

STUDIES ON POLYESTER ELASTOMERS USING PALM OLEIN FOR DRUG DELIVERY

*G. S. Prabha Littis Malar¹, S. Begila David²

^{1,2} Post Graduate and Research Department of Chemistry,
Scott Christian College(Autonomous), Nagercoil, India

ABSTRACT

The objective of this study is to assess whether a biodegradable elastomer, poly(1,2-ethanediol-co-polyol citrate) and poly(1,6-hexanediol-co-polyol citrate), would be a suitable material to engineer elastomeric scaffolds for cartilage tissue engineering. Polyester elastomers obtained from palm olein are biopolymers in the sense that they are generated from renewable natural sources. In this work, polyesters were obtained by thermal poly condensation method on the effect of palm olein-derived polyols with non-toxic monomers such as citric acid, 1,6-hexanediol, 1,2-ethanediol without addition of catalyst or solvents. The prepared epoxy resin and polyol were characterized using FT-IR and ¹H-NMR. Newly synthesized polyesters were characterized by FT-IR, ¹H-NMR, Solubility studies, TG-DTA, SEM analysis, Soil burial method and mechanical analysis. These polyesters exhibit wide range of mechanical and degradation profiles that can be tuned by the choice of monomers.

KEY WORDS : palm olein; epoxidation; polyol; biopolyester; tissue engineering

1.0 INTRODUCTION

Palm olein is a liquid fraction of palm oil consists of mainly mono-unsaturated triacylglycerol (TAG), POP (42.8%) and di-unsaturated TAG, POO (35.7%). Epoxidation is a simple and efficient method for introducing a new reactive group and useful properties and wide use in a variety of applications. Due to the high reactivity of the oxirane ring, epoxides can also act as raw materials for synthesis of polyesters [1]. Synthetic polyesters have become an integral part of various biomedical and engineering fields, such as tissue scaffolding and therapeutic delivery. In recent years, biodegradable polyesters have attracted much attention as green materials in biomedical engineering, soft tissue engineering and drug delivery, where cell-seeded constructs are designed to replace damaged or diseased tissues [2, 3]. Vegetable oils are excellent renewable source of raw materials for the manufacture of polyesters have high strength, stiffness, environmental resistance and long life [4]. Citric acid was chosen as a multifunctional monomer to enable network formation. It was found that the citric acid can be reacted with a variety of hydroxyl containing monomers at relatively mild conditions [5]. Mean while, it can also participate

in hydrogen bonding interactions within a polyester network [6]. This work refers initially bio-polyesters have the advantage of mimicking many features of extracellular matrix and the polymerization of palm olein via peroxide linkages during the use of this polymeric peroxide in the polymerization of ethylene glycol to obtain palm olein derived polyols refers to conversion of double bonds to hydroxyl groups [7]. Herein we report the synthesis and studies of polyesters: Poly (1,2-ethanediol-co-polyolcitrate) (PPEC) and Poly (1,6-hexanediol-co-polyolcitrate) (PPHC).

2.0 EXPERIMENTAL

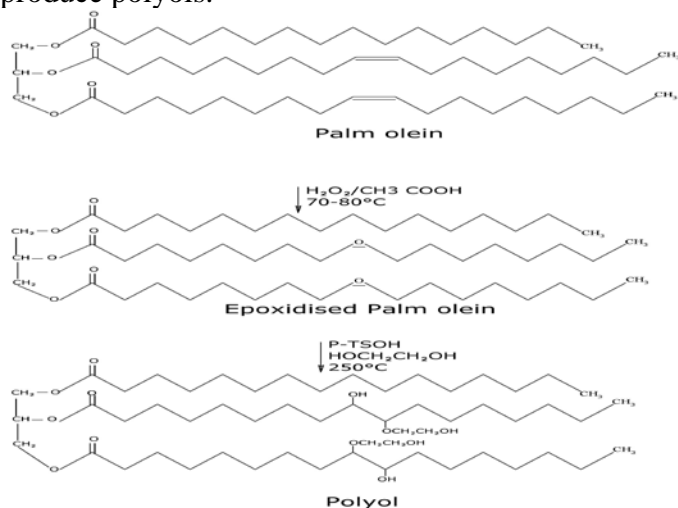
2.1 MATERIALS AND METHODS

The oil used in this study was food grade (Gold Winner) refined palm olein commercially available in supermarkets. Citric acid (100%), H₂O₂ (99.9%), glacial acetic acid(100%) were purchased from Sigma Aldrich chemical Co. and used as such. 1,6-hexanediol and 1,2-ethanediol (100%) monomers were supplied by Sigma Aldrich Co. and used as such.

2.2 PREPARATION OF EPOXIDISED PALM OLEIN

Palm olein was epoxidised using glacial acetic acid with H₂O₂ (50%) were placed in a 250 ml round bottomed flask and the mixture was heated

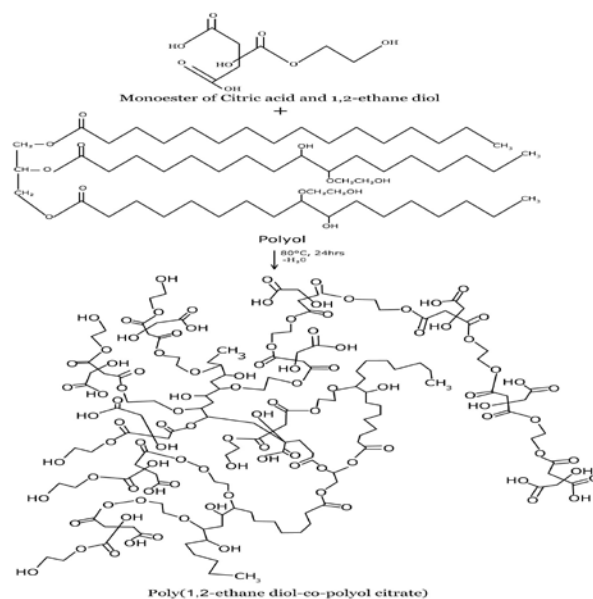
upto 70°C - 80°C for 10h. In order to remove excess H₂O₂, warm water was added to the mixture and the organic phase of the mixture was separated using separating funnel and were collected in a beaker. Thus obtained epoxidised palm olein were treated with ethylene glycol in presence of p-toluenesulphonic acid at 250°C to produce polyols.



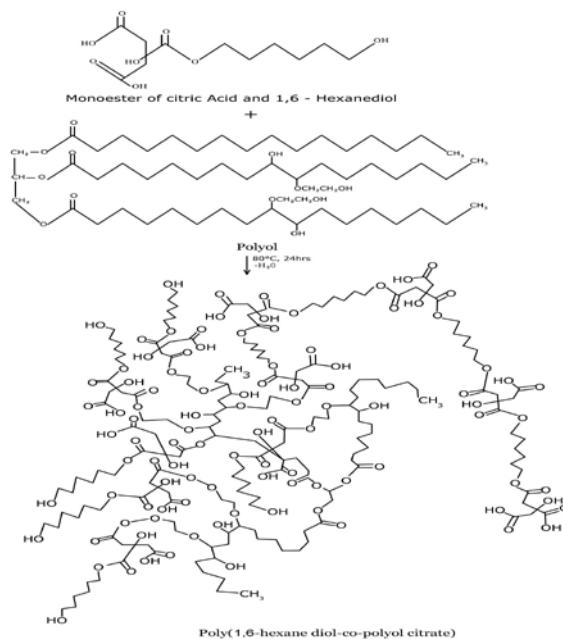
Scheme 1. Synthesis of Polyol from Palm Olein

2.3 SYNTHESIS OF POLYESTERS

Synthesis of aliphatic polyesters was carried out by two stage thermal poly condensation technique. At first stage a prepolymer was prepared by carrying out equimolar amount of diol and acids were placed in a 250 ml round bottomed flask and the mixture was heated upto 140°C -145°C for 30 minutes under a constant stream of nitrogen. At second stage the resultant prepolymer was postpolymerized by crosslinking with polyol at different molar ratios, films were cast into glass plate and placed in an air oven maintained at 80°C for 24 h, polyesters were obtained.



Scheme 2. Synthesis of Poly (1, 2-ethanediol-co-polyol citrate)



Scheme 3. Synthesis of Poly (1, 6-hexanediol-co-polyol citrate)

2.4 POLYMER CHARACTERISATION

Fourier transform infrared (FTIR) spectra of polymers were obtained using THERMO NICOLET, AVATAR 370 FTIR SPECTROMETER with KBR crystal in the range of 4000 - 400 cm⁻¹ at 27°C. The ¹H-NMR spectra for epoxy resin, polyols and pre-polymers were dissolved in DMSO and recorded using BRUKER AVANCE III, 400 MHz FT NMR SPECTROPHOTOMETER. The chemical shift

in ppm for ^1H NMR Spectra were obtained relative to TMS as internal reference. TG/DTA thermo grams of the post-polymers were obtained at a scanning speed of $10^\circ\text{C min}^{-1}$ in the range of $40^\circ\text{C} - 700^\circ\text{C}$ under the flow of nitrogen gas using PERKIN ELMER, DIAMOND TG/DTA. The SEM analysis of the post polymers were obtained using JOEL MODEL JSM 6390 LV at $5 \times$ to $300,000 \times$ SEI magnification. The mechanical property of polyester films were measured using the UTM equipped with 500N load cell. The dog bone shaped polymer film strips were cut according to ASTM standard ($45 \times 5 \times 2\text{mm}$, length \times width \times thickness) and pulled at a strained rate of 10 mm min^{-1} . Values obtained were used to construct stress strain curve. Young's modulus were calculated from the initial slope of the curve.

2.5 SOIL BURIAL METHOD

Garden soil (1200 g) was taken in different pots. A weighed amount (0.5 g) of each of the samples that is, PPEC and PPHC were placed in the beaker such that the soil covered the polymer from all the sides. The pots were covered with the aluminum foil and kept at room temperature. The weight of all the samples PPEC and PPHC were taken at regular interval of time (10 days) to check for any weight loss. Percent weight loss as a function of number of days was determined as total percent weight loss after 2 months was calculated as:

$$\% \text{ Weight loss} = \frac{\text{Initial weight at the beginning} - \text{Final weight after ten days}}{\text{Initial weight at the beginning}} \times 100\%$$

Weight Loss after every 10 days =

$$\frac{\text{Initial weight before ten days} - \text{Final weight after ten days}}{\text{Initial weight before the 10 days}} \times 100$$

2.6 SOLUBILITY STUDIES

The solubility content of the polyesters was measured in various organic and inorganic solvents. Cylindrical disc of about 7cm were cut using cork borer from cross linked polymer film. The discs were pre-weighed to know the initial mass (W_0) and suspended into 15 ml of solvent

at room temperature (27°C). The films were removed from the solvent after one week blotted dry with filter paper and weighed (W_s). The dried samples were weighed to find the dry mass (W_d). The sol-gel fraction was calculated using the formula:

$$\text{Sol}\% = [(W_0 - W_D) / W_D] \times 100$$

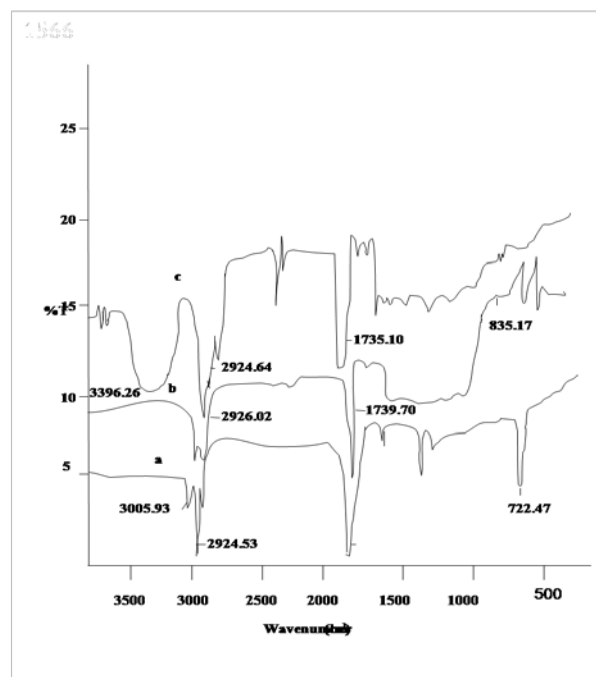


Fig 1. FTIR spectra of Palm Olein (a) Epoxidised Palm Olein (b) and Polyol (c)

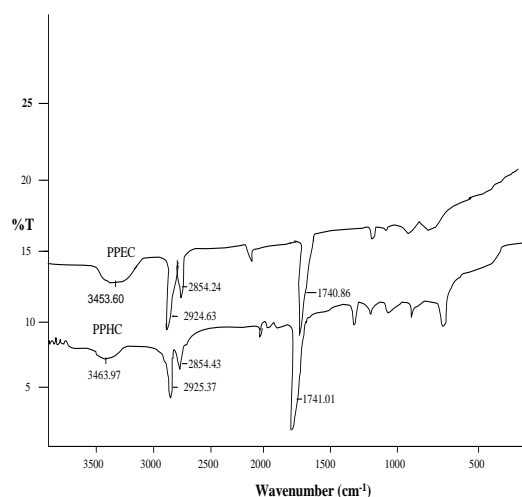


Fig 2. FTIR spectra of PPEC and PPHC

3.0 RESULTS AND DISCUSSIONS

3.1 FT-IR ANALYSIS

The FT-IR Spectra of palm olein, epoxidised palm olein and the prepared polyol are shown in

fig.1. As can be noted, the signature of the double bonds, C=C-H stretch at 3005.93 cm^{-1} and C=C stretch at 1463.14 cm^{-1} completely disappear in the epoxidised oil. The spectra of epoxidised oil clearly shows the epoxy groups C-O band at 835.17 cm^{-1} . The other peaks are 724.54 (methylene in-phase rocking), 1170.54 (ester, antisymmetric stretch), 1458.51 (methyl antisymmetric deformation) and 1739.07 (esters, aliphatic C=O stretch) cm^{-1} . The epoxy group (C-O band at 835.17 cm^{-1}) disappear in the spectra of polyol, confirming the oxirane opening [8]. Most importantly, the spectra of polyol shows broad hydroxyl stretching peak at around 3396.26 cm^{-1} , confirming the incorporation of the hydroxyl groups. The FTIR spectra of all the synthesized prepolymers and polyesters show a strong absorption band at around 1740.86 cm^{-1} , 1741.01 cm^{-1} (esters, aliphatic C=O stretch) thus confirmed the formation of polyesters [9,10] are shown in Fig 2. The bands shows at around 1173.27 cm^{-1} , 1171.06 cm^{-1} were assigned to C-O stretching of ester group. The band shows at 1462.42 cm^{-1} due to aliphatic C-C stretching. The band shows at 2854.24 cm^{-1} , 2924.63 cm^{-1} , 2854.43 cm^{-1} and 2925.37 cm^{-1} were assigned to methylene (-CH₂-) groups for the diacids/diols and aliphatic C-H stretching of the polyesters. The broad stretch at 3453.60 and 3463.97 cm^{-1} was attributed to the stretching vibrations of the hydrogen bonded carboxyl and hydroxyl groups [11, 12].

3.2 ¹H-NMR ANALYSIS

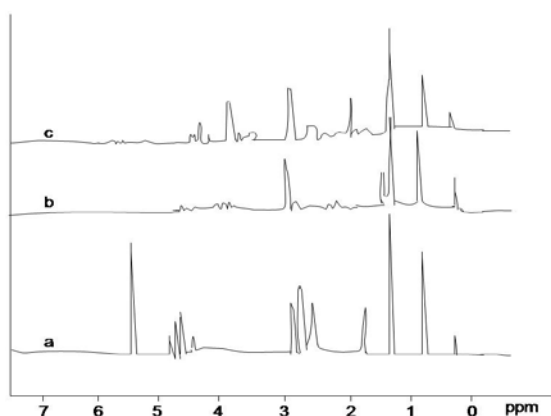


Fig 3. ¹H-NMR Spectra of Palm Olein (a),

Epoxidised Palm Olein (b) and Polyol (c)

The ¹H-NMR spectra recorded from palm olein, epoxidised palm olein and polyol are shown in Fig 3. The spectra shows the double bond hydrogen olefinic proton (-H-C=C-H-) between 5.2 - 5.4 ppm. This peak almost disappeared for epoxidised palm olein due to the conversion of double bonds from palm olein [13]. The peak at 5.2 - 5.4 ppm is observed to almost disappear in the spectra of polyol and it shows appearance of new peaks between 3.6 - 4.27 ppm correspond to the methylinic proton (-H-C-OH) and the proton associated with -OH groups [14].

3.3 THERMAL ANALYSIS

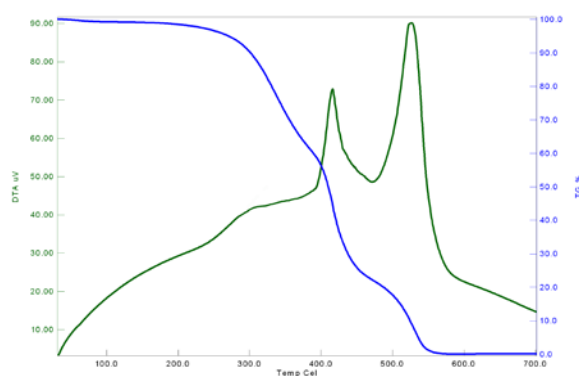


Fig 4. TG/DTA thermogram of PPEC

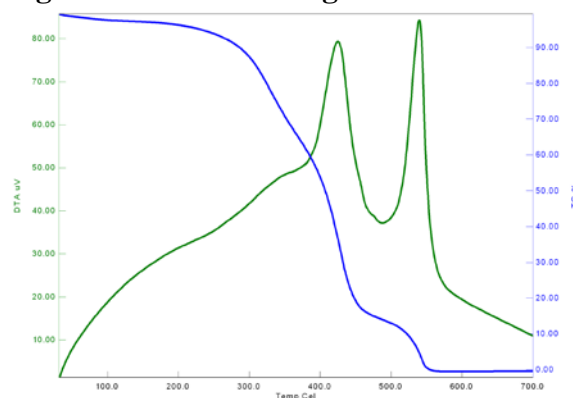


Fig 5. TG/DTA thermogram of PPHC

Figures 4 and 5 reveals the TG/DTA thermogram of polyesters PPEC and PPHC. In the TGA trace of polyesters PPEC and PPHC, the first mass loss upto 5% corresponds to dehydration and is complete around 250°C and the second stage decomposition takes place between 250°C and 500°C [15]. The weight loss around 100% in the last stage of thermal degradation may be due to the depolymerisation. Differential thermal analysis shows two isotherms a weak one around

400°C and a strong one around 550°C. The thermal studies showed that the synthesized polyesters were thermally stable.

3.4 SEM ANALYSIS

Scanning electron micrograph of PPEC and PPHC at x3000 magnification represented in figures 6 and 7 respectively. Surface sem images of the polyesters are homogeneously distributed which can be attributed to the well adhesion of the cells on the surface and so it meet the varying requirements of biomedical field [16, 17].

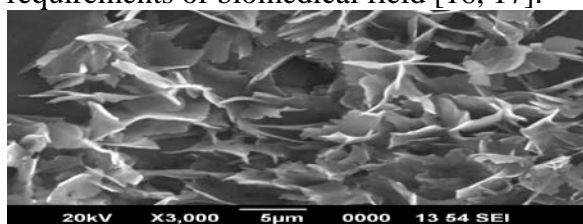


Fig 6. SEM image of PPEC before Soil Burial

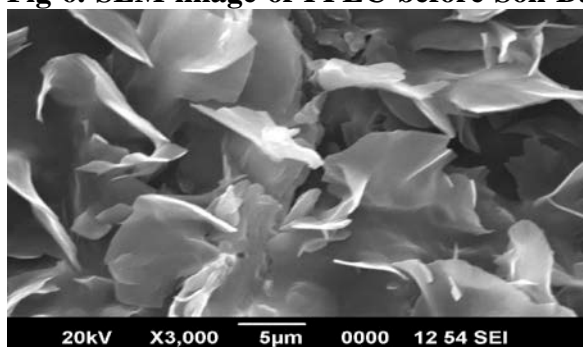


Fig 7. SEM image of PPHC before Soil Burial

3.5 SOLUBILITY STUDIES

The polyesters PPEC and PPHC are soluble in chloroform, carbon tetrachloride and sodium hydroxide. The prepared polyesters are insoluble in hexane, ethanol and acetone. The low sol content indicates the successful incorporation of crosslink network during post polymerization, since inter- molecular forces and strong hydrogen bonding exist in the polyesters as evidenced by FTIR analysis [10].

3.6 SOIL BURIAL METHOD

Scanning electron micrograph of PPEC and PPHC at x3000 magnification represented in figures 8 and 9 respectively. After two months of

soil burial, the sem images of the polyesters were unevenly distributed and also increases the gap when compared to fig 6 and 7. The polyesters PPEC degraded faster than PPHC. This was due to diols with decreasing number of methylene units faster the degradation rate [18, 19].

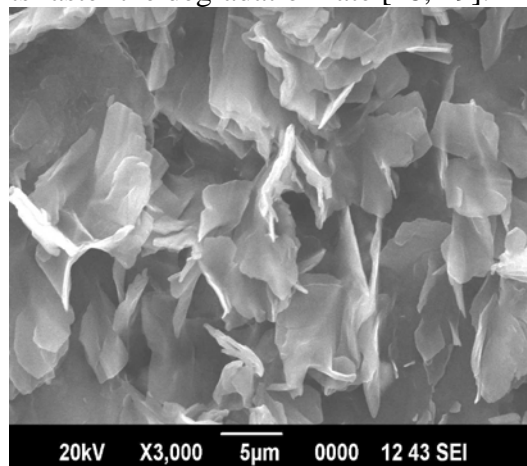


Fig 8. SEM image of PPEC after Soil Burial

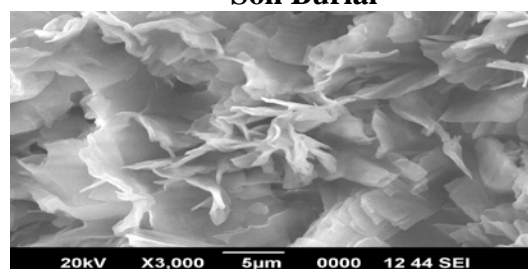


Fig 8. SEM image of PPHC after Soil Burial

3.6 MECHANICAL ANALYSIS

The mechanical properties of PPEC and PPHC were evaluated in Table1. The mechanical properties of amount of citric acid increased, the ultimate tensile strength and young's modulus increases and elongation at break decreases. This explains a strong hydrogen bonding between -COOH and -OH group contribute to the strength of the elastomer. From Table 1, the sample PPEC possess more elastomeric than PPHC due to higher percentage of elongation.

Table 1. Mechanical Properties of PPEC and PPHC (Ratio = polyol : prepolymer)

Name of the Polyesters	Ratio	Tensile Strength (MPa)	Elongation at Break (%)	Young's Modulus(MPa)
------------------------	-------	------------------------	-------------------------	----------------------

	1:1	0.823	59.7	1.378
PPEC	1:2	0.853	57.5	1.483
	1:2.5	0.876	56	1.564
	1:1	0.914	55.1	1.658
PPHC	1:2	0.952	52.8	1.803
	1:2.5	0.990	48.8	2.028

3.7 ANTIMICROBIAL ACTIVITY

Antimicrobial activity of polyesters do not show any activity against to test bacteria and fungi. This may be due to the presence of electron releasing group and cannot readily diffuse across the bacterial cell walls [20].

4.0 CONCLUSION

Citric acid-based biodegradable polyesters namely Poly(1,6-hexanediol-co-polyol citrate) and Poly(1,2-ethanediol-co-polyol citrate) were synthesized by melt condensation technique without using any catalysts. The thermal studies revealed that the elastomers were thermally stable. The thermal and mechanical properties of the polyesters showed that PPHC had better crosslinking than that of PPEC. The sem images shows that the samples can be used in tissue engineering due to their cell adhesion. The two copolyesters were found to be freely soluble in chloroform, carbon tetrachloride and sodium hydroxide. The prepared polyesters are insoluble in water, hexane, ethanol and acetone. Thus it is indicated that the choice of monomers influence the physical properties of the elastomers so it can potentially meet the requirements of various biomedical applications.

REFERENCES

[1] Darfizzi Derawi., and Jumat Salimon., Optimization on Epoxidation of Palm Olein by Using Performic Acid. E-Journal of Chemistry, 7, 1440 - 1448 (2010).
 [2] Yang J., Webb A.R., Hageman G., and Ameer G.A., Novel citric acid-based biodegradable

elastomers for tissue engineering. *Advanced Materials*, 16, 511 - 516 (2004).

[3] Nijst C.L., Bruggeman J.P., and Karp J.M., Synthesis and characterization of photocurable elastomers from poly(glycerol-co-sebacate). *Biomacromolecules*, 8, 3067 - 3073 (2007).

[4] Meier MAR., Metzger J.O., and Schubert U.S., Plant oil renewable resources as green alternatives in polymer science. *Chemical Society Reviews*, 36, 1788 - 1802 (2007).

[5] Patricia B. Malafaya., Gabriela A. Silva., and Rui L. Reis., Natural- origin polymers as carriers and scaffolds for biomolecules and cell delivery in tissue engineering applications. *Advanced Drug Delivery Reviews*, 59, 207 - 233 (2007).

[6] Khot S.N., Lascala J.J., Can E., Morye S.S., Williams G.I., and Palmese G.R.

Development and application of triglyceride-based polymers and composites. *Journal of Applied Polymer Science*, 82, 703 - 723 (2001).

[7] Gryglewicz S., Piechocki W., and Gryglewicz G. Preparation of polyol esters based on vegetable and animal fats. *Bioresource Technology*, 87, 35 - 39 (2003).

[8] Petrovic Z.S., Zlatanovic A., Snezana C.L., and Fiser S., Epoxidation of soybean oil in toluene with peroxyacetic and peroxyformic acids-kinetics and side reactions. *European Journal of Lipid science and Technology*, 104, 293 - 299 (2002).

[9] Lee L .Y., Wu S.C., Fu S.S., Zeng S.Y., Leong W.S., and Tan L.P., Biodegradable elastomer for soft tissue engineering. *European Polymer Journal*, 45, 3249 - 3256 (2009).

- [10] Djordjevic I., Choudhury N.R., Dutta N.K., and Kumar S., Synthesis and Characterisation of novel citric acid-based polyester elastomers. *Polymer*, 50, 1682 - 1691 (2009).
- [11] Xie D., Chen D., Jiang B., and Yang C., Synthesis of novel compatibilizers and their application in PP/nylon-66 blends. I. Synthesis and Characterisation. *Polymer*, 41, 3599 - 3607 (2009).
- [12] Song D.K., and Sung Y.K., Synthesis and Characterisation of biodegradable poly(1,4-butanediol succinate). *Journal of Polymer Science*, 56, 1381 - 1395 (1995).
- [13] Campanella A., Baltanas M.A., Capel-Sanchez M.C., Campos-Martin J.M., and Fierro J.L., Soybean oil epoxidation with hydrogen peroxide using an amorphous Ti/SiO₂ catalyst. *Green Chemistry*, 6, 330 - 334 (2004).
- [14] Guo A., Cho Y., and Petrovic Z.S., Structure and properties of halogenated and nonhalogenated Soy-based polyols. *Journal of Polymer Science. Part A. Polymer Chemistry*, 38, 3900 - 3910 (2000).
- [15] D'Antone S., Bignotti F., Sartore L., D'Amore A., Spagnoli G., and Penco M., Thermogravimetric investigation of two classes of block copolymers based on poly(lactic-glycolic acid) and poly(ϵ -caprolactone) or poly(ethylene glycol). *Polymer Degradation and Stability*, 74, 119 - 124 (2001).
- [16] Ma Z., Mao Z., and Gao C., Surface modification and property analysis of biomedical polymers used for tissue engineering. *Colloid Surface B*, 60, 137 - 157 (2007).
- [17] Russell S. D., and Daghljan C. P., Scanning electron microscopic observations on deembedded biological tissue sections: Comparison of different fixatives and embedding materials. *Journal of Electron Microscopy Technique*, 2, 489 - 495 (1985).
- [18] Ding T., Liu Q.Y., Shi R., Tian M., Yang J., and Zhang L.Q., Synthesis, characterization and invitro degradation study of a novel and rapidly degradable elastomer. *Polymer Degradation and Stability*, 91, 733 - 739 (2006).
- [19] Kang Y., Yang J., Khan S., Anissian L., and Ameer G.A., A new biodegradable polyester elastomer for cartilage tissue engineering. *Journal of Biomedical Material and Research*, 77A, 331-339 (2006).
- [20] Mangesh D.Teli., Ravindra D. Kale. Polyester nanocomposite fibers with antibacterial properties. *Advances in Applied Science Research*, 2, 491 - 502 (2011).