



The effects of auxiliary electric field within the electrohydrodynamic atomization encapsulation chamber on particle size, morphology and collection efficiency



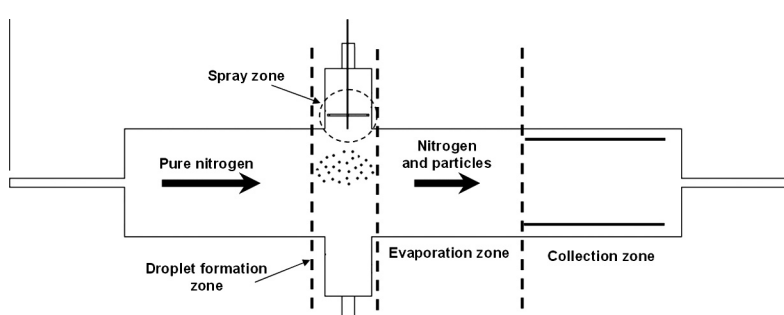
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HIGHLIGHTS

- A high voltage plate added in the chamber to induce auxiliary electric field (AEF).
- FEM calculations helped to examine the influence of flow and electric fields.
- AEF enhanced the collection efficiency but did not affect particle size distribution.
- AEF damaged smoothness of the particles when high voltage was applied to the plate.

GRAPHICAL ABSTRACT



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ABSTRACT

Electrohydrodynamic atomization (EHDA) or electrospray has been lately applied to fabricate drug carriers in the dosage forms of polymeric micro- and nano-fibers and particles. In the current study, EHDA process was performed in a glass encapsulation chamber to facilitate the formation of solid pharmaceutical particles after solvent evaporation from the electrosprayed droplets. High voltage nozzle and ring are enclosed in the named EHDA encapsulation chamber together with a grounded collecting plate. The unique feature of the design was an additional aluminum plate located a few centimeters above the collecting plate which was positively charged using a high voltage supplier. Furthermore, a simple finite-element model was generated to investigate the efficacies of flow and electric fields. This work aimed to investigate the effect of the auxiliary electric field on particle collection efficiency, morphology and size distribution. The final results show that application of the auxiliary electric field can clearly enhance particle collection efficiency in comparison to the EHDA process without auxiliary electric field. Additionally, it was established that the particle size distribution was not considerably influenced by the auxiliary electric field. On the contrary, the smoothness of the particles can be affected by the auxiliary electric field especially when a high voltage is applied to the flat plate.

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1. Introduction

Many new technologies and products have been developed during the last few years in the area of medicine and pharmacy. For instance, polymeric nano- and microparticles in biodegradable form are found among a group of pharmaceutical products that are

broadly employed in drug delivery applications [1–3]. Different methods, such as double emulsion, single emulsion and solvent evaporation are typically used to produce biodegradable polymeric nano- and microparticles. However, the most obvious drawbacks in these methods are the wide size distribution and the difficulty in scaling up the process. Most significantly, functionalities of drugs were possibly compromised as a result of exposure to organic solvents, aqueous organic interfaces, and high shear stress [4–6].

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Electrohydrodynamic atomization (EHDA) is a fairly recent technique for fabricating biodegradable polymeric micro- and nanoparticles for pharmaceutical applications. EHDA is a technique in which electrical forces are used to atomize a liquid solution. Various applications such as electrospray ionization in mass spectroscopy [7], thin film deposition [8], fabrication of pharmaceutical products [9–10], and drug encapsulation using polymeric particle production [11–14] can be considered for EHDA process.

As mentioned, EHDA have been used recently in pharmaceutical applications to fabricate different structures. EHDA was employed to generate corticosteroid aerosols between 1 and 5 μm with a small size distribution standard deviation and with an elevated efficiency such that adequate fine particles are fabricated to make uptake of corticosteroid to patients practicable and efficient [9]. Corticosteroids, as a cluster of relevant drugs, are employed in cancer treatment to limit the growth of tumors. An electrospray technique was also presented to generate coaxial electrospray liquid jets with diameters falling in the micron and sub-micron ranges. In the same study, monodisperse capsules were produced with diameters varying between 10 and 0.15 μm over a wide range of operating parameters [15].

In addition, the study of EHDA was extended towards the production of biodegradable polymeric micro and nano-particles. A few processing parameters associated with the fabrication processes such as solution flow rate, organic salt, surfactants, and polymer concentrations, and setup configurations on the size and morphology of pharmaceutical particles were examined [16]. It came to our attention that most of these named research works have placed focus on the release properties and morphology of the final polymeric particles. In contrast, a fundamental understanding regarding the application of EHDA to a production process and collection method is missing in the literature. This aspect is particularly important in the optimization of the process for production of pharmaceutical particles with the objective for achieving better quality and higher collection efficiency.

In EHDA process for pharmaceutical applications, PLGA (poly-lactic-co-glycolic acid) is generally used in the fabrication of micro and nano-particles for controlled release applications. Particle size plays a significant role in determining the period of sustained release rate [17–18] and is therefore an important engineering parameter from the viewpoint of design. The therapeutic capabilities of fabricated pharmaceutical particles are drastically affected by their size. In most cases, the drug release rate is enhanced under the conditions of larger surface to volume ratio, higher surface diffusion or surface erosion of the particles. Therefore, the capability to control the size of the fabricated particles offers a method to regulate or fine-tune the drug release properties.

The efficiency of particle collection and also the residual solvent in the fabricated particles were experimentally studied in our previous work [13]. Both factors are remarkably essential to the design of EHDA system particularly from the operating costs view. Higher particle collection yield is exceedingly advantageous because the raw materials used for fabrication of pharmaceutical particles are generally expensive. In other words, the collection yield is very essential in determining the operation cost of this process because of its direct linkage with the amount of raw materials needed. Nevertheless, there is a lack in literature regarding better understanding on this process from the operational point of view for scaling up of this type of pharmaceutical particle fabrication process.

In comparison to our recently published work [13], in the current study, one additional flat plate is positioned a few centimeters above the collecting plate, which is connected to a positive high voltage generator. Indeed, the target in this process is the enhancement of the particle deposition on the collecting plate using the additional electric field. The influences of an external electric field

on the motion and evaporation of highly charged droplets and their subsequent deposition have been previously studied. Yao et al. studied the solvent evaporation effect in EHDA process in an encapsulation chamber for pharmaceutical particle fabrication [14].

In summary, this work investigates the effects of an external electric field on the motion and deposition of highly charged particles. This phenomenon is studied in pharmaceutical particle fabrication process in an enclosed glass chamber, as a technical application of EHDA method, for other factors rarely addressed in the literature. The present study intends to examine the effect of Auxiliary Electric Field (AEF) on particle trajectory and deposition in the EHDA encapsulation chamber (Fig. 1). Furthermore, the influences of the auxiliary electric field on particle size distribution, morphology, and collection efficiency are examined.

1.1. Main zones in encapsulation chamber

As mentioned, EHDA process for fabricating pharmaceutical micro- and nano-particles is generally performed in an encapsulation chamber which can be seen in Fig. 1. Fig. 2 demonstrates that five main zones can be distinguished within the encapsulation chamber. These contain firstly a region in which pure nitrogen flows to carry the fabricated particles. Spray zone is the second region which comprises the nozzle and the ring where solution injection, atomization, and droplet breakup are observed. Thirdly, a droplet formation zone is exactly placed under the spray zone. In this zone, the jet formed at the apex of the needle is affected by the strong electric forces in the spray region; as a result, atomization to charged fine droplets occurs. Fourthly, there is an evaporation area wherein solvent evaporation from the droplets and conversion to fine solid particles take place. Afterwards, these solid particles are traveling towards the collecting plate. Lastly, solid particles are either deposited on the collecting plate or traveling towards the outlet in a collection zone. In an ideal system where the only forces acting in the EHDA system are electric forces, the particle collection efficiency can simply reach a high level close to 100%. This consideration is mostly reported in the literature. However, in a practical system, drag force as well as geometrical dimensions of the chamber also have significant effects on particle collection efficiency [13]. Henceforth, there is a delicate balance between the drag force and the electrical field force to determine the direction of the particles; towards the collecting plate (electrical forces dominant) or towards the outlet (drag force dominant).

2. Materials and methods

2.1. EHDA process

The experimental setup comprised one for each of the following items: nozzle electrode, ring electrode and flat plate electrode, all enclosed within a glass chamber (Fig. 1). High electric potential (relative to ground) was applied to the nozzle, ring and flat plate electrodes while the collecting plate was grounded.

The new generation of the chamber used in these experiments was modified from the one used in previous studies [8,14,16]. More details about the differences between these two generations of the chamber and merits of the new generation can be found in our recent study [13].

The spray zone includes the nozzle-ring configuration and the surrounding space within the chamber. The nozzle, the ring and the flat plate electrodes were independently connected to three high-voltage DC power supplies (Glassman High Voltage Inc., NJ, USA). The electric field within the chamber was fine-controlled by the high voltage difference combinations for the EHDA process

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