

# **ELECTROSPINNING PARAMETERS FOR ORGANIC POLYMERS FOR NANOFIBER PRODUCTION**

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## **ABSTRACT**

Nanofibre is a type of fibre with the sizes of nano scale. It can be produced by several methods but the most conventional way is by electrospinning process. Electrospinning process is using the concept of different charges between the collector and the solution and therefore from the tips of the Taylor cone shoot out jet of fibre to the collector and thus, nanofibre is produced. There are several parameters which will affect the morphology of the nanofibre. Among is the applied voltage, capillary to ground distance, concentration of the solution, volatility of the solution and also the conductivity of the solution. Nanofibre has been used in biomedical field, filtration, protective material, sensors, nanofibre reinforced composites and many more. In this research, polyethylene oxide (PEO) will be used as the material to fabricate the nanofibre and aim to fabricate out linear shape nanofibre. The PEO solution is prepared by dissolving the PEO powder into solvent whether is water or ethanol and stirred for more than 8 hours using magnetic stirrer for the solution to reach homogeneous state. Then the solution will undergo electrospinning process. The nanofibre which have been fabricate will undergo field emission scanning electron microscopy (FESEM) to study the morphology of the nanofibre. From the result that have obtained, it is clearly that with 5wt% of 900k MW of PEO mix with 5wt% of ethanol as solvent will fabricate out linear shape nanofibre.

## **ABSTRAK**

Nanofibre adalah sejenis serat dengan saiz skala nano. Ia boleh dihasilkan oleh beberapa kaedah tetapi cara yang paling konvensional adalah dengan proses electrospinning. Proses electrospinning menggunakan konsep caj berbeza antara pemungut dan cecair dan oleh itu dari hujung kon Taylor menembak keluar jet serat ke pengumpul dan dengan itu nanofibre dihasilkan. Terdapat beberapa parameter yang akan memberi kesan kepada morfologi nanofibre. Antara ialah voltan yang digunakan, jarak kapilari ke pengumpul, kepekatan cecair, volatility cecair dan juga konduksi cecair. Nanofibre telah digunakan dalam penapisan, bidang bioperubatan, bahan perlindungan, sensor, nanofibre bertetulang komposit dan banyak lagi. Dalam kajian ini, polyethylene oxide (PEO) akan digunakan sebagai bahan untuk menghasilkan nanofibre dan juga bertujuan untuk menghasilkan bentuk nanofibre linear. Cecair PEO disediakan dengan melarutkan serbuk PEO ke dalam pelarut sama ada air atau ethanol dan dikacau melebihi daripada 8 jam menggunakan pengacau magnet untuk cecair untuk mencapai keadaan homogeneous. Kemudian cecair itu akan melalui proses electrospinning. Nanofibre yang telah dihasilkan akan menjalani analisis field emission scanning electron microscopy (FESEM) untuk mengkaji morfologi nanofibre itu. Dari keputusan yang diperolehi, adalah jelas bahawa dengan 5wt % daripada 900k MW PEO bercampur dengan 5wt % etanol sebagai pelarut akan menghasilkan bentuk nanofibre linear.

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## **LIST OF ABBREVIATIONS**

MW	Molecular Weight
PEO	Polyethylene Oxide
RPM	Rotate per minutes
kV	kilo Volt
cm	centimetre
ml	millilitre
h	hour
FESEM	Field Emission Scanning Electron Microscopy

# 1 INTRODUCTION

## 1.1 Background

Nanofibre, also called superfine or ultrathin fibre (Usman A., Yaqiong Z., Xungai W. & Tong L., 2011) are type of fibre with nano scale diameter. With such small scale of fibre, exist some very intriguing characteristics like huge surface area to volume ratio, vast diversity of surface functionalities and resilient mechanical strength according to Chengjun Z., Raymond C., Rhonna W. and Qinglin W.. Also by controlling the parameters like concentration of polymer solution, type of solvent and concentration of the solvent used, voltage used, the polymer solution injection flow rate etc. during the electrospinning process, we can fabricate out different kind of morphology nanofibre like beaded nanofibre, elongated nanofibre and linear shape nanofibre. With such interesting properties, nanofibre has so many useful application in many field like filtration, protective material, sensors, nanofibre reinforced composites and many more. Since nanofibre is very useful, many researches have been done on the nanofibre. Below is the pie chart about the research field on the nanofibre.

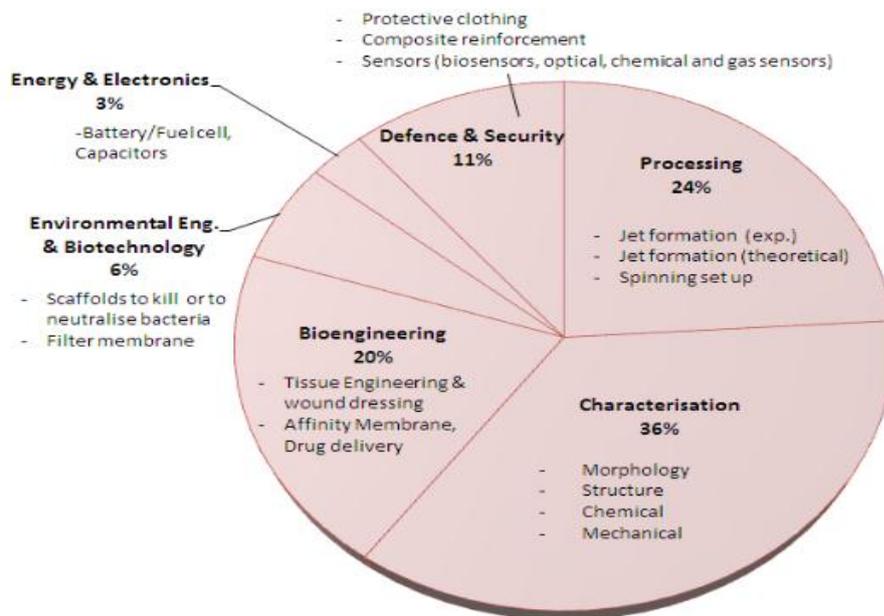


Figure 1-1: Division of Research on electrospun polymer nanofibre (from Zeynep K.,2011)

One of the applications of nanofibre is the controlled drug release. The high surface area to volume ratio has made nanofibre as potential materials for controlled drug released. To have steady and stable drug release profile, the desired morphology of nanofibre is linear shape nanofibre. There have been almost 200 different types of polymer used on producing controlled drug released nanofibre.

## ***1.2 Statement of problem***

Drug delivery system is a mechanism to deliver therapeutic agents into the body. Some examples of the primitive approaches are chewing leaves and roots of medical plants or inhalation of soot from the burning of medical substances. These methods of drug delivery lack of consistency and uniformity (John Wiley & Sons,2006). With the advancement of technology, new drug delivery system has been developed and one of the potential drug delivery system is by using nanofibre.

Nanofibre exhibit many properties like high surface area to volume ratio like with a diameter of 100nm have a ratio of geometrical surface area to mass of approximately  $100\text{m}^2/\text{g}$  (Audrey F. & Ioannis S. C., 2003). which is one of the properties that are desired in the drug released system which will give higher overall release rate than bulk materials like pills or needle injection. According to Jian F., Xungai W., and Tong L., electrospinning process will have little influence on the drug activity so when fabricating drug loaded nanofibre, the drug will not lost it properties during the electrospinning process. An ideal drug release system is in controlled manner in which the drug will be released at a predictable rate. Therefore, linear shape of nanofibre is preferable morphology in drug delivery system as linear shape will minimize the initial burst release of drug.

### ***1.3 Motivation***

In tissue engineering, the fibre can also be used as carriers in controlled drug release, delivering prolonged or better targeted drug delivery. Drug-loaded nanofibres can be prepared by co-dissolving solutions of guest pharmaceutical active ingredients and the host polymer by traditional single-fluid electrospinning. Different types of controlled drug release profiles such as immediate, pulsatile, delayed, sustained and biphasic releases have been achieved using electrospun nanofibre (Deng-Guang Yu et.al, 2012). Initial burst is likely to occur as the large surface area, drug distribution or the amorphous status of the drug. We need to maintain desired drug concentration in the blood within the desired period to have a controlled drug release profile. Therefore, we would like to eliminate the initial burst effect by fabricating out linear shape nanofibre.

There has been almost 200 different types of polymer used on producing controlled drug released nanofibre using material like ketoprofen, ferulic acid, but very less research have been done on using polyethylene oxide solution. Controlled drug released nanofibre must meet some requirement like having desired drug concentration release to the blood within desired time and the elimination of initial burst effect. Therefore, experiment will be conducted on using 2 different molecular weight of polyethylene oxide, which is 400,000(400k) and 900,000(900k) molecular weight (MW) to fabricate out linear shape nanofibre.

### ***1.4 Objectives***

The following are the objectives of this research:

- To fabricate out linear shape nanofibre using PEO only.

### ***1.5 Scope of this research***

The following are the scope of this research:

- i) To study the effect of concentration of polymer solution on the morphology of the nanofibre.
- ii) To analyze the morphology of the nanofibre.

## ***1.6 Organisation of this thesis***

The structure of the remainder of the thesis is outlined as follow:

Chapter 2 provides a description of the history of the electrospinning process along with the detailed description on the process. Effect of parameter toward the nanofibre also will be discussed, the application of nanofibre and the properties of polyethylene oxide.

Chapter 3 gives a review of the experiment methodology consisting preparation of the polymer solution, electrospinning process and the analysis of the morphology of nanofibre.

Chapter 4 is description on the result that have obtained and discussion about the result.

Chapter 5 is the conclusion of this thesis

## 2 LITERATURE REVIEW

### 2.1 History of Electrospinning Process

1<sup>st</sup> record of discovering the deformation of liquid due to electrostatic force is William Gilbert around year 1600. William Gilbert was a physician and president of the Royal College of Physician. According to Nick T., Jonathan J. S., Mark P. S., Hussam R., & Kathleen H., Gilbert used rubbed amber and caused deformation of a liquid drop which later known as the Taylor cone.

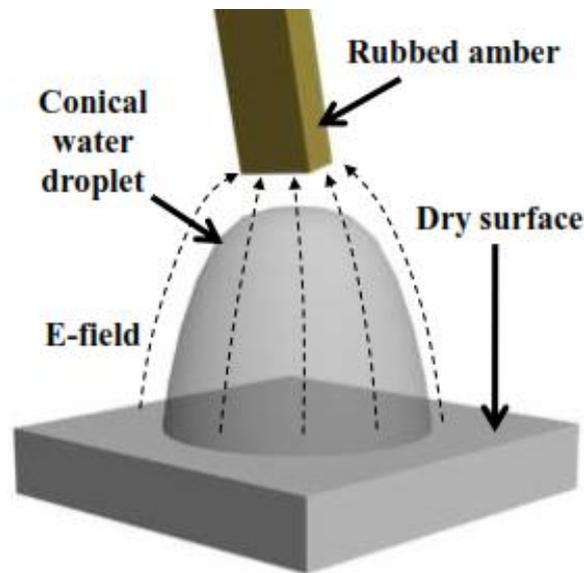


Figure 2-1: Rubbed Amber Cause Deformation of Water Droplets (from Tong H.W. & Wang M., 2009)

After the discovery of the deformation of water droplet, Formhals, in 1934 had managed to use electric charge to spin synthetic fibre with relatively small in diameter. But there are some disadvantages on Formhals works due to the close distance between the collector and polymer solution. This lead to the formation of loose web structure and the fibre tend to stick to the collector. Close distance between the collector and polymer solution caused the solvent does not complete evaporate making the fibre stick to the collector. In his second attempt, Formhals had distanced the collector and the polymer solution and has mitigated much of the problem from the 1<sup>st</sup> attempt (T.J. Sill and H.A.

von Recum, 2008). Anton Formhals have at least 22 patents regarding the electrospinning process and some of his drawing can be seen in the following figure.

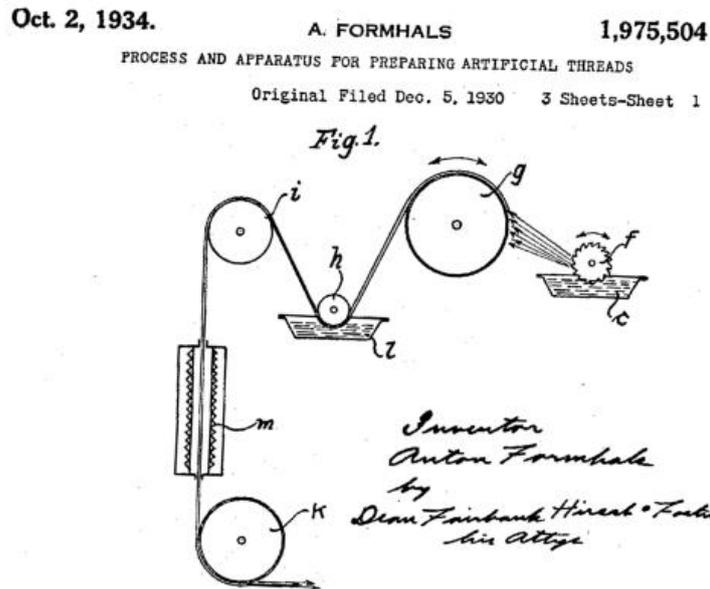


Figure 2-2: Drawing of Anton Formhals of Electrospinning ( from S.De Vrieze & K.De Clerck, N/A)

After Formhals, the electrospinning technology seems to be lie dormant until Simons design an apparatus proven that fabrication of nanofibre is feasible. Simon show that ultrafine fibre can be produced through the electrospinning process and with less viscous solution will produce finer but shorter fibre while high viscous solution will produce longer but thicker fibre. (Pirjo H., 2008)

At the same time, another person has expanded Formhals work electrospinning. Although Formhals have founded the method of using electric charges to synthesis fibre, but it is not him that coin the term Taylor cone. It was Taylor who was research on the jet forming process. He found out that when the polymer solution is applied electric charges on it, the round meniscus of the solution will develop into a cone shape. This cone shape was later on called Taylor cone. Taylor also found out the fibre produced have small diameter is because the fiber jet is ejected from the tip of the cone (T.J. Sill and H.A. von Recum, 2008).



Figure 2-3: Formation of Taylor Cone at the Tip of a Needle (from Oldrich J. & Stanislav P., 2010)

After Taylor and Simon, in 1971, electrospinning research was continuing by Baumgarten and he had made a significant find out on the effect of voltage toward the production of fibre. Upon reaching a certain critical voltage supply to the solution, fluid stream will form instead of breaking into droplets. The following figure shows the droplets and fluid stream. (HuaJun Z., 2007)

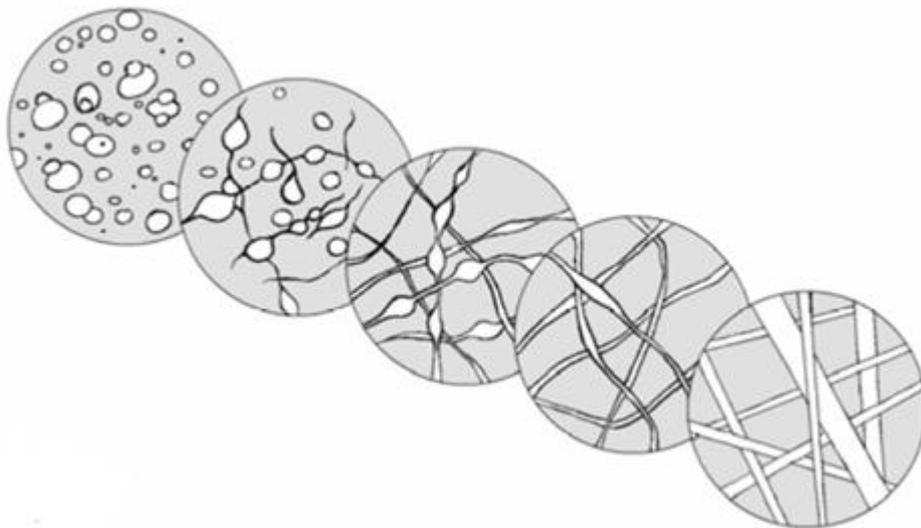


Figure 2-4: Formation of Droplet to Fluid Stream (from Pirjo H., 2008)

Since then, more and more researches have been done on the fabrication of nanofibre by different kind of solution. Papers and patent have been increasingly published regarding this technology. The following figure show the statistic data on the research paper and patent that have been publish regarding nanofibre.

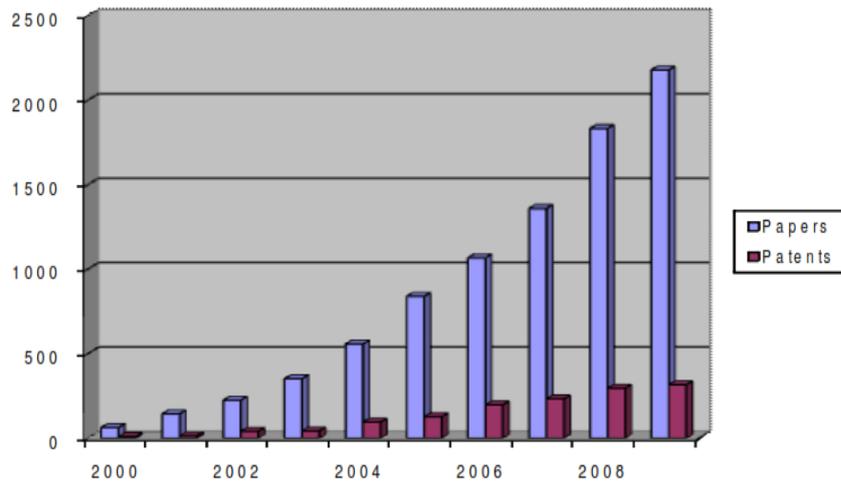


Figure 2-5: Statistic Data of Research Paper and Patent on Nanofibre. (from Oldrich J. & Stanislav P., 2010)

## 2.2 *Electrospinning Process*

There are number of methods like self-assembly, template synthesis, drawing, phase separation and electrospinning (Zheng M.H., Y.Z. Zhang, M.Kotako & S.Ramakrishna, 2003). All these method can be used to fabricate out the nanofibre but most of these method lack of scalability(Ghansham F., D.B. Jadhav & S.S. Chavan ,2013). Therefore, among all these methods, the best method for fabricate nanofibre for research purpose is through electrospinning method. Electrospinning, a process which has been known for more than 100 years, is a combination of 2 techniques, electrospray and spinning (Seema Agarwal et.al, 2008). The main component of an electrospinning equipment consist of a high voltage power supply, a dissolved polymer in a syringe with a conductive nozzle which is the needle and an electrically grounded plate set with a certain distance from the conductive nozzle (Christopher C.C., 2008).

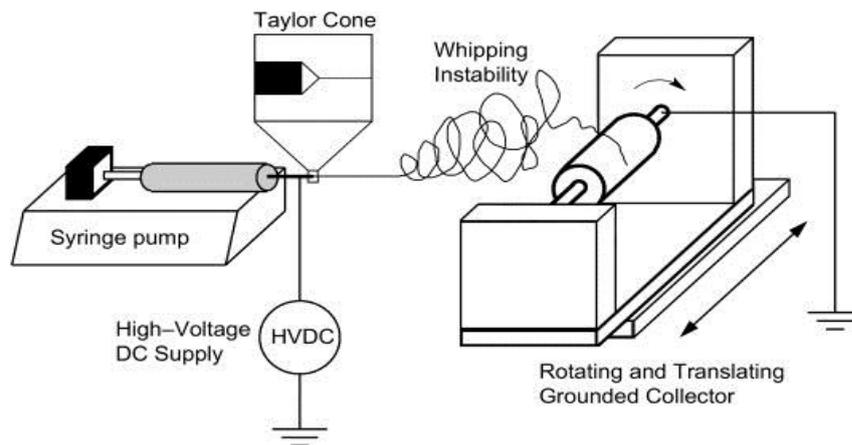


Figure 2-6: Schematic of a typical electrospinning system (T.J. Sill and H.A. von Recum, 2008)

Nanofibre is formed by the elongation of electrified jets of polymer solution. When applying charges into the fluid, the charges move through the fluid faster than the shape of fluid changes. The interaction between charged ion create the liquid jet while the surface tension of the fluid favours sphere-like shapes with smaller surface area per unit mass. The leading edge of the solution changes from rounded meniscus to a cone called Taylor cone. With enough electrical potential to exceed the surface tension of the polymer solution, droplet deformation occur, a charged fluid jet is ejected from the tip toward the opposite electrodes, the collector. The nozzle and the collector are set at a distance large enough so that before the fluid reached the collector, the solvent is evaporated during the travelling of fluid from the tips of Taylor cone to the collector.

According to HuaJun Z., depending on the solution prepared, with high enough viscosity, if the viscosity is not high enough, continuous jet will break into droplets which is caused by the instability of the liquid called Rayleigh instability. Therefore, different morphology structure of the fibre like beads, branches and buckling coils or zigzags can be achieved by controlling the parameter like applied voltage, the solution flow rate, the polymer weight concentration, the nozzle-to-ground distance and in some solutions, the concentration of ethanol (S.A. Theron et.al, 2004).

Various shape of electrospun fibre also been fabricated for different application like wound dressing and nerve conduit. Also, to broaden the usefulness of the nanofibre, kinds of post treatment like conglutination, by vapour coating, by chemical treatment of the surfaces, and by thermal processing toward the nanofibre have been applied. Thus the nanofibre has been quite an important material in many fields such as filtration and

separation, catalysis, electronics, protective clothing. One of the fields is biomedical field. Tissue engineering, drug release, wound dressing and enzyme immobilization are few example of the biomedical field which have some breakthrough with the nanofibre.

### 2.3 Effect of Parameter on Nanofibre

Fabrication of nanofibre may sound like very easy process, but is actually a very delicate process which involves many parameters that will affect the morphology of nanofibre (H.S. Wang, G.D. Fu & X.S. Li, 2009). There are several parameters which will affect the morphology of the nanofibre produced. Parameters like applied voltage, capillary to collector distance, the concentration of the polymer, the volatility of the solvent used and the solution conductivity. With increasing applied voltage, the shape at the Taylor cone will be altered. At low voltage, Taylor cone will be formed but as the voltage increased, formation of the Taylor cone is decreased which will lead to the formation of beaded nanofibre.

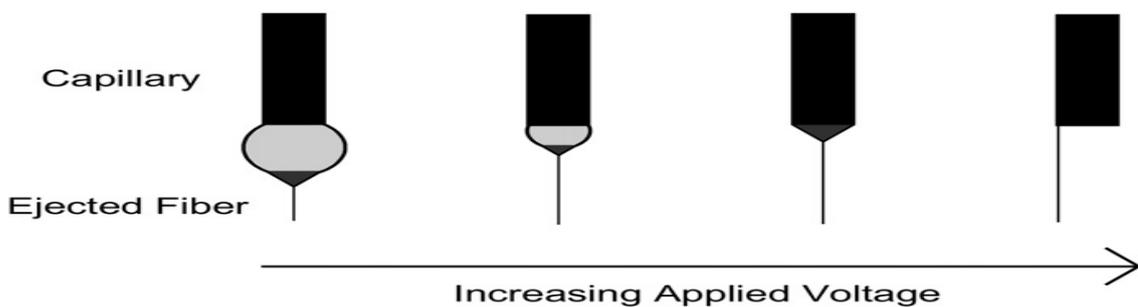


Figure 2-7: Formation of Taylor Cone at Different Applied Voltage (T.J. Sill and H.A. von Recum, 2008)

Capillary to collector distance play a role in determining the morphology of the nanofibre produced. The diameter is decreased with increasing distances from Taylor cone. With shorter distance between capillary and collector will lead to inadequate drying of the polymer fibre which leads to the formation of beaded nanofibre. (Zeynep K.,2011)

According to C. Riberio, V. Sencadas, C. Caparros, J. L. Gomez & S.L. Mendez, the solution concentration and molecular weight of the polymer is the most important parameter. For the solution to be able undergo electrospinning, the concentration play a very important role. If the solution is too dilute, the formation of nanofibre is likely will not occur due to the polymer fibre will break up to droplets before reaching the collector. But if the solution is too concentrated, the nanofibre also

will not be formed because of the high viscosity. While for the molecular weight, beaded nanofibre will be formed with low molecular weight but with high molecular weight, large diameter of nanofibre will be formed. (H.S. Wang, G.D. Fu & X.S. Li, 2009)

The volatility of the solvent will affect the porosity of the nanofibre. With higher volatility of the solvent will increase the surface area of the nanofibre by exhibit pores on the surface of the nanofibre. Finally is the conductivity of the solution, with higher conductivity of the solution, the nanofibre will have a smaller diameter. The following table is the summary of the effect of process parameter on the morphology of the nanofibre.

<b>Parameter</b>	<b>Effect on Nanofibre Morphology</b>
Viscosity/concentration	<ul style="list-style-type: none"> <li>• Low concentration/viscosities yielded defect in the form of beads and junctions.</li> <li>• Increasing concentration/viscosity reduced the defects.</li> <li>• Fibre diameter increased with increasing concentration/viscosity.</li> </ul>
Flow rate	<ul style="list-style-type: none"> <li>• Lower flow rates yielded fibre with small diameters.</li> <li>• High flow rates produced fibres that were not dry upon reaching the collector.</li> </ul>
Polymer molecular weight	<ul style="list-style-type: none"> <li>• Increasing molecular weight reduced the number of beads.</li> </ul>
Voltage	<ul style="list-style-type: none"> <li>• Too high voltage, beading was observed.</li> </ul>
Distance between tip and collector	<ul style="list-style-type: none"> <li>• Minimum distance required to obtain dried fibre.</li> </ul>

Ambient parameters

- Increased temperature caused a decrease in solution viscosity, resulting in small fibres.
  - Increasing humidity resulted in the appearance of circular pores on the fibres.
- 

Table 2-1 – Parameter and its Effect on the Morphology of the Nanofibre (Quynh P.P. & Antonios G.M., 2006)

#### ***2.4 Application of Nanofibre in Drug Delivery System***

Some of the common drug delivery system are taking pills or needle injection into the blood stream. With the advancement of technology, there has been some development on the drug delivery system. To develop new and improved drug delivery system, several drug carriers like hydrogels, microspheres, nanoparticles have been develop for over the past few years. Among these drug carries, nanofibre was also being explored as new drug delivery system.

Nanofibre is produce by electrospinning of polymer solution. By controlling parameters like applied voltage used when electrospinning, the flow rate of polymer solution, the polymer weight concentration, the nozzle-to-ground distance, we can control the morphology of the nanofibre to be beads, branches and buckling coils or zigzags. But from the point of view of drug delivery, the main advantages by using nanofibre as drug delivery is high surface area to volume ratio, targeted delivery of drug. Besides that, through electrospinning process, it also gives us the advantage to tune the porosity and the ability to manipulate the nanofibre composition in order to get the desired properties and function.

To deliver drug using nanofibre, these agents have been incorporated into the nanofibre. This is accomplished by electrospinning the mixture of polymer and drug in the same solvent. But the releasing of drug from this drug loaded nanofibre does not showed a very satisfied result. Initial burst effect is shown followed by smooth release of the drug. This is most likely because of the drug distribution in the nanofibre. To achieve sustained drug releasing, modification has been made on electrospinning. Conventional electrospinning is using single fluid to electrospin. The new technique is

using 2 fluids or even multiple fluids to electrospin. Using 2 fluid or multiple fluid to electrospin is called coaxial or multiple coaxial electrospinning. With these techniques, the drug is being encapsulated and hence reduces the effect of initial burst.

The materials used to electrospin are also very important as well. For drug delivery system, when choosing material for the fabrication of nanofibre, material that will degrade is generally more popular as it does not require to be taken out once it is implant inside the organisms. Things to be worry is that, biodegradable nanofibre will affect the drug delivery profile. The nanofibre may be starts to degrade when the drug being release causing high concentration and reached toxic level. Many researches have been done using different type of material for the fabrication of nanofibre for drug delivery system. Table below show some materials that have been used in the past for the drug delivery system (T.J. Sill and H.A. von Recum, 2008).

<b>Electrospun mat</b>	<b>Drug</b>
Poly(caprolactone) PCL	Diclofenac sodium Tetracycline hydrochloride Resveratrol Gentamycin Sulfate Biteral
Poly(lactic acid) PLA	tetracycline hydrochloride and mefoxin
Poly(caprolactone-D,L-lactide)	Diclofenac sodium
Poly(vinyl alcohol) PVA	Diclofenac sodium Tetracycline hydrochloride Sodium salicylate, naproxen,indomethacin
Poly(maleic anhydride-alt-2-methoxyethyl vinyl ether)	Diclofenac sodium
Poly(lactide-glycolide) (PLGA)	Paclitaxel (anticancer) Tetracycline hydrochloride
Poly(ethylene-co-vinylacetate)	tetracycline hydrochloride
Gelatin	Centella asiatica-herbal extract
Cellulose acetate	Vitamin A and E

Table 2-2 - Some of the representative electrospun systems studied for drug-release applications (Seema Agarwal et.al, 2008)

## ***2.5 Polyethylene Oxide (PEO) as the Material for Electrospinning***

There has been extensive research on other material on producing nanofibre but less research has been done on using polyethylene oxide (PEO). PEO has been use in doing other biomedical research like hydrogels for controlled drug release purpose.

For being non-toxicity, high water solubility, insensitivity to pH of biological medium and ease of production, polyethylene oxide is one of the most important materials in pharmaceutical industry (Ning Wu et.al, 2004). It is also a biodegradable synthetic polymer, which is approved for internal use in food, cosmetic personal care product and pharmaceutical (Moustafa M.G. Fouda et.al, 2012). Thus it is believed that PEO also can be used to fabricate a controlled protein drug release nanofibre.

## 3 MATERIALS AND METHODS

### 3.1 Overview

This paper presents a process of producing protein drug loaded nanofibre. This process is carried out using electrospinning equipment. Basically, this experiment will be divided into 3 parts. First part is the polymer solution preparation. Then the solution will undergo electrospinning process. Then the product of the electrospinning process, which is the nanofibre, will undergo morphological analysis by field emission scanning electron microscope (FESEM).

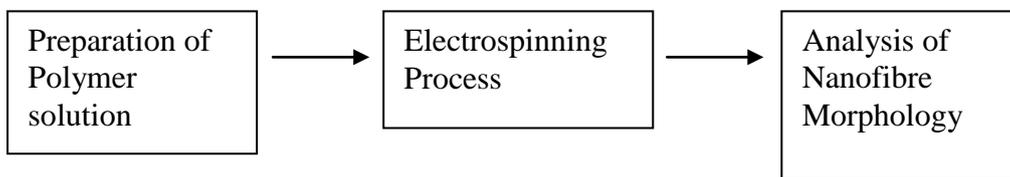


Figure 3-1 : Work Flow of the Experiment

### 3.2 Chemicals/Materials

Polyethylene oxide from Sigma Aldrich Company (molecular weight: 400,000 and 900,000), bovine serum albumin (BSA), distilled water, ethanol, needle (Becton Dickinson & Company, USA), syringe (Becton Dickinson & Company, USA), container, electrospinning equipment (Electrosis, Nano Fiber Production System), magnetic stirrer.

### 3.3 Polymer Solution Preparation

PEO polymer solution is prepared at room temperature by dissolving PEO powder (1.5wt% of 900k PEO) into the solvent, ethanol solution with 10wt% concentration. Mixture of PEO with solvent will be stirred for at least 8 hours using magnetic stirrer to reach homogeneous state.



Figure 3-2 : Polymer Solution will prepared in this Container

Different concentration of polymer solution (1wt% of 900k and 400k PEO + 5wt% of ethanol solution, 5wt% of 900k PEO + 5wt% of ethanol solution) will be mix in order to study the effect of concentration of polymer solution toward the morphology of nanofibre. After stirring for 8 hours, the solution will be mix with bovine serum albumin and stir again for another 15minutes for bovine serum albumin to dissolve into the solution. Then the solution will be left for 15min for the bubble that have form in the solution to bubble out from the solution.

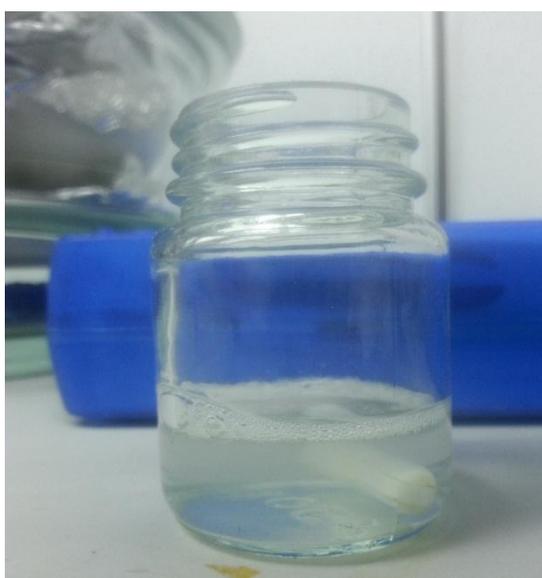


Figure 3-3 : Polymer Solution is Left for Bubble to Bubble out