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# ELECTROSPRAY METHOD: PROCESSING PARAMETERS INFLUENCE ON MORPHOLOGY AND SIZE OF PCL PARTICLES

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## ABSTRACT

The polymeric microparticles using electrospray technique have been used effectively as the drug carrier, whereby controlled release of drug. The electrosprayed particles morphology and size dictated the degradation of polymer matrix, therefore they influenced the release profile from drug loaded microparticles. The effects of electrospray processing parameters (flow rate, applied voltage and distance from the tip of needle to collector) on morphology and size of polycaprolactone (PCL) particles were investigated by scanning electron microscopy (SEM) and ImageJ software. In this research, the PCL solution was prepared by dissolving PCL in Dichloromethane at 4.5 % solution. In addition, processing parameters such as the flow rate (0.5 mL/h, 1 mL/h, 1.5 mL/h, 2 mL/h and 4 mL/h), the applied voltage (15 kV, 18 kV and 24 kV) and the collecting distance (15 cm, 20 cm, and 25 cm) were changed to examine the effects of them on size and morphology of PCL particles. The results indicated that at the suitable electrospraying parameters (18 kV, 1.5 mL/h, 20–25 cm), microparticles have obtained the uniform and stable morphology while at higher flow rate (2 mL/h and 4 mL/h), the particles were deformed and had bigger size.

*Keywords:* morphology, electrospray, microparticles, polycaprolactone.

## 1. INTRODUCTION

Electrospray method is a one–step process to fabricate biodegradable polymer microparticles with appropriate features such as size and morphology for drug carrier applications. Morphology and structure of electroprayed particles influence the release of drugs. Therefore, size and morphology controlled microparticles was able to control the release of drugs [1–4]. Some main factors which affect morphology (such as polymer concentration and solvent) or influence size and size distribution of particles (such as applied voltage, flow rate and collecting distance) were described in many studies. For instances, size and morphology of poly(lactic/glycolic) acid (PLGA) particles were controlled by adjusting solvent, molecular

weight, nozzle diameter and flow rate as these studies of Yao [5], Meng [6] and Jafari–Nodoushan [7]. Other polymers were used to fabricate electrosprayed microspheres with homogeneous and stable morphology such as chitosan [8, 9], polylactide acid (PLA) and PCL (Polycaprolactone) [1, 10, 11].

In drug delivery applications, polymer types were chosen based on their desirable properties, and then the release of drug from the polymer matrix. Polyester such as PLGA, PLA and PCL are degraded by hydrolysis of ester linkage. The degradation of PLGA and PLA is faster than PCL since they have more ester groups in their structure than PCL. Therefore, PLGA and PLA particles were suitable for shorter time drug delivery while PCL particles were effective for longer time system due to the slow degradation of PCL [12, 13]. This research investigated the effects of electrosprayed processing parameters such as flow rate, the applied voltage and the collecting distance on the morphology and size of PCL microparticles. The particles morphology was observed by SEM imagines. Size and size distribution of particles were evaluated by ImageJ and Minitab software.

## 2. MATERIALS AND METHODS

### 2.1. Materials

Dichloromethane (DCM) was purchased from Prolabo – France, 99 % purified. Polycaprolactone (PCL) (Mw = 75 – 90 kDa) was purchased from Sigma–Aldrich. PCL pellets were dissolved in DCM with 4.5 % concentration (w/w).

### 2.2. PCL microparticles production by electrospraying

The polymeric solutions were stirred using a magnetic stirrer for 2–3 h at room temperature. Then, the PCL solution was prepared in a 20 mL syringe and set up in a pump with the adjustable flow rate (Micropump Top–5300, UK, flow rate from 0.1 mL/h – 999.9 mL/h). The high voltage was applied to stainless steel needle (type Gauge 20G) on top of the syringe and the collector plate which was covered with aluminum foil. When the electrosprayed droplet flew from the tip of the needle to the collector, the solvent evaporated and solid microparticles were collected in aluminum foil. The processing parameters were adjusted by changing the flow rate (0.5, 1, 1.5, 2 and 4 mL/h), a high voltage (15, 18 and 24 kV) and collecting distance (15, 20 and 25 cm) during spraying. This process was carried out at room temperature. After electrospraying, the PCL microparticles were dried at room temperature for 2 days to remove solvent completely.

### 2.3. Characteristics of electrosprayed particles

Morphology of microparticles was observed by the Hitachi S–4800 Scanning Electron Microscopy (SEM) – Japan at Nanotechnology Laboratory, R&D Center, Saigon Hi–tech Park, Vietnam. Samples were platinum coated by using a sputter coater under vacuum environment. The accelerating voltage of SEM was 5 kV during scanning. The diameter of the electrosprayed particles was measured by using standard SEM images coupled with the ImageJ program (v.1.50i of National Institute of Health, USA). Then the Minitab Software (version 17.1.0 of Minitab Inc., Australia) was operated to calculate mean size and size distribution of microparticles.

## 3. RESULT AND DISCUSSION

### 3.1. Effect of flow rate on size and morphology of PCL particles

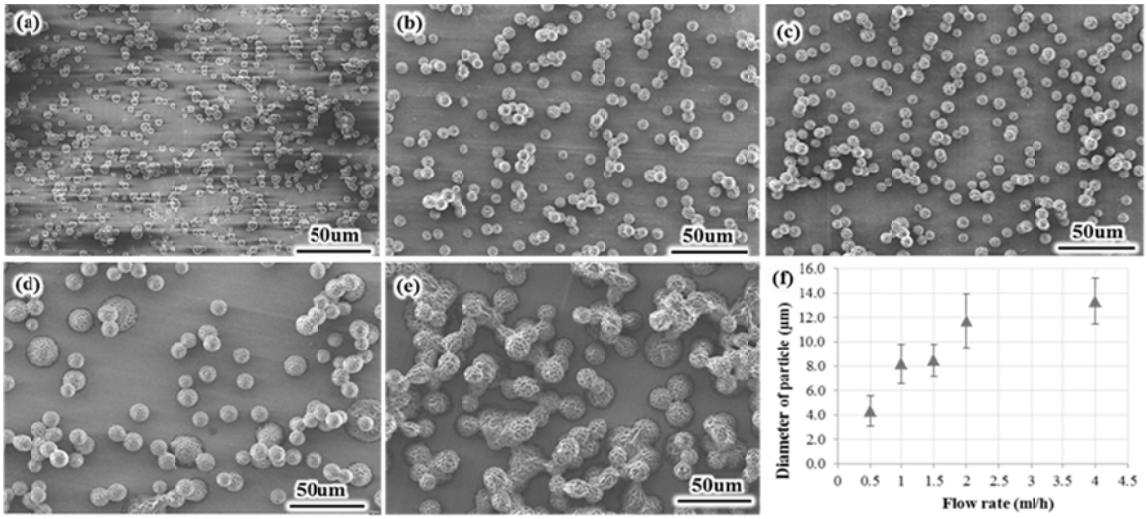


*Figure 1.* SEM images (a–e) of PCL microparticles of 4.5% PCL in DCM with different flow rate (a) 0.5 mL/h, (b) 1 mL/h, (c) 1.5 mL/h, (d) 2 mL/h, (e) 4 mL/h, (f) diameter of particle of mentioned flow rate (collecting distance: 20 cm, voltage: 18 kV, 20G).

The SEM images showed that the irregular and heterogeneous particles were formed at the flow rate of 0.5 mL/h (Figure 1a). Most of microparticles were spherical shape at flow rate from 1 mL/h to 4 mL/h (Figure 1b, c, d, e). However, at 2 mL/h and 4 mL/h, the particles were deformed and aggregated when they influence the collector since the solvent still present inside of particles (Figure 1d, e). The average diameter of particles was increased from 4.35 µm to 13.32 µm when the flow rate increased from 0.5 mL/h to 4 mL/h (Figure 1f).

*Table 1.* Average size and standard deviation of PCL particles in different elecstropraying process.

| Electrospraying parameters | | | Number of particles studied | Average diameter (µm) | Standard deviation (µm) |
|---|---|---|---|---|---|
| Flow rate (mL/h) | Collecting distance (cm) | Applied voltage (kV) | | | |
| 1.5 | 20 | 15 | 500 | 9.034 | 1.349 |
| 1.5 | 20 | 18 | 500 | 8.454 | 1.329 |
| 1.5 | 20 | 24 | 500 | 6.320 | 1.357 |
| 1.5 | 15 | 18 | 400 | 11.730 | 2.357 |
| 1.5 | 25 | 18 | 500 | 7.934 | 1.759 |
| 0.5 | 20 | 18 | 500 | 4.347 | 1.242 |
| 1.0 | 20 | 18 | 500 | 8.176 | 1.623 |
| 2.0 | 20 | 18 | 500 | 11.702 | 2.226 |
| 4.0 | 20 | 18 | 170 | 13.32 | 1.874 |

At the same period of time, with higher flow rate (2 mL/h, 4 mL/h), the solution volume ejected from the tip of the needle increased so the size of particles was bigger. Low flow rate (0.5 mL/h) caused small droplet and high charge density, the small particles were generated by

strong Coulomb fission. The homogeneous microspheres were obtained at flow rate of 1.0 mL/h and 1.5 mL/h. The standard deviation of particles size using 1.5 mL/h is the lowest value (1.329 µm) (Table 1). Therefore, flow rate was fixed at 1.5 mL/h in next experiments.

### 3.2. Effect of applied voltage on size and morphology of PCL particles

SEM images showed that the microspheres were generated at various applied voltage (15, 18 and 24 kV) whereas 4.5% PCL concentration and parameters of flow rate (1.5 mL/h), needle gauge (20G), collecting distance (20 cm) were fixed (Figure 2). The average diameter of PCL particles decreased when the applied voltage increased (Figure 3). This was a result of the field strength increasing at higher applied voltage.

According to Table 1, the average diameters of microspheres were decreased to 9.03 µm, 8.45 µm and 6.32 µm when applied voltage was increased, however the standard deviation of them was approximately (1.35, 1.33 and 1.36 µm).

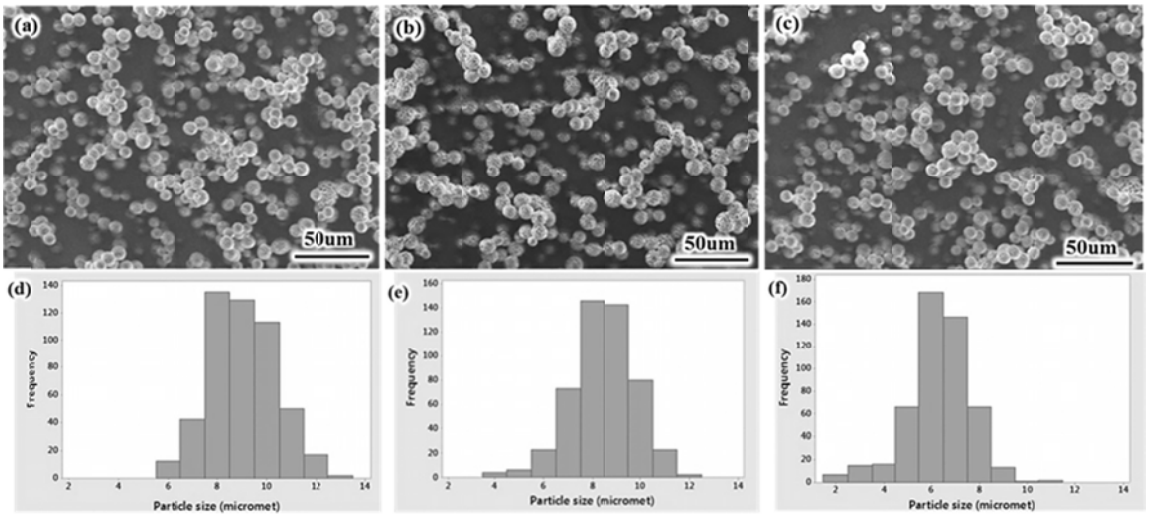


*Figure 2.* SEM images and the size distribution histograms of PCL particles with different applied voltage. (a, d) 15 kV, (b, e) 18 kV, (c, f) 24 kV (collecting distance: 20 cm, flow rate: 1.5 mL/h, 4.5% PCL in DCM, 20G).

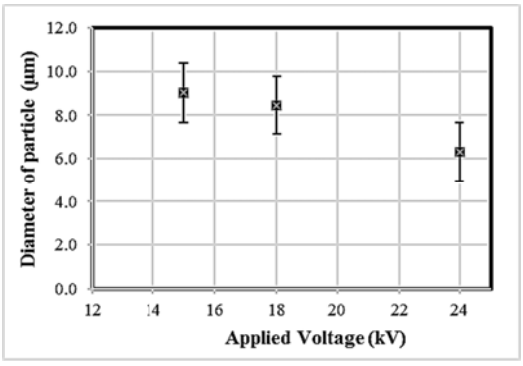


*Figure 3.* The effect of the applied voltage on the average diameter of PCL particles (4.5 % PCL in DCM, collecting distance: 20 cm, flow rate: 1.5 mL/h, 20G).

### 3.3. Effect of distance from the tip of needle to collector on size and morphology of PCL particles

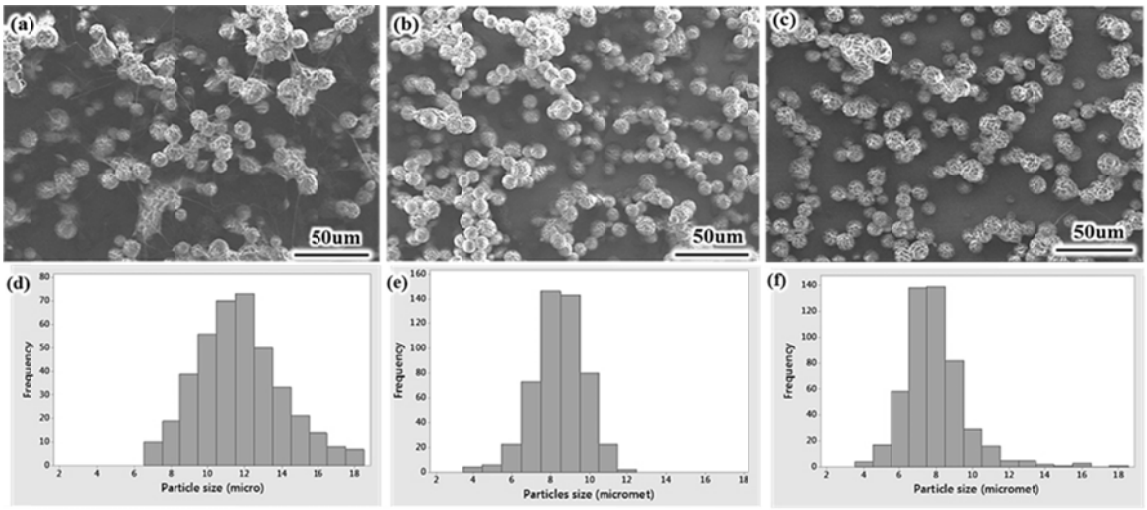


*Figure 4.* SEM images and the size distribution histograms of PCL microparticles with different collecting distance. (a, d) 15 cm, (b, e) 20 cm, (c, f) 25 cm (voltage: 18 kV, flow rate: 1.5 mL/h, 4.5 % PCL in DCM, 20 G).

Despite using the same parameters, 4.5% PCL in DCM, applied voltage of 18 kV, needle gauge 20G and flow rate of 1.5 mL/h, the morphology of microparticles was different when adjusted the distance from the tip of needle to collector.

At collecting distance of 15 cm, there was a variety of particle morphology such as sphere, fiber, microbeads, etc. while microspheres were only formed at 20 cm (Figure 4a, b). The explanation for this phenomenon is that the electrospray was in multi–jet mode at 15 cm due to high electric field forces. Thus the morphology of particles was heterogeneous and irreproducible such as microbeads, fiber and particles with a tail. Furthermore, increasing the collecting distance to 20 cm, the polymer chains had time to diffuse inside the droplet and rearranged structure, the particle morphology was spherical. However, when the distance was increased to 25 cm, the morphology of the particles turned to heterogeneous spheres (Figure 4c) and the size distribution of particles became broader than at 20 cm (Figure 4d, e, f), consequence of the generated satellite and secondary droplets.

According to Table 1, the average diameter of particles reduced from 11.73–7.93 µm when the collecting distance was increased gradually (15–25 cm) (Figure 5). Because of increasing distance, Coulomb fission divided droplets into smaller particles when they flew from the needle to the collector. The uniform size of particles which using collecting distance of 20 cm was the highest (standard deviation is 1.329) so that it was the optimized value in this research.

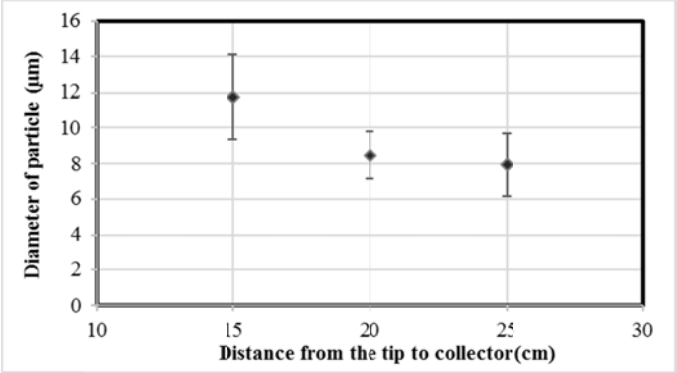


*Figure 5.* The effect of distance from the tip of needle to collector on the average diameter of PCL particles (4.5% PCL in DCM, flow rate: 1.5 mL/h, voltage: 18 kV, 20G).

## 4. CONCLUSION

The flow rate is a main processing parameters effects morphology of electrosprayed particles. Increasing flow rate from 0.5 mL/h to 2 mL/h caused bigger electrosprayed particles size, but the aggregation happened when the flow rate increased to 4 mL/h. Furthermore, the desirable microspheres were formed using a suitable set of parameters: flow rate of 1.5 mL/h, applied voltage of 18 kV and collecting distance of 20 cm. The size of the PCL microsphere increased when the flow rate increased and the voltage and the collecting distance decreased. The results demonstrated that the electrospraying technique was an effective method for fabricating monodispersed spherical microparticles.

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