Journal of Science and Technology **55** *(1B) (2017) 216–222*

TAYLOR CONE–JET MODE IN THE FABRICATION OF ELECTROSPRAYED MICROSPHERES

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Received: 30 December 2016; Accepted for publication: 5 March 2017

ABSTRACT

In this study, electrospray modes were investigated to clarify their effects on the morphology and size of polycaprolactone (PCL) particles. The result indicated that electrosprayed microspheres with homogeneous and stable morphology were fabricated by using cone–jet mode and suitable electrospray processing parameters. Besides, the PCL solution was created by dissolving in dichloromethane with different concentrations such as 3.5%, 4%, 4.5% and 5%. The scanning electron microscopy (SEM) micrographs pointed that electrosprayed PCL microspheres were formed by using 4.5 % polymer solution. In addition, the reproducible and homogeneous morphology of PCL microparticles were obtained at the following set of parameters: applied voltage of 18 kV, flow rate of 1.5 mL/h and distance tip to collector of 20 cm. Moreover, at the collecting distance of 15–25 cm, the flow rate of 1.2–1.8 mL/h and applied voltage of 18 kV the cone–jet mode was generated. It was an effective electrospray mode to create stable and homogeneous microspheres.

Keywords: electrospray, microspheres, homogeneous, cone–jet mode.

1. INTRODUCTION

Electrohydrodynamic (EHDA) is an interesting method in recent year because of its application in large medicine such as drug delivery system and tissue engineering. Besides, electrospray possesses more advantages to produce drug loaded polymeric microparticles compared to other methods such as emulsion, precipitation and spray drying [1]. In more details, some advantages of electrospray method are the high permeability to small drug molecules, the high drug loading capacity and encapsulation efficiency, the simple one–step process and the controlled ability of drug release through ester linkage degradation. Furthermore, the drug loaded PCL particles using electrospraying have slow degradation rate compared with poly (lactic acid) (PLA) and poly (lactic–co–glycolic acid) (PLGA), therefore it is more suitable for long term delivery system [2–4]. Since the morphology and size of electrosprayed particles influences on the release of drug and the degradation of particles, they need to be controlled [5–

7]. In some research, the monodisperse and reproducible particles obtained when were fabricated in the cone–jet mode. It is the most stable spraying mode and creates a uniform size of particles. Besides the cone–jet modes, some electrospray modes such as dripping, spindle, oscillating–jet and multi–jet mode can be observed when changing the electrical force [8–10]. However, they are the undesirable modes due to their instability and unpredictability. In more details, multi–jet mode and oscillating–jet generate the satellite and secondary droplets, resulting in a broader size distribution and unrepeatable particles shapes. In case of dripping and spindle mode, the particles are bigger and deformed because the solvent still exists in them [9, 11]. In Vietnam, some studies of Huynh D. P. and his group related to producing electrosprayed microspheres were published such as the chitosan microspheres [12] and the biodegradable polyester microspheres [13].

In this study, the effect of PCL concentration on the formulation of electrosprayed microspheres was investigated and the optimized value was chosen for next step. And then we revealed the varying electrospray modes by changing the applied voltage between tip and collector, flow rate or the collecting distance. Finally, the electrospray processing parameters in the cone–jet mode area were used to fabricate microspheres. The result demonstrated that the PCL microspheres obtained the homogeneous and reproducible morphology and the monodisperse size.

2. MATERIALS AND METHODS

2.1. Materials

Polycaprolactone (PCL) (M_w = 75–90 kDa) was supplied by Sigma–Aldrich, USA. Dichloromethane (DCM) was purchased from BDH Prolabo Chemicals, France, 99 % purified.

Electrosprayed solutions were prepared by dissolving PCL in DCM with different concentrations, included 3.5 %, 4 %, 4.5 % and 5 % (w/w). The polymeric solution was stirred by a magnetic stirrer at room temperature within 2–3 h to ensure the entire polymer was absolutely dissolved. Then, the dilute solution was stored within 15–30 min to remove bubbles completely.

2.2. PCL microparticles production by electrospraying

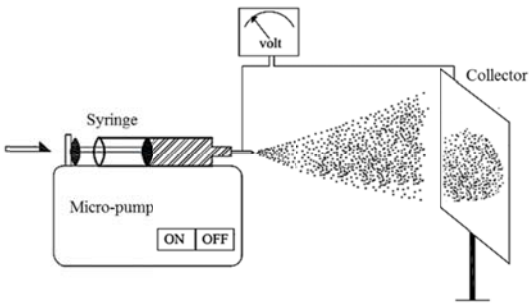

Figure 1. Setup electrospraying process.

PCL solutions were loaded in a 20 mL syringe with a stainless steel nozzle 20 G. The high voltage was applied to the needle at the tip of the aluminum foil (collector) at 18 kV. The distance between the tip of the needle and collector was fixed at 20 cm. The flow rate of electrosprayed solution was adjusted by a micro–pump from 0.5 mL/h to 2 mL/h (step 0.5 mL/h) (Figure 1). Then the samples on aluminum foil were dried at room temperature for 48 hours to evaporate solvent totally.

2.3. Classification spraying modes of electrospray method

Polymer concentration in DCM was fixed at 4.5% PCL, needle Gauge 20G. Besides, the flow rate (mL/h) was adjusted from 0.5 mL/h to 2.0 mL/h (step 0.1 mL/h) and distance from tip to collector was changed from 2.5 cm to 25 cm with an interval of 2.5 cm by removing the collector. Applied voltage was set at different values such as 12 kV, 15 kV, 18 kV and 24 kV. Electrospray modes were recorded by Camera Digital (Canon Powershot 300 HS) during the electrospraying (Figure 2).

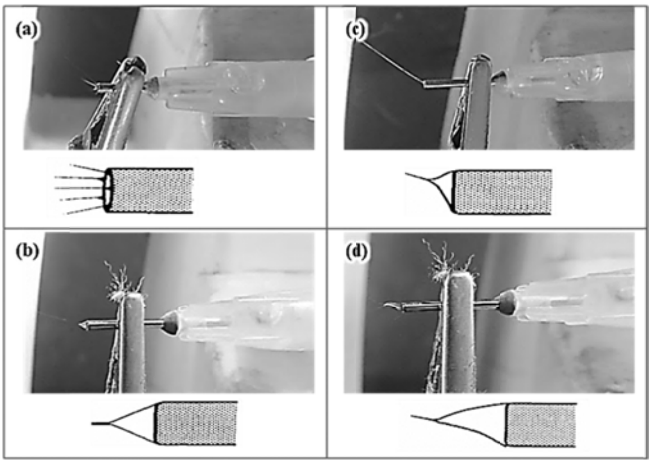

Figure 2. Spraying modes of electrospraying (a) multi – jet, (b) cone – jet, (c) oscillating – jet, (d) spindle.

The following electrospray modes were observed in this research included multi–jet, cone–jet, spindle and oscillating–jet mode. In the multi–jet mode, many jets were simultaneously ejected from the tip of the needle without forming droplets (Figure 2a). This mode developed from the cone–jet mode when the electric field force was strengthened at higher voltage and lower flow rate. The Taylor cone at the tip of the needle was observed in the cone–jet mode and it is the most stable and the most used mode (Figure 2b). In the oscillating – jet mode, the jet was projected from the tip of the vacant cone and changed its position regularly (Figure 2c). At the spindle mode, no regular droplet is ejected from the tip of the needle, only the elongated liquid appeared. After that, the spindle drops can separate into smaller droplets of different sizes due to the electrostatic force (Figure 2d) [8].

2.4. Characteristics of electrospray particles

PCL microparticles were observed by Scanning Electron Microscopy (SEM), Hitachi S–4800, Japan (Nanotechnology Laboratory, Saigon Hi–tech Park, Vietnam). In order to obtain the precise morphology of the particles, the measurement from random locations with different magnifications is essential. The accelerating voltage of SEM was 5 kV during scanning. After having the most appropriate SEM morphology result, the average size diameter and the size distribution were determined by Minitab Sofware (v.17.1.0 of Minitab Inc., Australia) and the ImageJ program (v.1.50i of National Institute of Health, USA).

3. RESULT AND DISCUSSION

3.1. Effect of PCL concentration on morphology of particles

Polymer chain entanglements, which generated during electrospraying process, were responsible for the final morphology of microparticles. In other words, when the chain entanglements were obtained significantly, microspheres were formed [14]. Moreover, the polymer concentration decided the formulation of chain entanglements so that the effect of PCL concentration on particle morphology was investigated.

Figure 3 indicated that the microparticles were hollow with low PCL concentration (3.5%) and spheres with higher PCL concentration (4 % and 4.5 %). By increasing the polymer concentration to 4 %, the number chain entanglements also were intensified and created distorted microspheres. Especially, perfect microspheres were obtained at 4.5 % PCL solution. However, when the PCL concentration (5 %) was too high, beaded fibers were mostly obtained since a lot of chain entanglements were created (Figure 3d). Therefore, we fixed 4.5 % PCL concentration and only changed the flow rate and collecting distance to examine the electrospray modes in next step.

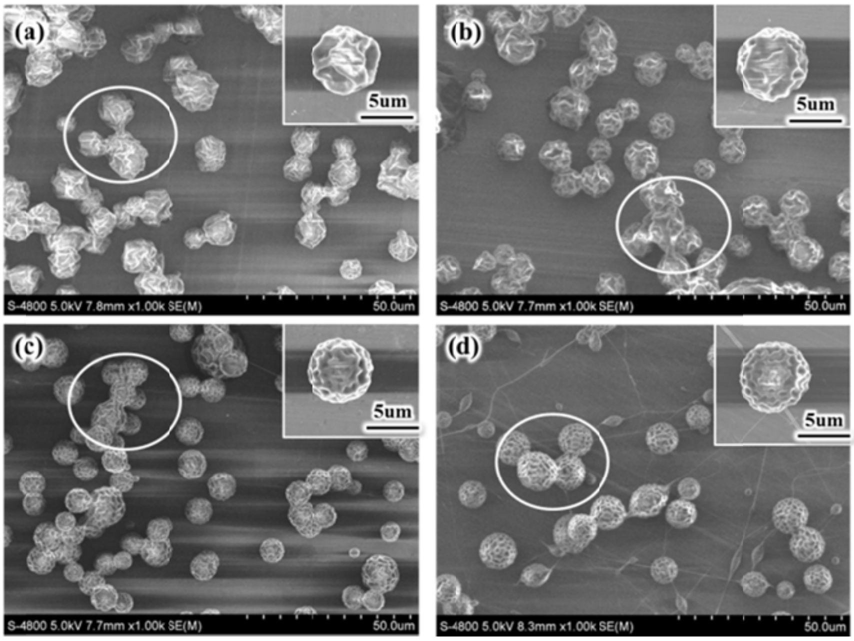

Figure 3. SEM images of PCL microparticles with different concentration in DCM: (a) 3.5 %, (b) 4 %, (c) 4.5 %, (d) 5 % (collecting distance: 20 cm, flow rate: 1.0 mL/h, voltage: 18 kV).

In addition, solvent inside microspheres had evaporated during it flew from the tip of the needle to the collector. The surface of microspheres had been wetting if solvent still remained inside, as a result, microspheres had tendency to agglomerate together. At the same processing parameters such as collecting distance, applied voltage and flow rate, the surface wetting property of particles had increased belong to the increased amount of solvent in PCL solutions. Because of that, the agglomeration together of microspheres reduced when the PCL concentration was raised up from 3.5 % to 5 % as showed on Figure 3.

3.2. Investigation spraying modes of electropspraying to obtain the homogeneous and stable particle morphology

The electrospray mode significantly effects on not only morphology but also the size of the microparticles. This research investigated the cone–jet mode area because it was the most stable mode and generated a mostly uniform size of particles. Thereby we can reduce the number of experiments when we revealed the effect of electrospraying parameters on the morphology and size of microparticles.

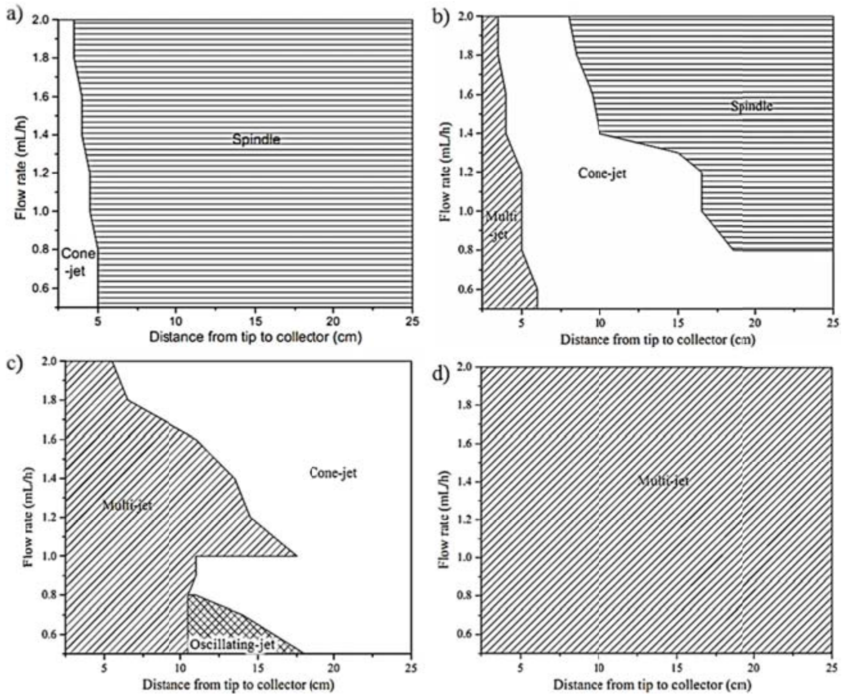

Figure 4. Mode selection maps to generate electrospraying modes (a) 12 kV, (b) 15 kV, (c) 18 kV, (d) 24 kV.

At low applied voltage (12 kV), the spindle mode was formulated when the flow rate was lower 2 mL/h and the collecting distance was from 5 cm to 25 cm as shown in Figure 4a. This phenomenon was explained that surface tension of PCL solution was higher than coulomb fission so that the polymer drops ejected on the top of the needle had irregular shapes, like the spindle (Figure 2d). When the collecting distance was shorter (2.5–5 cm), the cone jet mode was formed thanks to stronger electric field force but this area was narrow. Increasing voltage to 15 kV, the spindle mode area decreased while the cone–jet mode area increased, resulting in the multi–jet mode. And continuously increasing voltage to 18 kV, the spindle mode disappeared and the multi–jet mode area was larger, especially at the short collecting distance from 2.5–10 cm (Figure 4b, c). The reason is that the electric field force strengthened by a high potential or a short distance from the tip to the collector so that it overcame the surface tension of polymer solution. In addition, at 18 kV the oscillating–jet area appeared when the collecting distance increased from 10 cm to 18 cm and the low flow rate of 0.5–0.8 mL/h. This phenomenon is a result of electric field reducing and the presence of a small solution volume ejected from tip of needle. Increasing flow rate above 0.8 mL/h generated the cone–jet mode, consequence of a greater volume of solution.

Figure 4d showed that the multi–jet mode occurred continuously at voltage 24 kV although the flow rate changed from 0.5 to 2.0 ml/h and the distance from tip to collector changed from 2.5 cm to 25.0 cm. The explanation is that the voltage applied to the needle and the collector was so high that it overcame the surface tension of the polymer droplets. This led to the separation of a primary droplet into many small jets. Therefore, satellite particles appeared and the particles were heterogeneous and irregular morphology.

The cone–jet area was the largest when applied voltage was 18 kV, so we chose this value to fabricate the electrosprayed microspheres in next step.

3.3. Fabrication of PCL microspheres by electrospraying in cone –jet mode area

At electrospraying parameters, including 4.5 % PCL in DCM, 18 kV, 20 cm and flow rate 1.5 mL/h, the PCL microspheres were formed with a homogeneous morphology and size ranged from 4 µm to 12 µm. SEM images of PCL microprarticles showed that all electrosprayed particles had wrinkle surfaces due to a quick evaporation of DCM solvent. During the electrospraying process, there was a competition of solvent evaporation from the surface of droplets and polymer diffusion. DCM had a high evaporation rate (vapor pressure is 57.3 kPa, 25 °C), so that the skin of microspheres was solidified when the solvent in the surface of the droplets evaporated. And then, solidified skin moved to the droplet center and caused the surface particles wrinkled (Figure 5a).

At this condition, the average diameter was 8.454 µm with standard deviation was 1.329 and displayed monomodal size distribution as Figure 5b.

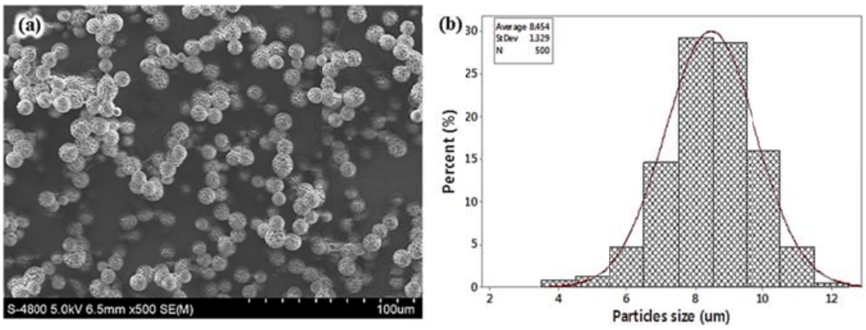

Figure 5. SEM images (a) and the size distribution histogram (b) of PCL particles with processing parameters: 4.5 % PCL in DCM, applied voltage 18 kV, flow rate 1.5 mL/h, collecting distance 20 cm, 20 G.

4. CONCLUSION

The PCL suitable concentration in DCM was 4.5 % to fabricate the electrosprayed microspheres. Increasing the electrical force by increasing voltage or decreasing the distance from tip to collector, the electrospray mode changed from spindle to cone–jet to multi–jet mode. Only when fabricating the electrospray particles in the cone –jet mode area, the monodisperse and reproducible particles were generated. This result indicated that the cone–jet area obtained at 18 kV, 15–25 cm, 0.5–2 mL/h or at 15 kV, 5–15 cm, 0.5–1.4 mL/h.

Acknowledgment. This research is funded by Vietnam National University Ho Chi Minh City (VNU–HCM) under grant number B2015–20a–01.

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