Review Article

Application of Electrospray Atomization (EA) – A Review Article

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Abstract

Electrospray atomization (EA) uses a high voltage to generate particles (electrospray) or fibers (electrospinning) while avoiding the use of heat or aggressive solvents representing an alternative to other thermal techniques that lead to some bacterial damages. While electrospraying may take several forms, in the cone-jet mode of operation (widely known as the Taylor cone), a jet shoots off the tip of the cone and breaks into droplets, as a result of the Rayleigh-Plateau instability, driven by surface tension. EA (electro refers to electric energy; hydrodynamic refers to fluid dynamics applied to liquids; and atomization refers to making bulk liquid into fine droplets) is a process where a liquid jet breaks up into fine droplets under influence of an external electrical field. In electrospinning, the polymer fluid does not break up into droplets but instead forms a slender, continuous liquid filament due to the suppression of the Rayleigh-Plateau instability by the effect of surface charge and the viscoelastic response of the jet. EA offers an approach for processing fine particles including charging, dispersing, coating and deposition.

Keywords: Electrospray, Electrospinning, Atomization, Encapsulation

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Introduction

Encapsulation of bacteria is an alternative that provides protection for living cells exposed to an adverse environment. It also helps food materials to resist processing and packaging conditions, improving taste, aroma, stability, nutritional value and product appearance. One of the encapsulation methods is EA (Electrospray Atomization) or EHDA (Electro Hydro Dynamic Atomization), which uses a high voltage to generate particles (electrospray) or fibers (electrospinning) while avoiding the use of heat or aggressive solvents representing an alternative to other thermal techniques that lead to some bacterial damages.

Typically, the EA process works at room temperature and allows the use of biopolymers in water solutions, avoiding the use of organic solvents, just by adjusting the process parameters and/or changing the solution properties through the addition of proper additives. Both electrospray and electrospinning technique has shown a great potential in the biomedical industry.

These techniques have recently appeared as an alternative to other drying processes and it has a tremendous potential in the food science area for the development of novel functional ingredients. Nonetheless, formulating encapsulated bioactive can still be challenging in the food industry because of the limiting use of food grade and generally regarded as safe (GRAS) materials as encapsulants.

The final products from Electrospinning and electrospraying are structure wise different but the technologies are similar. Final products of electrospinning are nanofibers, however, the electrospraying results are spherical bodies - microparticles deposited onto the support material.

Electrospinning and electrospraying, these two technologies act as "sister" technologies for polymer based nanomaterials production. Almost the same devices and arrangements are used for both of these technologies (**Figure 1**). Although the final products are different, they can be used separately or together. The main products of electrospinning are nanofibers. Nanofibers and nanofibrous layers are used in wide range of application nowaday. By the use of electrospraying technology produce a product that is Nanobeads. Nanobeads can be used mainly in medicine or special filtration. The nanofibers and nanobeads can be produced from a pure polymer material or there can be use of another material as an additive. One of such materials can be spherical fullerenes, which bring its special properties. Such composite nanomaterials can finally achieve better properties with minimal weight or surface changes. Needle or needle-less technologies has been used for both, electrospinning and electrospraying [1].

William Gilbert is a first scientist who observed and recorded an electro hydrodynamic atomization (EHDA) phenomena, also called electrospray atomization [3]. In 1750, Jean-Antoine (Abbé) Nollet, a French Clergyman and physicist, reported the earliest observation on electrospray, Literature demonstrating that if the container is electrified or put close to the electrical ground and then passed the water, water would aerosolize [4]. Around one century later,

Lord Kelvin invented a setup composed of two liquid nozzles that were bridged to opposite collection reservoirs and demonstrated that differences in kilovolt scale will be occurring due to the small differences in charging between water dripping from the nozzles [5]. In 1882, Lord Rayleigh theoretically evaluated the charge that a liquid droplet could carry to the greatest extent, known as the "Rayleigh limit", which was confirmed experimentally 100 years later [6, 7]. The first patent related to EA setup appeared in 1900 [8]. Zeleny conducted the electrospray experiment with ethanol and photographed a cone-jet in 1914 [9]. In 1960's, Taylor developed a mathematical description of the EA process, simulating the conical shape of the liquid phase in the presence of an electrical field that became known as Taylor cone later on [10]. In the 1980's, Fenn and coworkers performed a series of studies that eventually made electrospray capable of introducing dissolved analytes into the gas phase for mass analysis [11]. John Bennett Fenn won the Nobel Prize in Chemistry in 2002 because of his contribution to electrospray ionization for analyzing biological macromolecules [12].

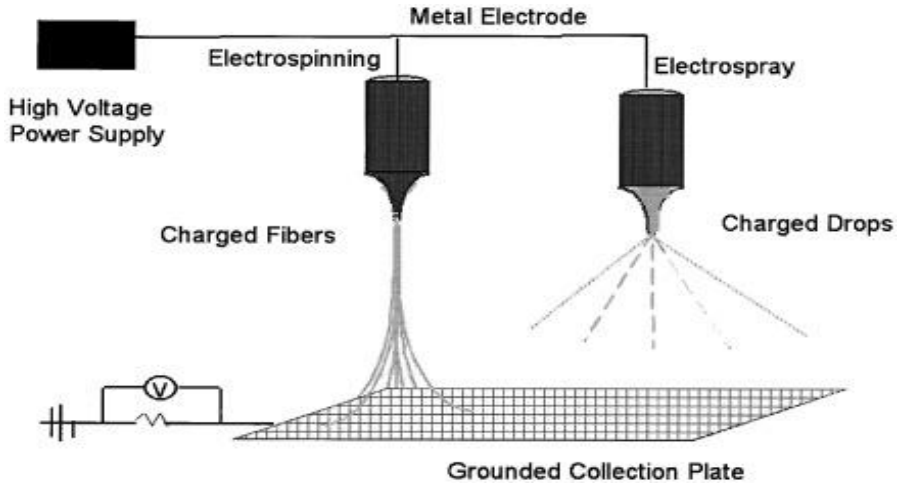

Figure 1 Difference between the end product of electrospray and Electrospining [2]

EA (Electrospray atomization)

Principles and Basic Setup

The basic setup for EA consists of several major components: a syringe pump, a syringe, a metal needle serving as a nozzle, a high voltage power source and a grounded substrate serving as a collector (**Figure 2**).

Some EA setups employ a closed chamber where air/nitrogen flow transfers particles toward collecting filters. The use of the chamber reduces the evaporation of solvents and facilitates the formation of smaller particles with smoother surface morphology [13, 14].

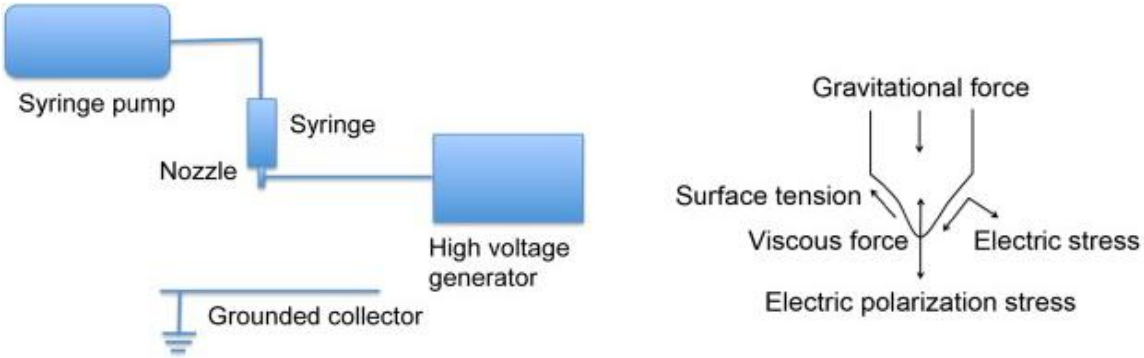

Figure 2 Schematic illustration of (a) basic setup of EHDA and (b) major forces on the spraying cone [15]

Different Applications of EA (Electrospray atomization)

From last two decades number of research work has been carried out on the application of electrospray atomization. Different applications of EA can be categorized as:

- Food processing applications
- Drug/gene/virus delivery applications

- Imaging contrast agent applications
- Cell/tissue encapsulation applications
- Sensing applications

Food processing applications

An Electrospray atomization (EA) Technology used for formulating of micro-and nanoparticulate for various pharmaceutics. In addition, EA technique has been used for food processing. Notable examples are as follows. In 2011, Gorty and Barringer demonstrated that the electro spraying of chocolate is a new approach, which allows chocolate to be atomized due to the existence of an electric field, can achieve a thin and even coating of chocolate [16]. The same group also demonstrated confectionery coating (cocoa butter, cocoa butter equivalent, and lauric butter) using electrospray that offered greater and more complete coverage than non-electrospray coating [17]. Production of very fine, near-monodisperse chocolate particles was also demonstrated by electrospraying chocolate suspensions [18]. In a different study, the formation of zein nanoparticles and encapsulation of curcumin (a food coloring and active ingredient) in particles by EA was examined [19]. Same study further tested the performance of curcumin-loaded zein nanoparticles in semi-skimmed milk coloring, showing the potential of obtaining milk-based products with different shades and chromaticities through the addition of various amounts of curcumin-loaded zein nanoparticles. Additionally, the preparation of solid lipid nanoparticles (stearic acid (SA) and ethylcellulose (EC)) containing an active ingredient (maltol) was demonstrated by electrospraying [20].

Drug/gene/virus delivery applications

EA is a promising technology for encapsulating both hydrophobic and hydrophilic drugs into polymeric particles [21]. For hydrophobic drugs, they can be simply mixed with polymers and dissolved in organic solvents to form a solution that can be electrosprayed to form micro-and nanoparticles. It was also demonstrated that the encapsulation of paclitaxel, a hydrophobic drug in polylactic-co-glycolic acid (PLGA) microparticles using electrospray, exhibited sustained release of paclitaxel for more than 30 days [22, 23]. Subsequent study examined the performance of paclitaxel-loaded PLGA microparticles on the topical delivery of paclitaxel for the treatment of C6 glioma tumors inoculated subcutaneously in BALB/c nude mice [24]. It was shown that microparticles with 20 percent drug loadings had a good performance where the suppression of tumor growth was observed for about 10 days after the first administration. Comparing to other formulations (discs), microparticles generated by EA are normally more effective in suppressing tumor growth because of its inhibited burst release and the latter linearly sustained release.

Imaging contrast agent applications

EA has been used to produce contrast agents for various imaging applications. The utilization of microbubbles as contrast agents for the delineation and perfusion of tissues evokes a great deal of interest in ultrasound imaging. Edirisinghe's group first demonstrated the fabrication of microbubble suspensions containing uniform bubbles smaller than 10 μm in size based on co-axial electrospray [25]. The same research group further prepared phospholipid-coated microbubble suspensions with diameters of 3–7 μm [26, 27]. They found these bubbles had high structural stability and their size remained almost the same for 160 minutes at room temperature. However, the mean bubble diameter decreased dramatically and then became stable at around 1–2 μm after 20 minutes under the human body temperature. Unfortunately, there is no report on *in vivo* studies of microbubbles generated by this technique.

Cell/tissue encapsulation applications

This method is successfully applied on encapsulation of probiotic strain. Encapsulation is generally mentioned as a way of protecting bacteria against severe environmental factors. Encapsulation goal is to create a favorable micro-environment in which the bacteria will survive during processing and storage and released at appropriate sites (e.g. small intestine) in the digestive tract. In some reports, the benefits of probiotics strain encapsulation also consider that encapsulation protect probiotics against low gastric pH similarly for liquid-based products such as dairy products.
Encapsulation is done by some physicochemical or mechanical process in that a substance is entrapped in a material in order to produce particles with diameters of a few nanometres to a few millimetres. So, the prepared capsules contain two parts, small particles that contain an active agent that is first part and second part is core material surrounded by a coating or shell. The shell materials used for encapsulation include a variety of polymers, carbohydrates, fats and waxes, depending on the core material which needs to be protected.

In the particular case of probiotic, the probiotic strain needs to be protected all the time, from the production of cells, during processing of product, till consumption of the probiotic food product. The principal factors against which they need to be protected are: processing conditions (temperature, oxidation, shear, etc.), desiccation (for dry food products), storage conditions (packaging and environment: moisture, oxygen, temperature, etc.), degradation in the gastrointestinal tract (low pH in stomach and bile salts in the small intestine) [28].

Production of uniform alginate beads with sizes ranging from 200 μm to 2 mm under high flow rates using a modified electrospray setup has also been carried out [29]. The encapsulation of HepG2 cells in alginate beads was also performed. Encapsulation of B50 neuroblasoma rat cells in alginate beads by EHDA showed that the cells inside gel beads remained viable after encapsulation and maintained their ability to reattach and proliferate after being released [30].

Encapsulation of human mesenchymal stem cells (hMSCs) in alginate has been carried out using EHDA and these cell-laden capsules were further incorporated in hydrogel [31]. The gel loaded with microcapsules was employed as a patch for myocardial infarction repair in a rat model, showing the improvement of retention of hMSCs and cardiac function.

Experimental setup for EA

The key component of an experimental set up for EA is a coaxial nozzle that consists of an outer needle and an inner needle. Two immiscible liquids, or liquid and gas, are injected into the outer and the inner needles, with the flow rates controlled by two syringe pumps, respectively. A ring-shaped electrode or a ground electrode is placed below the nozzle at a specific distance. A high voltage ranging from several kilovolts to tens of kilovolts is applied between the nozzle and the electrode. Under the elevated electric field, a Taylor cone is formed at the tip of the nozzle and the jet flow of the inner and the outer liquids is eventually broken into multilayer droplets. The droplets are collected by either a ground electrode or a container underneath the electrode. A light source and camera system are used for continuous monitoring of the process [32].

EA process on freeze-dried Bifidobacterium longum subsp. infantis

The coating was a three-step process carried out at room temperature and at 40 percent relative humidity [32].

- In the first step, an initial layer of coating particles was electrosprayed over the collector
- Secondly, the freeze-dried powder with a viability of ~10 log cfu/g was spread out over the initial electrosprayed material layer
- Finally, atop coating layer was electrosprayed directly over the freeze-driedmaterial to achieve full encapsulation

The overall encapsulated product was then collected and mechanically mixed to achieve a more homogeneous coating of the freeze-dried powder with the fine electrosprayed particles.

Sensing applications

Metal oxides have been used as sensing materials for various types of gases due to their simplicity, small dimensions and low cost. Matsushima and coworkers prepared the films composed of multiple layers of SnO_2particles on the glass substrates utilizing the electrospray pyrolysis approach [33]. The particles showed sensing properties for H_2. Cusano and coworkers demonstrated the SnO_2 layer deposition on the silica optical fiber via electrospray pyrolysis for the detection of sub-ppm ammonia concentrations in water environments [34]. The results of room temperature adsorption experiments revealed the high sensor resolution of 80 ppb, good recovery characteristics, high repeatability and short response time. Metal oxides including Cu-doped SnO_2, WO_3, and In_2O_3 thin films were also fabricated using electrospray deposition for sensitive and selective detection of hydrogen sulfide [35, 36]. It was shown that Cu-SnO_2 films could readily detect very low concentrations of H_2S when the operating temperatures were 100 and 200°C.

Conclusion

EA offers a simple but robust method of producing particles with well-controlled size, morphology, structure, and shapes for various applications. EA also offers a means for processing fine particles including charging, dispersing, coating and deposition. Although substantial progress has been achieved, additional efforts are still needed in the

development and applications of EA on the fabrication and processing of particulate materials. For example, while particles with sizes in tens of nanometers have been achieved, the flow rates used in those studies are usually very low, resulting in a very low production rates. Devices and technologies should be further developed to enhance production rate, in particular, for the fabrication of particles less than 100 nm. Also production of micro- or nano-particulate materials with well-controlled properties will expand the array of applications. Also future studies are required in biomedical applications including drug delivery and regenerative medicine for understanding the mechanism and effectiveness of EA.

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Publication History
Received 17th May 2018
Revised 20th June 2018
Accepted 05th July 2018
Online 30th July 2018