

Electrospun PLA/PCL Fibers with Tubular Nanoclay: Morphological and Structural Analysis

Hazim J. Haroosh,¹ Deeptangshu S. Chaudhary,¹ Yu Dong²

¹Department of Chemical Engineering, Curtin University, Perth, WA 6845, Australia

²Department of Mechanical Engineering, Curtin University, Perth, WA 6845, Australia

Received 17 March 2011; accepted 9 August 2011

DOI 10.1002/app.35448

Published online 28 November 2011 in Wiley Online Library (wileyonlinelibrary.com).

ABSTRACT: Biodegradable polymers are good candidates for a wide range of applications in tissue engineering and drug delivery because of their biocompatibility, their degradation, mechanical properties, and offer a sustained release of encapsulated drugs. The electrospun polymer nanofibrous materials can be used as carriers for hydrophobic and hydrophilic drugs. This research work focused on poly(lactic acid) (PLA) and blends of PLA with poly(ϵ -caprolactone) (PCL) that are reinforced with different concentrations of halloysite nanotubes (HNTs) and various cosolvents for electrospinning including chloroform : acetone, chloroform : methanol, and dichloromethane (DCM) : *N,N*, dimethylformamide (DMF). The fibers produced from the DCM : DMF system without HNTs were more uniform resulting in smaller fiber diameters as compared to the chloroform : methanol system due to the increased solution

conductivity. The addition of HNT nanoparticles produced electrospun fibers with large diameters because the viscosity of the solution increased. Cosolvent was important in determining fiber diameters because it strongly influenced the solution viscosity and conductivity. HNTs had relatively small impact on the growth of a crystalline morphology in PCL–HNT composites. The solvent mixture of chloroform : methanol was better for PLA-based systems since PLA was found to have slightly higher crystallinity and larger enthalpy value indicating the improved structural orderness in the PLA polymer matrix. © 2011 Wiley Periodicals, Inc. *J Appl Polym Sci* 124: 3930–3939, 2012

Key words: electrospinning; nanocomposites; poly (lactic acid); poly (ϵ -caprolactone); X-ray diffraction; differential scanning calorimetry

INTRODUCTION

Electrospinning is a multipurpose polymer processing technique in which a stream of a melt or polymer solution is connected to a high electric field, resulting in formation of nanoscaled fibers. It offers a promising way to fabricate continuous fibers with diameters ranging from nano- to microscaled level.¹ The electrospun nonwoven fabrics consisting of ultrafine fibers were found to have wide applications such as separation filters, carbonaceous materials,¹ and scaffolding for tissue engineering in biomedical fields, tissue repair substitutes, and carriers for drug delivery platform due to their high specific surface area and porous structure.²

Polymers have been commonly used in several applications in the pharmaceutical industry as carrier for tissue engineering and drug delivery. Till now, electrospinning has been used for the fabrication of a numerous biodegradable polymers for drug delivery, such as poly (lactic acid) (PLA), poly

(ϵ -caprolactone) (PCL), poly (glycolic acid) (PGA), poly (lactide-*co*-glycolide) (PLGA), and polyurethane (PU) as well as natural proteins including collagen, gelatin, and elastin.³

High molecular weight poly (lactide) (PLA) provides better mechanical strength and integrity to the scaffold⁴ and thus are promising for clinical uses because the acidic environment induced by the degradation of the polymer helps to reduce the bacteria growth and promote epithelization. This is mainly due to their biocompatibility and the flexibility they offer in terms of their degradation profiles and mechanical properties.² Additionally, Poly(ϵ -caprolactone) (PCL) is well known for its slow biodegradability, high biocompatibility, and good drug permeability.^{5,6} Halloysite nanotubes (HNT) are clays belonging to the kaolinite family. HNT is in tubular shape with lengths in the range of 1–3 μm and diameters in size of 100–300 nm. It has been recently reported that owing to the hydroxides groups in the HNT structure, the incorporation of HNT within PLA polymer can resist the negative effect of PLA acidic environment.⁷ In addition, many solvents exist for successful electrospinning, and therefore it is essential to choose an appropriate solvent system that should be able to improve solution parameters and allow polymers to spin with good properties.^{8–10}

Correspondence to: D. S. Chaudhary (d.chaudhary@curtin.edu.au).

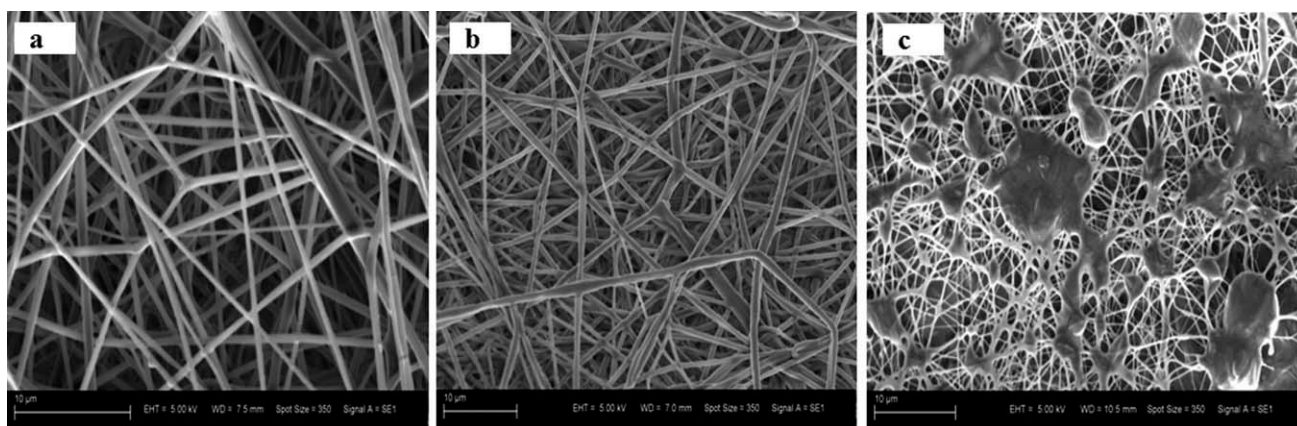


Figure 1 SEM micrographs of electrospun PLA : PCL fibers by using DCM : DMF as a solvent and containing various PLA : PCL blend ratios by weight (a) 1 : 0, (b) 3 : 1, and (c) 1 : 1. The scale bar in the micrograph is 10 μm .

The focus on this study is to understand the effect of the cosolvents and the addition of HNT nanoparticles in PCL/PLA blend system. Because PCL is widely used as long-term implantable devices, blending with PLA and HNT can deliver a new drug delivery system with sustained release property for a range of applications in tissue engineering and drug delivery. For this reason, this study will investigate the electrospun fiber diameters of biopolymer blend of high molecular weight of PLA with low molecular weight of PCL.

EXPERIMENTAL

Materials

Poly (ϵ -caprolactone) PCL ($M_n = 33,000 \text{ g mol}^{-1}$) was purchased from Daicel Chemical Industries, Japan, poly lactide acid (PLA) 3051D, $M_n = 93,500 \text{ g mol}^{-1}$, $T_g = 65.50^\circ\text{C}^{11}$ was supplied by NatureWorks USA, and halloysite nanotubes (HNT) from Imerys tableware Limited, New Zealand, while dichloromethane (DCM), dimethylformamide (DMF), chloroform, and methanol were purchased from Sigma-Aldrich, used without any purification.

Electrospinning

Electrospinning was carried out using 8% wt/v PLA solution mixed with 15% wt/v PCL at different ratios of 1 : 0, 3 : 1, and 1 : 1 with three solvents, namely DCM : DMF at 3 : 1, chloroform : methanol at 2 : 1 and chloroform : acetone at 2 : 1. The HNT suspension was added at 1% wt/v and 2% wt/v to the polymer solution for all solvents and was homogenized for 30 min under ultrasonication. For electrospinning process, the solutions were transferred to a 10-mL syringe pump with 20-G needles. The flow rate of polymer solution was 2 mL h^{-1} , and the applied positive voltage was in the range of

25–28 kV. The resulting fibers were collected on a flat aluminum foil. The distance between the needle tip and the target was 13–15 cm. The thickness of the fiber mat ranged from 300 to 450 μm .

Viscosity of solutions

The viscosity of solution was measured by using Visco 88—a portable viscometer from Malvern instruments (UK), with built-in temperature sensor, and supplied with a double gap measuring geometry to provide extra sensitivities when measuring low viscosity fluids.

Scanning electron microscopic (SEM) studies

The morphology of electrospun nanofibers was studied by an EVO 40XVP scanning electron microscope

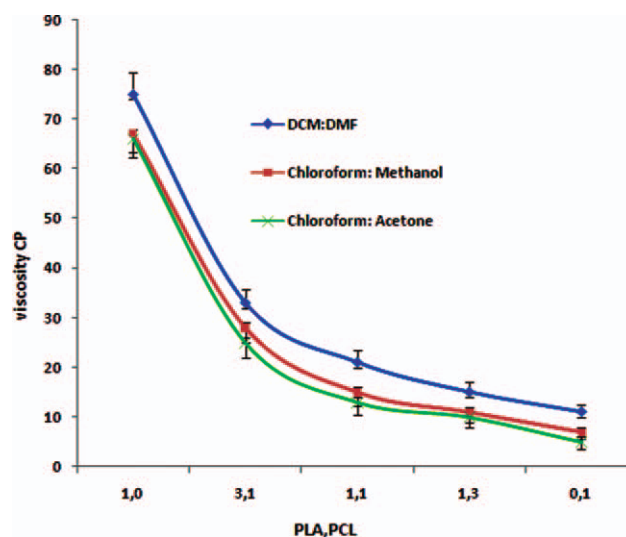


Figure 2 Viscosity of different percentages of PLA : PCL solutions dissolved in the mixture of DCM : DMF, chloroform : methanol, and chloroform : acetone. [Color figure can be viewed in the online issue, which is available at [wileyonlinelibrary.com](http://www.interscience.wiley.com).]

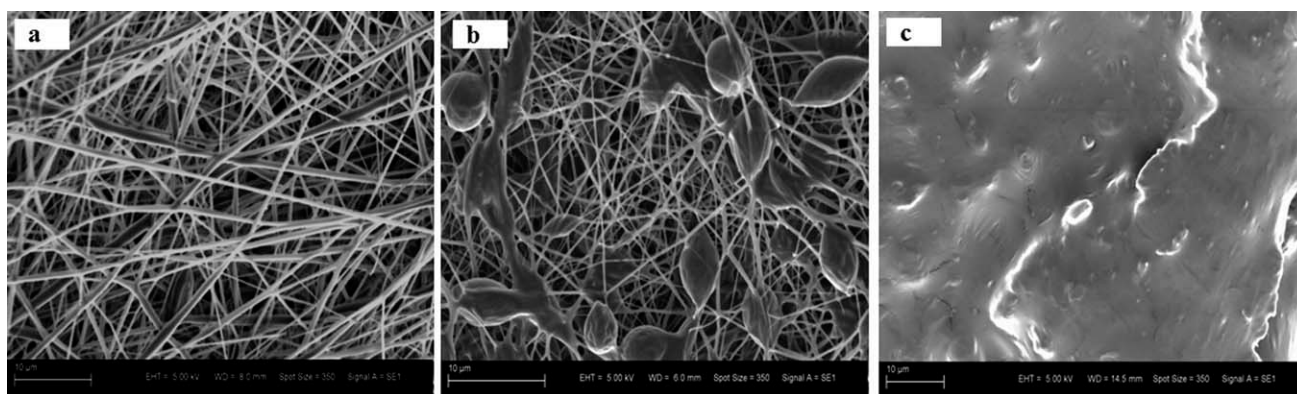


Figure 3 SEM micrographs of electrospun PLA : PCL fibers by using chloroform : methanol as a solvent and containing various PLA : PCL blend ratios by weight (a) 1 : 0, (b) 3 : 1, and (c) 1 : 1. The scale in the micrograph is 10 μm .

(Germany) and the accelerating voltage was set at 5 kV. Before SEM observation, the samples were sputter-coated with platinum. Fiber diameter was calculated from the SEM images by using an in-house developed scanning program, which analyzes a minimum of 50 fibers from a scanned SEM image, and includes a statistical deviation of 15%.

X-ray diffraction (XRD)

A total of 11 samples were chosen from the complete set of electrospun fiber samples to investigate the crystallinity and thermal properties which would highlight the interaction between the nanoclay and the polymer matrix. These samples were identified based on a Design of Experiment (DoE) analysis using commercial statistical software, MINITAB

LLC, version 3.2. XRD measurements of the prepared samples were performed in a Bruker Discover 8 diffractometer (Germany) operating at 40 kV and 40 mA using Cu $K\alpha$ radiation that was monochromatized with a graphite sample monochromator with a 2θ range from 5° to 30° at a scanning rate of $0.05^\circ \text{ s}^{-1}$. The basal spacing of the silicate layered was determined from the Bragg's equation, $\lambda = 2d\sin\theta$ (where θ is the diffraction position and λ is the wavelength). Igor software package (Wavemetrics, Lake Oswego, Oregon) was used for curve fitting. Composite crystallinity was calculated based on a peak fitting procedure. The fitted coefficients were calculated based on minimized values of Chi-square using the Levenberg–Marquardt algorithm. Each fitting procedure was repeated eight times with different initial inputs to ensure the data reproducibility.

TABLE I
Dielectric Constant for Solvents

	DMF	Methanol	Acetone	DCM	Chloroform
Dielectric constant	38.3	33	21	9.1	4.8

Differential scanning calorimetry (DSC)

DSC was performed using a DSC6000 Perkin Elmer (USA) with Cryofill liquid nitrogen cooling system. Approximately 10 mg of fibers were sealed in aluminum pans and their thermal behavior was analyzed

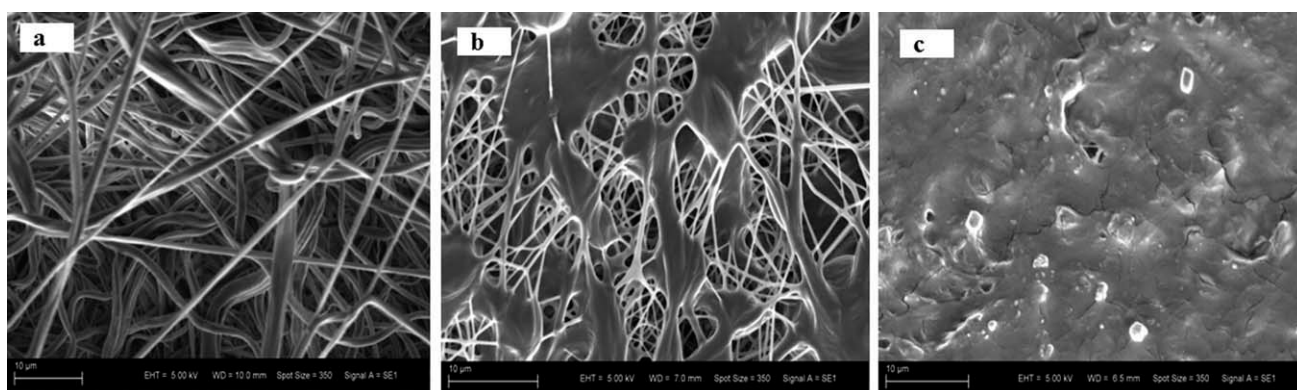


Figure 4 SEM micrographs of electrospun PLA : PCL fibers by using chloroform : acetone as a solvent and containing various PLA : PCL blend ratios by weight (a) 1 : 0, (b) 3 : 1, and (c) 1 : 1. The scale in the micrograph is 10 μm .

TABLE II
Summaries of the all Average Fiber Diameters (in nm)
for all Structures

Cosolvents	PLA : PCL (1 : 0)	PLA : PCL (3 : 1)	PLA : PCL (1 : 1)
DMF : DCM	450 (± 25)	490 (± 30)	250 (± 40)
Chloroform : methanol	510 (± 25)	325 (± 40)	NA
Chloroform : acetone	570 (± 30)	375 (± 45)	NA

during heating and cooling between 30 and 180°C with a ramp rate of 10°C min⁻¹.

RESULTS AND DISCUSSIONS

Without HNT loading

Figure 1(a) shows that using PLA in DCM : DMF led to homogenous fibers with the average diameter of 450 nm with a large variation in fiber diameters. Increasing the amount of PCL to PLA (1 : 3) resulted in fibers with average diameter of 490 nm with maximum and minimum diameters of 800 and 230 nm, respectively. Moreover, increasing the percentage of PCL (1 : 1) caused beads and inhomogeneity in structures with a decrease in diameter to 250 nm with maximum and minimum diameters of 425 and 130 nm, respectively as shown in Figure 1(c). This

indicates that by lowering the solution viscosity, the fiber diameter can be reduced, but to a great extent inhomogeneity occurs in the fiber structure, which is a possible reason for the beads to occur in the electrospinning process.

Figure 2 gives the result of viscosity of different percentage of PLA : PCL solutions dissolved in the mixture of DCM : DMF, chloroform : methanol, and chloroform : acetone. It can be seen that increasing PCL amount led to the decrease of solution viscosities; Only 33% PCL lowered the blend viscosity by more than 50%, regardless of the solvent while beyond 50% of PCL in the blend, the drop of solution viscosity is not so significant.

Figure 3(a) shows that using PLA dissolved in chloroform: methanol produced fibers with the average diameter of 510 nm and with a maximum diameter of 740 nm. Increasing the percentage of PCL to PLA (1 : 3) produced fibers with beads with the average fiber diameter of 325 nm with maximum and minimum diameters of 390 and 260 nm, respectively and by increasing the percentage of PCL to (1 : 1) there was no fiber structure obtained.

Considering that the solution viscosity is critical in forming fibers, Figure 2 shows that the viscosity was significantly reduced by the addition of PCL in 1 : 1 ratio and its effect on the electrospun fibers was the

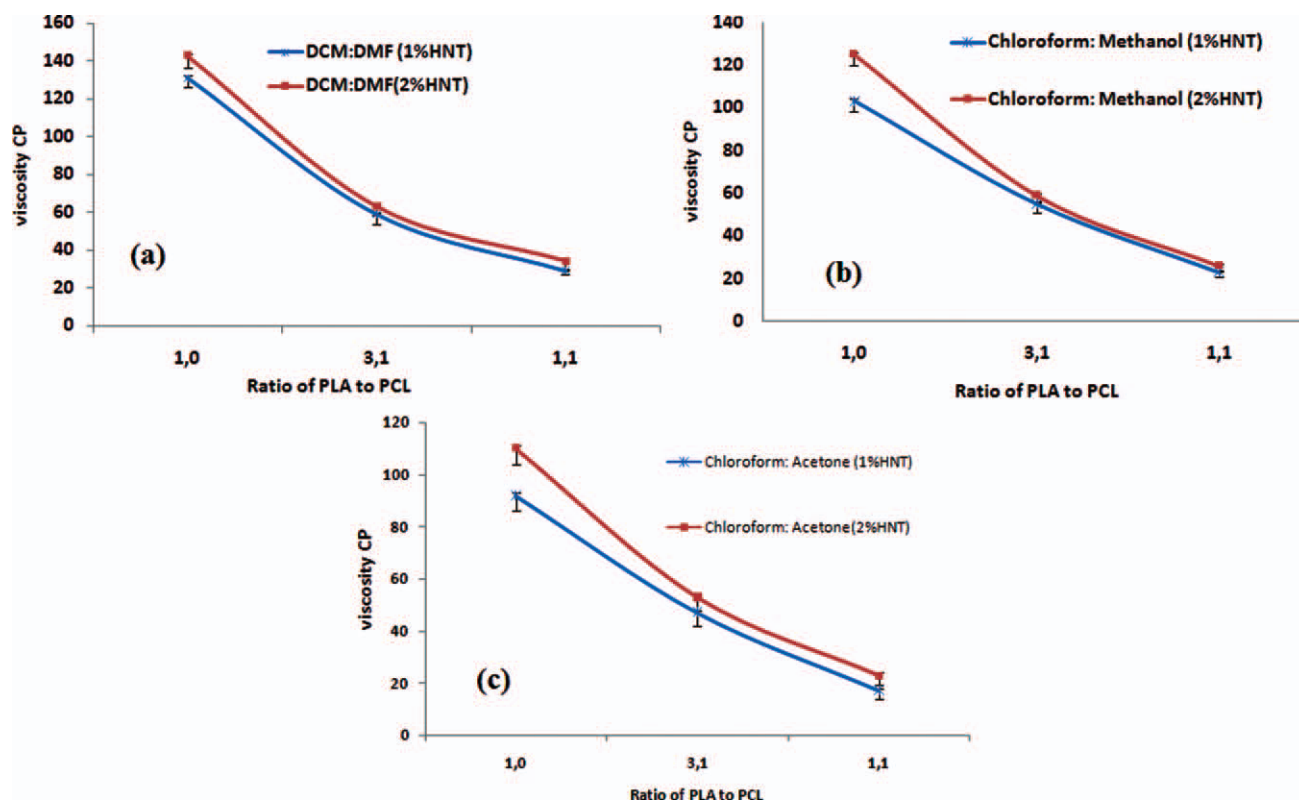


Figure 5 Viscosity of different percentage of PLA : PCL solutions dissolved in the mixture of (a) DCM : DMF with HNT (b) chloroform : acetone with HNT (c) chloroform : methanol with HNT. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

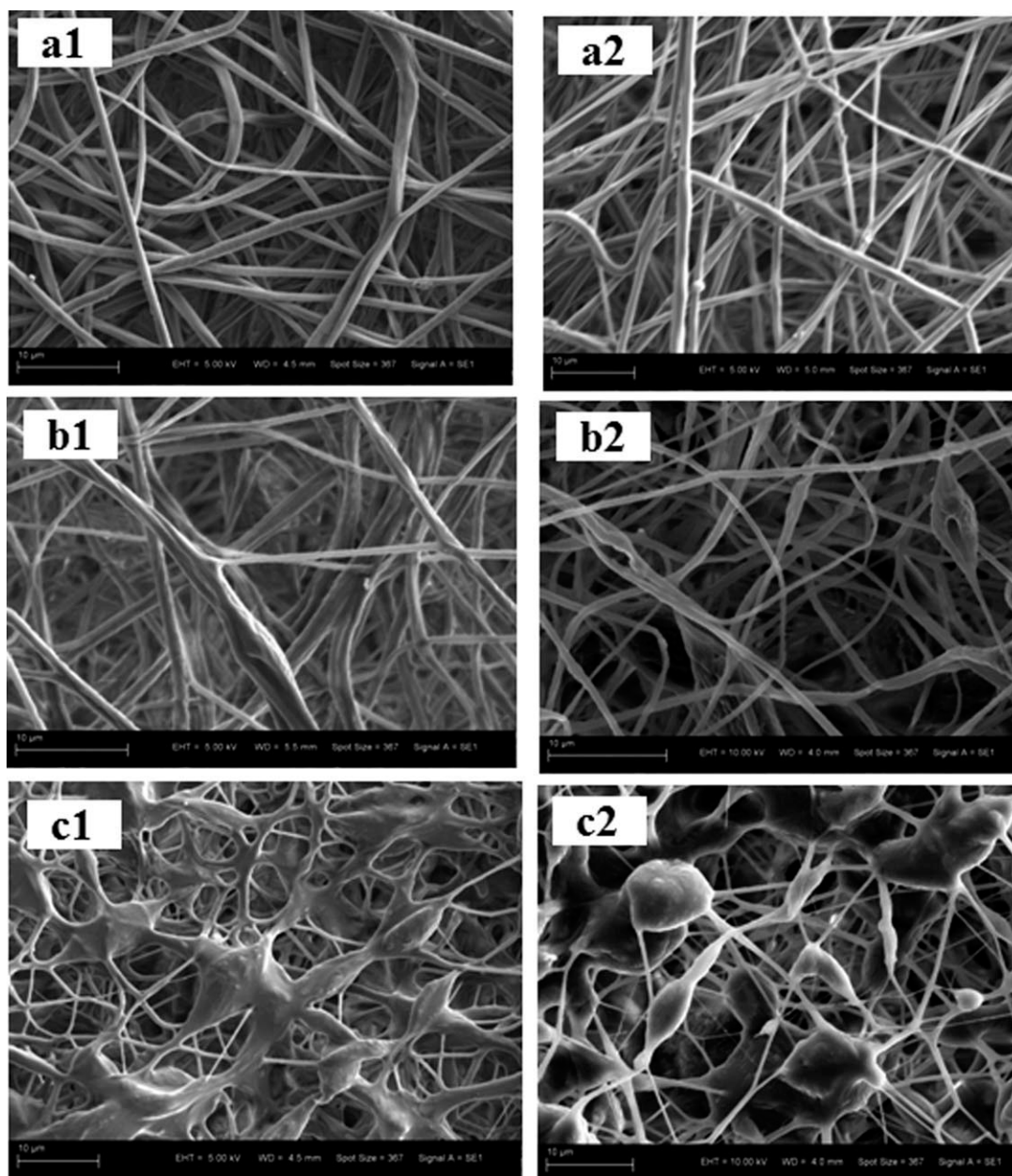


Figure 6 SEM micrographs of electrospun PLA : PCL fibers by using chloroform : methanol as a solvent and containing various PLA : PCL blend ratios (a1) 1 : 0, (b1) 3 : 1, and (c1) 1 : 1 with 1 wt % of HNT and (a2) 1 : 0, (b2) 3 : 1, and (c2) 1 : 1 with 2 wt % of HNT. The scale in the micrograph is 10 μm .

same as seen with DCM : DMF solvent. The fibers produced from the DCM : DMF system (all percentages) were uniform, resulting in fibers with smaller diameters, as compared to fibers obtained from chloroform: methanol system and this is because the conductivity of DCM : DMF solution is higher than the chloroform: methanol solution. DMF has a higher dielectric constant than methanol while DCM has a higher dielectric constant than chloroform as shown on Table I. As a result, increasing the conductivity aided in the production of uniform charge density and beads-free fibers, and also higher conductivities yielded smaller fibers as shown earlier.¹²

Figure 4(a) demonstrates that electrospun PLA dissolved in chloroform : acetone led to produced fibers with average diameter of 570 nm with the maximum diameter of 775 nm, while increasing the amount of PCL to PLA (1 : 3) produced fibers with inhomogeneity in structure and the average diameter reduced to 375 nm with the maximum diameter of 600 nm. Further increase in PCL led to no fiber formation as shown in Figure 4(c). Table II summarizes the average fiber diameters for all structures. The significance of the solution conductivity can be gauged from Tables I and II. For all polymer blends systems, fibers diameters and structural

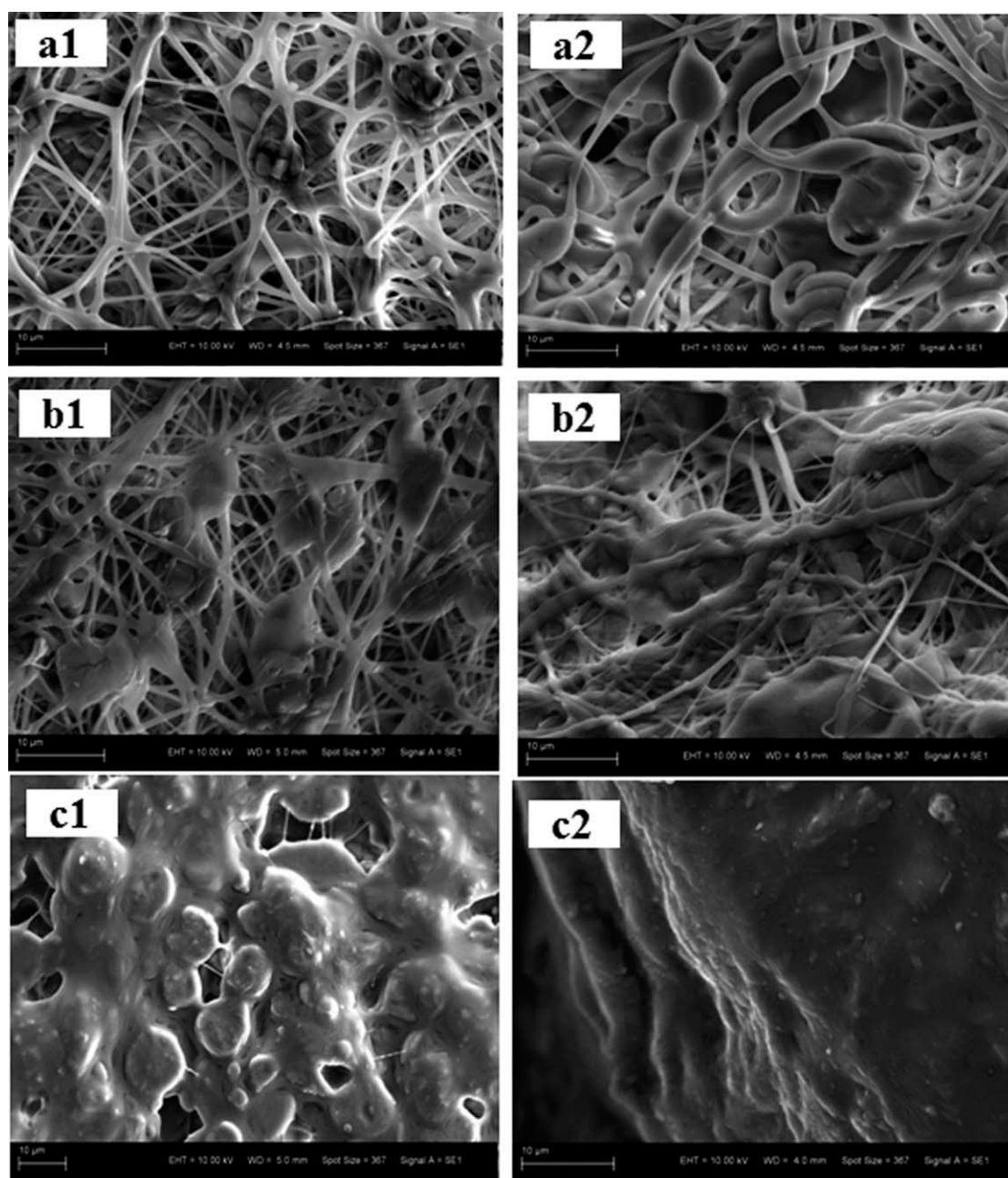


Figure 7 SEM micrographs of electrospun PLA : PCL fibers by using DCM : DMF as a solvent and containing various PLA : PCL blend ratios (a1) 1 : 0, (b1) 3 : 1, and (c1) 1 : 1 with 1 wt % of HNT and (a2) 1 : 0, (b2) 3 : 1, and (c2) 1 : 1 with 2 wt % of HNT. The scale in the micrograph is 10 μ m.

homogeneity showed the strong correlation with solvent types used.

Effect of HNT loading

With the addition of nanoclays, solution viscosities tend to increase even though the overall trend was decreasing as the PCL content increased, as illustrated in Figure 5, which is similar to results reported elsewhere.¹³ Figures 6–8 show that using PLA and PLA : PCL blends at different percentages

have significantly dissimilar behavior. It is evident that the addition of nanoclay always increased the fiber diameters. This is because HNT increases the electrical conductivity and the viscosity of the solution.⁷ Table III summarizes the average fiber diameters for 1 and 2 wt % HNT. When compared with samples without HNT loading, Figure 6 revealed that using PLA and PLA : PCL blend in chloroform : methanol with HNT produced good fibers in the 450 nm range, especially for PLA : PCL (3 : 1). In addition, the high volatility of methanol allowed for

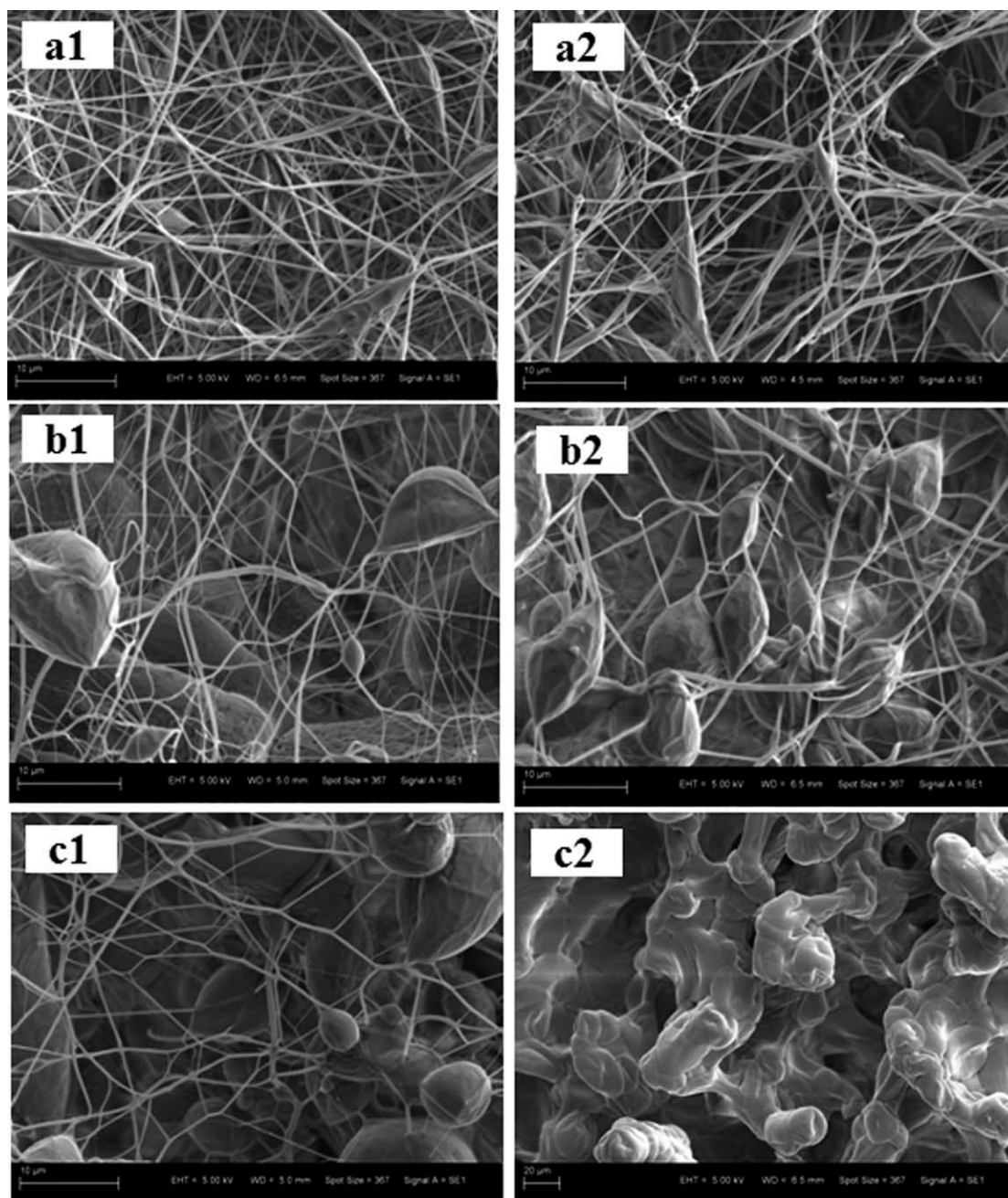


Figure 8 SEM micrographs of electrospun PLA : PCL fibers by using chloroform : acetone as a solvent and containing various PLA : PCL blend ratios by weight (a1) 1 : 0, (b1) 3 : 1, and (c1) 1 : 1 with 1 of HNT and (a2) 1 : 0, (b2) 3 : 1, and (c2) 1 : 1 with 2 wt % of HNT. The scale in the micrograph is 10 μ m.

adequate evaporation of the solvent before the deposition of fibers on the collector plate, leading to the formation of the highly fibrous structure.¹⁴

On the other hand, as shown in Figure 7, electrospun PLA and PLA : PCL blend in DCM : DMF with HNT produced significantly thicker fibers as compared to samples without HNT. This occurred despite an increase in the solution conductivity. During the electrospinning process, it was observed that the solution had some flow difficulty due to the increased viscosity of the solution, and most likely,

the electric potential could not overcome the effect of the increased viscosity leading to a failure in forming a polymer jet.¹⁵ Furthermore, unlike methanol, the low volatility of DMF led to reduced solvent evaporation leading to fibers that were wet at the collector plate.¹⁶

When compared with SEM images of fibers from chloroform : acetone solution, it can be seen that fibers from chloroform: acetone (Figure 8) have the smallest diameter, but also they show a greater amount of bead formation. Hence, high conductivity

TABLE III
Summaries of the Average Fiber Diameters (in nm) for All Structures with HNT

Cosolvents	PLA : PCL (1 : 0)		PLA : PCL (3 : 1)		PLA : PCL (1 : 1)	
	1% HNT	2% HNT	1% HNT	2% HNT	1% HNT	2% HNT
DMF : DCM	950 (± 45)	1100 (± 45)	730 (± 75)	NA	NA	NA

All fiber diameters are in nm and NA refers to no fiber obtained.

of the solution may not overcome the surface tension and increased viscosity of the solution by using a low volatile solvent.

Crystallinity and thermal property analysis

As seen from the X-ray diffraction patterns (Fig. 9), the electrospun samples indicated a mix of intercalated morphologies depending upon the type of solvent used. Observed in Figure 1(a), crystallinity (%C) of polymer matrices within composite materials could be calculated on the basis of a peak fitting procedure developed by Lopez Rubio et al.,¹⁷ which is widely used for synthetic polymer and it is better in reflecting the crystalline content than the traditional two-phase model.

The method used here took into account irregularities in crystals that were expected to coexist in semi-crystalline materials and avoided the underestimation (two-phase method did not consider the diffuse scattering from non-perfect crystalline structure) of the crystalline content. Using the Levenberg–Marquardt algorithm, a curve fitting exercise was repeated eight times with different initial inputs and Gaussian shape of the fitted curve was confirmed to reflect the best fitting results. As Ungar¹⁸ suggested, the crystallinity for samples was calculated as,

$$X_c = \sum_1^n AC_i/A_t$$

where AC_i is the area under each fitted crystalline peak with index i and A_t is the total area under the diffractogram pattern. Table IV outlines the peak basal spacing for the nanoclay filled samples and also the relative crystallinity as calculated from the XRD raw data. Based on Table IV data, the key finding is that the addition of low molecular weight PCL to PLA and to PLA nanocomposites reduces the overall crystallinity and that the addition of nanoclay has relatively smaller impact on the growth of a crystalline morphology during the fiber electrospinning process. The fact that the fibers were obtained with relatively higher amorphous morphology is very beneficial to drug loading efficiencies and to improve the drug dispersion within the polymer matrix. Interestingly, Figure 9 shows that the poly-

mer–nanoclay interaction is strong enough to achieve a large intercalated structure within the amorphous region, and moreover, it appears that the addition of PCL enhances this effect (Samples No. 2 and 4). This has significant implication in drug loading capacity of biopolymers where the intercalated nanoclay structure would be able to accommodate higher wt % of drug molecules. Finally, (chloroform : methanol) samples (Samples No. 3 and 2) indicate that in presence of PCL, the polymer–solvent interaction is capable of dispersing the nanoclay within the polymer matrix; from two distinct morphologies appearing at around $2\theta = \sim 9^\circ$ (nearly exfoliated) and around $2\theta = \sim 22^\circ$ (long-range ordered structure) for PLA only samples, a single broad amorphous region was seen with the addition of PCL (Sample No. 2).

The DSC results in Table IV shows that by blending PLA with PCL there was a significant decrease in T_g compared with the fibers produced with PLA (about a 20°C reduction). Nevertheless, there was only a small change in T_m . Additional 2% of HNT led to a small decrease in T_g values for PLA : PCL blend nanofibers except for pure PLA in (DMF : DCM) and PLA : PCL with 2 wt % of HNT dissolved in (chloroform : methanol). However, the T_m values again showed no significant change for most samples. The interesting aspect was the apparent influence of solvents on the T_g and T_m values of the

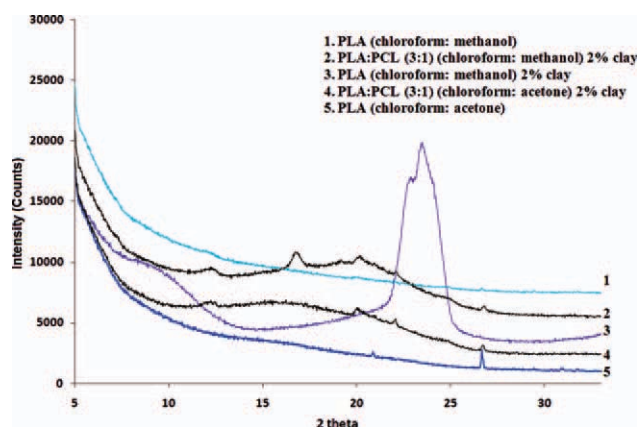


Figure 9 X-ray diffraction plots for selected samples showing the relative position of the intercalation peak due to addition of nanoclay in PLA or PLA-PCL samples with different solvents. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

TABLE IV
The DSC Results for PLA and PLA : PCL Nanocomposites with and Without HNT and with Different Cosolvents

Sample	X_c (%) [*]	T_g (°C)	T_m (°C)	ΔH_m (J g ⁻¹)
PLA – (DCM : DMF)	18.75	62.87	157.96	31.16
PLA – 2% HNT (DCM : DMF)	15.46	64.75	155.36	30.9
PLA – chloroform : methanol	12.58	66.41	155.41	25.64
PLA – 2% HNT (chloroform : methanol)	13.45	58.51	153.91	24.79
PLA – (chloroform : acetone)	15.78	63.22	155.16	25.42
PLA – 2% HNT (chloroform : acetone)	9.12	58.89	155.12	23.38
PLA : PCL, 3 : 1, DCM : DMF	5.45	46.43	153.93	17.05
PLA : PCL, 3 : 1, 2% HNT (DCM : DMF)	3.16	44.13	153.89	15.23
PLA : PCL, 3 : 1, (chloroform : methanol)	8.72	45.62	154.47	24.57
PLA : PCL, 3 : 1, 2% HNT (chloroform : methanol)	4.24	46.44	154.41	17.15

Calculation were repeated for three sets of samples and standard deviation for the T_g and T_m values are <1%.

blends. For example, PLA in (DCM : DMF) showed a T_g of 62.87°C and T_m of 157.96°C while, PLA in (chloroform : methanol) showed a T_g value of 66.41°C and T_m value of 155.41°C. Moreover, in presence of 2% nanoclay, the above two samples in their respective solvents showed T_g values of 64.75 and 58.51°C, respectively. Given this increasing–decreasing behavior with the addition of nanoclays, at this stage it is difficult to confirm whether such effect was dominated by the solvent mixture. It is also seen that the addition of low molecular weight PCL to the PLA matrix lowered the overall crystallinity, and this is evident from the smaller ΔH_m values for the PLA : PCL blends regardless of the solvent used. In summary, the DSC data strongly suggest that the solvent mixture of chloroform: methanol helps the PLA matrix attain relatively great structural orderness (slightly higher crystallinity but larger enthalpy value) and the addition of PCL matrix enhances the intercalated structure.

CONCLUSIONS

This investigation focused on the morphological evolution of PLA and blends of PLA with low molecular weight PCL reinforced with different concentrations of tubular halloysite nanoparticles and different cosolvents using fiber electrospinning. The fibers produced from the DCM : DMF system without HNT nanoparticles were more uniform, resulting in smaller fiber diameters as compared to chloroform : methanol system and this is directly related to the increased solution conductivity in the case of DCM : DMF mixture. The addition of HNT nanoparticles produced fibers with large diameters because the solution viscosity increased by the addition of HNT. HNT also increased solution conductivity for chloroform : methanol cosolvent with PLA-PCL blend, which resulted in uniform fibers, especially in PLA : PCL system with polymer ratio of 3 : 1. In addition, the high volatility of methanol allowed faster solvent evaporation leading to fibers with smaller diameters. Electrospun PLA and its blends

in DCM : DMF with HNT produced significantly thicker fibers as compared to samples without HNT, which was attributed to the increasing viscosity and low volatility of the solvent to negate the effects of higher conductivity of the solution. Key insights into processing blends of PLA-PCL were obtained including (1) the choice of cosolvent is important in determining fiber diameters of PLA-PCL blend because the cosolvents strongly influence the viscosity and conductivity of the bulk solution; (2) the dispersion of nanoparticles and their interaction with low molecular weight polymers such as PCL is significant in that their interactions influence the solution viscosity and conductivity to determine the fiber diameter; (3) there was a slighter growth of a crystalline morphology during the fiber electrospinning process when the interactions between low molecular weight PCL and HNT had happened; (4) when compared to the different cosolvents, the solvent mixture of chloroform : methanol is more suitable for PLA based systems because it can increase the structural orderness in PLA matrix.

The authors acknowledge Curtin Microscopy unit for technical assistance for the SEM. The authors also thank Applied Physics lab for assisting with XRD.

References

- Han, J.; Chen, T.; Branford-White, C.; Zhu, L. *Int J Pharm* 2009, 382, 215.
- Cui, W.; Li, X.; Zhu, X.; Yu, G.; Zhou, S.; Weng, J. *Biomacromolecules* 2006, 7, 1623.
- Heydarkhan-Hagvall, S.; Schenke-Layland, K.; Dhanasopon, A.; Rofail, F.; Smith, H.; Wu, B.; Shemin, R.; Beygui, R.; MacLellan, W. *Biomaterials* 2008, 29, 2907.
- Kim, K.; Luu, Y.; Chang, C.; Fang, D.; Hsiao, B.; Chu, B.; Hadjiargyrou, M. *J Controlled Release* 2004, 98, 47.
- Luong-Van, E.; Grøndahl, L.; Chua, K.; Leong, K.; Nurcombe, V.; Cool, S. *Biomaterials* 2006, 27, 2042.
- Kenawy, E.; Abdel-Hay, F.; El-Newehy, M.; Wnek, G. *Mater Chem Phys* 2009, 113, 296.
- Touny, A.; Lawrence, J.; Jones, A.; Bhaduri, S. *J Mater Res* 2010, 25, 857.

8. Arumugam, G.; Khan, S.; Heiden, P. *Macromol Mater Eng* 2009, 294, 45.
9. Buschle-Diller, G.; Cooper, J.; Xie, Z.; Wu, Y.; Waldrup, J.; Ren, X. *Cellulose* 2007, 14, 553.
10. Han, J.; Branford-White, C.; Zhu, L. *Carbohydr Polym* 2010, 79, 214.
11. Haque, P.; Barker, I.; Parsons, A.; Thurecht, K.; Ahmed, I.; Walker, G.; Rudd, C.; Irvine, D. *J Polym Sci A Polym Chem* 2010, 48, 3082.
12. Pham, Q.; Sharma, U.; Mikos, A. *Tissue Eng* 2006, 12, 1197.
13. Bhardwaj, N.; Kundu, S. *Biotechnol Adv* 2010, 28, 325.
14. Jiang, H.; Fang, D.; Hsiao, B.; Chu, B.; Chen, W. *Biomacromolecules* 2004, 5, 326.
15. Um, I.; Fang, D.; Hsiao, B.; Okamoto, A.; Chu, B. *Biomacromolecules* 2004, 5, 1428.
16. Hsu, F.; Hung, Y.; Liou, H.; Shen, C. *Acta Biomater* 2010, 6, 2140.
17. Lopez Rubio, A.; Flanagan, B.; Gilbert, E.; Gidley, M. *Biopolymers* 2008, 89, 761.
18. Ungar, T. *Script Mater* 2004, 51, 777.