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Effect of Glutamic Acid as Additional monomer in Biodegradable Poly(xylitol sebacate glutamate) Polymer

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Abstract

Xylitol-based polyesters such as poly(xylitol sebacate) PXS are said to be the potential new materials for tissue engineering due to their adjustable mechanical and degradation properties. However, the result indicates that the elastomers are very soft and have a low elongation at break. Therefore, to increase the mechanical strength and minimize the rate of degradation, glutamic acid was added as the third monomer into the PXS. Novel Poly (xylitol Sebacate Glutamate) (PXSG) was successfully synthesized through melt polycondensation without using any harsh solvents and catalysts. The mixture was synthesized at 120°C for about 8 hours. Post polymerization process was carried out in the oven at 100 °C for three days to develop the crosslink network formation. Several testing and characterization were conducted to evaluate the effect of glutamic acid concentration in the polymer. From the result, FTIR spectroscopy confirmed the ester bond formation, tensile strength and Young's modulus increased significantly while the percent of elongation at break and degradation rate decreased as the glutamic acid ratio increased.

Keywords: Biodegradable polymer; tissue engineering; polyxylitol; glutamic acid; polymer scaffolding

1. Introduction

Xylitol- based polyester has been a major interest among scientist in developing biodegradable materials for tissue engineering applications due to its excellent balance properties between drug or biomolecule attachment and controlled degradation of the resulting polyesters [1]. It is considered advantageous among other polyols because it holds tunable properties in mechanical, crystallinity, hydrophilicity, and degradation rate by altering each monomer's feeding ratios [2, 3]. The inert property and unlikely to have deleterious effects on cells are other factors that make xylitol a popular choice to be utilized to make polyol-based polymer [1].

Previously, poly (xylitol citrate) (PXC) and xylitol and poly (xylitol sebacate) (PXS) were successfully synthesized using citric acid and sebacic acid as the co-monomer, respectively [4]. Unfortunately, both PXC and PXS polyesters exhibit inadequate modulus, which is very soft and deform easily. The Young's modulus value of PXC is only 0.0058±1.2 MPa, and PXS polyester is 0.82±0.15 MPa. In this study, glutamic acid was used as a third monomer to yield hydrophilic polyesters with a high degree of elasticity and therefore produced polymer with outstanding mechanical properties. The usage of extra acid to react with alcohols with multiple functions in polycondensation reaction will produce a high degree of elasticity and escalate the polyesters' hydrophilic level [5]. Carboxylic groups on the glutamic acid backbone chain allow the formation of hydrogen bonding and salt bridge, increasing the strength and stiffness of the polymer chain and promising to produce materials with better mechanical properties [6][7].

2. Experimental

2.1. Preparation of samples

Xylitol, which acts as a base was obtained from Sigma Aldrich, Sebacic Acid from Merck Milipore, and

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Glutamic Acid from R&M Chemicals. The three monomers were blended in a reaction flask for 8 hours at 130 °C. The mixture was then cast into PTFE mold and cured in an oven for three days to obtain a film shape sample. Monomer ratios of PXSG are shown in Table 1.

Table 1 :Formulation ratio of PXSG polymer

Formulation	Mol ratio		
	Xylitol (X)	Sebacic acid (SA)	Glutamic acid (GA)
PXSG 1	1.0	0.474	100
PXSG 2	1.0	0.340	24
PXSG 3	1.0	0.346	24

2.2. Characterization and testing

Perkin Elmer UATR Two (Spectrum Two) spectrometer was performed to analyze the bonding in PXSG polyesters. The spectrums in the scale from 370 to 4000 cm^{-1} were recorded. INSTRON testing machine was used according to ASTM D638 with the speed of 50 mm/ min, to measure Young's modulus, tensile strength, and elongation at break of the samples, a dumbbell shape of 5 samples for each formulation was prepared with measurement of 15cm x 2cm.

2.3. In vitro degradation

This test was carried out to obtain the weight loss of PXSG polyester. The method to test biodegradability was referred to in the previous research conducted by Kim *et al.* [8]. Three slabs for each formulation were cut into 1 cm x 1 cm and soaked in phosphate buffer saline (PBS) and Sodium Hydroxide (NaOH) solution at 37 °C. The samples were taken out and weighed at different periods, rinsed with water, dried to constant weight in an oven, and weighed again. Percentage of weight loss and water uptake was calculated by the initial weight of the sample (W_0), weight measured at a certain period (W_T), and dried sample weight (W_D) data by using equation (1) and (2) below [9]:

$$Weight\ loss\ (\%) = Wo - Wd / Wo \times 100 \quad \text{Equation (1)}$$

$$Water\ uptake\ (\%) = Wt - Wo / Wo \times 100 \quad \text{Equation (2)}$$

3. Result and discussion

3.1. Characterization

As shown in Figure 1(a), PXSG polyester shows the broad peaks of OH^- groups at 3364.48 cm^{-1} and 3294.26 cm^{-1} attributed to xylitol's pentafunctionality. The result depicted that the hydroxyl peak gradually weakened with decreasing the initial amount of sebacic acid and increasing the amount of glutamic acid. Simultaneously, the degree of esterification was enhanced with an increase in the initial ratio of glutamic acid to xylitol [10]. In Figure 1(b), the spectra show the carbonyl (C=O) stretching peaks for PXSG elastomer. The absorbance band between 1696.75 cm^{-1} and 1670.50 cm^{-1} was attributed to the carbonyl (C=O) stretching vibrations of ester and carboxyl group, which confirmed ester's formation in all polymers [11].

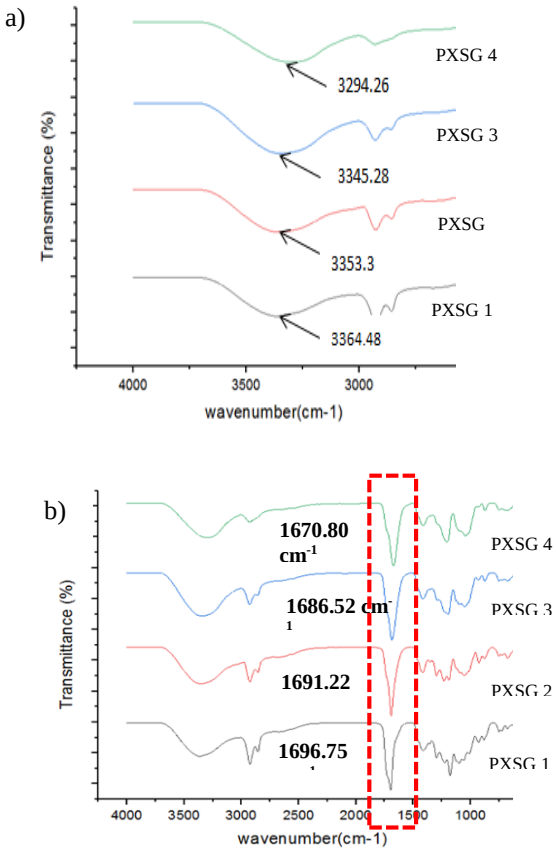


Fig. 1. (a) The shifting of the hydroxyl group in PXSG polyesters' FTIR spectra and (b) The FTIR spectra of PXSG polyesters.

3.2. Mechanical properties

The data obtained from the tensile test showed an increase in the tensile strength with an increasing amount of glutamic acid in the formulation (Figure 2). Tensile strength of PXSG 1 was 3.09 MPa, which was the lowest as compared to PXSG 2, PXSG 3, and PXSG 4 with 6.17 MPa, 8.2 MPa, and 12.7 MPa, respectively. These results indicated that the increasing amount of glutamic acid could improve the stiffness of materials [12], and this may due to the increase in intermolecular bonding by the densely packed molecules [13].

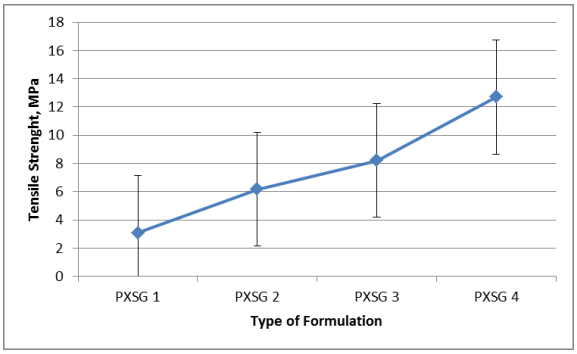


Fig. 2. Effect of Glutamic Acid Ratio on Tensile Strength on PXSG polyester.

The elongation at break (Eb) data presented in Figure 3, shows a decreasing trend with an increase in glutamic acid ratio. PXSG 1, with 347.9% had the highest value of Eb among other PXSG polyesters. The introduction of glutamic acid led to the reduction in flexibility of polymers. It can be seen that there is a large range of tunable mechanical properties for PXGS elastomers available by varying the feeding monomer ratios [7].

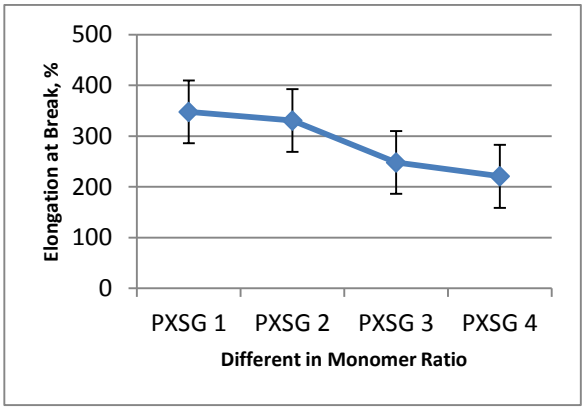


Fig. 3. Effect of Monomer Ratio on Elongation at Break on PXSG polyester.

From the result, it can be observed that Young's modulus increased with the extra glutamic acid ratio. The lowest value of Young's modulus of PXSG 1 was 0.8 MPa, and the highest value was PXSG 4, with 3.4 MPa. More segment of glutamic acid may increase in intermolecular bonding in the polymer matrix chain.

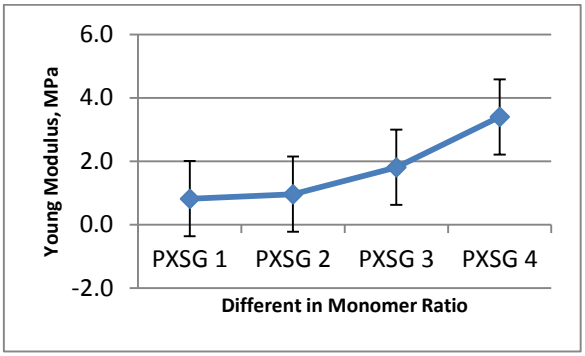


Fig. 4. Effect of Monomer Ratio on Young's Modulus on PXSG polyester.

3.3. Biodegradable properties

In biodegradable polymers, high crosslink density is responsible for reducing the degradation rate and this could be achieved by introducing a high amount of the third monomer in the formulation [12]. Figure 5 shows the remaining weight over time profiles of the PXSG polyester during degradation in phosphate buffer solutions (pH = 7.4, 37 °C) within 5 weeks. The final remaining weight of PXSG 1, PXSG 2, PXSG 3, and PXSG 4 were 71.85%, 75.88%, 81.42% and 84.17% from the original weight, respectively. It showed that the remaining weight of PXSG increased as the amount of the third monomer increased, which is in agreement with a previous report [10]. The result may be obtained through the formation of longer hydrophobic chains that do not allow water molecules to penetrate the structure [5].

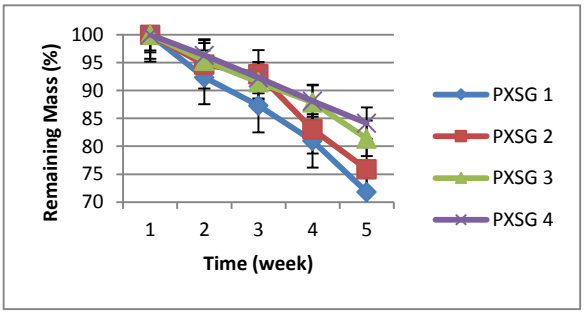


Fig. 5. Remaining weight of the PXSG polyester during degradation in Phosphate Buffer Solutions (pH = 7.4, 37 ◦C).

Figure 6 demonstrates the changes in pH values of PBS contained PXSG polyesters during the mass-loss process. The initial value of PBS solution was 7.4. The data demonstrated that the pH of media containing PXSG polyesters was significantly lower in the first week, indicating the extraction of short chains from the polymer network had occurred [4]. The pH value decreased from 7.4 to 6.56, 6.52, 6.48, and 6.46 for PXSG 1, PXSG 2, PXSG 3, and PXSG 4, respectively. The reduction in pH is due to the acidification from the cleaved chains [14]. The mechanism for acidification of PXSG polyesters is proposed by the unreacted carboxylic acid (-COOH) groups in the matrix and of the carboxylic acid groups formed by hydrolysis of the PXSG ester (-COOR) groups [14]. The mechanism is shown below:

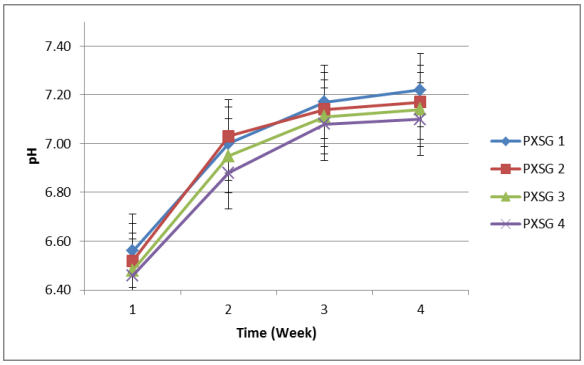
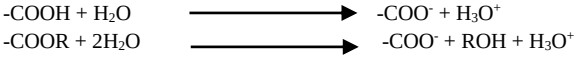


Fig. 6. Changes in pH value of PBS soaked with PXSG polyesters.



4. Conclusions

Biodegradable poly (xylitol sebacate glutamate) (PXSG) polyester was casted by polycondensation of xylitol, sebacic acid, and L-glutamic acid. In conclusion, the addition of L-glutamic acid as a third monomer successfully enhanced the mechanical properties of tensile strength and Young's modulus. However, it led to a decrease of elongation at break. The results indicated that a large range of tuneable mechanical properties for PXGS polyester could be obtained by varying the number of monomer ratios. As expected, the degradation rate of the PXGS polyesters decreased due to the formation of more crosslinks. For better application in the biomedical industry, it is highly recommended that other researchers vary the ratio of xylitol and add any other polymer to make it more compatible with the human body environment.

5. Conflicts of interest

There are no conflicts to declare.

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