단당류로부터 유도된 새로운 생분해성 폴리에스테르의 합성 및 특성화 연구: 폴리에틸렌갈락타레이트

정근수, 박종래
서울대학교 재료공학부

Synthesis and Characterization of Novel Biodegradable Polyester Derived From Monosaccharide: Poly(ethylene galactarate) (PEGA)

Keunsoo Jeong and Chong Rae Park
Carbon Nanomaterials Design Laboratory, Hyperstructured Organic Materials Research Center(HOMRC) and Department of Materials Science and Engineering, Seoul National University, Seoul 151-744, South Korea
crpark@snu.ac.kr

1. Introduction

Conventional biodegradable polymers which are aliphatic polyesters showed some limitations in their application due to lack of desirable hydrophilicity and reactive functional groups. The presence of pendant functional groups imparts some hydrophilicity and makes it possible to conjugate other functional molecules such as anti-cancer drug or gene, etc.

This study is aiming at synthesizing new functional aliphatic polyester via polymerization of galactaric acid, natural monosaccharide containing four hydroxyl groups. In conventional synthetic routes of the functional aliphatic polyesters, multi-step protection-deprotection procedures are generally required to introduce the functional groups, but we tried to simply introduce the functional groups via polymerization of monosaccharide without complicating protection-deprotection procedures. Chemical and physical properties were examined to see its applicability in biomedical areas.

2. Experimental

2.1. Synthesis of Poly(ethylene galactarate) (PEGA)

PEGA was synthesized by polymerization of bis(2-hydroxy ethylene)galactarate (BHEG), which is organic derivatives of galactaric acid (GA). In synthesis of BHEG, 0.02 mol of GA and 0.5 wt% of catalyst were added into various amounts of EG. The reaction mixture was refluxed at 120 ~140 ℃ for 12 ~ 24 hours. The solution was then cooled to RT and dissolved in MeOH. And the product was precipitated using $CHCl_3$. The product, BHEG, was finally purified by repeated recrystallization from methanol and dried under vacuum at 50 ℃ for 48 hours.

0.02 mol BHEG and 0.5 wt% of catalyst were added into 20 ml of EG. The reaction mixture was heated to 120 ℃. Then, the reaction was proceeded at a reduced pressure of around 1 torr. At the end of the reaction, the crude condensation product dissolved in DMF and subsequently precipitated into acetone. Precipitates were dried under vacuum at 50 ℃ for 48 hours.

2.2. Degradation of Poly(ethylene galactarate) (PEGA)

1 g of PEGA powder with proteinase K or without proteinase K was well suspended in 50 ml of PBS. And then, the mixture was stored in shaking incubator at 37 ℃. After 24, 48, and 72 hours, the each samples was filtered and dried under vacuum.

3. Results and Discussion

The chemical structure of PEGA was confirmed by FT-IR and ^{1}H NMR. From the spectra of PEGA, formation of ester bond between GA and EG was observed by the presence of C=O bond of the ester linkage at 1735 cm^{-1}, and the peak caused by C-O bond of primary alcohol, the end group of BHEG, at 1040 cm^{-1} is disappeared because primary alcohol is converted to ester linkage through esterification of BHEG. And a broad peak is observed at 3400 cm^{-1}, indicating that PEGA has pendant hydroxyl groups.

In ^{1}H-NMR spectrum of BHEG, two peaks due to protons of ethylene group can be found at 4.32 ppm (-COOC$\underline{H}_2$C$\underline{H}_2$OH) and 3.82 ppm (-COOCH$_2$C$\underline{H}_2$OH), which can not be found from GA . And two peaks of GA at 4.20 ppm (-OOCC$\underline{H}$CHCHC$\underline{H}$COO-) and 3.75 ppm (-OOCCHC$\underline{H}$C$\underline{H}$CHCOO-) are shifted to 4.12 ppm and 4.05 ppm, correspondingly. In ^{1}H-NMR spectrum of PEGA, two peaks of BHEG at 4.12 ppm and 4.05 ppm are broadened and merged, so just one peak is observed at 4.10 ppm. Two peaks due to protons of ethylene group in BHEG are observed at just 4.32 ppm in PEGA.

Table 1 shows the change in the molecular weight of PEGA catalyzed by the various catalyst systems, the number average molecular weight is increased from 6,100 to 9,000 with various catalysts and is maximized to 9,000 when H_2SO_4 and Sb_2O_3 as a cocatalyst were used.

Degradation behavior of PEGA was measured by weight loss. The weight loss of PEGA is shown in Figure 3 in the presence or absence of proteinase K, enzyme. When proteinase K was used, the rate of weight loss of PEGA is higher than without proteinase K, and the remaining weight was about 20% with proteinase K and about 60% without proteinase K after 7 days.

Table 1. Molecular weight of PEGA

Catalyst	Mn	Mw	Yield
None	5,900	6,100	70.3
SnO	6,100	6,400	72.9
H_2SO_4	6,700	7,100	87.5
Sb_2O_3	6,500	6,700	89.8
H_2SO_4 + Sb_2O_3	7,900	9,000	93.2

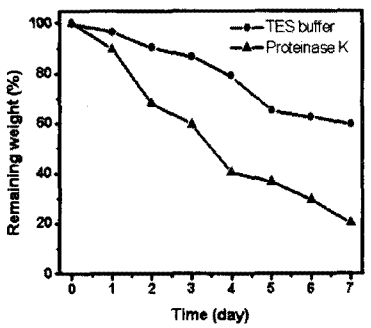

Figure 4. Hydrolytic degradation with TES buffer and proteinase K

4. Conclusion

In this study, novel functional biodegradable polyester was synthesized via polymerization of GA, monosaccharide. The optimal polymerization condition was 120 ℃ for 18 hours under 1 torr. The maximum weight average molecular weight was 9,000 when Sb_2O_3 and H_2SO_4 were used together as the cocatalyst. The enzymatic degradation was effective on degradation of PEGA. PEGA would be a candidate at pharmacological application for controlled drug delivery.