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Effects of Solution Viscosity on the Fabrication of Polycaprolactone (PCL)/Chitosan Nanofibers

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Abstract: Over the past few decades, electrospun nanofiber has been introduced as one of the suitable drug carriers for drug delivery application. A special property exhibited by the nanofiber is that it has an extremely high surface area to volume ratio which makes it suitable to be applied in this application. In fact, there has been a lot of considerable interest in developing electrospun nanofiber using an electrospinning technique. In this study, a synthetic polymer, Polycaprolactone (PCL) was blended with a natural polymer, chitosan to fabricate electrospun nanofibers for drug delivery application. The ratio of the polymer blending composition for PCL/Chitosan was varied. The solution viscosity was measured by a viscometer. The morphology of the nanofibers was observed using a Scanning Electron Microscopy (SEM) and wettability was measured using a water contact angle measurement. At suitable polymer blend composition and viscosity, it was possible to fabricate electrospun nanofibers with diameter of 85-120 nm. It was also observed that the wettability of the nanofibers was 63.03±6.02°.

Key words: Polycaprolactone, Chitosan, electrospinning, electrospun nanofibers, drug delivery, Scanning Electron Mcroscopy (SEM)

INTRODUCTION

In general, pharmaceutical drug use exists at present is in the form of solid pills, liquid and injectable forms. The conventional forms can cause problems such as partial degradation before reaching the desired target and can lead to reduced therapeutic effect (Vilar *et al*., 2012). Considering this matter, drug delivery system has been developed to control the administration of drugs through a medium that allows it to be used to the targeted body parts and this leads to the introduction of nanofiber as a suitable drug carriers. Electrospun nanofiber is suitable because it has special properties which have a high surface area and short diffusion path length (Mahoney *et al*., 2012; Sun and Li, 2011).

Polymer blending is one way to combine the positive features of different polymers into a single system. This method is an approach to develop a new biomaterial that has a combination of characteristics that obviously cannot be obtained by a single polymer (Ratajska and Boryniec, 1998). Blending of synthetic and natural polymer can produce desired properties of nanofiber (Lim *et al*., 2014). In this study, PCL and Chitosan were used to fabricate nanofibers. PCL is a synthetic polymer. It is widely used in drug delivery system due to its availability, biodegradability and good mechanical properties (Martino *et al*., 2011; Roozbahani *et al*., 2013; Sarasam and Madihally, 2005). Since, PCL is hydrophobic, it will reduce the tendency of cell adhesion to the electrospun nanofiber (Kim *et al*., 2006; Lim *et al*., 2014). On the other hand, natural polymer Chitosan is hydrophilic (Roozbahani *et al*., 2013), biodegradable and nontoxic (Sun and Li, 2011).

To fabricate nanofiber for drug delivery system, there are many techniques established such as phase separation, self-assembly (Pillay *et al*., 2013; Rathinamoorthy, 2012) template-directed synthesis (Hulteen *et al*., 1997) drawing (Jayaraman *et al*., 2004) and electrospinning (Mahoney *et al*., 2012). However, electrospinning technique is more preferable in nanofiber fabrication, since, it can fabricate continuous nanofibers. Besides, it mimics extracellular matrix and applicable for producing ultrafine fiber (Lim *et al*., 2014; Pillay *et al*., 2013). The process is simple and versatile (Yu *et al*.,

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2009). It utilizes high voltage source that will create sufficient electrostatic force to the polymeric solution which results in the formation of very fine nanofibers. Although, electrospinning is frequently describes as simple process, still there are several parameters need to be considered to obtain the desired fiber such as properties of the solution (viscosity, conductivity, molecular weight and surface tension), processing parameters (applied electric field, distance of tip to collector and flow rate) and the ambient conditions (humidity and temperature of surrounding) (Bhardwaj and Kundu, 2010).

In the current study, the main objective was to explore the effect of viscosity level of PCL/Chitosan solution on the formation of nanofibers. Chitosan can be blended with PCL at a low blend ratio. The blend ratio was varied which formed different levels of polymer concentration and viscosity. It is believed that the solution viscosity factor is important because it may affect the formation of the nanofiber in terms of morphology, diameters of nanofiber and the surface properties (Mahoney *et al*., 2012). In general, low viscosity of polymer solution produces fibers containing beads and increasing the viscosity will increase the diameter of fiber. Meanwhile, at certain level of viscosity, it is possible to produce bead-free nanofibers and the nanofiber is difficult to form when it exceeds the threshold of the suitable viscosity level. It has been proven that at very low or very high viscosity results in unsuccessful formation of continuous nanofiber (Bhardwaj and Kundu, 2010; Doshi and Reneker, 1995). Drugs can be incorporated in this nanofiber and the drug incorporated nanofibers can be used as delivery vehicle at the wound sites.

MATERIALS AND METHODS

PCL pellets (MW = 70,000-90,000), Chitosan with medium molecular weight, 98% acetic acid and 99.8% formic acid were purchased from Sigma-Aldrich.

Preparation of PCL/Chitosan-based solution: Four types of polymer solutions were prepared from different blend ratio of PCL and Chitosan by dissolving both polymers in a mixture of 3 mL of Acetic Acid (AA) and 7 mL of Formic Acid (FA). The solution was magnetically stirred (500 rpm) at room temperature using a magnetic stirrer. The time taken for the solution to completely dissolve was about 2-3 h. The viscosity of polymer solutions was measured at room temperature by using a Brookfield LVDV-II+PRO rotational viscometer (Brookfield Engineering Labs., Inc., Middleboro, MA, USA) using a SC4-18 spindle.

Fabrication of PCL/Chitosan-based electrospun nanofibers by electrospinning: PCL/Chitosan solutions were electrospun using electrospinning unit and were pumped from a 5 mL syringe with a needle gauge 21. The voltage applied was in the range of 18–22 kV. The electrospinning was carried out at room temperature (24±1°C) with (50±5%) relative humidity. The distance between the tip to collector screen was set at 10 cm and the flow rate was 1.0 mL/h. The syringe needle was connected to a power supply. The electrospun fibers produced were collected at the grounded collector.

Characterization: Morphology of the PCL/Chitosan electrospun nanofibers was studied by SEM (Hitachi TM 3000, Japan) and images obtained were analyzed using Image J Software. The wettability of PCL/Chitosan electrospun nanofibers was determined through contact angle measuring system (VCA Optima by AST Products) with distilled water. About 1 μL of water was dropped three times at different places of the nanofibers and the contact angle was determined.

RESULTS AND DISCUSSION

Viscosity measurement: Table 1 shows the viscosities for different polymer solutions measured by viscometer. This study used a solvent system of AA:FA (3:7). It was chosen as it could dissolve PCL and chitosan at some specific blend ratio and these solvents were less-toxic than other volatile solvents (Steyaert *et al*., 2012). From Table 1, it was observed that sample A had the highest viscosity compared to the other samples. On the other hand, the viscosity of sample C was the lowest. The amount of chitosan is responsible for higher viscosity of sample D than sample C. By increasing the amount of the Chitosan, it gave larger impact on the viscosity of the solution compared to PCL.

Morphology of PCL/Chitosan-based electrospun nanofiber: Figure 1a, b shows unsuccessful fabrication of electrospun nanofibers from sample B and D. From sample A and C, nanofibers were successfully fabricated

Table 1: Viscosity measurements by viscometer

Samples	PCL/Chitosan (w/w) (g)	Viscosity centipoise (cP)
A	1.0/0.05	219.7
B	0.8/0.10	209.0
C	0.8/0.05	167.5
D	0.6/0.12	197.0

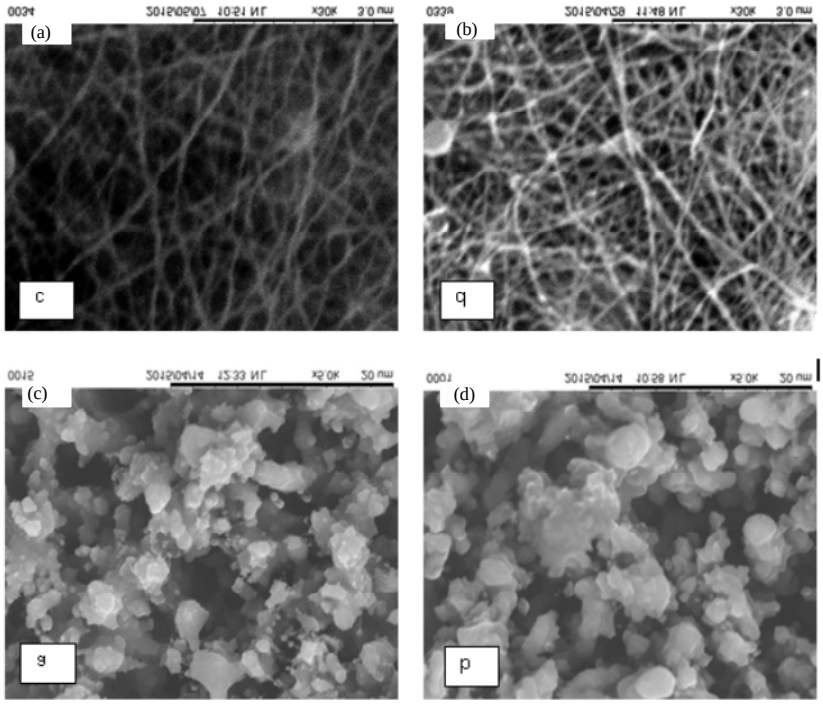


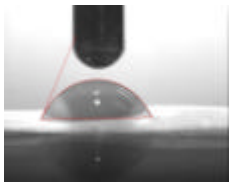
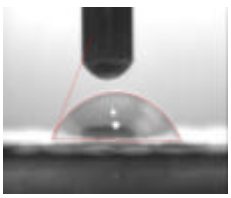
Fig. 1: SEM micrographs of unsuccessful and successful PCL/Chitosan based electrospun nanofibers: a) Sample B; b) Sample D; c) Sample A and d) Sample C

Fig.1c, d. It was observed that both the fibers had the diameter within the range of 85-120 nm. The amount of the Chitosan controlled the increase in polymer solution viscosity, however, there is a limitation of Chitosan amount for PCL/Chitosan polymer blend solution. The amount of Chitosan affected the nanofiber formation. Only 0.05 (w/w) Chitosan produced nanofibers (Sample A and C) and 0.1 (w/w) or more Chitosan did not obtained the fiber (Sample B and D). The average fiber diameter obtained from sample A and C did not have much difference. A research conducted by Stolnik *et al.* (2012) states that the nanofiber having diameter >200 nm are most likely be isolated by spleen and removed by phagocytes. Hence, a suitable diameter of the nanofiber that enables it to be applied in the drug delivery system is within the range of 10-100 nm (Goldberg *et al.*, 2007).

Water contact angle measurement: Three different measurements for each sample were carried out and the average was calculated. The measurement was done after 3 sec of water droplets gets contact with the surface of nanofiber. The contact angles for each sample are listed in the Table 2.

The contact angle between sample A and C did not have much difference and both the nanofibers were hydrophilic. In drug delivery application point of view, it is desirable to obtain a nanofiber which has hydrophilic properties. By applying a hydrophilic nanofiber, the drugs can be delivered to the targeted part of body, since, it has good interaction with body fluids.

Table 2: Water contact angle of PCL/Chitosan-based electrospun nanofibers

Samples	Average water contact angle (°)	
Sample A (10.5% w/v)	63.03±6.02	
Sample C (8.5% w/v)	62.57±7.90	

CONCLUSION

PCL/Chitosan based electrospun nanofibers were successfully fabricated from different polymer blend ratios. At optimum polymer blend ratio, polymer concentration and viscosity, fabrication of nanofibers was

possible. The viscosity factor has a significant effect on the morphology, diameter and the properties of the PCL/Chitosan based electrospun nanofiber. The range of fiber diameters of nanofibers was 85-120 nm and the water contact angle measurement showed that the nanofibers had hydrophilic property. Further investigations are needed to use this nanofiber for drug loading and delivery application.

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