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# Hybrid Nanofibre Matrix for Regenerative Therapy Fabricated by Electrospinning: Effects of Process Parameters on the Fibre Efficacy

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## Abstract

Electrospinning has drawn great attention in the fabrication of nanofibre matrix that applies electrostatic potential to draw molten polymer jet as nanofibre onto a collector. This study aims at fabricating hybrid Polycaprolactone (PCL)/Polyethylene Glycol (PEG) nanofibre matrix for regenerative therapies. To optimize the electrospinning system, the effects of various process parameters (e.g. polymer solution concentration, polymer solution flow rate, power supply voltage and collector distance) on the efficacy of the nanofibre were investigated. The process parameters directly influenced the efficacy of the nanofibre, and the optimized values of the parameters were found to be polymer solution concentration of 10 wt% PCL and PEG each component, polymer solution flow rate of 8 ml/h, power supply voltage of 21 kv and collector distance of 14 cm. The thermal properties (e.g. melting temperature, Tm and melting enthalpy, J/g) of the polymers (before and after electrospinning) were also determined through Differential Scanning Calorimetry (DSC) and Thermo-gravimetric Analysis (TGA) to study whether the electrospinning process change the thermal properties of the polymers. It was observed that the electrospinning process rendered to increase both the melting temperature and melting enthalpy of the polymers. The preliminary results demonstrate the suitability of electrospinning system to fabricate hybrid PCL/PEG nanofibre matrix, and also offers the potential of developing hybrid nanofibre matrix which could better meet the structural and functional requirements of living tissues for regenerative therapies.

**Keywords:** Hybrid; PCL; PEG; Nanofibre; Electrospinning; Process parameters; Tissue Engineering

## Introduction

Tissue engineering is a rapidly growing area which combines the fields of biology, medicine and engineering to improve the quality of human health by repairing and/or regenerating the diseased/damaged tissues and organs often using scaffolds as temporary support [1]. Spectacular progresses in the fields of biochemistry, cell and molecular biology, genetics, biomedical engineering and materials science have given a huge boost in developing biodegradable polymeric scaffold suitable for tissue engineering applications [2]. The scaffolds which are expected to mimic the structure and functions of the native Extracellular Matrix (ECM), support the growth and formation of tissues in regenerative therapies [3]. The scaffolds should have interconnected pore networks of appropriate size and distribution to support tissue integration and vascularization. Besides, the scaffolds should be biodegradable and bioresorbable as the tissue will eventually replace the scaffold, and also should have suitable surface chemistry to support cell adhesion and growth [4,5].

Electrospun nanofibre matrices have great potential as tissue engineering scaffolds because they mimic the nanoscale properties of the ECM of human body [6]. Synthetic polymers are well-known as materials to be used for tissue engineering scaffolds as they satisfy most of the requirements in compared to other materials [7]. For instance, polycaprolactone (PCL), polyethylene glycol (PEG) and *polylactic-co-glycolic acid* (PLGA) are widely used as tissue scaffold materials in bone, cartilage, liver, heart and nerve regeneration due to their biodegradable property that leads their easy removal from the body by natural metabolic cycle [4]. To date, electrospinning is a champion in processing materials such as polymers, composites, ceramics and even metals into nanofibre matrix [8] for tissue scaffolding due to its versatility, cost-effectiveness and simplicity.

To attain required characteristics of the electrospun nanofibre remains a great challenge, which can be manipulated by a number of process parameters. Pham et al. [9] classified the overall parameters associated with electrospinning system as i) polymer solution properties, ii) control variables and iii) ambient conditions. Generally, these parameters influence the scaffolds' morphological and eventually biomechanical properties. Therefore, these parameters need to be studied and optimized to produce nanofibre scaffolds as required. Within the scope, this study focuses on investigating the effects of polymer solution properties (e.g. concentration and flow rate) and the control variables (e.g. power supply voltage and collector distance) on the efficacy of the electrospun nanofibre towards the optimization of the electrospinning process to fabricate PCL/PEG hybrid nanofibre matrix.

Thermal properties of the electrospun nanofibres are important as they might modulate the biomechanical properties of the fabricated nanofibres for tissue engineering applications [10-12]. The thermal properties (e.g. melting temperature, Tm and melting enthalpy, J/g) of the polymers (before and after electrospinning) have also been evaluated via thermo-gravimetric analysis (TGA) and differential scanning calorimetry (DSC) to study the effect of the electrospinning process on the polymer's thermal properties.

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## Materials and Methods

### Polymers/Solvents used

Polycaprolactone (PCL) in pellet form and polyethylene glycol (PEG) in flake form were purchased from Sigma-Aldrich (USA). Various solvents, such as dichloromethane, methyl acetate, tetrahydrofuran, acetic acid, acetone, and dimethylformamide were purchased from Merck (Germany). All chemicals were of analytical grade and were used without further modification/purification.

### Preparation of polymer solutions

All the above mentioned solvents were used to investigate which one dissolved PCL & PEG polymers efficiently to fabricate nanofibre matrix. Through intensive experimental iterations the dichloromethane was found to be the most efficient solvent for preparing the PCL/PEG polymer solution, and thus it was decided to be used throughout the fabrication process of nanofibre matrix. PCL/PEG hybrid polymer solutions of various concentrations were prepared using dichloromethane solvent. The used concentrations of PCL and PEG (each component) were of 5 wt%, 10 wt% and 15 wt% as presented in Table 1.

A magnetic stirrer was utilized to prepare the homogeneous polymer solutions. The magnetic bar was merged into the beaker having the solid polymers and solvent. The beaker was placed onto a stirrer that applied a magnetic field rendering a rapid rotation of the magnetic bar that enhanced and/or ensured the proper dissolution and/or mixing of the polymers producing a hybrid polymer solution. The rotation speed of the magnetic bar was set at 750 rpm.

### Electrospinning system

This method uses high voltage power supply to generate a potential difference between the polymer solution and the collector, which electrospins nanofibres that are deposited onto the collector. A polymer solution was suspended in a syringe with needle, which was held by surface tension, and the flow rate of the polymer solution was controlled by a programmable syringe pump (NE 1000, USA). A high voltage power (ESP0P-10W DDP, Gamma High Voltage, USA) was supplied to both polymer solution (via needle tip) and the collector. The potential difference between the needle tip and the collector created an unstable electric field. As the electric potential increased, the droplet of the polymer solution at the needle tip elongated to form a taylor cone. When a critical voltage was reached, repulsive electric force opposed the surface tension of the polymer solution thus leading to the formation of a polymer jet. As the jet traveled, the solvent evaporated and fibres were deposited/collected onto the collector. The schematic diagram of the electrospinning system is illustrated in Figure 1.

### Variation/Optimization of process parameters

There are a number of process parameters such as i) polymer solution concentration, ii) polymer solution flow rate, iii) power supply voltage, and iv) distance between collector and needle tip that seem to have direct effect on the efficacy of the electrospun nanofibre. These parameters were studied towards the optimization of the electrospinning process to fabricate PCL/PEG hybrid nanofibre matrix with properties as required for any specific application. Usually three values of each parameter were used to investigate their effects on the fibre efficacy and ultimately to determine the optimum set of these process parameters. Three different polymer solution concentrations used were of 10 wt%, 20 wt% and 30 wt% (i.e., 5 wt%, 10 wt% and 15 wt% of PCL and PEG each). The polymer solution flow rates were set to be at 8 ml/h, 13 ml/h and 18 ml/h. The applied power supply voltages were varied to be of 12 kv, 17 kv and 22 kv. The distances between needle tip and collector were selected to be of 10 cm, 15 cm and 20 cm. Through an intensive series of trial fabrication the optimum process parameters were found to be as follows: i) polymer solution concentration of 20 wt% (i.e. 10 wt% of PCL and PEG each), ii) polymer solution flow rate of 13 ml/h, iii) power supply voltage of 17 kv, and iv) collector distance of 15 cm. These optimized parameters were utilized for all further fabrications to investigate the effect of any specific parameter by varying one parameter iteratively, while other three parameters were kept unchanged.

### Morphological characterization

The morphologies of different electrospun nanofibre matrices were observed via scanning electron microscope (SEM) (FEI, USA) under high vacuum with an accelerating voltage of 15 kv, a current of 60-90 mA and at a working distance of about 2 cm.

### Thermal properties analyses

The thermal properties (e.g. melting temperature, Tm and melting enthalpy, J/g) of the polymers (before and after electrospinning) were studied using differential scanning calorimetry (DSC) (Mettler Toledo, USA) and thermo-gravimetric analysis (TGA) to investigate the effect of the electrospinning process on the polymer's thermal properties. Five types of samples (e.g. raw PCL, raw PEG, electrospun PCL, electrospun PEG and electrospun hybrid PCL/PEG) were analysed.

## Results and Discussion

### Effects of polymer concentration

The concentration of the polymer solution is one of the most important parameters in the fabrication of nanofibre matrix. In this study, three different concentrations of PCL/PEG polymer solutions numerically 10 wt%, 20 wt% and 30 wt% (i.e., 5 wt%, 10 wt% and 15 wt% of each PCL/PEG component) in dichloromethane solvent were investigated. The SEM images of the expected nanofibre matrices are presented in Figure 2. It was observed that at lower concentration of polymer solution (e.g. 10 wt%) the polymer jet was intermittent as it travelled and thus producing no true continuous nanofibre matrix on the collector (Figure 2a) rather dispersed polymer was deposited onto the collector. At this condition, the jet contained more solvent than the polymer. As the jet travelled, the solvent was evaporated leaving very limited amount of polymer that could not produce continuous fibre onto the collector. Likewise, too high polymer solution concentration (e.g. 30 wt%) also rendered no formation of polymer jet. This might

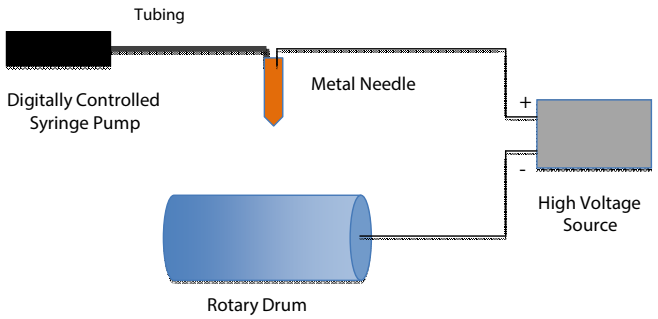


**Figure 1:** The overall experimental set-up for the electrospinning process.

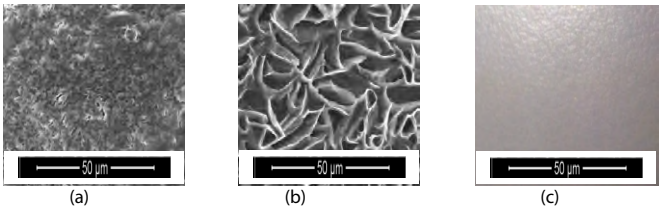


**Figure 2:** SEM images of PCL/PEG hybrid electrospun nanofibre matrix demonstrating the influence of the variation of polymer solution concentration on the fibre efficacy, while other parameters remained constant (polymer solution flow rate of 8 ml/h, power supply voltage of 17 kv, and collector distance of 15 cm).

be due to very high surface tension at the tip of the taylor cone, which could not be opposed by the applied electric potential. Thus, there were no traces of polymers onto the collector (Figure 2c). Therefore, the optimum polymer concentration was considered to be of 20 wt% of PCL/PEG (i.e., 10 wt% of PCL and PEG each component) in dichloromethane. This optimum PCL/PEG polymer solution concentration was used throughout the study.

## Effects of polymer flow rate

The fibres were spun from the optimum polymer solution concentration of 10% (w/v) PCL and 10% (w/v) PEG in dichloromethane at three different polymer flow rates such as 8 ml/h, 13 ml/h and18 ml/h. The fibres were fabricated applying the voltage of 21 kv and collected onto a flat collector of 10 cm distance from the needle tip. The SEM images of the fibres produced at different polymer solution flow rates are shown in Figure 3, which clearly demonstrates the effects of polymer solution flow rate on the nanofibre efficacy. It was observed that the lower flow rate (e.g. 8 ml/h) produced thinner fibre (Figure 3a) and the fibre diameter increased with the increase of polymer solution flow rate. In contrast, at too high flow rate (e.g. 18 ml/h) thicker and even smeared fibres were observed. It was believed that the thicker and smeared fibres were produced because of the excess amount of polymer dispensing due to the increased flow rate that resulted in the formation of droplet at the tip of the spinneret. When the size of the droplet is too big to suspend at the tip of the spinneret, it either drops from the tip or is carried along with the jet to the collector [11]. Too high flow rate caused beading in the fibres since the polymer jet/droplet did not have sufficient opportunities to uniformly elongate and/or dry properly prior to reaching the collector. At higher flow rate of 18 ml/h higher number of beads was formed (Figure 3c) in compared to at lower flow rate of 13 ml/h (Figure 3b). Some other researchers also investigated the relationship between polymer flow rate and the fabricated fibre diameter, and observed the similar phenomena [9].

## Effects of applied voltage

The effect of the applied voltage on the efficacy of nanofibre matrix is illustrated in Figure 4. The fibres were spun from the optimal PCL/PEG polymer solution applying three different voltages of 12 kV, 17 kV and 22 kV. It was observed that at lower voltage (e.g. 12 kV) the fibres tended to be thicker and even formed beads (Figure 4a). The increase of voltage decreased the probability of bead formation. In contrast, the thinner fibres were produced at higher voltage (e.g. 22 kV). This was because when higher voltage was applied a higher electrostatic force was created causing the jet of polymer to travel faster. Thus relatively lesser polymer solution was available at the tip of the taylor cone that resulted in thinner polymer jet to be released to form the fibre (Figure 4c). Wannatong et al. [11] stated that the effect of applied potential on the electrospun fibre efficacy was caused by three major forces namely, the body, the electrostatic and the drag forces. It was also commented that besides the fibre diameter, the applied voltage might also affect the fibre orientation/alignment. At lower potential the tangential speed of the depositing charged jet is higher than the approaching speed that renders the depositing jet to be drawn away resulting in partial alignment of the electrospun nanofibre. On the other hand, at higher potential the approaching speed of the charged jet is higher than the tangential speed that leads to the random deposition of the charged jet on the collector. It is deduced that the alignment of the electrospun nanofibre depends very much on the trajectory of the charged jet prior to deposition on the collector. The optimum applied voltage was found to be 17 kV that showed better fibre efficacy (Figure 4b).

## Effects of collector distance

Controlling the distance between the needle tip and the collector had been considered to be one of the efficient ways to modulate the electrospun nanofibre diameter and morphology [9]. In this study, the effect of collector distance on the fibre efficacy was studied by setting three different collector distances at 10 cm, 15 cm and 20 cm. Similar to the effect of applied voltage, at shorter collector distance (e.g. 10 cm) relatively thicker filament was produced (Figure 5a), and the increase of collector distance led to the formation of thinner fibre. This could be because of the fact that when the polymer jet travelled longer distance in the electrostatic field the whipping occurred that resulted in thinner fibre. Furthermore, when the polymer jet travelled longer distance it experienced more elongation that reduced the fibre cross-section for mass balance, and thus the thinner fibre was produced (Figure 5c). In this study, the collector distance of 15 cm was considered to be optimum that demonstrated better fibre efficacy (Figure 5b) among all three distances of 10 cm, 15 cm and 20 cm.

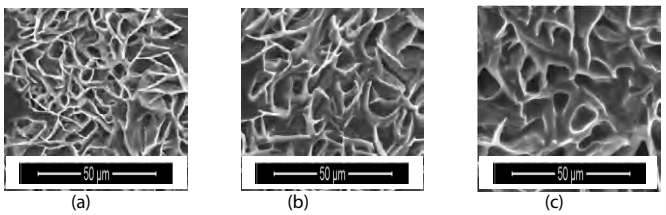


**Figure 3:** SEM images of PCL/PEG hybrid electrospun nanofibre matrix demonstrating the influence of the variation of polymer solution flow rate on the fibre efficacy, while other parameters remained constant (polymer solution concentration of 20 wt%, power supply voltage of 17 kv, and collector distance of 15 cm).

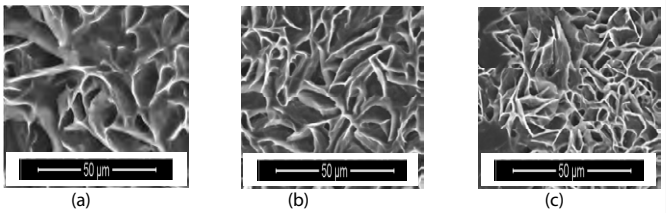


**Figure 4:** SEM images of PCL/PEG hybrid electrospun nanofibre matrix demonstrating the influence of the variation of power supply voltageon the fibre efficacy, while other parameters remained constant (polymer solution concentration of 20 wt%, polymer solution flow rate of 8 ml/h, and collector distance of 15 cm).

## Thermal properties

The thermal analyses data (e.g. melting temperature, Tm and melting enthalpy, J/g) of the polymers (before and after electrospinning) obtained through DSC and TGA are presented in Table 2. It was observed that the melting temperature and melting enthalpy of both PCL and PEG increased upon electrospinning process. It could be due to the phenomenon that the electrospinning process caused better alignment of the polymer chains that resulted in increase of melting temperature and melting enthalpy. This means that higher temperature and energy are required to break the better aligned polymer chains, which indeed indicates the improvement of strength of the electrospun fibre. This aspect needs to be further confirmed through mechanical test, which is already in plan for the next study. It is worth noting that the melting temperature and melting enthalpy of electrospun hybrid PCL/PEG laid in between that of PCL and PEG, which exhibited close inheritance of the processed hybrid polymer with the initial constituent polymers. Dhakate et al. [10] also observed that the electrospun matrix showed improvement in thermal properties in compared to the initial raw polymer.

## Conclusions

The hybrid PCL/PEG nanofibre matrix was successfully fabricated by electrospinning system. The effects of various process parameters such as, polymer solution concentration, polymer solution flow rate, power supply voltage and collector distance on the nanofibre efficacy were investigated to optimize these parameters. All these parameters had direct influences on the efficacy of the nanofibre, and the optimized values of the process parameters like, polymer solution concentration, polymer solution flow rate, power supply voltage and collector distance were found to be 20 wt% (10 wt% of PCL and PEG each component), 8 ml/h, 17 kv and 15 cm, respectively. The thermal analyses were also conducted through DSC and TGA to study whether the electrospinning process affect the thermal properties (e.g. melting temperature, Tm and melting enthalpy, J/g) of the electrospun polymer. It was observed that the electrospinning process resulted in increase of both melting temperature and melting enthalpy of the polymers. The preliminary qualitative results encourage going for further detail quantitative analyses including cell culture study, which are already in plan for the next study. In conclusion, the electrospinning system demonstrates the suitability of fabricating PCL/PEG nanofibre matrix, and also offers the potential of developing hybrid nanofibre matrix that could better meet the structural as well as functional requirements of living tissues for regenerative therapies.

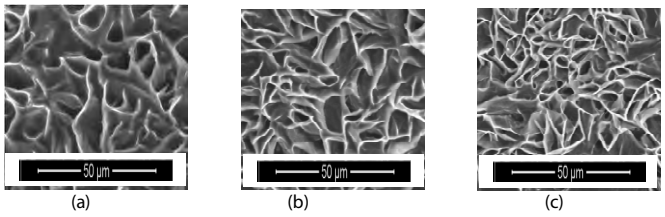


**Figure 5:** SEM images of PCL/PEG hybrid electrospun nanofibre matrix demonstrating the influence of the variation of collector distanceon the fibre efficacy, while other parameters remained constant (polymer solution concentration of 20 wt%, polymer solution flow rate of 8 ml/h, and power supply voltage of 17 kv).

| Polymer Samples | PCL Concentration | PEG Concentration | Solvent Concentration |
|---|---|---|---|
| 1 | 5wt% | 5wt% | 90% |
| 2 | 10wt% | 10wt% | 80% |
| 3 | 15wt% | 15wt% | 70% |

**Table 1:** Various polymer solutions showing the respective components' concentrations.

| Sample | Melting Temperature (Tm, °C) | Melting Enthalpy (J/g) |
|---|---|---|
| Raw PCL | 62 | 55 |
| Raw PEG | 66 | 58 |
| Electrospun PCL | 65 | 59 |
| Electrospun PEG | 69 | 62 |
| Electrospun PCL/PEG | 67 | 60 |

**Table 2:** The thermal properties (melting temperature, Tm and melting enthalpy, J/g) of the polymers before and after electrospinning.

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