/1,50/1,100/1)

Characterization of $PCEC_{800}$

Figure 4 and 3(b) are respectively the NMR and GPC results of $PCEC_{800}$. The results are consistent with $PCEC_{200}$. And from Figure 4(d), we can see that as the ratio of CL/PEG increases, both of NMR and GPC are displayed that the molecular of $PCEC_{800}$ was gradually increases.

Table 1 lists the specific reaction conditions and molecular weight, molecular weight distribution for each set of reactions. From Table 1 we can see that by comparing the changes in the molecular weight of PEG under the same conditions(respectively number of 1,4,8), then we can conclude that the molecular weight of PCEC increases with the increase in the molecular weight of PEG within the scope of the experimental study.

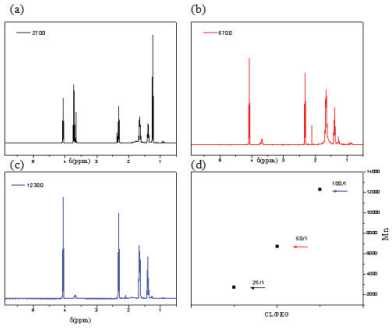

FIGURE 4. (a-c)The ^{1}H-NMR of $PCEC_{800}$(Mn=2700,6700,12300,molecular weight calculated by ^{1}H-NMR), (d)The relationship between the ratio of CL/PEG and the molecular weight of $PCEC_{800}$

TABLE i). The molecular weight and molecular weight distribution of PCEC

Number	Mn(PEG)	Time(h)	Concentration of CL(mol/L)	CL/PEG	Mn[a]	Mn[b]	Mw/Mn (PDI)[b]
1	200	12	2	50/1	1600		
2		12	3	50/1	2400		
3		12	4	50/1	3600		
4	400	12	2	50/1	2800	8522	1.38
5		24	2	50/1	5400	11888	1.39
6		36	2	50/1	2800	18654	1.30
7	800	12	2	25/1	2700	6128	1.33
8		12	2	50/1	6700	12588	1.33
9		12	2	100/1	12300	14875	1.42

[a] means calculated by ^{1}H-NMR
[b] means calculated by GPC

CONCLUSION

In this paper, We successfully prepared 3 sets of PCEC block polymers of different molecular weights derived from PEG (respectively PEG_{200}, PEG_{400}, PEG_{800}), and experiments show that with the increase of reaction concentration, reaction time and CL/PEG ratio, the molecular weight of the PCEC increases; in addition, the results show that with the PEG molecular weight increases, the molecular weight of PCEC also shows an increasing trend. Based on this, in the future our team plans to prepare ene-functional PCEC, then add some cross-linker to cross-link the polymer chains, the UV-curing of the materials will achieved by a click chemistry reaction. And we also can give material different physical and chemical properties by changing the structure and functional groups of the polymer. Further more, our team plan to introduce various reactive groups into the material to prepare a photo-curable material for 3D printing with multi-responsibility to make it more widely used.

ACKNOWLEDGMENTS

This material is based upon work funded by Natural Science Foundation of China (No. 21274131, No. 51273178 and No. 51303158), the Natural Science Foundation of Zhejiang Province (No. LY15E030005 and No. LY17E030006), and the Xin Miao Talent Program of Zhejiang Province (No.2018R403052).

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