

Mechanical and thermal properties of biodegradable hydroxyapatite/poly(sorbitol sebacate malate) composites

Tham Weng Hong¹,
Mat Uzir Wahit^{1*},
Mohammed Rafiq Abdul Kadir²,
Wong Tuck Whye¹

Address:

¹ Enhanced Polymer Research Group, Department of Polymer Engineering, Faculty of Chemical Engineering, Universiti Teknologi Malaysia, Johor Bahru, 81310, Malaysia.

² Medical Implant Technology Group, Faculty of Biomedical Engineering & Health Sciences, Universiti Teknologi Malaysia, Johor Bahru, 81310, Malaysia.

* Corresponding author

Tel: +607 553 5909

Fax: +607 558 1463

e-mail: mat.uzir@cheme.utm.my

Abstract – In this project, novel hydroxyapatite (HAp)/poly(sorbitol sebacate malate) (PSSM) composites for potential application in soft tissue engineering were developed. The composites consist of the biodegradable polyester prepared from sorbitol, sebacic acid, malic acid and various amount of HAp (5, 10, and 15 wt%). The effects of different weight percents of HAp on the properties of composites were studied. Fourier transform infrared (FT-IR) spectroscopy was performed to analyze chemical interactions between HAp/PSSM. Tensile tests and differential scanning calorimetry (DSC) were conducted to evaluate the mechanical and thermal properties of HAp/PSSM composites. Tensile testing on HAp/PSSM composites showed that their mechanical properties improved with increasing concentration of HAp. The Young's modulus and tensile strength of the composites ranged from 16.20 ± 1.73 to 23.96 ± 2.56 MPa and 626.96 ± 81.04 to 1026.46 ± 105.12 MPa, respectively. The glass transition temperature (T_g) of all the samples was slightly higher than room temperature.

Keyword: *Biodegradable, Composites, Hydroxyapatite, Mechanical properties, Tissue engineering*

1. Introduction

Synthetic biodegradable polymers as biomaterials have been one of the research focuses in the last decade. Biodegradable polymers offer advantages over ceramic- and metallic-based biomaterials as they can be manipulated to exhibit a wide range of mechanical, degradation and physiochemical properties (Pasupuleti et al., 2011). In particular, biodegradable aliphatic polyesters have recently received attention for their potential use in biomedical applications due to their degradability and biocompatibility (Gunatillake et al., 2003). Aliphatic polyesters can be synthesized from monomers endogenous to human metabolism and in the other hand, degraded via hydrolysis in aqueous medium into non-toxic carboxylic acid and hydroxyl group short chain oligomers or monomers (Gunatillake et al., 2003).

Hydroxyapatite (HAp) ($\text{Ca}_{10}(\text{PO}_4)_6(\text{OH})_2$), which is a form of calcium phosphate has been widely investigated for both dental and orthopedic applications due to their outstanding biocompatibility and osteoconduction (Jayabalan et al., 2010, Nejati et al., 2008, Sadat-Shojai et al., 2010). However, the brittleness of calcium phosphate and formation of microcracks induced during harsh processing conditions limited the application of hydroxyapatite to non-load bearing parts of the skeleton (Burdick et al., 2011, Chung et al., 2011). In order to overcome these limitations, many research groups have combined biodegradable polyesters with HAp to form composite (Rizzi et al., 2001, Sharifi et al., 2011). Until now, HAp has been incorporated with synthetic polymers such as poly(L-lactide) and poly(lactic-co-glycolide) (Russias et al., 2006, Zhang et al., 1999), poly(ϵ -caprolactone) (PCL) (Choi et al., 2004), polyhydroxyalkanoates (Misra et al., 2006), poly(1,8-octanediol citrate) (Chung et al., 2011, Qiu et al., 2006), and poly((1,2-propanediol-sebacate)-citrate)

(Lei et al., 2009). Findings have shown that under certain conditions, incorporation of HAp particles can improve the mechanical properties of the polyesters.

Bruggeman et al. (2008) had recently described the synthesis and characterization of a biodegradable polyester elastomers without the present of catalysts or solvent, referred to as poly(sorbitol sebacate) (PSS), for soft tissue engineering application. The mechanical properties and degradation rates of these elastomers can be altered by varying the type of polyols and the synthesis conditions. Furthermore, synthesis method for PSS is very simple and does not require expensive raw materials. However, PSS exhibited low tensile strength and modulus, which limit their applications where higher load-bearing is required (Bruggeman et al., 2008). In order to improve the mechanical properties of PSS, multifunctional monomer such as citric acid or tartaric acid has been incorporated to act as secondary crosslink agent. The resulting polyesters, poly(sorbitol citrate sebacate) (PSCS) and poly(sorbitol tartarate sebacate) (PSTS) showed significant improvement in mechanical properties (Pasupuleti et al., 2011).

Herein, we report the synthesis and characterization of hydroxyapatite/poly(sorbitol sebacate malate) (HAp/PSSM) composites. The monomers including sorbitol (Bruggeman et al., 2008) and sebacic acid (Wang et al., 2002) are endogenous to human metabolism and polyester based on malic acid (Wan et al., 2007) were found to be biocompatible. The preparation of the composites was carried out by catalyst-free polycondensation, which can avoid the toxicity induced by catalyst or initiator during polymerization reaction that would reduce the biocompatibility of the composites. We hypothesized that the mechanical properties of PSS can also be improved after adding a multifunctional monomer, malic acid into the polymer. Moreover, the incorporation

hydroxyapatite is expected to further increase the mechanical properties of the composites. The tensile and thermal properties of the composites were evaluated.

2. Research methodology

2.1. Synthesis and characterization of HAp/PSSM composites

Sorbitol (S), sebacic acid (SA), and hydroxyapatite (HAp) were purchased from Sigma Aldrich (Malaysia). Malic acid (MA) was purchased from R & M Chemicals (Malaysia) and tetrahydrofuran (analytical grade) was purchased from Merck (Malaysia). All chemicals were used as received. The synthesis of HAp/PSSM composites was adapted from a technique that has previously been described (Lei et al., 2009, Qiu et al., 2006). Briefly, equimolar amounts of the polyol and diacids (S:SA:MA = 1:1:1) were mixed with various amount of HA (5, 10, 15 wt%) in a reaction flask. The mixture was melted under stirring at 150-155 °C under a constant flow of nitrogen gas. Following melting, the reaction was continued for 1 h to create the PSSM prepolymer with HAp. The prepolymer was cast into PTFE mold with ~1 mm thickness and kept in an oven at 110°C for 2 days for post-curing to obtain HAp/PSSM composites. The composites with 0, 5, 10 and 15 wt% of HAp were named as C0, C5, C10, and C15, respectively.

2.2. Characterization of HAp/PSSM composites

Fourier transform infrared (FTIR) spectroscopy was carried out on a Perkin Elmer Spectrum One spectrometer (UTM, Malaysia) to analyze the chemical bonds of prepolymers and the composites. The samples were scanned in spectrometer over the range of 4000-600 cm^{-1} . The glass transition temperatures (T_g) of cured composites were characterized using a

differential scanning calorimeter (Mettler-Toledo DSC822^o/400, SIRIM, Malaysia) operating in nitrogen atmosphere. The samples were heated from -50°C to 200°C at 10°C/min, cooled from 200°C to -50°C at 10°C/min and subsequently heated for second cycle up to 200°C at 10°C/min.

The sol contents (low molecular weight of polyesters that can dissolve in tetrahydrofuran) and the swelling degrees of the composites were simultaneously tested from the following methods (Liu et al., 2009a, Liu et al., 2009b). The small square samples (1 cm x 1cm with 1 mm in thickness) were weighted (W_1) and soaked in tetrahydrofuran (20mL). Samples were taken out 24 h, the solvents on its surface were absorbed using filter papers and the weights W_2 were recorded. Then the sample was dried completely to the final weight of W_3 in an oven. Sol content was calculated as $S = (W_1 - W_3)/W_1 \times 100$, and swelling degree was reported as $Q = (W_2 - W_3)/W_3 \times 100$. The average values were taken from three samples for each composite.

Tensile test was conducted at room temperature on Lloyd tensile LRX testing machine (UTM, Malaysia) equipped with 2.5kN load cell. Briefly, the dumbbell-shaped samples according to ASTM standard D638 (26 x 4 x 1.5 mm, length x width x thickness) were prepared and pulled at a rate of 50 mm/min. For all the composites, five specimens were tested and the values were averaged.

3. Results and Discussion

3.1. Characterization of chemical structure

The aliphatic polyester, PSSM and HAp/PSSM composites were successfully prepared via polycondensation without the presence of catalyst and the reaction scheme for PSSM was shown in Fig 1. The prepolymers and composites of HAp/PSSM were characterized by FTIR. Fig. 2 shows the FTIR spectra for HAp, prepolymer C0, prepolymer C5, prepolymer C10, and prepolymer C15, while the spectra for C0, C5, C10 and C15 were shown in Fig.3. The peaks corresponding to the HAp structure include the broad peaks at 1091 cm^{-1} and 1039 cm^{-1} were assigned to vibration of phosphate group, the peaks at 1629 and 3435 cm^{-1} were corresponded to the hydroxyl group in the adsorbed water, while the double peak at 1414 and 1448 cm^{-1} was attributed to the carbonated impurities in the structure of HAp (Rehman et al., 1997, Sadat-Shojai et al., 2010). The intense peak within $1695\text{-}1740\text{ cm}^{-1}$ in the spectrums of prepolymers and composites were assigned to carbonyl (C=O) groups, which proves the presence of ester bonds and carboxylic groups. The carbonyl peak in the composites' spectra are sharper compare to the prepolymers' spectra, this demonstrated that most of the diacids monomers had reacted to form polyester. Also, there is a small shift to the right (1730 cm^{-1}) in carbonyl peak of C5, C10, and C15 compare to sample C0, this changes may be attributed to the formation of hydrogen bonding between C=O groups of PSSM and the surface hydroxyl (-OH) group of HAp. The peaks at 2931 and 2850 cm^{-1} were assigned to the methyl groups. The broad peak at 3450 cm^{-1} in the spectrums of prepolymers should be assigned to hydroxyl groups on the unreacted monomers, terminal hydroxyl groups in the PSSM matrix and the hydroxyl groups on the surface of HAp. On the other hand, the stretches observed in the composites' spectrum at 3450 cm^{-1} should be attributed to hydrogen bonded hydroxyl groups

and unreacted hydroxyl groups remained in the polyester molecular chains (originating from monomers with multifunctional groups).

3.2. Glass transition of HAp/PSSM

The thermal data for the composites were listed in Table 1. The glass transition temperature (T_g) for HAp/PSSM composites ranged from 39.83 to 42.61°C. The values indicate that the composites are stiff at room temperature. Glass transition temperature usually reflect the ability of polymer chains to move freely which are normally affected by chemical crosslink, hydrogen bonding and physical interaction between polymer matrix and HAp particles. Herein, increasing HAp loading cause the T_g of the composites to become higher. The presence of HAp particle in the PSSM hindered the formation of random crosslink network in the matrix, which will lower the T_g; In contrast, the presence of malic acid as secondary crosslink agent and HAp particles will also hindered the mobility of the polymer chains, which could increase the T_g (Lei et al., 2009). In this situation, the effect of the low mobility of the polymer chains predominates and thus, the glass transition temperature increased.

3.3. Sol contents and swelling degrees of HAp/PSSM composites

The results from swelling tests showed that the composites were composed of the sols (can dissolve in tetrahydrofuran) and the gels (cannot dissolve in tetrahydrofuran). A small part of sols which can be dissolved in some solvents often appeared in polyester matrix, and these sols usually act as plasticizers and contribute to the formation of hydrogen bonding (Liu et al., 2009a). Generally, high sol content indirectly means lower polymerization degree and

crosslink density. Listed in Table 2, the sol contents and swelling degrees ranged from 10.05 to 14.25% and 81.99 to 127%, respectively. The swelling degrees decreased with the increase of HAp weight percent, mainly because of the volume effect of the increased HAp particles and more physical adsorptions. The sol content of composites C5 and C10 was slightly higher than C0 (pure PSSM polymer). This may be due to many sols enclosed by the HAp particles. This hindered the curing of low molecular weight polymer chain cured into the polyester network. This is in agreement with previous finding reported by (Liu et al., 2009a).

3.4. Mechanical properties

Fig. 4 and Table 1 show the tensile stress-strain curves and test results for HA composites containing 0, 5, 10, and 15wt%, respectively. Previously, PSS elastomer reported by Bruggeman *et al.* (2008) exhibited Young's modulus, tensile strength, and ultimate elongation of 0.37 MPa, 0.57 MPa, and 192%, respectively. When malic acid was added as secondary crosslink agent to form PSSM, the mechanical properties of the polymer increase significantly. PSSM polymers achieved a Young's modulus of 626.96 MPa, tensile strength of 16.20 and elongation at break of 49.04%. Malic acid reacted with free hydroxyl group in sorbitol to form polyester chains and random crosslinking within the polymer network which result in a higher degree of crosslinking and thus, a stiffer thermoset was obtained.

The tensile strength and modulus of the composites increased gradually with increase HAp loading, ranged from 16.20 to 23.96 MPa and 626.96 to 1026.46 MPa, respectively. Meanwhile, the presence of HAp reduced the flexibility of the composites as the elongation at break decreased from 49.04 to 10.10% when HAp content increased from 0 to 15 wt%. From the result, it was obvious that the mechanical properties of the polymer after incorporation of

malic and HAp particles had increase and can cover many biomedical applications. The high stiffness allows HAp/PSSM could be used in bone tissue engineering such as repairs/replacements for cartilage (0.7-15.3 MPa), ligament (65-541 MPa), tendon (143-2310 MPa), and cancellous bone (50-500 MPa) (Burdick et al., 2011). It is also possible to tune the mechanical properties of the composites by varying the reaction time and temperature, monomer feed ratio, particle size of HAp and choice of diol and/or diacids.

4. Conclusion

The HAp/PSSM composites were successfully developed in this project. All these raw materials, such as, sorbitol, sebacic acid, malic acid and hydroxyapatite are biocompatible to human body. The preparation of the composites is relatively simple as it does not involve the use of harsh solvent and catalyst. The incorporation of HAp particle improved the mechanical properties of PSSM polymers.

Acknowledgement

This work is supported by Universiti Teknologi Malaysia (UTM) and funded by Ministry of Science, Technology and Innovation for E-Science grant (Vote No: 79400). All these financial supports are highly grateful.

References

- Bruggeman, J. P., Bettinger, C. J., Nijst, C. L. E., Kohane, D. S. and Langer, R. 2008. Biodegradable Xylitol-Based Polymers, *Adv Mater* 20. 1922-27.
- Burdick, J. A. and Mauck, R. L. 2011. *Biomaterials for Tissue Engineering Applications: A Review of the Past and Future Trends*, 1 ed, SpringerWienNewYork, Germany.
- Choi, D., Marra, K. G. and Kumta, P. N. 2004. Chemical synthesis of hydroxyapatite/poly(ϵ -caprolactone) composites, *Materials Research Bulletin* 39. 417-432.
- Chung, E. J., Sugimoto, M. J. and Ameer, G. A. 2011. The role of hydroxyapatite in citric acid-based nanocomposites: Surface characteristics, degradation, and osteogenicity in vitro, *Acta Biomaterialia* 7. 4057-4063.
- Gunatillake, P. A. and Adhikari, R. 2003. Biodegradable synthetic polymers for tissue engineering, *European Cells and Materials* 5. 1-16.
- Jayabalan, M., Shalumon, K. T., Mitha, M. K., Ganesan, K. and Epple, M. 2010. Effect of hydroxyapatite on the biodegradation and biomechanical stability of polyester nanocomposites for orthopaedic applications, *Acta Biomaterialia* 6. 763-775.
- Lei, L., Li, L., Zhang, L., Chen, D. and Tian, W. 2009. Structure and performance of nano-hydroxyapatite filled biodegradable poly((1,2-propanediol-sebacate)-citrate) elastomers, *Polymer Degradation and Stability* 94. 1494-1502.
- Liu, Q., Wu, J., Tan, T., Zhang, L., Chen, D. and Tian, W. 2009a. Preparation, properties and cytotoxicity evaluation of a biodegradable polyester elastomer composite, *Polymer Degradation and Stability* 94. 1427-1435.
- Liu, Q., Tan, T., Weng, J. and Zhang, L. 2009b. Study on the control of the compositions and properties of a biodegradable polyester elastomer *Biomedical Materials* 4. 9.
- Misra, S. K., Valappil, S. P., Roy, I. and Boccaccini, A. R. 2006. Polyhydroxyalkanoate (PHA)/Inorganic Phase Composites for Tissue Engineering Applications, *Biomacromolecules*

7. 2249-2258.

Nejati, E., Mirzadeh, H. and Zandi, M. 2008. Synthesis and characterization of nano-hydroxyapatite rods/poly(l-lactide acid) composite scaffolds for bone tissue engineering, *Composites Part A: Applied Science and Manufacturing* 39. 1589-1596.

Pasupuleti, S. and Madras, G. 2011. Synthesis and degradation of sorbitol-based polymers, *Journal of Applied Polymer Science* 121. 2861-2869.

Qiu, H., Yang, J., Kodali, P., Koh, J. and Ameer, G. A. 2006. A citric acid-based hydroxyapatite composite for orthopedic implants, *Biomaterials* 27. 5845-5854.

Rehman, I. and Bonfield, W. 1997. Characterization of hydroxyapatite and carbonated apatite by photo acoustic FTIR spectroscopy, *Journal of Materials Science: Materials in Medicine* 8. 1-4.

Rizzi, S. C., Heath, D. J., Coombes, A. G. A., Bock, N., Textor, M. and Downes, S. 2001. Biodegradable polymer/hydroxyapatite composites: Surface analysis and initial attachment of human osteoblasts, *Journal of Biomedical Materials Research* 55. 475-486.

Russias, J., Saiz, E., Nalla, R. K., Gryn, K., Ritchie, R. O. and Tomsia, A. P. 2006. Fabrication and mechanical properties of PLA/HA composites: A study of in vitro degradation, *Materials Science and Engineering: C* 26. 1289-1295.

Sadat-Shojai, M., Atai, M., Nodehi, A. and Khanlar, L. N. 2010. Hydroxyapatite nanorods as novel fillers for improving the properties of dental adhesives: Synthesis and application, *Dental Materials* 26. 471-482.

Sharifi, S., Shafieyan, Y., Mirzadeh, H., Bagheri-Khoulenjani, S., Rabiee, S. M., Imani, M., Atai, M., Shokrgozar, M. A. and Hatampoor, A. 2011. Hydroxyapatite scaffolds infiltrated with thermally crosslinked polycaprolactone fumarate and polycaprolactone itaconate, *Journal of Biomedical Materials Research Part A* 98A. 257-267.

Wan, Y., Feng, G., Shen, F. H., Balian, G., Laurencin, C. T. and Li, X. 2007. Novel

Biodegradable Poly(1,8-octanediol malate) for Annulus Fibrosus Regeneration, *Macromolecular Bioscience* 7. 1217-1224.

Wang, Y., Ameer, G. A., Sheppard, B. J. and Langer, R. 2002. A tough biodegradable elastomer, *Nat Biotech* 20. 602-606.

Zhang, R. and Ma, P. X. 1999. Poly(α -hydroxyl acids)/hydroxyapatite porous composites for bone-tissue engineering. I. Preparation and morphology, *Journal of Biomedical Materials Research* 44. 446-455.

Table 1. Mechanical and thermal properties of HAp/PSSM composites

Sample	Tensile strength at yield/MPa	Tensile Modulus/MPa	Elongation at break/%	Tg (°C)
C0	16.20 ± 1.73	626.96 ± 81.04	49.04 ± 4.30	39.83
C5	19.74 ± 1.71	710.56 ± 100.34	36.06 ± 6.70	40.71
C10	22.13 ± 4.73	875.42 ± 157.58	27.04 ± 3.50	41.47
C15	23.96 ± 2.56	1026.46 ± 105.12	10.10 ± 2.10	42.61

Table 2 Sol content (S) and swelling degree (Q) of the composites with different weight percents of HAp

HAp (wt%)	Q (%)	S (%)
0	127.72	12.29
5	123.07	14.25
10	100.04	13.24
15	81.99	10.05

Fig. 1 Synthesis of poly(sorbitol sebacate malate) polymer

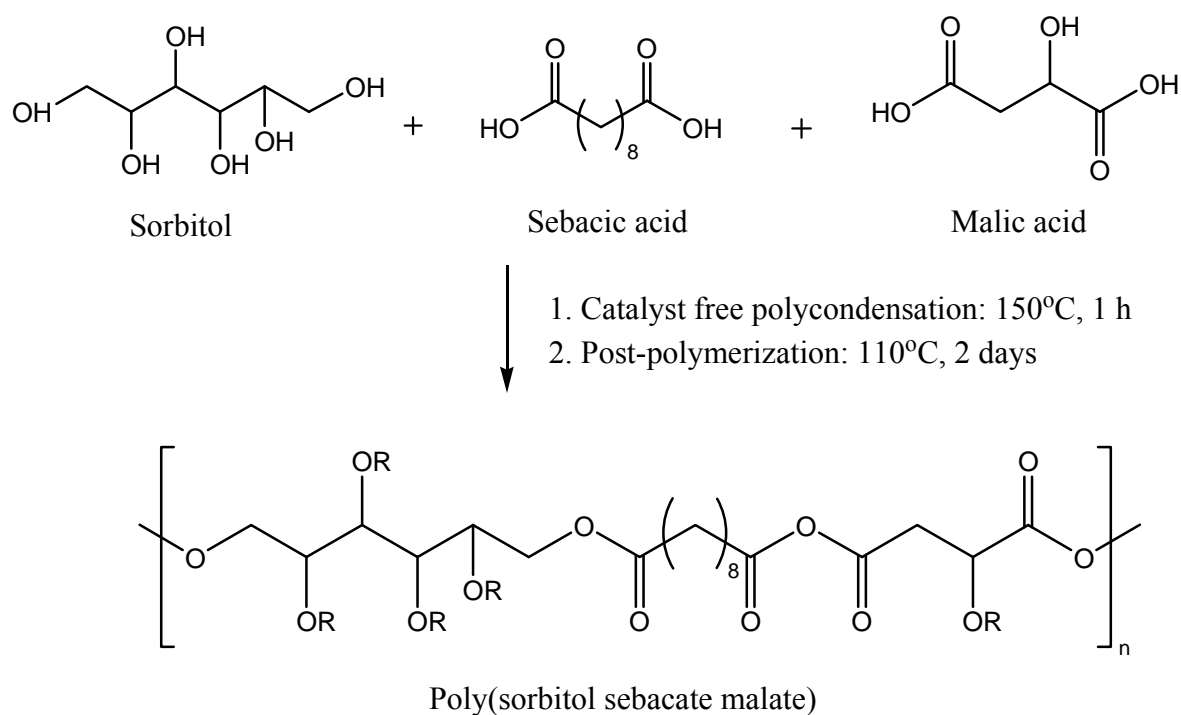


Fig. 2 FTIR spectra for HAp, prepolymer C0, prepolymer C5, prepolymer C10, and prepolymer C15

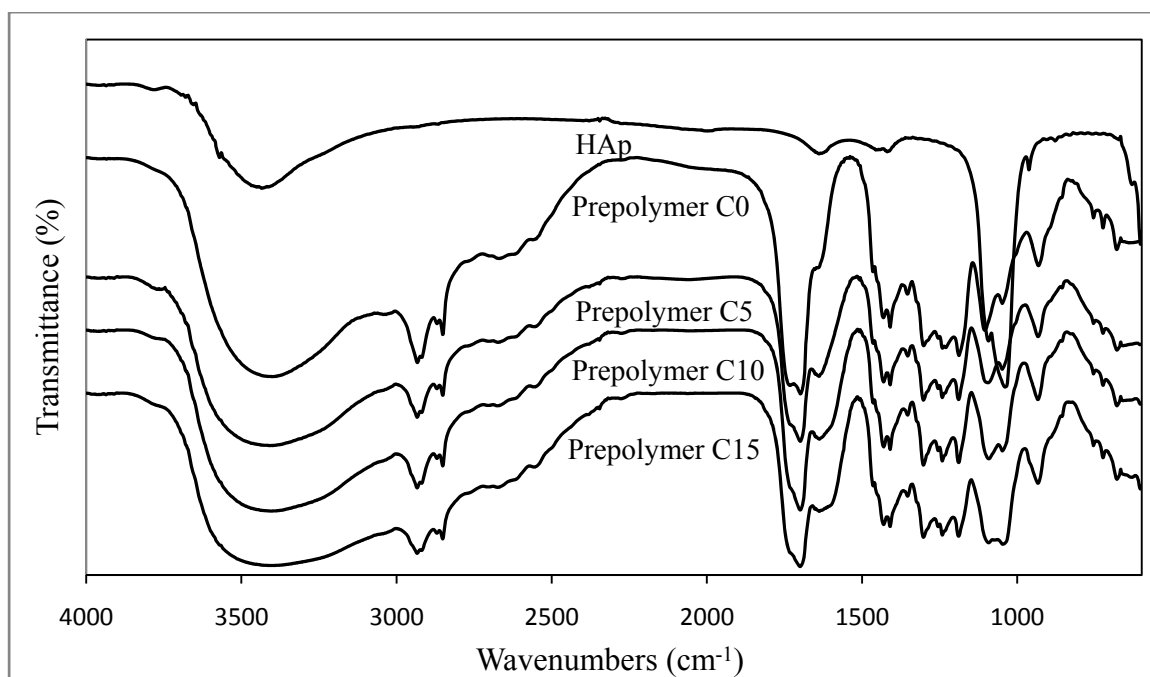


Fig. 3 FTIR spectra for C0, C5, C10, and C15

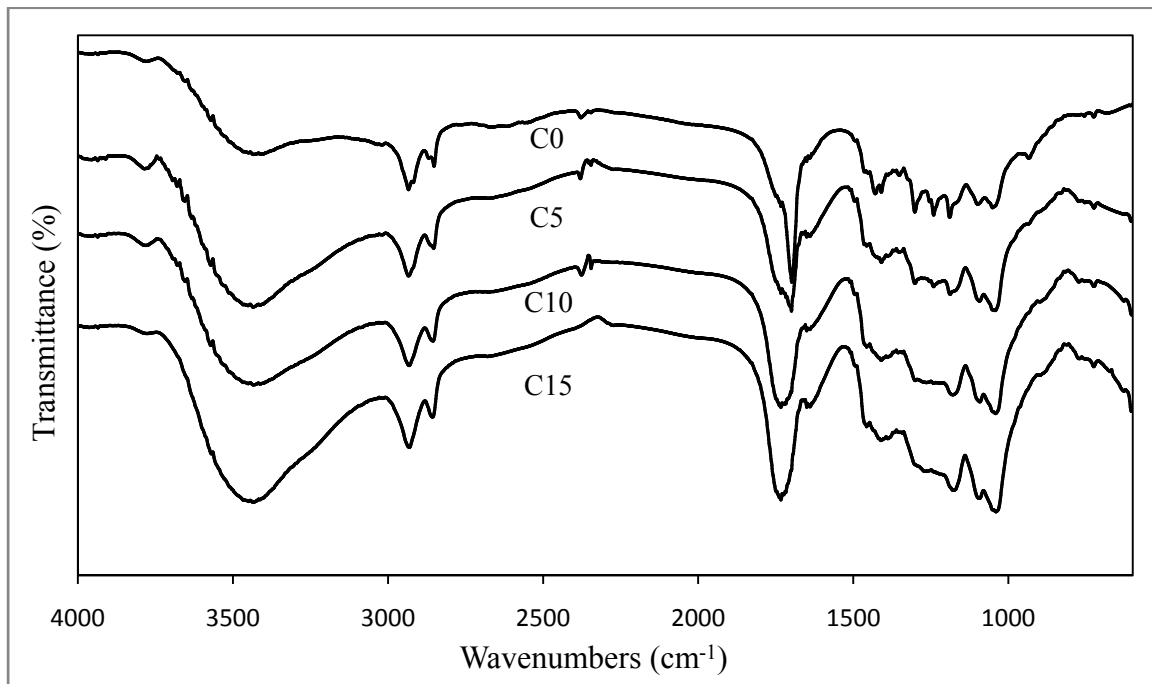


Fig. 4. Typical tensile stress versus strain curves for composites (C0, C5, C10, and C15)

