On the Fabrication of Microparticles Using Electrohydrodynamic Atomization Method

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Abstract — A new approach for the control of the size of particles fabricated using the Electrohydrodynamic Atomization (EHDA) method is being developed. In short, the EHDA process produces solution droplets in a controlled manner, and as the solvent evaporates from the surface of the droplets, polymeric particles are formed. By varying the voltage applied, the size of the droplets can be changed, and consequently, the size of the particles can also be controlled. By using both a nozzle electrode and a ring electrode placed axisymmetrically and slightly above the nozzle electrode, we are able to produce a Single Taylor Cone Single Jet for a wide range of voltages, contrary to just using a single nozzle electrode where the range of permissible voltage for the creation of the Single Taylor Cone Single Jet is usually very small. Phase Doppler Particle Analyzer (PDPA) test results have shown that the droplet size increases with increasing voltage applied. This trend is predicted by the electrohydrodynamic theory of the Single Taylor Cone Single Jet based on a perfect dielectric fluid model. Particles fabricated using different voltages do not show much change in the particles size, and this may be attributed to the solvent evaporation process. Nevertheless, these preliminary results do show that this method has the potential of providing us with a way of fine controlling the particles size using relatively simple method with trends predictable by existing theories.

Index Terms — Electrohydrodynamic Atomization; Polymeric Particles; Single Taylor Cone Single Jet; Size Control.

I. INTRODUCTION

Currently there are many ways to fabricate drug delivery particles. These includes spray drying method, emulsion method, dialysis method etc. Electrohydrodynamic Atomization (EHDA) is another way for the fabrication of such polymeric particles, although simply calling EHDA as the method of fabrication is a misnomer, and it warrants further discussion.

The EHDA method is essentially a two-step process for the fabrication of polymeric drug delivery particles. Polymer and drug dissolved in organic solvent are first pumped through a nozzle. The nozzle is applied with a high potential difference. The electrical field formed will cause the jet emitted from the nozzle to disintegrate into mono dispersed droplets in the micrometer range. The droplets are formed in a cross flow of nitrogen gas. Solvents will then evaporate from the surface of the droplets, and as the amount of solvent decreases, the droplets will then be transformed into polymeric particles with homogenously dispersed drugs in the polymer matrix. Thus, the EHDA is involved in the first part of the fabrication process, and the solvent evaporation process is an important second step in the fabrication of particles.

Rayleigh¹²³⁴ in the late 1800s is the first to observe that by applying an electrical potential to a liquid jet, the stability of the jet is changed. A slight charging will increase the stability of the jet, while a large charging will cause instability of the jet. Basset⁵ in 1984 gave a theoretical stability analysis of a thin liquid jet based on the perfect conductor model. The perfect conductor model assumes that the liquid has infinite conductivity and all charges are concentrated on the surface of the jet. This will cause a tangential surface stress, and with the set in of fluid motion, the viscous stress would also be needed to be taken into account. This would mean that the dominant stresses in this model would be the surface tension stress, the electrical tangential surface stress, and the viscous stress.

He found theoretically that increasing the charge density of the surface will cause instability under short wavelength disturbances and increases the growth rate of the instability (Fig. 1). Zeleny⁶ in the 1910s also gave a qualitative description of the different type of spray mode that can occur by applying different voltages to the nozzle. Glotin⁷ and Nayyar and Murty⁸ analyzed the problem using the perfect dielectric model, where the conductivity is assumed to be zero, and the electrical stress is imparted to the jet by the polarization stress of the dielectric material. Due to the absence of the surface charge, there is no tangential surface stress, and consequently the viscous stress can also be ignored. This would mean that the dominant stress would be the electrical polarization stress, and the surface tension

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stress. They found theoretically that increasing the electrical field will instead stabilize the jet (Fig. 2), contrary to what Basset has found. Taylor\(^9\) in 1966 realized that both perfect models are not good approximations and he together with Melcher introduced the Leaky Dielectric Model\(^10\), which assumes that surface changes can exist on the surface of a dielectric fluid. Saville and Mestel used the Leaky Dielectric Model and the theoretical prediction is much closer to reality. Recently, Hohman \etal\(^{11}\) also did a theoretical analysis and the results are able to explain the increased stability at low charge density and low electrical field strength.

In 1955, Vonnegut and Neubauer\(^12\) first explored the idea in using electrical stress to breakup thin liquid jet to form monodispersed droplets and particles. In recent years there is revival in the interest of using the EHDA method for the fabrication of micrometer size polymeric drug delivery particles. The potential advantages of using the EHDA method are given by the following points: 1. Micrometer range particles can be fabricated using nozzle size that has a length scale of 1 to 2 order larger; 2. No heating is needed and the fabrication can be done in room temperature; 3. The particles are very monodispersed if suitable operating parameters are used.

**II. EXPERIMENTAL**

**A. Materials**

Dichloromethane (DCM) is used as the solvent. It has a conductivity of about 0.0023 microsiemens per centimeter. Commonly used EHDA solvents, such as Ethylene Glycol, has a conductivity of about 0.69 microsiemens per centimeter. The low conductivity of Dichloromethane plays a big part in the explanation of the results of the experiments.

Polycaprolactone (PCL) from Sigma Aldrich is the polymer used for the fabrication of polymeric drug delivery particles. It has a molecular weight of about 65000. The concentration off PCL in DCM is 5% by weight.

Taxol, or the generic name Paclitaxel, from Bristol-Myer-Squibb, is the anti-cancer drug that is being encapsulated for delivery. The concentration of Taxol in PCL is 1% by weight.

**B. Apparatus**

A simple setup is rigged for the investigation of the process of the EHDA process (Fig. 3). The nozzle is a 29 gauge spinal tap needle with a flat tip. The ring is made of copper with a copper tube diameter of 4 millimeters and a ring diameter of 4 centimeters. It is placed axisymmetrically with regard of the nozzle, and the centre of the ring is 1 centimeter above the tip of the nozzle. The ground needle is a 26 gauge spinal tap needle and is placed 10 centimeters away from the tip of the nozzle. The apparatus is placed inside the fume hood and the experiments are

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**Fig. 1:** Dispersion relationship for perfect conductor based on Basset analysis. \(m\) is the non-dimensionalized wavenumber, \(k\) is the non-dimensionalized growth rate, and \(E\) is the non-dimensionalized surface charge density. The non-dimensionlized wave number is inversely proportional to the surface disturbance wavelength, and the droplet size is proportional to the surface disturbance wavelength.

**Fig. 2:** Dispersion relationship for perfect dielectric based on Nayyar and Murty analysis. The meaning of the parameters are similar to Fig. 1, except \(E\) is the non-dimensionalized electrical field strength.

**Fig. 3:** The Electrohydrodynamic Atomization setup. For the experiments, \(d_n\) is 220 microns, \(d_r\) is 4 cm, \(l_{RF}\) is 1 cm, \(l_{NG}\) is 10 cm. The solvent used is Dichloromethane (DCM), and has 5% by weight of Polycaprolactone (PCL) as solute.
done in ambient air.

To measure the droplet size, Phase Doppler Particle Analyzer is used. Two different pairs of laser are focus at the point of interest. The size of the droplets is determined by the interference pattern observed on the droplets, and the velocity of the droplets is determined by the Doppler shift detected.

The particles are collected directly on the Scanning Electron Microscope sample studs. The samples are then coated with platinum and observed using the Scanning Electron Microscope. The size of the particles is determined using SmileView software.

C. Methods

There are various spray regimes that can be encountered when an electrical potential is applied to the nozzle. In this set of experiments, all the particles are fabricated in the Single Taylor Cone Single Jet regime. In this regime, there is a liquid cone located at the tip of the nozzle. At the tip of the cone, a single stable thin jet is emitted. The jet, under the influence of surface tension and the electrical stress, will breakup in the varicose mode, and droplets will be formed.

Using both a nozzle electrode and a ring electrode (Fig. 3), we were able to produce a Single Taylor Cone Single Jet13 (Fig. 4) for a wide range of voltages applied to the nozzle and the ring. If only a single nozzle electrode were used, the range of voltage permissible for the formation of the Single Taylor Cone Single Jet would be limited, and at high voltage, we would get the Multiple Cone mode14 (Fig. 5), which was undesirable because of the more polydispersed spray.

To achieve the Single Taylor Cone Single Jet regime, we first set the nozzle voltage to a certain fixed value. We then increased the ring voltage from zero until the dripping mode can be observed. The ring voltage is then reduced until the Single Taylor Cone Single Jet regime is achieved.

The reasons for the fabrication of the particles in the Single Taylor Cone Single Jet mode are two fold. Firstly, in the Single Taylor Cone Single Jet mode, only a minor amount of secondary droplets and satellite droplets are formed. This will ensure the monodispersity of the spray. Secondly, the electrohydrodynamics of the thin jet under the influence of surface charges and axial electrical field are relatively well developed and thus we are able to predict the trend of the process.

III. RESULTS AND DISCUSSION

A. Phase Doppler Particle Analyzer

Preliminary results from the Phase Doppler Particle Analyzer (PDPA) have shown that the droplet size increases with increasing voltage applied. This trend can be seen in Table 1. This result fits the trend predicted by the electrohydrodynamic theory of the Single Taylor Cone Single Jet based on the Perfect Dielectric fluid Model. In our experiments, Dichloromethane is used, which has a very low conductivity. This may explain why the Perfect Dielectric Model fits the trend of the present study. Our results show agreement with a perfect dielectric model by Glonti. Furthermore, the results also fit the analysis by Hohman et al. using a leaky dielectric model, when the conductivity and surface charge density in the analysis is assumed to be low. Comparing our results with Hartman’s15 analysis, we see that we have the opposite trend. This is due to the fact that they are using solvents that have conductivity that are two orders of magnitude higher than what we are using. The higher conductivity would cause a higher surface charge density, and the

<table>
<thead>
<tr>
<th>Nozzle Voltage</th>
<th>Ring Voltage</th>
<th>Mean Size of Droplets</th>
<th>Standard Deviation of Mean Size Measured</th>
</tr>
</thead>
<tbody>
<tr>
<td>7.0</td>
<td>5</td>
<td>15.67</td>
<td>10.76</td>
</tr>
<tr>
<td>8.5</td>
<td>6</td>
<td>19.38</td>
<td>6.00</td>
</tr>
<tr>
<td>10</td>
<td>9</td>
<td>19.96</td>
<td>5.97</td>
</tr>
<tr>
<td>12.5</td>
<td>10</td>
<td>20.55</td>
<td>5.89</td>
</tr>
</tbody>
</table>

Table 1: Mean size and standard deviation of EHDA microparticles. Notice the increase in mean size as the voltage on the nozzle and ring is increased.
tangential surface stress and the viscous stress cannot be neglected in this case. This would mean that the analysis is more akin to the solution based on a perfect conductor theory.

B. Particle Fabrication

By changing the voltage applied to the electrodes, we are able to fabricate particles of various sizes. Although the size of the particles does not show a clear trend, we can see from Fig. 6 that particles fabricated at a much lower voltage have a smaller diameter than do particles fabricated at a high voltage. A large voltage difference is needed before any clear difference in particle size can be detected. The morphology of the particles fabricated is largely determined by the solvent evaporation process. According to Raula\textsuperscript{16}, a small droplet has a higher chance of forming into particle with a smooth surface and solid core, while a large droplet has a higher chance of forming into particle with a shriveled surface and a porous core. This explains the difference in morphology between the two different particles in Fig. 6. In this set of experiments, the particles are fabricated in ambient air. This increases the rate of solvent evaporation, which will also cause shriveled surface\textsuperscript{16}. This explains why the morphology of the particles is worse than previous works\textsuperscript{17}.

In order to fabricate particles with a smooth morphology and a solid core, we will need carefully control the conditions so that the rate for solvent evaporation is low, and increase the resident time of the particles in the chamber so that all the solvent is evaporated before the particle is collected.

IV. CONCLUSION

These preliminary results has shown that this method has the potential of fine controlling the particles size using relatively simple method with trends predictable by existing theory. The particle morphology is largely dependent on the solvent evaporation process, and a careful control of the process condition is needed to produce particles that have good morphology.

V. REFERENCES