Chapter 8 A review on electrospinning technologies and their potential use in the Biomedical Industry

Capítulo 8 Una revisión sobre las tecnologías de electrohilado y su uso potencial en la Industria Biomédica

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Abstract

Electrospinning is a technique to obtain new fibrous structures from synthetic or natural polymers for the development of materials used in pharmaceutical and biomedical industries, among others. However, the low production rate of electrospinning has limited industrial application. This review comments on the various electrospinning technologies to increase productivity based on specific examples from the literature.

Review, Nanofibers, Electrospinning

Resumen

El electrospinning es una técnica para obtener nuevas estructuras fibrosas a partir de polímeros sintéticos o naturales para el desarrollo de materiales utilizados en la industria farmacéutica y biomédica, entre otros. Sin embargo, la baja tasa de producción del electrospinning ha limitado su aplicación industrial. En esta revisión se comentan las distintas tecnologías de electrospinning para aumentar la productividad a partir de ejemplos concretos de la literatura.

Revisión, Nanofibras, Electrospinning

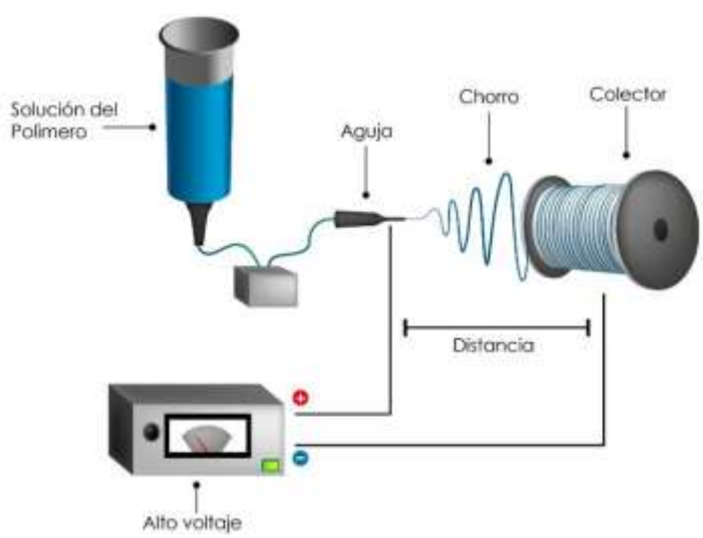
1 Introduction

Electrospinning is a versatile manufacturing technique used to produce continuous fibers from natural or synthetic polymers with diameters ranging from nanometers to microns. This technique allows one to manipulate the different variables of the process and properties of the solution to obtain fibers with specific physical characteristics such as composition, porosity and contact surface per unit volume, alignment and morphology (Erickson *et al*., 2015, Haider *et al*., 2018, Patil *et al*., 2017) among others.
At present, electrospinning is seeing increased interest because the resulting nanofibers are finding applications in biomedicine (Ibrahim & Klingner, 2020), as well as in the textile industry (Mirjalili & Zohoori, 2016), environment (García-Zamora *et al*., 2019), and food and packaging industry (Kumar *et al*. 2019). In this chapter, the different electrospinning techniques are described, classified according to their operating principle: nozzle and free surface methods. The basic configuration of electrospinning, the different injectors, the variables that affect electrospinning and their microstructure, as well as the biomedical applications of coaxial and free-surface injectors, are also described.

1.1. Electrospinning basic configuration

Electrospinning is the increasingly lauded technique for the manufacture of continuous, thin fibers and consists of a high voltage power supply, a needle connected to a syringe, and a metal collector, with the large electrical potential difference applied between the needle and metal collector. In Figure 8.1, the key components of an electrospinning machine are presented.

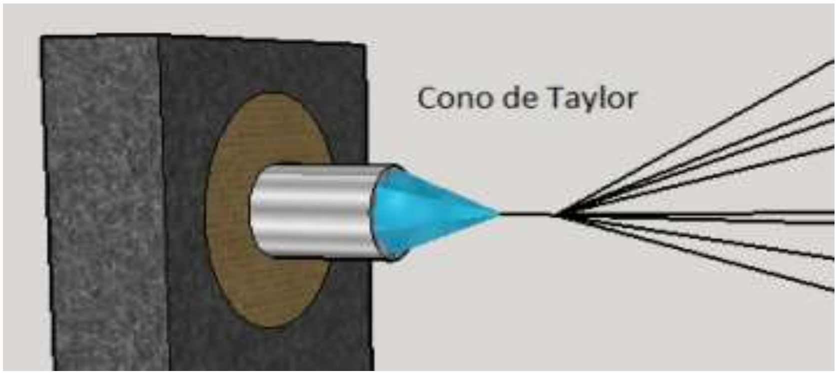
Figure 8.1 Schematic diagram of the electrospinning process



(Adapted from Jiang, Carbone, & Lo, 2015)

Initially, the polymer solution is held at the tip of the needle due to surface tension. When the electrical potential is applied, the hemispherical surface of the polymer drop at the tip of the needle elongates to form a conical shape known as the Taylor cone (Figure 8.2). The formation of the cone immediately precedes the formation of the fibers (Cano *et al*., 2010; Jiang, Carbone & Lo, 2015).

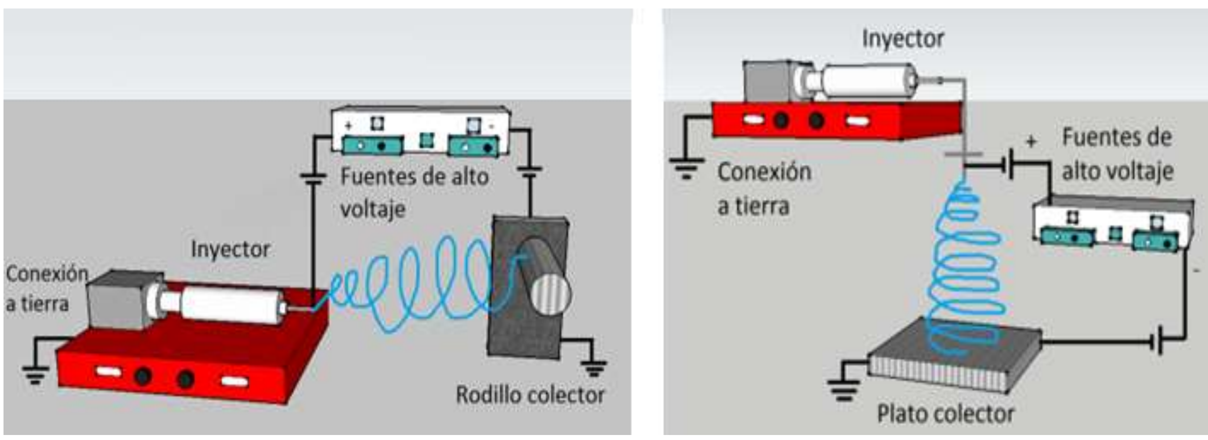
Figure 8.2 Formation of a Taylor cone in capillary



(Taken from Olguin, Fuentes, 2016)

Subsequently, the nanofibers are deposited randomly on the collector forming veils or films and can be manufactured using a stationary collector or a rotating dynamic collector. There are two configurations in electrospinning equipment, horizontal (Figure 8.3a) and vertical (Figure 8.3b). The first one is called a horizontal electrospinner since the injector and the collector are in the same plane, unlike the vertical electrospinner, in which the collector is located in the normal direction just below the injector. Most electrospinners have the horizontal configuration, since this configuration presents fibers with fewer defects such as drops or beadings.

Figure 8.3 Installation diagram for a) horizontal electrospinner b) vertical electrospinner

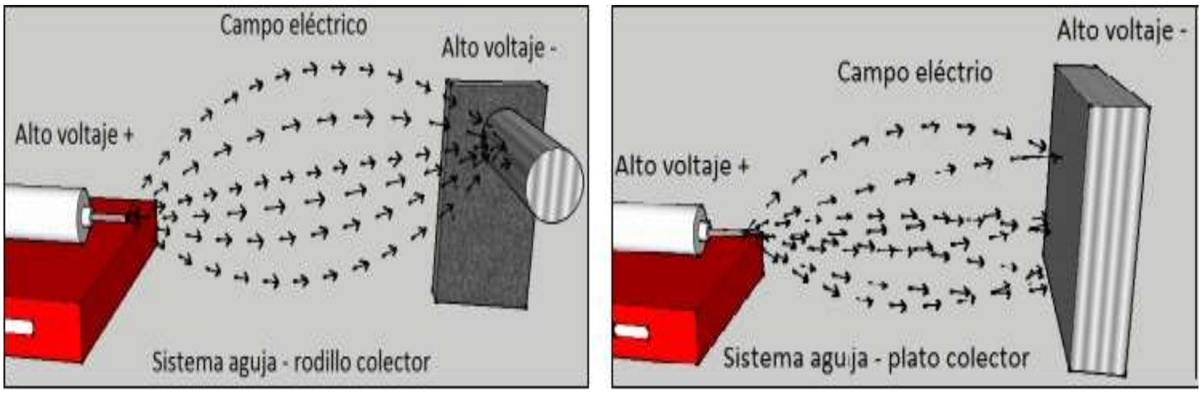


(Taken from Santacruz Vázquez, V. et al., (2017)

It is essential to consider the physics of the electric field that occurs between the injector and the collector of the electrospinner. Because the electrostatic force is the phenomenon that dominates the process, the electric field that acts on the drop of polymeric solution drags the fibers in an axial or tangential direction depending on the configuration of the equipment.

In Figure 8.4, a diagram of the trajectory of the charged particles in the electric field for the two types of collector is shown. If the system is needle-roller, the electric field will simulate an ellipsoid under which the polymer solution from the injector will travel to the collector. If the system changes to that of a plate collector, the electric field can be described as a truncated ellipsoid (Sahay, Thavasi, & Ramakrishna, 2011).

Figure 8.4 Configuration of the electric field in electrospinning equipment



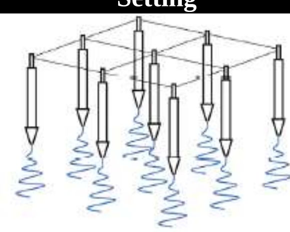
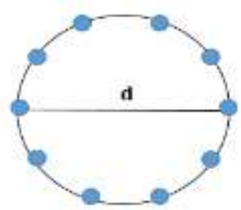
(Taken from Olguin, Fuentes, 2016)

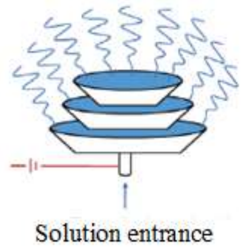
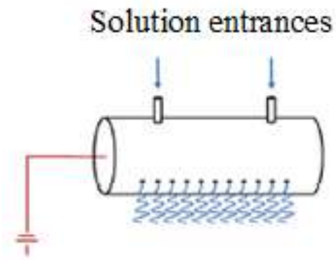
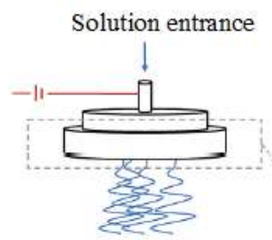
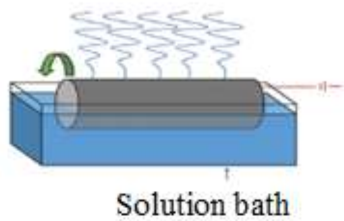
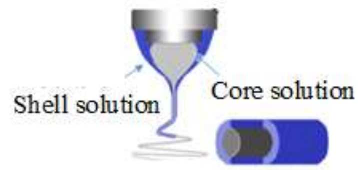
In the same way, the injectors have different configurations, among them the simple needle injector also called a capillary injector, coaxial injector and multi-injector (Yao, Chang, Ahmad, & Li, 2016).

1.2 Technologies used in the electrospinning process

The needle injector is the most widely used configuration according to the reported literature and was the first injector designed for the electrospinning process (Huang, Zhang, Kotaki, & Ramakrishna, 2003). It consists of a plunger or syringe that has an electrically charged capillary attached and that serves as a duct for the supply of the fluid to be electrospun. This injector has disadvantages such as: low feed flow rate, impossibility of obtaining fibers from immiscible mixtures (Tang *et al*., 2016; Vyslouzilova *et al*., 2017), and low productivity (<1 g/h). This last problem has been resolved with modified injectors classified into nozzle and free surface methods (Vass *et al*., 2019). The first method refers to injectors in which the solution is fed directly to multiple needle arrays, while the free surface injectors refer to those in which a greater number of Taylor cones can be formed, and the jets of liquid can freely leave the surface of the solution. Table 8.1 presents a diagram and the different characteristics of several types of multiple injectors used in the electrospinning process.

Table 8.1 Productivity data and diagrams of the different multiple injectors used in the electrospinning process

Author	Productivity	Setting
Theron *et al.,* (2005) used a 9-needle configuration	Productivity 0.1-1 g / h. Voltage 10 kV.	 Taken from Theron *et al.* (2005)
Tomaszewski & Szadkowski, (2005) compared three different arrangements of 10 nozzles arranged in linear, concentric, and elliptical forms: The concentric configuration presented higher process stability and fiber quality. They used PVA solutions.	Productivity 60 mg / h Voltage 20 kV.	 Taken from Tomaszewski & Szadkowski, (2005)

Jiang *et al.*, (2013) used a stepped pyramid configuration, where the formation of several jets was observed, for PVA solutions.	Productivity 2.3- 5.7 g / h Voltages 55-70 kV.	 Taken from Jiang *et al.*, (2013)
Varabhas *et al.*, (2008) used a porous tube configuration of 13 cm long with 20 holes, with a solution of polyvinylpyrrolidone.	Productivity 0.3- 0.5 g / h Voltage 40-60 kV.	 Taken from Varabhas *et al.*, (2008)
Zhou *et al.*, (2009) employed a flat electrode configuration with 4 holes. A polyethylene oxide solution was used.	Productivity 1.68 g / h Voltage 19.8 - 21.0 kV.	 Taken from Zhou *et al.*, (2009)
Niu *et al.*, (2009) employed cylindrical and disc nozzles for use in polyvinyl alcohol solutions. Bhattacharyya *et al.*, (2016) used the free surface electrospinning method from a star-shaped wire electrode, using polyvinyl alcohol solutions.	Cylindrical nozzles Productivity 6 g/h Voltage greater than 57 kV. Disc nozzle Productivity 6.5g/h Voltage 62kV	 Taken form Niu *et al.*, (2009)
Yoon *et al.*, (2018) conclude that coaxial electrospinning allows functional macromolecules, such as proteins and drugs, to be encapsulated in a single step.		 Taken from Yoon *et al.*, (2018)

Free surface electrospinning presents high productivity although is limited to non-volatile solutions. This method is suitable for large-scale nanofiber production. Despite multiple nozzle methods resulting in a lower productivity, it is possible to better control the distribution of the fibers (Noyan *et al.* (2018). Table 8.2 presents the advantages and disadvantages of these methods.

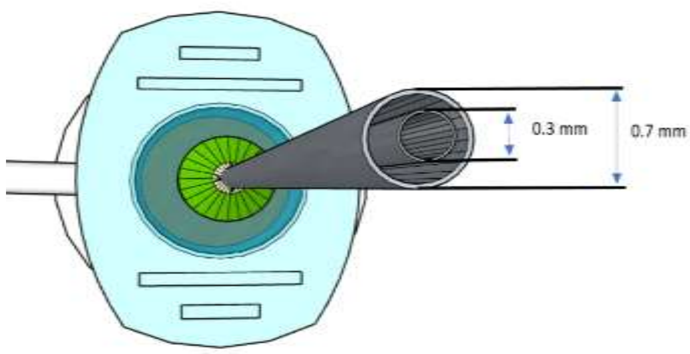
Table 8.2 Advantages and Disadvantages of Multiple Nozzle and Free Surface Electrospinning

Electrospun method	Advantage	Disadvantages
Multiple electrospinning: nozzles	Lower potential difference requirement. Adequate control of the fibers. Ability to form specific fiber structures such as core-shell, porous and multicomponent fiber.	Possibility of the solution clogging the outlet at the tips of the nozzles. Interaction between jets that cause repulsion and deflection of the jet.
Free surface electrospinning	Higher production rate. No problems associated with the nozzles, such as clogging with the solution.	Reduced control of the jets. Difficulty obtaining multi-component fibers. Higher potential difference requirement.

1.3 Coaxial injector

The coaxial injector (Figure 8.5) is a modification of the conventional electrospinning process that involves the provision of multiple feed systems for simultaneous electrospinning. Generally, a matrix arrangement of needle injectors is used, allowing the injection of an internal solution into an external one, to produce continuous coated or hollow nanofibers (Rojas *et al.*, 2020). The coaxial electrospinning configuration implies a core-shell nozzle that is coupled to the material deposits respectively (Gualandi *et al.*, 2015; Yarin, 2011). When applying the voltage to the injector, the formation of the Taylor cone occurs, and the internal fluid remains inside as the core of the fiber, while the external fluid encapsulates the internal fluid, while allowing the evaporation of the solvent. It has been reported that the fibers obtained from a coaxial injector present a greater encapsulation efficiency of active compounds compared to the fibers obtained in a simple injector (Cuvellier *et al.*, 2018; Chen *et al.*, 2020).

Figure 8.5 Diagram of a coaxial injector



The importance of the coaxial injector lies in the possibility of producing polymer / organic compound and polymer / inorganic compound biphasic fibers, whose properties include high surface-volume ratio, porosity, pore size and adjustable diameter from fluids with different physical and chemical (Yao, Chang, Ahmad, & Li, 2016; Ahmed & Ikram, 2016; Quin *et al*., 2018). The use of the coaxial injector in electrospinning equipment permits the obtention of sophisticated fibers with innovative nanoscale architecture (branched, tube yarn, multichannel, porous, etc.) for drug administration, engineering fabrics, nanoelectronics, energy storage devices and sensors (Pant, Park & Park, 2019; Zhang *et al*., 2015; Huang *et al*., 2018). Table 8.3 shows the results of recent investigations that report on creating electrospun fibers using a coaxial injector and the operating conditions used. From this information, it can be concluded that this injector represents an opportunity for the development of new materials.

Table 8.3 Operating conditions for obtaining electrospun fibers with a coaxial injector

Feed flow rate (mL/h) Core /Shell		Distance Needle-Collector (cm)	Voltage (kV)	Fiber Diameter (nm)	Polymer	Authors
0.094 0.189	1.5	12	18.5	70	PEG PA6	Babapoor, Karimi, Golestaneh, & Mezjin (2017)
0.1	0.2	15	19	200	PLA PVA	Alharbi *et al.* (2018[a])
0.02-0.05	0.01-0.040	15	7-8	590-1170	PAN PEGME	Noyan *et al.* (2018)
0.2	1.3 1.5 1.7	20	20	420	Epoxi-amine Pullulan	Cuvellier *et al.* (2018)
0.1	0.4	10	25	-	SSC GELATIN	Isik, Altay, & Capanoglu (2018)
0.8	0.8	25	25	516-403	PAN ZnO	Methaapanon *et al.* (2019)
0.2	0.4	15	12	100	OIL PMoA/PAN	Zhang *et al. (*2019)
0.06	0.06	10	26	500	SSI-GO SPEEK	Wu *et al.* (2019)
0.4	1.3	13	25	671	PLA/CS	Afshar *et al.* (2019)
0.6	0.12	15	14	112	PAN/SDBS	Peng *et al.* (2019)
0.6	0.3	-	18	573-624	PCL GAS	Chen *et al.* (2020)

1.4 Variables that affect electrospinning process

The process of elecrtrospinning is governed by three aspects: the characteristics of the solution, the process variables, and variables corresponding to the surrounding environment all of which interact to determine the characteristics of the resultant fiber. Table 8.4 summarizes the effects of the variables corresponding to each of these aspects (Nagihan, Pinar, & Filiz, 2014).

Table 8.4 The effects of various **v**ariables and parameters on the electrospinning process

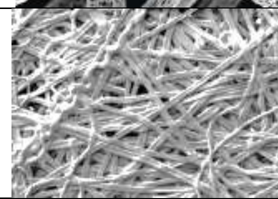
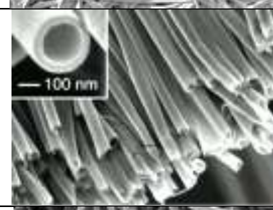
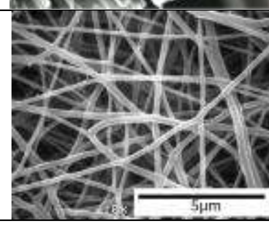
Aspect	Dependent variable	Effect	Effect on fiber feature
Solution	Concentration	An increase in the solute concentration increases the solution's viscosity and consequently the fiber diameter. Conversely, if the solution is of insufficient concentration, it breaks into drops generating instability in the Taylor cone, preventing electrospinning.	Fiber Size and fiber morphology.
	Surface tension	The value of the tension surface depends on the polymer and the solvent, since a decrease in this parameter will reduce the possibility of the formation of drops and favors the formation of the Taylor cone.	Veil Uniformity.
	Conductivity	Experimentally it has been shown that an increase in conductivity brings with it a decrease in the fiber diameter.	Fiber Diameter
	Dielectric constant of the solvent	A solution with a high dielectric constant result in fibers with a reduced diameter and reduces the probability of defects, drops, or beading.	Fiber formation
Process	Voltage	A critically important parameter. A higher voltage favors the formation of thinner fibers and prevents the formation of drops.	Fiber Diameter
	Feed flow rate	A low supply flow rate generates a more stable Taylor cone, evaporating the solution in a gradual way avoiding defect formation in the fiber. An increased flow results in a corresponding increase in fiber diameter.	Veil Uniformity.
	Injector distance to manifold	This parameter is related to the properties of the solution; an ideal distance must be determined that allows obtaining suitable fibers and evaporation of the solvent.	Fiber Morphology
Environmental	Humidity	An increased ambient moisture level favors the existence of circular pores on the surface of the fibers.	Veil Uniformity.
	Temperature	A critical parameter due temperature affects the solution viscosity, thermal conductivity, vapor pressure etc.	

(Adapted from Duque Sánchez, Rodríguez & López, 2013)

1.5 Types of microstructures obtained by the electrospinning process

Different types of structures in the electrospun fibers can be obtained, according to the application (Wang *et al.*, 2011). These structures are classified into porous, flat, hollow, and branched fibers (Table 8.5).

Table 8.5 Classification of the structure of micro and nanofibers obtained by electrospinning

Name	Source	Shape
Porous	Pores are generated when the solvent used to dissolve the polymer is thermodynamically unstable and when subjected to an electric field the solvent coexists in two phases, liquid and gaseous. (Li & Hsieh, 2006)	
Flat	Flattened nanofibers occur when high molecular weight polymers electrospun fibers impact against the collector (Yu *et al*., 2014).	
Hollow	Hollow structures are achieved by using a coaxial electrospinning head of the tube-shell type. The polymer is injected through the shell and through the internal tube a compound that is immiscible with the external polymer is passed (Li, McCann, & Xia, 2005).	
Branched	Branched structure is obtained when electrospun primary jets form branches prior to arriving at the collector. due a balance between electrostatic forces and surface tension of the polymeric solution (Huang, Zhang, Kotaki & Ramakrishna, 2003).	

1.6 Most commonly used polymers electrospinning process

Electrospinning technique is restricted to polymeric substances that allow the formation of fibers, and for the selection of electrospinning polymers, specific physical and chemical properties such as density, electrical conductivity, viscosity, molecular weight of the polymer must be considered, as well as polymer-solvent interactions (Frenot & Chronakis, 2003). A wide variety of electrospinning polymers have been reported; however, polymers of natural origin have the advantage of being biocompatible and immunogenic in comparison with synthetic ones (Liao *et al*., 2018). Among them are collagen, elastin, silk, gelatin, chitosan etc. (Horng Lin, Kuang Chen, Lin Huang, & Chieh Huang, 2015). Table 8.6 lists some of investigations carried out with electrospun biopolymers.

Table 8.6 Biopolymers most frequently used for electrospinning

Polymers	Fibers uses	Operation conditions	Reference
Gelatin and poly-caprolactone	Pharmaceutical industry	Solution 10% w/v. Feed flow rate 1 mL/h. Applied voltage 0.5, 0.8, and 0.3 kV.	Zhang, Ouyang, Lim, Ramakrishna, & Huang, (2004)
Jelly	Nutritional products	Solution in a range of 7 to 20% w/v. Feed flow rate 0.1 and 1 mL/h. Applied voltage 28 and 35 kV.	Nagihan, Pinar, & Filiz, (2014)
Gelatin and polyvinyl alcohol	Packing industry	Solutions 10% w/v. Feed flow rate 0.5 mL/h. Applied voltage 15, 20 and 25 kV.	Horng Lin, Kuang Chen, Lin Huang, & Chieh Huang, (2015)
Jelly	Biomedical industry	Solutions 2.5 to 15% w/v. Feed flow rate 0.8mL/h. Applied voltage 10 to 16 kV.	Huang, Zhang, Kotaki, & Ramakrishna, (2003)
Chitosan and PVA	Management Drugs	Feed flow rate 0.6 mL/h. Applied voltaje 22 kV.	Roya *et al.*, (2016)
Chitosan and PVA	Biomedical industry	Solution of QS/PVA 30/70 Feed flow rate 0.5 mL/h. Applied voltage 20 kV.	Koosha, & Mirzadeh, (2015)

1.7. Biomedical Applications of Coaxial and Free Surface Injectors

Coaxial and free-surface electrospinning have potential applications in the biomedical industry; such fibers are used as tissue engineering scaffolds, wound dressings, and drug delivery devices (Table 8.7). The controlled release of incorporated drugs is a very important feature, especially for toxic drugs such as doxorubicin. Electrospun nanofibers allow controlled drug release in order to minimize negative side effects for patients. In most cases, drug molecules are incorporated into coaxial fibers, in which the drug is introduced into the core of the fiber and are protected by biopolymeric materials in the shell, allowing sustained release.

Table 8.7 Uses of coaxial and free surface injectors and their biomedical applications

Injector type	Application	Author
Coaxial	Controlled release of hygroscopic drug poly (DL-lactic acid) and dimethyloxalylglycine fed into the core and poly (3-hydroxy butyrate) fed into the fiber shell.	Wang *et al.* *(*2010)
Coaxial	Chemotherapy against ovary cancer. The doxorubicin is dispersed in the solution of PVA solution into the core and PVA and chitosan solution located in the shell.	Yan *et al.* *(*2014)
Coaxial	Controlled release for wounds dressings. Sodium hyaluronate located in the core and cellulose acetate in the shell.	Li *et al*. (2014)
Coaxial	Proliferation of Schwann cells. Laminin localized in the nucleus and poly (L-lactide) -co-poly (ε - caprolactone) in the shell.	Kijeńska *et al.* (2014)
Coaxial	Tissue regeneration. The antibiotic metronidazole is incorporated into the core of poly (ε - caprolactone) providing good mechanical properties, while the shell of zein provides good biocompatibility and a hydrophobic barrier for the prolonged release of the drug from the core.	He *et al*. (2017)
Coaxial	Antibacterial material as dressing for wounds and filtration against *Escherichia coli*. Polylactic acid was located in the nucleus and chitosan solution in the shell.	Nguyen *et al.* *(*2011)
Free sueface	Antibacterial properties against *Escherichia coli* gram - negative and *Staphylococcus aureus* gram - positive. Chitosan / PVA / $AgNO_3$ or Chitosan / PVA / TiO_2 nanofibers.	Wang *et al.* (2016)
Free surface	Anti-inflammatory activity and analgesic effect. Niflumic acid and polyvinylpyrrolidone nanofibers.	Radacsi *et al.* *(*2019)
Free surface	Microbicide. PVA fibers with Tenofovir.	Krogstad & Woodrow (2014)

Conclusions

In this review, research articles on electrospinning and its applications in materials for the medical and pharmaceutical industries have been evaluated. Electrospun nanofiber structures have great potential to be applied in processes that use membranes due to their high porosity of up to 90% and a large specific surface area. Therefore, the authors comment on the need to develop injectors that allow higher efficiency of the electrospinning technique and thereby increase the feasibility for large-scale production of these nanostructures.

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