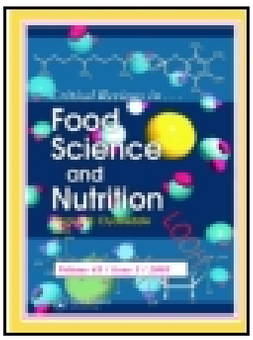

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Principles of Electrospraying: A New Approach in Protection of Bioactive Compounds in Foods

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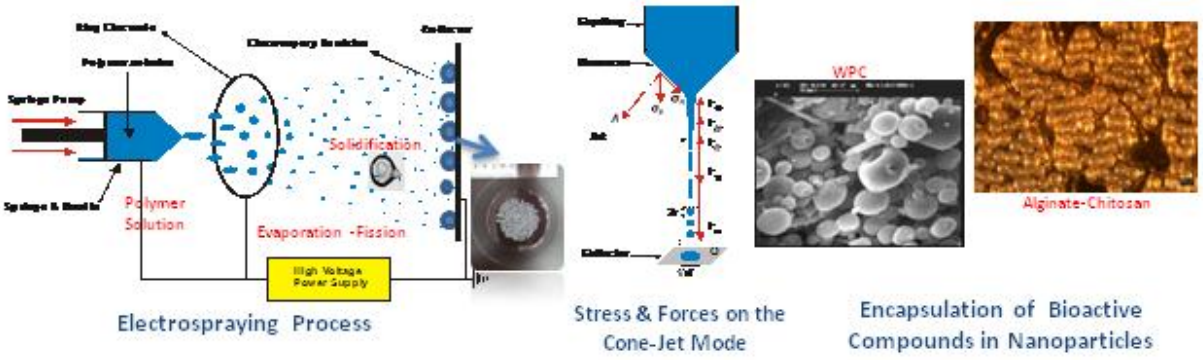
Highlights:

- The electrospraying technique and its application for encapsulation is reviewed;
- The choice of encapsulating materials for electrospraying is examined;
- Principles and fundamentals of electrospraying are outlined;
- Comprehensive discussion on the electrospraying process & conditions is presented;
- Recent advances & future trends of electrospraying in the food industry are described.

Abstract

Electrospraying is a potential answer to the demands of nanoparticle fabrication such as scalability, reproducibility and effective encapsulation in food nanotechnology. Electrospraying (and the related process of electrospinning) both show promise as a novel delivery vehicle for

supplementary food compounds since the process can be carried out from an aqueous solution, at room temperature and without coagulation chemistry to produce matrices or particulates in the micro-and nano-range. The presentation of core materials at the nanoscale improves target ability to specific areas of the digestive tract and gives improved control of release rate. Adoption of these electrohydrodynamic atomization technologies will allow the industry to develop a wide range of novel high added value functional foods. To optimize production conditions and maximize throughput, a clear understanding of the mechanism of electrospraying is essential. This paper presents a comprehensive review of the principles of electrospraying to produce nanoparticles suitable for food technology application, particularly for use in encapsulation and as nanocarriers.



Keywords

Electrospraying, Bioactive Compounds, Capsules, Nanoparticles, Encapsulation, Safe Delivery System

1. Introduction

The increase in consumer demand for functional foods with superior nutritional values, lower levels of synthetic preservatives and better organoleptic properties may be addressed by the use of micro- or nano-scale encapsulated products: such foodstuffs are premium price products and are therefore equally attractive to food manufacturers. Due to their size and high specific surface area, micro- and nano-scale particles have high encapsulation efficiencies and demonstrate major potential for applications requiring controlled release and stabilization of a wide range of active ingredients as well as appropriate levels of biodegradability and biocompatibility (Eltayeb, Bakhshi, et al. 2013). Nanotechnology is commonly defined as the application and control of material at dimensions of ~1--100 nm (Eltayeb, Bakhshi, et al. 2013). Nanoencapsulation is the process of entrapping bioactive compounds in carrier materials at these nanoscale dimensions (Torres-Giner et al. 2016; Drosou et al. 2016; Paximada et al. 2017; Fathi et al. 2014). Bioactive compounds are essential or non-essential compounds ingested as foodstuffs (typically vitamins, antioxidants, or probiotic bacteria) that can be shown to have some beneficial effect on human health (Biesalski et al. 2009; Ezhilarasi et al. 2012; Chen et al. 2006).

The ability to reproducibly load bioactive molecules into polymeric micro- or nano-spheres particularly at the industrial scale is a challenge(Bock et al. 2011; Tripathi & Giri 2014; Eltayeb, Stride, et al. 2013). The survival and activity of encapsulated bio-compounds can be greatly attenuated by certain encapsulation techniques. For a given biopolymer, the structural morphology of the capsules, particularly in terms of size and shape may be controlled during the encapsulation process. During food processing and storage, bioactive compounds (such as probiotic bacteria)can be exposed to damaging factors such as temperature, oxidative stress,

acid-base changes, and molecular entrapment which can significantly affect their viability(Eltayeb, Bakhshi, et al. 2013; Cook et al. 2012; Gómez-Mascaraque et al. 2015a; Gomez-Mascaraque et al. 2016; Rocio Pérez-Masiá et al. 2015).During the passage through the gastrointestinal (GI) tract, probiotic bacteria are adversely affected by the enzymatic action of pepsin and the low pH of the stomach contents with the degree of antagonism depending on the sensitivity to the antimicrobial activity of bile salts and the protease rich conditions in the intestine (Tripathi & Giri 2014).

Encapsulation is used to protect bioactive compounds in stressful conditions, and also to improve their flow properties(Braithwaite et al. 2014; Rocio Pérez-Masiá et al. 2015; Ye et al. 2015).

Several techniques have been presented in the literature for the production of polymeric micro/nanoparticles containing bioactive components(Kwak 2014; Lassalle & Ferreira 2007; Rocío Pérez-Masiá, López-Rubio, et al. 2014; Gomez-Mascaraque et al. 2016; Torres-Giner et al. 2016; Jafari 2017).Such methods include solvent emulsification or solvent evaporation (Bilati et al. 2005; Jain 2000), salting-out and emulsification (McCarron et al. 2006; Pimentel-González et al. 2009), spray drying (Chavarri et al. 2012; Duongthingoc et al. 2014; Maciel et al. 2014), freeze or vacuum drying (Jiao et al. 2017; Zhao et al. 2017), spray chilling or cooling (Arslan-Tontul & Erbas 2017),supercritical fluid (SCF) processing(Santos et al. 2013; Xia et al. 2012), coacervation and precipitation (Hernández-Rodríguez et al. 2014; Lertsutthiwong & Rojsitthisak 2011), ionic-gelation (Bodmeier & Wang 1993; Katas & Alpar 2006), melt extrusion and injection (Verstraete et al. 2016), liposome entrapment (Ran et al. 2016) and inclusion complexation (Yankovsky et al. 2016).However, the processing conditions of certain of these techniques can be severe enough to significantly damage the structure of bioactive compounds

and to decrease the survival rate of probiotic bacteria (López-Rubio & Lagaron 2012; López-Rubio et al. 2012; Laelorspoen et al. 2014; Gomez-Mascaraque et al. 2016).These conditions include exposure of the bioactives to high temperatures, and exposure to organic solvents, or other agents which can affect the stability of sensitive nutrients and hinder their usage for food applications due to toxicity concerns related to solvent carry over (Chakraborty et al. 2009; López-Rubio & Lagaron 2011; Rocio Pérez-Masiá et al. 2015). These methods generally employ chemical cross-linkers and high speed stirring over long durations and typically result in inhomogeneous release profiles and lack of batch-to-batch reproducibility (Bock et al. 2011; Bohr et al. 2015). In addition, the size distributions of particles produced by emulsion-based techniques tend to be inhomogeneous and broad-spectrum, again resulting in lack of reproducibility. Similarly, some methods such as microfluidic devices, liposomes, solid lipid nanoparticles (SLN) and nanostructured lipid carriers (NLC) are characterized by rapid release, low encapsulation load, low stability in GI tract, a requirement for low viscosity raw material solutions and thus can be troublesome to implement on a commercial scale (Ran et al. 2016; Kanai & Tsuchiya 2016; Cirri et al. 2017; Park et al. 2017).Furthermore, the use of organic solvents, is an intrinsic disadvantage in many of these techniques since it can lead to the denaturation of bioactive compounds during processing, and an increase of variability in both encapsulation efficiencies and loading capacities (Yang et al. 2000).

Regarding encapsulation techniques, in recent years, electrodynamic atomization (electrospraying or electrospinning) has been proposed as a straight forward and versatile method for the production of micro- or nano-scale particles by the incorporation of bioactive agents, with

a number of advantages compared to traditional encapsulation techniques (Arya et al. 2009; Bock et al. 2012; Jaworek & Sobczyk 2008).

Electrodynamic atomization shows promise as a novel delivery vehicle for supplementary food compounds since the process can be carried out from an aqueous solution, and at low or ambient temperatures. It is moreover a one-step physical process, that does not chemically coagulate the product, and produces close tolerance small particle sizes, coupled with a high deposition efficiency of the charged spray on to uncharged target surfaces, and due to mutual electrostatic repulsion, an intrinsic lack of droplet agglomeration (Ghorani & Tucker 2015; Gómez-Mascaraque et al. 2016; Drosou et al. 2016; Bohr et al. 2012; Workman et al. 2014; Yang et al. 2013).The size of electrospray particles can range from hundreds micrometers down to several tens of nanometers (Jaworek 2007; Jaworek & Sobczyk 2008). Electrosprayed capsules can be generated from a wide range of biopolymers by modifying the physical characteristics of the aqueous solvent with appropriate additives (Rocio Pérez-Masiá et al. 2014).The advantages of applying coatings in the form of an electrostatic spray are higher transfer efficiency, and better control of the production process which leads to process cost reduction and a reduction in contamination of both the environment and the product (Abu-Ali & Barringer 2008; Gorty & Barringer 2011; Wang et al. 2015).

This technology has recently been applied to increase the stability of sensitive compounds during production, by reducing evaporation and degradation of volatile bioactives (particularly aromas), masking undesirable flavors such as polyphenols, increasing storage life by limiting exposure to oxygen, water or light, (important in the case of unsaturated fatty acids)and increasing the proportion of the ingested material (such as vitamins) that are available to the body (Donsì et al.

2011; Fathi et al. 2012; Khayata et al. 2012; Sáiz-Abajo et al. 2013). Electrospraying has been demonstrated as a method for the fabrication of food nanoparticles and nanocapsules, which offer an attractive alternative to the use of films (Gaona-Sánchez et al. 2015; Jaworek & Sobczyk 2008). For food applications, capsules are commonly preferred to fibers, since in addition to simplifying handling, dispersion within food products, and the subsequent incorporation into various products, they exhibit greater surface/volume ratios and, therefore, are expected to have better release profiles compared to large scale fibers (Hong et al. 2008; Gómez-Mascaraque et al. 2015a).

The aim of this review is to provide a comprehensive overview of the potential applications of the electrospraying technique in the production of micro- and nano-particles for the protection and safe delivery of bioactive compounds.

2. Principles and fundamentals of electrospraying

The principles of electrospraying technique are based on the capability of an electric field to act on a liquid drop, quantified by Lord Rayleigh in 1882, and further examined by Zeleny in 1914 and Taylor in 1964 (Rayleigh 1882; Taylor 1964; Zeleny 1914).Vonnegut and Neubauer (1952) were pioneers of applying voltage to generate micro-particles via electrical atomization. They demonstrated that a stream of highly electrified uniform droplets of about 0.1 mm in diameter can be fabricated by applying potentials of 5--10kV (DC) to liquids in small capillaries(Vonnegut & Neubauer 1952).The electrospraying process has been studied by numerous researchers (Chakraborty et al. 2009; Hayati et al. 1987; Cloupeau & Prunet-Foch 1990; Jaworek & Krupa 1999b; Jaworek & Krupa 1999a; Jaworek & Sobczyk 2008; Jaworek 2007). In this technique the electrostatic force induced by high voltage atomizes the liquid into

fine droplets and evaporation of the solvent is performed during the flight of the droplets toward the ground electrode (Jaworek 2007; Hao et al. 2013; Zhang & Kawakami 2010). The difference between electrospinning and electrospraying is related to the degree of molecular interaction in the spun or sprayed liquid. A high degree of interaction results in a fiber, and a lower degree in a particulate stream (**Fig.1**).

The device consists of a needle shaped spinneret, a ring electrode, a collector, a feed pump, and a power supply source. Usually, the needle (or spinneret) -- often a blunt hypodermic needle is connected to a high-voltage supply, while the ring electrode and a collector are grounded (**Fig.1**). Sometimes, the needle is grounded, while the collector or/and ring are at high voltage (Hao et al. 2013; Jaworek & Sobczyk 2008; Jaworek et al. 2009; Scampicchio et al. 2015; Zhang & Kawakami 2010; Xie & Wang 2007).It should be noted that the polarity of the electric field may affect the spinning rate, and some molecules are better at carrying a positive charge rather than a negative charge and vice-versa. In some cases, to maintain the spinning process over a wider range of flow rates, a protective electrode circular is used to generate a strong electric field near the tip of the needle(Guo et al. 2015).This circular shielding electrode can stabilize the liquid meniscus ejecting from the needle, particularly for low conductivity solutions (Jaworek 2007). It is reported that the uniformity of micro-encapsulation size is stabilized by an additional ring electrode (Teo & Ramakrishna 2006; Xie & Wang 2007; Zamani et al. 2013).For example, Xie and Wang (2007) studied the droplet formation and development of mono-dispersed micro-encapsulation of living cells with controllable size in electrospraying process. They applied two positive voltages to both the nozzle and the ring electrode. They discovered that with increasing

voltage applied to the ring electrode, the dripping frequency was decreased with the formation of slightly larger droplets (Xie & Wang 2007).

Chain entanglements of polymer solutions play a significant role in fiber or capsule formation during the electrospinning/spraying process. As previously mentioned, if the solution concentration is low, the jet is destabilized due to varicose instability and hence fine spherical bodies -- micro-particles are formed (Jaworek & Sobczyk 2008). These highly charged droplets self-disperse in space due to electrostatic repulsion, thereby preventing droplet agglomeration and coagulation (Jaworek 2007). The size distribution of the droplets is usually narrow and droplets are smaller than those available from conventional mechanical atomizers, perhaps below 1μm in diameter (Jaworek 2007). The disruption of droplets by electrostatic force was first observed and quantified by Rayleigh who showed that the high charge potential forces result in dividing charged droplet into smaller droplets. This was defined as Coulombic fission of the droplets which causes original dispersed droplet forming many smaller, more stable droplets(Rayleigh 1882). The bulk forces include electrodynamic forces, inertia, gravity, and drag forces all act on the charged droplet (**Fig.2**).

The electrodynamic force (F_e) is proportional to the electric field. The electrodynamic force occurs due to the electric field caused by the voltage inflicted on the needle as well as the area charge of any formerly emitted droplets (F_Q). Gravitational force (F_g) and Inertial force (F_σ) are presented as volume density. In addition, the drag force (F_η) is known for a moving droplet as the stokes drag and is proportional to the surrounding gas viscosity and jet velocity(Jaworek & Sobczyk 2008). The stresses on the jet surface, which deform its appearance work against the tensor of the surface tension of the liquid. Stress tensors include the electrodynamic stress tensor,

resulting from the surface charge density (Q) and the local electric field (Λ), stress tensor, caused by dynamic viscosity which is essential for liquid motion and is proportional to the gradient of liquid velocity normal to the inter-phase surface(σ_η), and the stress tensor caused by the inertia of the liquid, which is commensurate to the bigeminal product of local liquid velocity at the inter-phase surface (σ_ρ) (**Fig.2**) (Jaworek& Sobczyk 2008; Pozniak & Cole 2015).

When the induced droplet flows and deforms,(the Taylor cone), surface stresses act against surface tension include electro-dynamic stress (proportional to the charge density on the surface of the jet, and on the local electric field), pressure differential across the jet-air interface, and stresses due to liquid dynamic viscosity and inertia. This is illustrated by the following equation(Jaworek & Sobczyk 2008):

$$\boldsymbol{d} = \frac{\boldsymbol{Q^{aQ}\varepsilon^{a\varepsilon}\rho^{a\rho}}}{\boldsymbol{\sigma^{a\sigma}\gamma^{a\gamma}}} \qquad \textbf{(1)}$$

The constant α in this equation depends on the liquid permittivity and d: particle diameter, Q: volume flow rate, ε: permittivity of free space, ρ: liquid density, σ: liquid surface tension, and γ: liquid bulk conductivity. The derivation of this equation has been proved to hold as long as the field of electrospray continues to expand significantly (Jaworek & Sobczyk 2008).The main modes of electrospraying are the dripping and jet modes. Dripping modes are specific in that only fragments of the liquid are ejected directly from the needle. In this mode, the liquid is emitted in the form of relatively large drops (dripping mode and micro-dripping mode) and elongated spindles (spindle or multi- spindle) in the absence of continuous jetting. In jet modes, the liquid is elongated into a long, fine jet, which can be smooth and stable (cone-jet mode) or

can move in any regular way. In fact, the liquid protrudes from the nozzle as a long continuous jet which disintegrates into droplets downright at some distance from the tip of the nozzle. In this case, the jet disintegrates into droplets as a result of electrostatic forces (Jaworek & Sobczyk 2008; Jaworek & Krupa 1999a; Cloupeau & Prunet-Foch 1990).Sometimes, a few fine jets can also be observed on around the capillary axis. This special mode is known as the "multi-jet" mode. Other case modes include micro-dripping, spindle, multi-spindle, precession, and the oscillating-jet (Jaworek & Sobczyk 2008). Generally, dripping and micro-dripping modes occur at low voltages and if the solution is not viscous enough and the surface tension is too high (Luo et al. 2012). In most cases, the unstable cone-jet mode is observed whenever the flow rate is not commensurate to the used voltage out coming in an irregular mass transfer at the nozzle end, or the applied voltage is too high, or corona discharge occurs before enough charge is accumulated in the droplet at the nozzle end to form a stable conical shape (Luo et al. 2012; Xie & Wang 2007). Figure 3 shows sketches of the three most common forms of electrospraying.

Jaworek and Sobczyk (2008) stated that the most important mode of spraying is the cone-jet mode (Jaworek & Sobczyk 2008).

3. Encapsulating materials for electrospraying

The first step towards translating this technology for food applications is the definition of materials that can be used for electrospraying. There are a broad range of polymers which can be applied to entrap, coat or encapsulate substances of various types and characteristics. If intended for the encapsulation of food components the materials should ideally be food-grade substances that are Generally Regarded As Safe (GRAS) (Freiberg & Zhu 2004). In addition, the choice of wall materials depends on several factors such as their ability to self-assemble, the cost of raw

materials, ease of fabrication of delivery system, and regulatory status. Also, it should be considered that the size, morphology, charge, permeability, bioadhesion and environmental stability of nanocarriers are important (Pérez-Masiá et al. 2013; Abd El-Salam & El-Shibiny 2016; Martínez et al. 2012).As a result, materials with natural origin are often preferred because they comply more easily with the requisites of biocompatibility, biodegradability and absence of toxicity (Liu et al. 2008).Recently, attention has been focused on developing functional matrices by usingbiological origin substances such as proteins, carbohydrates and lipids to militate against the possible environmental and health risks caused by non-biodegradable materials (Aceituno-Medina et al. 2013).The use of food-grade polymers and biopolymers as bioactive delivery devices has been investigated for use in foodstuffs(Chen et al. 2006; Jones & McClements 2011) (**Table.1**).

3.1. Protein based encapsulating materials used in electrospraying

Among the several existing food-grade biopolymers, proteins are used as a food ingredient to improve food texture or sensory characteristics (Nieuwland et al. 2013). Protein hydrogels are accepted as appropriate substances for encapsulation in food applications, especially in liquid and semi-solid foods. Generally, they can be produced in controlled size ranges without any harmful effect on the sensory characteristics of the processed food (El-Salam & El-Shibiny 2015). The protein functional groups give them the ability to interact and protect binding with a broad spectrum of active compounds. Furthermore, they can have significant stabilizing effects on food texture (Heidebach et al. 2012; Tavares et al. 2014).Common protein based encapsulating materials used in electrospraying are whey protein isolate (WPI) (López-Rubio et al. 2012), whey protein concentrate (WPC) (López-Rubio & Lagaron 2012), soy protein isolate

(Xu et al. 2012), egg albumen (Wongsasulak et al. 2010), collagen (Bürck et al. 2013), gelatin (Songchotikunpan et al. 2008), zein (Brahatheeswaran et al. 2012), wheat gluten (Woerdeman et al. 2005), and casein (Nieuwland et al. 2013). Zein is a class of prolamine protein found in maize (corn) that is widely used in a variety of industrial and food applications (Shukla & Cheryan 2001). It is not soluble in water due to the large quantity of hydrophobic amino acid residues (glutamine, proline, leucine, and alanine) which constitute about 30% of the protein composition. This property can be beneficial for the encapsulation of bioactive compounds since cross-linking of the encapsulant polymer is not required (Moomand & Lim 2015b; Moomand & Lim 2015a).

Zein is a non-toxic polymer that is biocompatible and biodegradable and is used to produce films with adequate characteristics in terms of permeability and thermal resistance (Escamilla-García et al. 2013). Zein films and zein particles can be applied for the encapsulation of essential oils (such as omega-3), essential micronutrients (such as folic acid), controlled released of additives (such as quercetin) or used as an active packaging material (such as the combination of gallic acid and zein used in flexible antimicrobial packaging) for food preservation (Rocío Pérez-Masiá et al. 2015; Torres-Giner et al. 2010; Patel et al. 2012; Alkan et al. 2011). They also can be administered as drug delivery vehicles, an application which has been demonstrated using curcumin as a model (Wang & Padua 2005; Hurtado-López & Murdan 2005; Gomez-Estaca et al. 2012).

Milk proteins have a number of advantages compared to other biomaterials commonly used in encapsulation of probiotics. Dianawati et al. (2013) have shown that compared to soy protein isolate, milk proteins provide more desirable protection for *Bifidobacteriumlongum*after freeze drying and during exposure to acid and bile (Dianawati et al. 2013).Several studies have shown

that whey proteins (WP) are considered as desirable biomaterial for encapsulation of probiotics (Lopez 2013; Poulin et al. 2011). Whey protein concentrate is the cheapest and most common form of whey protein, being a by-product of cheese production. Typically, whey protein comes in three major forms: concentrate (WPC), isolate (WPI), and hydrolysate (WPH). Pérez-Masiá, Lagaron, and Lopez-Rubio (2015) investigated lycopene encapsulation using a whey protein concentrate (WPC) from milk and two polysaccharides (dextran and chitosan) during electrospraying. The results showed that WPC presented the greatest encapsulation efficiency (around 75%) and better protected lycopene against both moisture and thermal degradation. This was ascribed to interactions between biopolymer and lycopene (Rocio Pérez-Masiá et al. 2015). Casein and its derivatives, have the advantage of gel generation initiated by acid or enzyme treatment at room temperature. This creates appropriate conditions for the encapsulation of bioactive compounds without adversely affecting their survival rate. Some common types of casein used in encapsulation of probiotics are native casein (Burgain et al. 2013) and sodium caseinate (Dianawati et al. 2013).

Gelatin has been extensively examined and tested for use in controlled drug release due to its biodegradability and electrical properties: it possesses unique gelation attributes and is commercially available at a low cost (Okutan et al. 2014). Gómez-Mascaraque et al. (2015) have investigated electrosprayed gelatin sub micronparticles as edible carriers for the encapsulation of polyphenols of interest in functional foods (Gómez-Mascaraque et al. 2015a). Also, Okutan et al. (2014)show that electrospun gelatin nanofibers may be used in foods for thickening and stabilizing purposes at smaller amounts giving more efficient results (Okutan et al. 2014). It was reported that gelatin cannot be electrospun at room temperature when dissolved in water as

gelation would occur (Erencia et al. 2014). The potentials of the electrospraying method for obtaining food-grade gelatin capsules in the submicron range for sensitive bioactive protection was studied by Gómez-Mascaraque, Lagarón, and López-Rubio (2015). In addition, they studied the impact of protein concentration on the size and morphology of the obtained particles (Gómez-Mascaraque et al. 2015a).

Gliadin is a class of protein present in wheat and several other cereals within the grass genus *Triticum.* Gliadins are a component of gluten and essential for giving bread the ability to rise properly during baking. Gliadins and glutenins are the two main compounds of the gluten fraction of the wheat seed (Gulfam et al. 2012). Recently, gluten has been used to develop nanospheres from bioactive compounds such as drugs, or fish oil (Liao et al. 2012).

Silk fibroin (SF) is a well-known biomaterial with applications in tissue engineering and drug delivery (Ye et al. 2015; Zhu et al. 2015). Silk fibroin is known to be a biocompatible material, and has several forms used for different applications. However, use of SF in the particle form is scarcely reported (Ekemen et al. 2013). Furthermore, Kim et al. (2015) studied the effect of shear viscosity on the generation of sphere-like silk fibroin micro-particles via electrospraying (Kim et al. 2015).

3.2. Carbohydrate based encapsulating materials used in electrospraying

Carbohydrates are suitable for encapsulation, because they are biocompatible, biodegradable, and possess high potentials for modification in order to achieve the required properties. Polysaccharide based delivery systems can interact with a broad spectrum of bioactive compounds through their functional groups, this makes them multi-purpose carriers for binding and entrapping a variety of hydrophilic and hydrophobic bioactive food ingredients. Also, they

are considered suitable shells under high-temperature processes due to their temperature resistance in comparison with lipid or protein-based delivery systems which might melt or become denatured (Fathi et al. 2014). Pérez-Masiá et al. (2014) have determined the solution characteristics and ease of electrospraying of several polysaccharides, such as dextran, maltodextrin, a resistant starch, pullulan and fructoligosaccharides (FOS), and two proteins (a whey protein concentrate from milk and a soy protein isolate), were evaluated as matrix materials, attempting to characterize and compare hydrocolloid aqueous solutions prepared with the physical properties of aqueous solutions made from spinnable polymers in water as polyvinyl alcohol (PVOH) and polyethylene oxide (PEO) (Rocio Pérez-Masiá et al. 2014).

Chitosan is a copolymer of N-acetyl-D-glucosamine and D-glucosamine and is obtained by the alkaline deacetylation of chitin (Sridhar et al. 2015). Chitosan is soluble in an aqueous acidic solution and hence avoids hazardous organic solvents for in the fabrication of micro/nanoparticles (Hejazi & Amiji 2003). It was reported that chitosan nano-formulations provide synergistic improvement of antimicrobial and anticancer drug activity (Ignatova et al. 2013; Smith et al. 2013). From a biopharmaceutical point of view, chitosan has the special property of adhering to mucosal surfaces, a fact that makes it a useful polymer for bioactive compounds and drug delivery(Lehr et al. 1992). The surface of chitosan nanoparticles is positively charged and thus, the particles are expected to be stable with minimum aggregation. Xu et al. (2006 & 2007), in two separate studies, investigated the encapsulation of bovine serum albumin (BSA) by electrospraying technique from chitosan and poly(lactide).In a survey, the chitosan in sprayed particles is cross-linked by tri-polyphosphate. In another survey, BSA is loaded onto particles by electrospraying an emulsion of BSA in a PLA solution (Xu & Hanna

2007; Xu et al. 2006). Chen and et al. (1995) studied electrospraying of conducting liquids for monodisperse aerosol production in the 4nm to 1.8μm diameter range. This experiment was performed using sucrose in solution and controlling the liquid electrical conductivity by adding small amounts of nitric acid (Chen et al. 1995).

Carrageenans are polymers of linear structure consisting of D-galactose units alternatively linked by α(1--3) and β(1--4) bonds (Gbassi & Vandamme 2012; Rokka & Rantamäki 2010). Rodrigues et al. (2011) noted that the addition of alginate, chitosan, xanthan gum, L-carrageenan, and WPC (50% protein) to the medium affected parameter the growth and the survival of the five strains of *Lactobacillus* and *Bifidobacterium* (Rodrigues et al. 2011).

Alginic acid, also called algin or alginate, is an anionic polysaccharide distributed widely in the cell walls of brown algae, where through binding with water it forms a viscous gum. Alginates are naturally occurring polysaccharides obtained from marine brown algae, and consist of two monomeric units, D-mannuronic acid (M) and L-guluronic acid (G) (Dong et al. 2013; Suksamran et al. 2009). Ghayempour and Mortazavi (2013) used coaxial jets for the production of micro/nanocapsules alginate solutions by electrospraying. The results showed that the average diameter of produced capsules varied from 80nm to 900μm (Ghayempour & Mortazavi 2013). Furthermore, Fukui et al., (2010) investigated the preparation of mono-dispersed polyelectrolyte (sodium alginate-chitosan) microcapsules by electrospraying. The diameters of the microcapsules were controlled in the range of 80-230μm by varying the operating conditions(Fukui et al. 2010).

Recently, electrosprayed maize starch (amylose and amylopectin) and its constituent nanoparticles were studied by Ghaeb, Tavanai, and Kadivar (2015), who examined the

application of electrospraying process for the production of amylose and amylopectin nanoparticles from maize starch with an average particle size around 100nm (Ghaeb et al. 2015).

3.3. Lipid based encapsulating materials used in electrospraying

Solid lipid nanoparticles based on stearic acid and ethyl cellulose have been used to encapsulate vanillin, ethyl-maltol and maltol flavors without measurable chemical interaction between the ingredients (Eltayeb, Stride, et al. 2013). The encapsulated nanoparticles (30-90nm) displayed enhanced stability against collapse and aggregation and limited flavor loss or degradation during processing and storage (Eltayeb, Stride, et al. 2013).In case of oils, the possibility of obtaining thin and evenly spread hydrophobic film coated with sunflower oil was investigated on conductive and non-conductive surfaces (Anu Bhushani & Anandharamakrishnan 2014; Khan et al. 2012). The droplet generation characteristics of ethanol in the presence of triglycerides; such as medium chain triglyceride oil and soy bean oil, were studied using single and multiple nozzle electrospraying systems fabricating triglyceride oil and droplets with an average diameter of ~2μm (Zhang et al. 2013).Common lysolecithin, an ionic surfactant, was used to increase the conductivity of a lipid spinning dope because lipids are non-conductive, and therefore not suitable for electrospraying (Khan et al. 2013). A water-oil emulsion was electrosprayed to produce thin edible barriers. The addition of an emulsifier (polyglycerol polyricinoleate) and whey protein isolate stabilized the jet and enhanced the water vapor barrier properties of the film respectively (Khan et al. 2013). Luo et al. (2012) used both electrospraying and electrospinning to produce near-monodisperse particles and electrospun fibers from a commercially available chocolate sauce based on invert sugar syrup, milk chocolate crumb (milk, sugar, cocoa mass), hydrogenated vegetable oil, dried glucose syrup, and fat reduced cocoa powder (Luo et al. 2012).

The formation of beads-on-string morphologies was characteristic of the electrospun chocolate fibres. Very fine fibres and what the authors describe as “satellite particles” were obtained during the transition between electrospraying and electrospinning. The continuous shape alterations of elongated spheres and thin fibers may have the potential for varying the micro-texture and mouth-feel of food products (Luo et al. 2012).

3.4. Synthetic based encapsulating materials used in electrospraying

Polyethylene glycol (PEG) hydrogels are applied for encapsulation and delivery of sensitive biologic ingredients including cells, drugs, and proteins due to resistance to protein adsorption, high biocompatibility, and versatile macromer chemistry (Lin & Anseth 2009). Encapsulation of bioactive compounds in PEG hydrogels, protects their activity and allows some control over their release rate and site (Zustiak & Leach 2011).Jain et al. (2015) studied the production of polyethylene glycol-based hydrogel microspheres by electrospraying. To facilitate the production of microspheres via electrospraying, they optimized the gelation time of PEG hydrogels by the Michael addition reaction between acrylate and thiol (Jain et al. 2015).Polylactide or polylactic acid (PLA) is a biodegradable thermoplastic aliphatic polyester derived from renewable resources, such as corn starch, tapioca roots, chips or starch, or sugarcane, and readily available in commercial quantities (Kwak 2014). Lu et al. (2015) prepared biodegradable microparticles with different morphologies from PLA by electrospraying (Lu et al. 2015). Their results revealed that the preparation of drug-loaded (the antibiotic Rifampin was the test drug) microspheres through electrospraying is a simple and efficient method and the processing parameters play an important role in obtaining high quality micro-carriers(Lu et al. 2015).

4. Processing conditions

Electrospraying process parameters such as solution and solvent properties, applied voltage, flow rate, needle gauge and tip to collector distance (TCD) need to be optimized in order to produce consistent product and to vary the size distribution of the particles. Numerous studies have shown that processing conditions influence if not control the size and morphology of micro- or nano-particles in electrospraying. Changes in the electrospraying conditions can determine whether the stream ejected from the needle is divided into spheres or irregular-shaped particles (Nath et al. 2013; Rocío Pérez-Masiá, Lagaron, et al. 2014).Bock et al. (2011) mentioned that during the electrospraying process, there are various parameters with interdependent effects on particle size, distribution, encapsulation efficiency, loading capacity and in-vitro release profiles (Bock et al. 2011). Particle size, surface morphology, density and distribution are some of the attributes that influence the efficiency of bioactive component and delivery carriers, hence, should be controlled (Bohr et al. 2015; Chen et al. 1995; Jain et al. 2015; Eltayeb, Bakhshi, et al. 2013; Gaona-Sánchez et al. 2015; Hwang et al. 2008; Lu et al. 2015; Bock et al. 2011).An increase in the magnitude of certain electrospraying parameters such as conductivity, and voltage applied to the solution is correlated with reduction in particle diameter. However, an increase in the magnitude of electrospraying parameters such as flow rate, viscosity, and percent solids the sprayed solution tends to increase particle diameter (Hartman et al. 2000; Yao et al. 2008). It is highly desirable to control the size of the capsule product as this property is strongly related to the stability and efficacy of delivery of the entrapped bioactive compounds. It is possible to produce particles with different morphologies and sizes by varying process parameters such as solution properties, processing conditions and ambient conditions. Understanding how each of

these processing parameters influences particle morphology and dimensions is essential for proper process control.

4.1. Polymer solution

Polymer type, molecular weight, and concentration are the three crucial factors that determine the feasibility of electrospraying and morphological characteristics of particles produced (Jaworek & Sobczyk 2008). Changes in polymer concentration and molecular weight affect the viscosity and surface tension of the solution, and so greatly affect the nature of the electrosprayed product. In general, the solubility of a polymer increases as the molecular weight decreases. However, other important physical properties such as viscosity, strength, flexibility and the degree of molecular chain entanglement (Shenoy et al. 2005) increase with molecular weight (Treloar 1970). If the polymer concentration is not high enough, the jet is destabilized due to varicose instability and hence fine spherical bodies -- micro-particles are formed (Jaworek & Sobczyk 2008).The size of particles can be controlled by changing the concentration of dissolved or suspended substance (Jaworek 2007). Rocío Pérez-Masiá et al. (2014) have investigated surfactant-aided electrospraying of low molecular weight carbohydrate polymers (maltodextrin and commercial resistant starch) from aqueous solutions. They have reported that higher surfactant concentrations led to smaller capsules, related to lower surface tension and higher conductivity of the solutions (Rocío Pérez-Masiá, Lagaron, et al. 2014).Tan et al. (2009) showed that the size of the starch acetate nanospheres can be easily controlled by a number of simple and effective modifications, namely adjusting the polymer concentration in the chosen solvent acetone, the proportions of the water and organic phases, and the molecular weight and degree of substitution of the starch esters (Tan et al. 2009). Luo et al. (2011) showed a positive

linear tendency in electrosprayed chocolate particle diameter and diameter distribution range by increasing the sugar concentration in the chocolate suspension. Furthermore, they found that sugar concentrations of 30--35%w/w resulted in very fine, near-mono-disperse chocolate particles. Small additions of NaCl (as a electrolyte) at 1%w/w were found to reduce the average particle diameter and modify the monodispersity of the particles fabricated (Luo et al. 2012).Marthina and Barringer (2012) evaluated the effect of lecithin content and cocoa butter on electrical resistivity and apparent viscosity under electrospraying. They found that the droplet size and width of the coating area were profoundly influenced by the resistivity and apparent viscosity of the sample (Marthina & Barringer 2012). Pérez-Masiá, Lagaron, and López-Rubio (2014) demonstrated that beads (capsules) formed at low polymer concentrations of PVOH and PEO, and raising the polymer concentration and the subsequent viscosity yielded fibers (Rocio Pérez-Masiá et al. 2014).Kim et al. (2015) studied the effect of silk fibroin (SF) concentration on the micro-particle shape. Their results showed that the shape of electrosprayed particles changed from irregular (6wt%) to oval (9wt%) and finally became spheroids (10wt%) as the SF concentration increased (Kim et al. 2015).

Recently, Gómez-Mascaraque, Lagarón, and López-Rubio (2015) examined the potential of the electrospraying technique to obtain food-grade gelatin capsules in the submicron range. They showed that fibres were obtained for the sample with the greatest protein concentration (i.e. 20%w/v, while pseudo-spherical particles typical of a discontinuous electrospraying process, with some residual fibrils, were produced at lower gelatin concentrations (i.e. 5-8%w/v) (Gómez-Mascaraque et al. 2015a).

4.2. Solvent

Solvents are the main components of any spraying feed solution and are therefore bound to have significant influence over the particle fabrication process and the characteristics of the particulate product. Two of the most important attributes influencing particle generation in a liquid spraying method are the solubility of the solutes in the solvent(s) and the drying kinetics of the solvent (Park & Lee 2009; Raula et al. 2004; Yao et al. 2008). If the evaporation rate of solvent is slow, particle morphology will be more spherical, since there is more time for the solvent to evaporate (Park & Lee 2009).

Significant polymer--polymer interactions are more common in so sparingly soluble solutions as the polymer chains can coil up, whilst in a more suitable solvent polymer-solvent system interactions are predominant and the polymer chains are more extended (Shenoy et al. 2005). The solubility of solutes in the solvent, generally remains constant during the evaporation process, unless more than one solvent is utilized with a distinct volatility and other solvent power for the solutes. In such cases, phase separation may happen among the liquid and solid phases and also the solid phases, leading to variation in the rate of the release of the bioactive compounds(Gilchrist et al. 2012).Many of the sensitive bioactive compounds used for the production of micro- or nano-particles do not dissolve in organic solvents and may lose bioactivity when dispersed in polymer solutions. To avoid this problem, some researchers have used the method of coaxial electrospinning/spraying, where the bioactive compounds and the polymer are dissolved in an aqueous core solution and surrounded by an organic shell solution. This is one of the methods available to overcome this problem by extruding the core and shell solutions via two concentric nozzles (Chakraborty et al. 2009). Bohr et al. (2015) studied the

influence of a double solvent system on particle generation, with an affirmation on the possible influence of polymer stream flight time on the resulting particle attributes, especially particle morphology, compound distribution and release in the electrospraying technique (Bohr et al. 2015). They indicated that further understanding of the influence of solvent systems on particle generation and the related particle specifications can be beneficial to particle engineering and help obtain better quality loaded particles (Bohr et al. 2015).

Moomand and Lim (2015) showed that at low polymer concentrations (10% w/w), regardless of the applied solvent, electrosprayed zein aggregates on the obtained collector were observed. But, at higher polymer concentration (20%w/w), the zein solution prepared in aqueous ethanol solvent resulted in smooth ribbon-like fibers while a combination of capsules and fibers were observed with zein solutions prepared in isopropanol solvent. They reported that the capsules were homogenously dispersed throughout the fiber mesh with maximum diameters of approximately 4μm and an average size of 1μm (Moomand & Lim 2015a; Moomand & Lim 2015b). Two different solvents were recently applied for the preparation of drug loaded PLGA particles, whereby the polymeric solution in dichloromethane(DCM) produced particles larger (3946±407nm) than when trifluoroethanol (TFE) is used (1774±167nm) (Prabhakaran et al. 2015).

4.3. Voltage

A crucial element in any electrospraying process is the application of high voltage to the polymer solution-variation of this voltage controls the electrical field strength between the spinneret and the collection point, and thus the strength of the drawing force. Once the charge is applied to the solution, the external electrical field initiates the electrospraying process when the electrostatic

force in the solution overcomes the surface tension of the solution (Wang & Stark 2010).Usually either negative and positive high voltages above about 6 kV are able to distort a polymer droplet into the diagnostic shape of a Taylor cone and cause jet initiation (Taylor 1964). Note that the balance between surface tension and the electrical force is critical in determining the initial cone shape of the polymer solution at the needle tip (Zong et al. 2002). To perform a successful electrospraying process from a polymer solution, the cone-jet mode could be formed only within certain range of applied voltages(Hartman et al. 2000).Hwang, Jeong, and Cho (2008) showed that the size of the particles is dependent on the relative flow ratio between the polymer solutions and the amount of voltage applied. They demonstrated that the dripping mode occurred at low voltages, and that micro-dripping occurred when the voltage increased to 6.7kV. They declared that the length of the cone-jet was progressively reduced as the electric field was enhanced (Hwang et al. 2008).Laelorspoen et al. (2014) showed that the size of the microcapsules significantly reduced from 543±88 to 312±69 and 259±62μm when produced at 4, 6 and 10kVby electrospraying of zein--alginate solutions (Laelorspoen et al. 2014).Jain et al. (2015) observed that upon increasing the applied voltage to 10kV during electrospraying of polyethylene glycol (PEG), a transition from dripping to jetting mode resulted in the formation of fine droplets(Jain et al. 2015).It has also been reported that voltages in the range of 0--12 kV were applied to electrospray three solutions with different sodium alginate concentrations to examine the effect of different voltages on the calcium alginate hydrogels size: the effect of voltage on the size of calcium alginate micro-hydrogel indicated that raising the voltage above a threshold of 8kV would lead to smaller particles. Significantly, the pressure-assisted electrospray through a

coaxial head was applied to produce the gel particles around 3μm, which is much less than the human tactile sensation threshold (Mehregan Nikoo et al. 2016).

4.4. Diameter of spinneret

The diameter of a spinneret (often a blunt hypodermic syringe needle)is inversely proportional to its gauge and hence smaller needles have a higher value of gauge. Stability of the Taylor cone is also dependent on the needle gauge (Jain et al. 2015). Needles with a small diameter are more appropriate for the stable fabrication of microparticles. However, viscoelastic solutions made of polymers with a high glass transition temperature (T_g) easily blocked fine nozzles during the electrospraying process (Jain et al. 2015).

The diameter of the droplets is typically about twice the jet diameter and by increasing the outlet orifice size the jet dimensions will be increased (Poncelet et al. 1999).Arya et al. (2009) showed that applying smaller gauges (20 and 22G) resulted in the sputtering of the polymer solution and micro- or nano-particles with narrow size range were obtained with the highest gauge (smallest diameter) of 26G (Arya et al. 2009). Jain et al. (2015) used 30, 21, and 18gaugeneedles to electrospray PEG. They obtained more stable Taylor cones as the needle gauge was reduced from 30 to 18G, while maintaining the voltage and flow rate constant at 10kV and 1ml.h^{-1}(Jain et al. 2015).Wang et al. (2015) evaluated the effects of the needle size on electrosprayed chitosan microspheres. They used needle gauge sizesof 32G, 30G, 30G and 28G, with inner diameters of 104, 138, 149 and 205μm, respectively. They showed that as the needle size increases, the size of the obtained chitosan microspheres increase slightly and the size distribution becomes wider (Wang et al. 2015).

4.5. Flow rate

The polymer solution flow rate determines the amount of solution available at the needle tip during electrospraying. For a given voltage, there is a corresponding flow rate if a stable Taylor cone is to be maintained. Modulation of droplet size by regulating flow rate under a cone-jet mode can help accurately set the dimension of electrosprayed droplets based on the flow rate of polymer solution (Guo et al. 2015). In the other words knowing this parameter allows for the prediction of the material's behavior in determining particle size. The unstable cone-jet mode can be observed when the flow rate is disproportionate to the applied voltage resulting in an irregular mass transfer at the nozzle end, or the applied voltage becomes too high, or corona discharge occurs before a sufficient charge can be accumulated in the droplet at the nozzle end to form a stable conical shape (Luo et al. 2012).

Generally, electrospraying at high flow rates leads to the generation of large size particles; since the rate of the jet that drips from the needle is higher, the solvent does not volatilize completely. In contrast, a low flow rate can lead to smaller particles, since the smaller rate of the jet, causes the greater volatilization of the solvent (**Fig.4**) (Ghayempour & Mortazavi 2013; Zamani et al. 2013).

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Hwang, Jeong, and Cho (2008) demonstrated that the morphology of the particles was influenced by the relative feed rate of the two polymer solutions. When the feed rate of a shell-forming solution is higher than the core-forming solution, the cone-jet mode will be a combination of an inner core solution surrounded by the shell solution (Hwang et al. 2008).

Luo et al. (2011) observed that when the flow rate was sufficiently high during the electrospraying of chocolate solutions, the unbalanced resulting forces applied to the liquid cause it to elongate in the direction of the electric field and take the shape of a jet before breaking off into particles of different sizes. They observed that at flow rates lower than 50μL/min, no stable jetting could be achieved (Luo et al. 2012). In addition, flow rate of 50μL/min showed better monodispersity in particle size distribution, whereas at 100 and 200μL/min flow rates, bimodal size distributions were observed. The average particle diameter was also increased from 0.14±0.06 mm to 0.18±0.05 and 0.20±0.09mm at the flow rates of 50,100 and 200μL/min (Luo et al. 2012).

4.6. Tip to collector distance (TCD)

The atomization of the droplet takes place between the needle tip, where the Taylor cone is formed and the collector. As may be expected, the TCD has a direct influence on flight time and the electrostatic field strength. TCD can influence particle size and specify the final product morphology through the evaporation rate of the solvent (Yao et al. 2008). When the distance of the collector is very small, the solvent does not have enough time to evaporate, and hence the particles will be big and unstable (Arya et al. 2009; Yao et al. 2008). Increasing the TCD results in longer flight times of droplet and solvent evaporation time, which tends to solidification of the particles before reaching the collector (Luo et al. 2012).

Luo et al. (2012) adjusted the collection distance between the nozzle tip and the substrate by setting it at 150mm during the electrospraying of a chocolate solution. They demonstrated that the particles were not effectively dried when the collector distance was less than 150mm. Significant merging of the as-sprayed particles could be observed in samples collected at a distance of 100mm due to flow motion of the “wet” particles on the substrate (Luo et al. 2012). This is an unusual observation, as more usually, coalescence is prevented by the electrostatic repulsion of the presumably like charged particles. Gaona-Sánchez et al. (2015) reported that even small distances from the collector in electrospraying particles can cause complete solvent evaporation, collapse of the particles, coalescence and broad size distributions. They showed that at distances of 1.5±0.5cm between the needle and collector, the formation of homogenous zein films occurs without the generation of electric corona discharge arcs, along with constant spraying in the electrospraying process (Gaona-Sánchez et al. 2015).

Jain et al. (2015) showed that under constant voltage conditions, applying a very low or high TCD, results in either wider diameter distribution or increase in the particle diameter of PEG (Jain et al. 2015). Guo et al. (2015) showed that the electrosprayed droplets collected on the cover glass at different distances from the tip had different morphologies (Guo et al. 2015). For a TCD of 3cm, droplets with round edges were obtained, which indicates that Coulombic fission had not occurred in these droplets. When the TCD was increased to 6cm, a fraction of the droplets broke into small pieces with ragged morphology. When the TCD increased further to 9cm, only small, fragmented droplets with ragged morphology were obtained. Moreover, these droplets showed two quite distinct dimensions resulting from the breakup of the primary droplets due to Coulombic fission (Guo et al. 2015). MehreganNikoo et al. (2016) demonstrated that smaller particles of calcium alginate micro-hydrogels could be formed at the small distance between the nozzle and cross-linking solution (3.5cm), but there seemed to be a high back pressure on the jet at this distance which resulted in an unstable stream with a flow rate lower than that achieved at 8cm. 8cm provided the most uniform dripping and so was chosen as the optimal distance between the nozzle and cross-linking solution. They also reported that increasing TCD 12.5 to 15.5cm tended to decreased particle size but the uniformity of the jet increased which is an important for commercial production (Mehregan Nikoo et al. 2016).

4.7. Ambient conditions

Ambient parameters particularly humidity and temperature are thought to influence morphology and the productivity of the electrospraying process. This is because a direct relationship exists between solvent evaporation and temperature as well as between the conductivity of the solvent and temperature (Chakraborty et al. 2009; Jaworek 2007; Kivikero 2010), in addition sufficiently

high humidity can prevent the operation of any electrostatic process. Electrospraying is performed at ambient temperature and mostly at atmospheric pressure. Thus, this method is compatible with fragile molecules that are sensitive to elevated temperature or shearing force (Abeyewickreme et al. 2009; Bohr et al. 2015).

Wu, Kennedy, and Clark (2009) studied polymeric particle formation via electrospraying at low atmospheric pressure. They reported that changes to the pressure had considerable effects on the microstructure and morphology of poly(e-caprolactone)(PCL) particles. The average particle size became larger as the chamber pressure decreased. They showed that in the electrospray PCL solutions with concentrations of 3, 5, and 7w/v %, while the pressure was reduced from 0 to 2250mmHg relative to ambient pressure, the average diameter of the solidified particles increased from 2.0±0.3 to 8.5±0.2μm. It was also revealed that under these conditions, the size distribution was narrower than at atmospheric conditions (Wu et al. 2009). Gorty and Barringer (2011) studied chocolate electrospray quality using two different outlet temperatures (35° and 50°C). Their results showed that electrical resistivity, apparent viscosity and apparent yield value of some samples reduced with increasing temperature (Gorty & Barringer 2011). Wang et al. (2015) preformed electrospraying of chitosan between25°and50°C. They observed that the average size of generated chitosan microspheres reduces as ambient temperature is increased, which they attribute to a temperature related reduction in the viscosity in the chitosan solution (Wang et al. 2015).

5. Applications of electrospraying in food industry

Electrospinning/spraying technique can be used for the encapsulation of materials such as vitamins, antioxidants, drugs, nutraceuticals, bacteria, viruses, DNA, and osteogenic or

dermatological growth factors. In this regard, the use of micro- or nano-particles produced by electrospraying has been of great interest in the food and biomedical fields, in particular in the field of protecting nutraceuticals (Bock et al. 2011; Laelorspoen et al. 2014; Rocio Pérez-Masiá et al. 2015; López-Rubio et al. 2012).Micro- or nano-particles produced through electrospraying act as reservoir systems capable of protecting bioactive compounds from their environment and enhancing their long term biological activity (Rocio Pérez-Masiá et al. 2015; López-Rubio & Lagaron 2012; Rocío Pérez-Masiá et al. 2015; Laelorspoen et al. 2014; Anu Bhushani & Anandharamakrishnan 2014). Ideally, using this method will be able to provide tailored release rates required by certain therapies, by controlling particle morphology, size and polymeric matrix. Also, this technique is demonstrated to be versatile basically for the delivery of a wide spectrum of biocompounds, ranging from small molecules to larger macromolecules (Nath et al. 2013).

5.1. Recent advances in encapsulation of bioactive compounds by electrospraying

Torres-Giner et al. (2010) studied the stabilization of omega-3 fatty acid (docosahexaenoic acid) (DHA) by encapsulation in zein ultrathin capsules produced by electrospraying. They found that the encapsulated omega-3 fatty acid showed a 2.5-fold decrease in the degradation rate constant. Significantly, the ultrathin zein-DHA capsules became more stable across relative humidity and temperature (Torres-Giner et al. 2010). Also, Moomand and Lim (2015) studied the effects of solvent and ω-3 rich fish oil on physicochemical properties of electrosprayed and electrospun zein particles and fibers (Moomand & Lim 2015a; Moomand & Lim 2015b).

In several studies, López-Rubio and coworkers worked on the properties of WPC capsules obtained through electrospraying for the encapsulation of bioactive compounds (López-Rubio &

Lagaron 2012; López-Rubio et al. 2012). López-Rubio and Lagaron (2012) fabricated WPC capsules through the electrospraying technique for the encapsulation of antioxidants (*β-carotene*). Their results showed that electrosprayed WPC capsules can be obtained for a wide pH range (López-Rubio & Lagaron 2012). Similarly, Pérez-Masiá et al. (2015) performed encapsulation of folic acid in matrix WPC and a commercial resistant starch by electrospraying and spray drying for nutraceutical applications. Their results revealed that both materials and encapsulation methods led to improved folic acid stability, particularly under dry conditions (Rocío Pérez-Masiá et al. 2015). It was emphasized that electrospraying is a promising technology in the food industry for encapsulation applications, since the capsules obtained presented similar morphological characteristics than those obtained through spray drying (Rocío Pérez-Masiá et al. 2015).Similarly, Bakhshi et al. (2012) applied the electrospraying technique to generate nano-sized particles of folic acid encapsulated in sodium alginate (Bakhshi et al. 2012).

In another study, Pérez-Masiá, Lagaron, and Lopez-Rubio (2015) studied the morphology and stability of edible lycopene-containing micro/nanocapsules fabricated through electrospraying (emulsion/coaxial electrospraying) and spray drying. They reported that even though encapsulation structures were obtained from all the matrices evaluated via both processing technologies, spray drying, as a consequence of the high temperatures needed in this process, influenced lycopene stability and very poor encapsulation efficiencies were found in this case (Rocio Pérez-Masiá et al. 2015).

5.2. Recent advances in encapsulation of probiotics by electrospraying

Recently reported research has shown that electrospraying is a practical method for the manufacture of food-safe encapsulated delivery systems, and hence that there is much potential

to design and develop encapsulated products for high-margin improved functionality products with matching delivery systems. The formulation of probiotic bacteria into microcapsules is a novel technique to decrease cell death during GI passage, as well as an opportunity to control release of these cells across the intestinal tract (Cook et al. 2012).

In several studies, López and et al studied the properties whey protein capsules obtained through electrospraying for the encapsulation of probiotic bacteria. This method has been used for encapsulation of *Bifidobacterium animalis Bb12*. Also, they have been found to increase the resistance of probiotic *Streptococcus thermophilus* and *Lactobacillus delbrueckii ssp. bulgaricus* against acid and bile salts (López-Rubio & Lagaron 2012; López-Rubio et al. 2012). Laelorspoen et al. (2014) studied on the microencapsulation of *Lactobacillus acidophilus* in zein--alginate core--shell microcapsules through electrospraying technique. They have demonstrated that after 2 h-incubation in simulated gastric fluid (SGF) at pH 1.2 with pepsin, the encapsulated *L. acidophilus* suffered only 1-log reduction, whilst the number of the non-encapsulated bacteria was reduced by about 5-log cycles (Laelorspoen et al. 2014). Also, Gomez-Mascaraque et al. (2016) have optimized the electrospray conditions for the microencapsulation of a model probiotic microorganism, *Lactobacillus plantarum*,within a whey protein concentrate matrix(Gomez-Mascaraque et al. 2016).

5.3. Recent advances in other applications in food industry by electrospraying

Luo et al. (2011), electrosprayed near-monodisperse chocolate particles for the confectionery industry to introduce an efficient and economical technique for altering the texture and mouthfeel of the food in terms of crispness and crunchiness. Their purpose was presenting a strategy to help producers improve declining sales growth rate in an economically saturated

chocolate market (Luo et al. 2012). Similarly, electrospraying of chocolate to obtain a uniform thin coat (Gorty & Barringer 2011) and production of cocoa butter microcapsules by coaxial electrospraying was also reported (Bocanegra et al. 2005). Eltayeb et al. (2013) produced nanoparticles of solid lipids, i.e. stearic acid and ethyl cellulose with sizes under 100nm by electrospraying to encapsulate maltol flavor. In this research, the maltol encapsulation efficiency and yield were 69.5% and 69%, respectively (Eltayeb, Bakhshi, et al. 2013). Ghaeb, Tavanai, and Kadivar (2015) showed that the electrospraying method is an efficient way of fabricating amylose, amylopectin and starch nanoparticle with an average particle size of around 100nm (Ghaeb et al. 2015).

In other study, Gómez-Mascaraque, Lagarón, and López-Rubio (2015) examined the electrosprayed gelatin sub-microparticles as edible carriers for the encapsulation of polyphenols with application in the development of functional foods. They applied the electrosprayed matrices (without the need of employing high temperatures or toxic solvents) to encapsulate (-)-epi-gallocatechin gallate as a model antioxidant molecule. They reported higher encapsulation efficiency than that reported for other encapsulation systems for the protection of catechins (close to 100%). They showed that encapsulation by the electrospraying method did not damage the bioactive compound as it retained its antioxidant activity (Gómez-Mascaraque et al. 2015a). Recently, electrostatic spraying was examined as a means of improving shelf-life of cupcakes by Kerr and Kerr (2015). Substantial quantities of breads, cakes and other baked goods suffer a loss of quality or must be discarded because of contamination by yeast and molds. They were electrosprayed a 5% potassium sorbate solution onto yellow cupcakes in less than 4 second. The results showed that electrostatic charging of potassium sorbate solutions improves overall

surface coverage, slows the onset of fungal/mold growth and limits subsequent growth compared with conventionally applied sprays (Kerr & Kerr 2015). The potential of electrospraying for thinner edible coatings with excellent barrier properties was also reported by producing the starch films (Pareta & Edirisinghe 2006), and hydrophobic film coating of sunflower oil (Khan et al. 2013).Uematsu et al. (2004) studied on surface morphology and biological activity of protein thin films produced by electrospray deposition. They generated biologically active proteins on α-lactalbumin, with the aim to make protein-based biomaterials, biosensors, and biochips (Uematsu et al. 2004).

6. Conclusions and Future Trends

The results surveyed in this paper show that electrospraying is a viable and practical method for the production of encapsulation and delivery systems. Electrosprayed polymer particles can be used as delivery system nutrients to protect them during processing and storage or during passage of the components to the target site in body. The advantages of using electrospraying technique to encapsulate food bioactives are a combination of sustained and controlled pay-load release, room temperature processing, reduced protein denaturation, and efficient encapsulation. All these enhancements can be accomplished using food grade polymers or bio-polymers. There is also scope to regulate the size distribution of the final product by manipulating processing parameters. This paper presents a comprehensive and detailed discussion of the basic story of the principles of electrospraying to produce nanoparticles including sections on processing, structure, property characterization and applications. The electrospraying process is applied to improve the quality of products based on oral ingested ingredients. Incorporation of the desired materials into the delivery carrier is generally a one-step commercially attractive process that

combines ease of processing, high encapsulation yield with excellent loading capacity. Modern electrospraying plant is effective, easy to use with low dead volume meaning the bioactive compounds have a low machine residence time before protective encapsulation. Size distribution is a critical parameter because particle size is strongly related to the release profile and bioavailability of the payload active bio-compounds the food product. Stable and steady jets are a good indication of close to mono-dispersed particles and hence repeatability. Larger polymer concentrations are employed in electrospinning to form continuous fibers, whereas electrospraying requires lower concentrations and lower intermolecular cohesion to generate micro- or nano-particles. Also, particle morphology is important as it influences both the accumulation of bioactive compounds and the release profile of entrained probiotic bacteria. The upper and lower processing ranges for polymer molecular weight vary widely depending on the polymer type and thence molecular chain entanglement behaviour. Choice of the spraying voltage is important in achieving a stable jet and thence stable particle production.

There is clear potential to develop electrosprayed particles to improve the design and function of novel products and delivery systems for functional food compounds, and there is a growing need for nanotechnology in the food industry. Electro-processing techniques afford promising tools for production bioactive compounds delivery systems for drugs, probiotic bacteria and nutraceutical materials. Electrospraying is a low energy and low-cost material processing technology, which is able to deliver these required products. We find ourselves in the early stages of the uptake of electroprocessing for the manufacture of high added value materials to satisfy increasing consumer demand for functional food products. The development of electrospraying will clearly continue to develop novel materials and the processes to make them.

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Table 1.Applied electrospraying polymers for encapsulation.

Based encapsulating materials		Ingredient (Bioactive Compounds)	Reference
Protein	Amaranth protein isolate (API)	Curcumin	(Aceituno-Medina et al. 2013; Blanco-Padilla et al. 2015)
	Casein	Lipase enzyme	(Xie 2003)
	Collagen	Drugs	(Nagarajan et al. 2014)
	Gelatin	(−)-Epigallocatechin gallate (EGCG)	(Gómez-Mascaraque et al. 2015b)
	Gliadin	Cyclophosphamide (Anticancer drug)	(Gulfam et al. 2012)
	Hordein	-	(Wang & Chen 2012)
	Silk Fibroin	Cisplatin	(Qu et al. 2014)
	Soy Protein Isolate (SPI)	α-linolenic acid	(Gómez-Mascaraque & López-Rubio 2016; Fabra et al. 2016)
		α-tocopherol	
	Whey protein concentrate (WPC)	*β*-carotene	(López-Rubio & Lagaron 2012; Rocío Pérez-Masiá et al. 2015; López-Rubio et al. 2012; Gomez-Mascaraque et al. 2016)
		Folic Acid	
		Bifidobacteriumstrains	
		Lactobacillus plantarum	
	Whey Protein Isolate (WPI)	Rosemary	(Colín-Orozco et al. 2014; Sullivan et al. 2014; Fabra et al. 2016)
		β-lactoglobulin	
		α-tocopherol	
	Wheat Gluten	Fish oil	(Tapia-Hernández et al. 2015)
	Zein-Alginate	*Lactobacillus acidophilus*	(Laelorspoen et al. 2014)
	Zein	Catechins	(Bhushani et al. 2017)
Carbohydrate	Amylopectin	-	(Stijnman et al. 2011)
	Alginate-Chitosan	*Lactobacillus plantarum*	(Coghetto et al. 2016)
	Alyssum homolocarpum seed gum	D-limonene	(Khoshakhlagh et al. 2017)
	Bacterial cellulose from	(−)-Epigallocatechin gallate	(Paximada et al. 2017)

	Komagataeibactersucrofermentans	(EGCG)	
	Cellulose	Natural pigment of red cabbage	(Wu et al. 2014; Devarayan & Kim 2015)
	Chitosan	(−)-epigallocatechin gallate (EGCG)	(Gómez-Mascaraque et al. 2016)
	Dextran	Lycopene	(Rocio Pérez-Masiá et al. 2015)
	Guar Gum	Folic Acid	(Rocío Pérez-Masiá et al. 2015; Stijnman et al. 2011)
	Inulin	Indomethacin	(Jain et al. 2014)
	Resistant Starch	folic acid	(Rocío Pérez-Masiá et al. 2015; Ghaeb et al. 2015)
	Maize starch		
	Tara Gum	-	(Stijnman et al. 2011)
Lipid	Stearic acid-Ethyl cellulose	Vanillin & Maltol	(Eltayeb, Bakhshi, et al. 2013)
Synthetic Polymer	Polyethylene glycol (PEG)	Cells, drugs & proteins	(Lin & Anseth 2009)
	Polylactic acid (PLA)	Rifampin	(Lu et al. 2015)

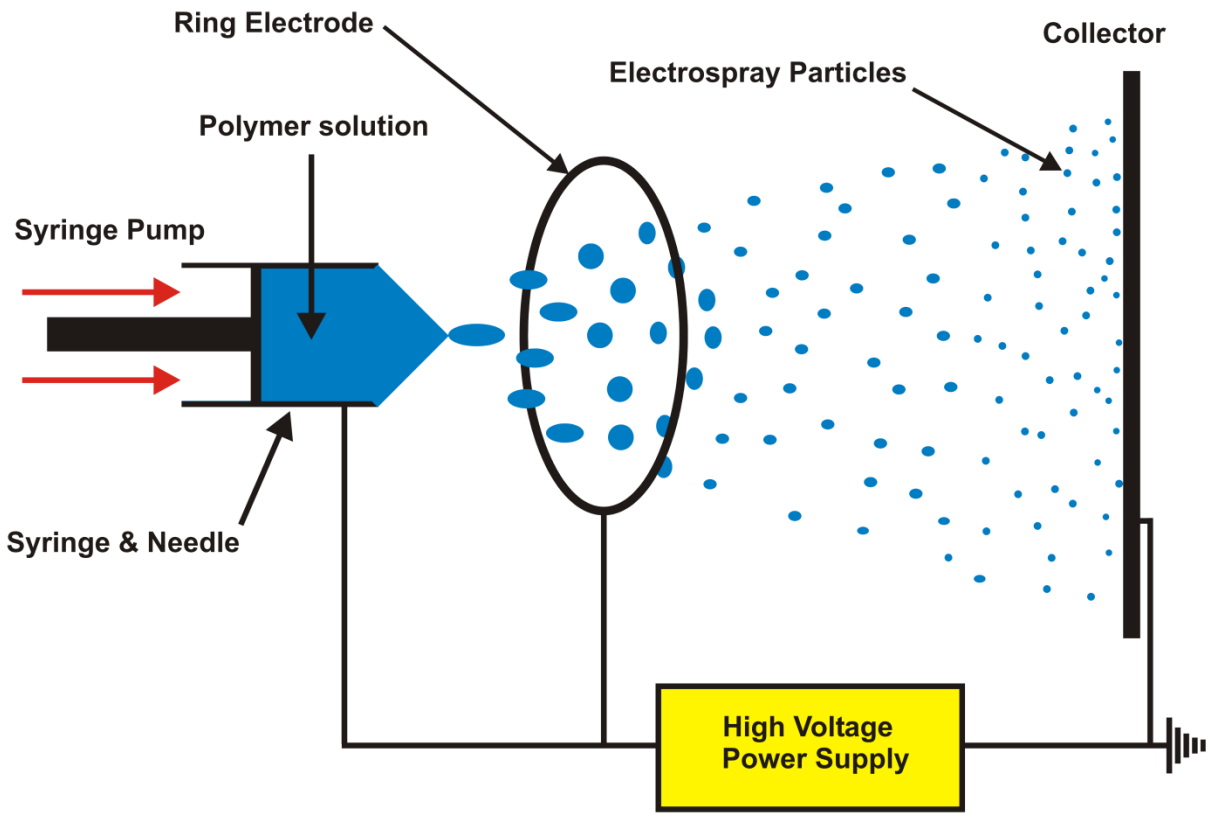

Figure 1. Schematic diagram of a basic electrospraying process.

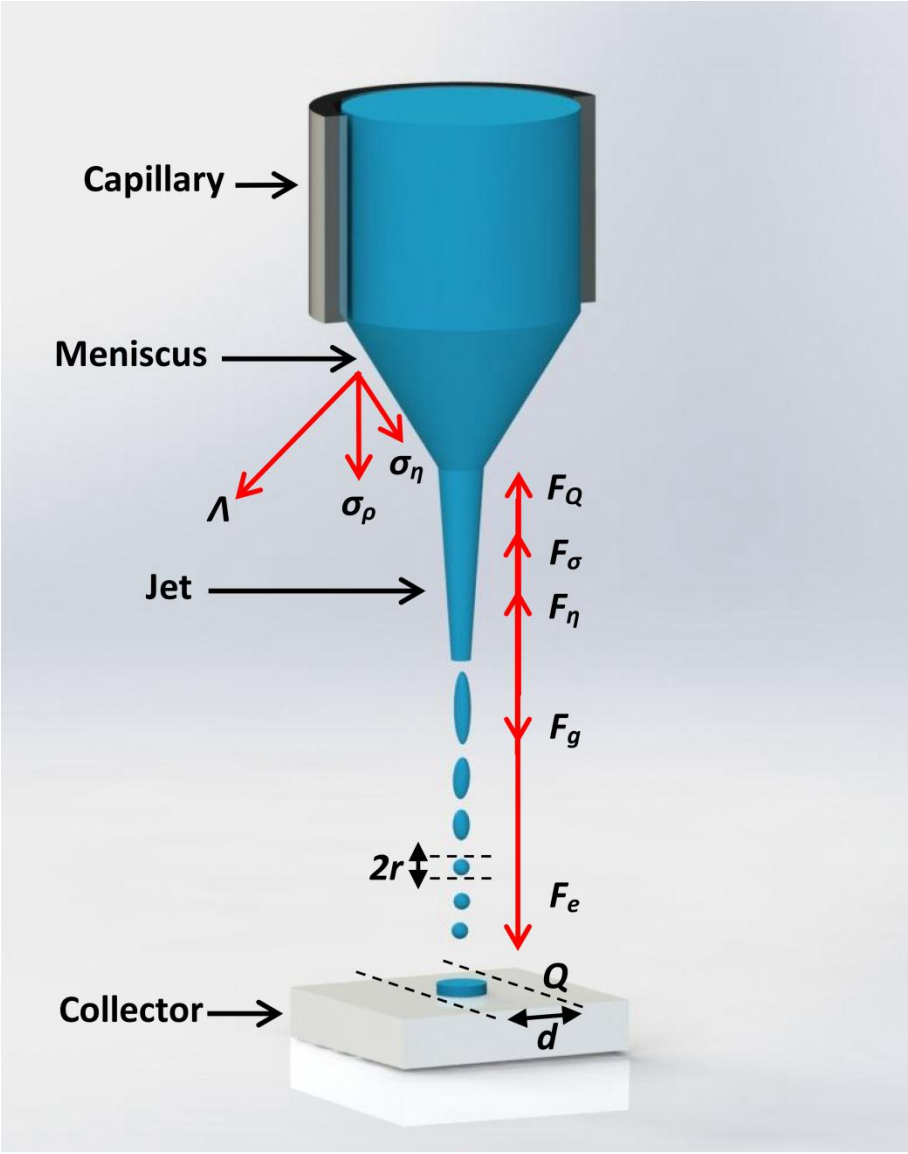

Figure 2. Schematic illustration of stresses and forces during the electrospraying process. The electrodynamic force (F_e), the area charge of any formerly emitted droplets (F_Q), Gravitational force (F_g), Inertial force (F_σ), Drag force (F_η), Surface charge density (Q), Local electric field (Λ), the gradient of liquid velocity normal to the inter-phase surface(σ_η), local liquid velocity at the inter-phase surface (σ_ρ).

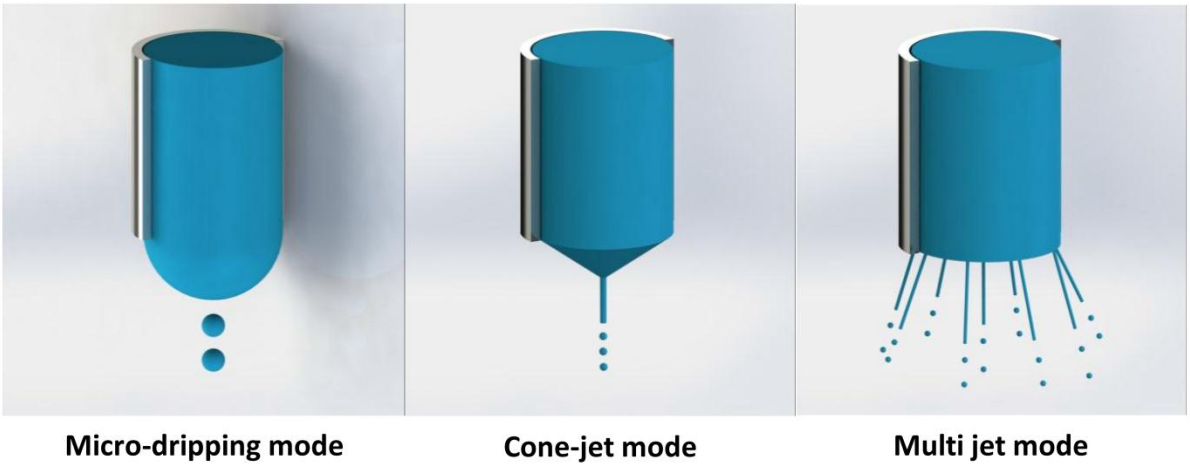

Figure 3. Common modes of electrospraying process

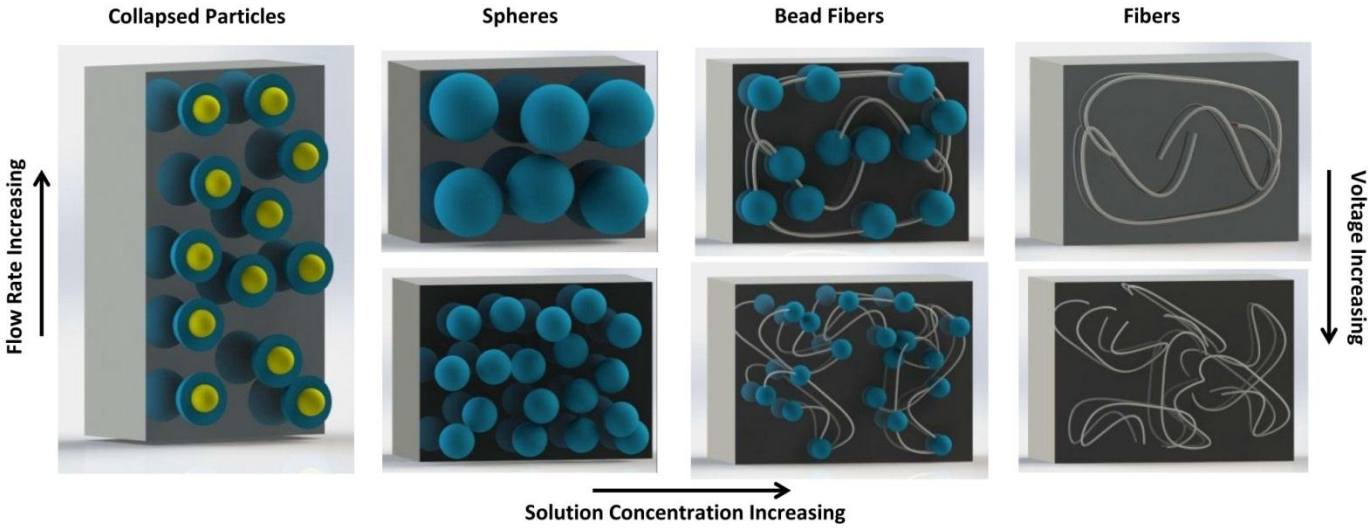

Figure 4. Schematic illustration of the effects of the concentration, flow rate, and voltage on electrosprayed/electrospun nano/microstructures.