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SYNTHESIS, CHARACTERISATION AND SWELLING STUDIES OF POLY(DIOL CITRATE-CO-DIOL SEBACATE) ELASTOMERS

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ABSTRACT

Polyester elastomers have emerged as promising biomaterials for drug delivery and tissue engineering. The potential biomaterials should be elastic and flexible, so as to mimic the mechanical properties of natural tissue. Herein, we report the design and synthesis of elastomers containing multifunctional non-toxic monomers; citric acid, 1,12-dodecanediol, 1,4-cyclohexanedimethanol, sebacic acid. The polyesters were characterized by FTIR, ¹H NMR spectroscopy, DSC and swelling experiments. The tensile tests and swelling experiments illustrate that the polymer were cross-linked elastomers. Thus the studies on the elastomers support the fact that the polymer properties can be tuned by the choice of the monomers.

Key Words: Citric Acid; 1,12-Dodecanediol; 1,4-Cyclohexanedimethanol; Bioelastomer; Polyester

INTRODUCTION

Synthetic polyester bioelastomers have emerged as an important class of biomaterials that find wide applications in drug delivery, tissue engineering, gene therapy and packaging (Barrett and Yousaf, 2009). Although a number of biodegradable elastomers have been developed, most of them require complex and costly synthesis procedures, which translate into higher manufacturing costs and hinder the commercial and clinical implementation of their use (Yang et al, 2006). Also, careful selection of monomers for biomaterial syntheses is essential for determining and controlling the functionality and biocompatibility of the biomaterials to be produced. Recently, there is an increased attention in using citric acid as a robust multifunctional monomer for biomaterial syntheses (Tran et al, 2009). In earlier works, several investigators have reported scaffolds fabricated from elastic polyesters based on multifunctional monomers, in particular polyoctanediol citrate (POC) or polyglycerol sebacate (PGS) (Yang et al, 2006). To our knowledge no study has systematically investigated citric acid-based polyesters in combination with aliphatic diols/diacids as comonomer by catalyst free reactions. Herein we report the synthesis and studies of two polyesters: Poly(1,12-dodecanediol citrate-co-1,12-dodecanediol sebacate) (P1) and Poly(1,4-cyclohexanedimethanol citrate-co-1,4-cyclohexanedimethanol sebacate) (P7). All the monomers used have been previously used in other biocompatible polymers and so cytotoxicity was expected to be low.

MATERIALS AND METHODS

Synthesis of the polyesters

The pre-polymers were synthesized by catalyst-free melt-condensation technique. Equimolar amounts of diol (DD or CHDM) and acids were placed in a three-necked round-bottom flask and the monomer mixture was first heated up to 160-165 °C followed by heating at 140-145 °C for 3 h under a constant stream of nitrogen. The pre-polymers thus obtained were dissolved in 1, 4-dioxane [20% w/w solution] and the resulting pre-polymer solution was used for film preparation without further purification (Djordjevic et al, 2009). Films for mechanical and structural analysis were cast into Teflon petri dishes and placed in an air oven maintained at 80 °C for 24 h for post polymerization of the pre-polymers.

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Polymer characterization

Fourier transform infrared (FTIR) spectra were obtained at room temperature (27 °C) using ABB MB 3000 FT-IR SPECTROMETER. Pre-polymer samples were prepared by a solution casting technique (5 % pre-polymer solution in dichloromethane) over a KBr crystal. The ^1H NMR spectra for pre-polymers were recorded using a JOEL NMR spectrometer. The pre-polymers were purified by precipitation in water with continuous stirring followed by freeze-drying and they were then dissolved in CDCl_3 in 5 mm outside diameter tubes. Solubility of all the prepolymers was determined in various solvents qualitatively. Differential scanning calorimetric (DSC) thermograms were recorded in the range of -70 °C to 150 °C using DSC Q200 V23.10 Build 79 at a heating rate of 1 °C min^{-1} under nitrogen. TGA thermograms were obtained under the flow of nitrogen gas at a scanning speed of 1 °C min^{-1} in the range of 50 - 600 °C using TGA Q50 V20.5 Build 30. The decomposition temperature (T_d) was defined as the temperature at which 5 % weight loss of the samples occurred. The mechanical properties of the polyesters were measured with Tinius Olsen h10K-S UTM testing machine the load cell is of 5 N. The dog bone-shaped polymer film strips were prepared according to ASTM D 628 (30 mm $\times$ 5 mm $\times$ 5mm; length $\times$ width $\times$ thickness) and pulled at a strain rate of 1 mm/min. Values were converted to stress-strain and plotted. Young's modulus was calculated from the initial slope of the curve of the tensile stress versus strain.

Swelling Experiments

The percentage swelling of the polyester was measured in DMSO as follows: 10 mm diameter discs of the polymer films were punched out from the film and soaked into 15 mL of DMSO at room temperature (27 °C). The discs were taken out of the solvent after 24 h and their weights were measured after wipe-cleaning their surfaces with a lint-free paper. The percentage swelling of the discs was calculated using the expression $[(M_w - M_o)/M_o] \times 100\%$, where M_o and M_w represent the disc masses in dry and wet conditions, respectively. After the swelling experiments, the discs were dried to constant weight and sol content was calculated using the expression $[(M_o - M_d)/M_d] \times 100\%$ where M_o and M_d represent the disc masses in pre and post swelling(dried) states.

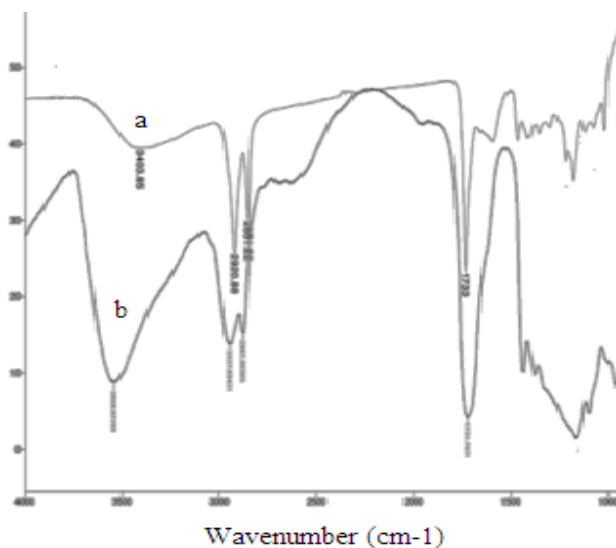


Fig 1: FTIR spectra of P1 (a) and P7 (b)

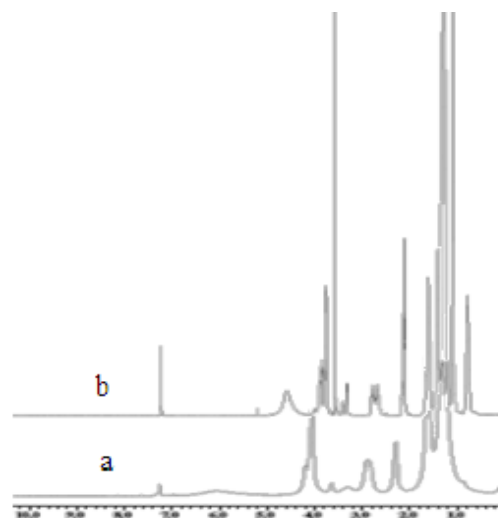


Fig 2: ^1H NMR spectra of P1 (a) and P7 (b)

RESULTS AND DISCUSSION

Polymer characterization

The FTIR spectra of all the synthesized pre-polymers (fig 1) show a strong absorption band at around 1733 cm^{-1} , which is characteristic absorptions of carbonyl stretching vibrations of ester groups and thus confirmed the formation of polyesters (Song et al (2003), (Pasupuleti et al, 2011) (Lei et al (2007). The

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bands centered at around 2921 and 2851 cm^{-1} were assigned to methylene ($-\text{CH}_2-$) groups for the diacids/diols and observed in all the spectra of the polyesters (Brioudea et al, 2007). The broad stretch at 3404 and 3506 cm^{-1} was attributed to the stretching vibrations of the hydrogen-bonded carboxyl and hydroxyl groups (Xie et al 2000) (Lee et al, 2009).

The purified pre-polymers were characterized by ^1H NMR. A proposed structural formula for the resulting copolyesters (Fig. 2) showed the correlation between the different structural components and the observed chemical shifts of the pre-polymers. The multiple peaks around 2.8 ppm, and 4.1 ppm (Djordjevic et al, 2009) (Pasupuleti et al, 2011) were attributed to the protons in $-\text{CH}_2-$ group and alcoholic $-\text{OH}$ group from citric acid. The peak at around 3.6 ppm could be due to the proton signal of $-\text{OCH}_2\text{CH}_2-$ from diol (Yang et al, 2006). The peaks at 0.9, 1.3 and 1.6 ppm were attributed to $-\text{CH}_2-$ protons of sebacic acid, 1, 12-dodecanediol and 1,4-cyclohexanedimethanol with the peaks overlapping in P1. The chemical shift value for $-\text{CO}-\text{CH}_2-$ group of sebacic acid was found at 2.3 ppm. Tensile tests on the polymer films revealed the Young's modulus (E) of the polymers P1 and P7 were 24.87 and 0.89 MPa respectively. The ultimate tensile strength was 3.45 and 0.41 for P1 and P7. The % elongation at break was 285 % for P1 and 120 % for P7. Figure 3 depicts the typical stress-strain curves of the synthesized polyesters. All the mechanical properties were higher for P1 when compared with P7. Thus it is evident that the mechanical properties of the elastomers can be controlled by substituting different diol units. This difference in properties could be useful for a variety of biomedical applications.

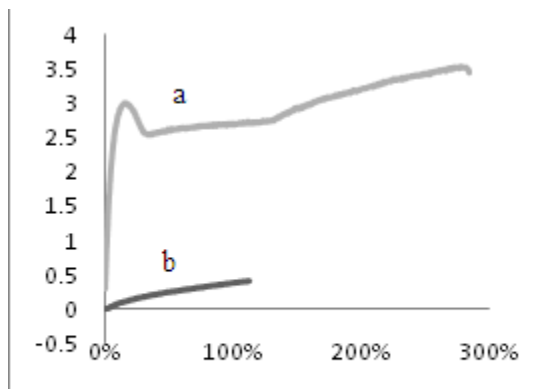


Fig 3: Stress-strain curves for P1(a) and P7 (b)

Thermal Analysis

The thermal studies revealed that the elastomers were thermally stable. The DSC analysis of both the polyesters showed T_g below room temperature, a characteristic feature that determined their elastomer-like behavior (Djordjevic et al, 2009). The T_g of P1 (13.58 $^{\circ}\text{C}$) was higher than P7 (-1.64 $^{\circ}\text{C}$). Since, T_g was associated with chain mobility of a polymer, the T_g values of the polyesters substantiated the formation of higher cross-linking in the case of P1 which had more methylene groups than that of P7.

Swelling Experiments

Equilibrium swelling was studied in DMSO which was chosen because of its high boiling point. The swelling experiments revealed that P1 and P7 swelled to 41% and 316 % of their original size respectively. The sol content of the polyester elastomers P1 and P7 was calculated as 2.5% and 4.6% respectively. The relatively small amount of the sol content confirmed the successful formation of polymer network. Although DMSO dissolved the pre-polymer, the final post-polymerized samples did not dissolve in DMSO even after soaking for several days. The low sol content indicated the very little presence of small oligomers trapped with the polymeric network. As the polymer-polymer intermolecular forces were high due to cross-linking and strong hydrogen bonding, the samples did not completely dissolve. This result was shown to be in agreement with the FTIR analysis which showed the presence of hydrogen bonded $-\text{OH}$ and $-\text{COOH}$ groups.⁴ The high swelling of the P7 in DMSO could be due to the weakening of the intermolecular interactions and disruption of physical cross links between the polymer chains. Also it could be due to lesser crosslink density than that of P1 polyester which had a more rigid network.

Conclusions

The polyester elastomers, poly (1,12-dodecanediol citrate-co-1,12-dodecanediol sebacate) (P1); poly (1,4-cyclohexanedimethanol citrate-co-1,4-cyclohexanedimethanol sebacate) (P7) were synthesized using melt

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condensation polymerization and thermal curing condition. The mechanical and thermal properties of the polyesters showed that P1 had better cross-linking than that of P7. Also, T_g evidenced their elastomeric nature. The polymers had appreciable swelling characteristics which substantiate their cross-linking abilities. Thus it is noticed that the choice of monomers can largely influence the physical properties of the elastomers so as to suit them for the requirements of various biomedical applications.

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