Electrospinning method to produce drug-loaded nanofibers for topical/ transdermal drug delivery applications

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Abstract: Electrospinning is the method for preparing drug-loaded nanofibers with ultrafine structure, a large surface area to volume ratio, and a high porosity with a small pore size. Among the other nanofiber production methods, electrospinning is the most cost effective one with simple tooling and, it is applicable to produce ultrafine fibers with a simple step-up production for drug delivery applications. The selection of the polymer as carrier for electrospinning and the production procedure design is crucial due to drug-polymer-solvent interactions and the other process parameters which would influence the physicochemical biocompatibility and characteristics. This technique can be applied to produce nanofibers of a wide array of polymer types: natural, synthetic polymers, or their blends. This review focuses on various electrospinning methods to produce drug loaded nanofibers, polymers used, electrospinning process parameters, their advantages and limitations for topical/transdermal drug delivery applications.

Key words: Nanofiber, electrospinning, topical drug delivery, transdermal drug delivery

Introduction

Modern polymeric drug delivery systems for topical/transdermal therapy are systems which are designed to release drug(s) to diseased sites of the skin in a consistent and a sustained release manner. In recent years, electrospun polymeric nanofibers have considered as drug delivery systems in wound healing, skin burn therapy as topical and transdermal drug delivery systems (Gomes et al., 2015).

Nanofibers can be produced using different techniques namely, drawing method, self-assembly, phase separation, and electrospinning. Among the other nanofiber production methods, electrospinning is the most cost effective one with simple tooling and, it is applicable to produce ultrafine fibers with a simple step-up production for drug delivery

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applications(Ulubayram et al., 2015).

Electrospinning is a simple method that utilizes electrostatic forces to produce nanofibers of polymer with unique characteristics including ultrafine structure, a large surface area to volume ratio, and a high porosity with a small pore size ranging from submicron to nanometer sizes (Pillay et al., 2013; Paaver et al., 2014).

Nanofibers have many advantages, such as high surface to volume ratio, porosity, and astructure that mimics the extracellular matrix structure, the production of mats and, furthermore the loading of drugs into nanofibers has improved their functions(Son et al., 2014). Electrospun nanofibers have been developed for skin tissue scaffolds, wound dressings as well as drug delivery applications includingAlzheimer drugs, antimicrobial and antifungal drugs, proteins, cosmeceuticals and genes(Arthanari et al., 2014; Gencturk et al., 2016; Esenturk et al., 2016).

The selection of the polymer to fabricate nanofibers with electrospinning technique is very important due to drug-polymer-solvent interactions which would influence the formation of nanofibers and the physicochemical properties and , morphology, mechanical properties, drug release (including burst effect), and biocompatibility of the final nanofibers (Paaver et al., 2014).This technique can be applied to generate nanofibers of a wide array of polymer types: natural polymers such as cellulose derivatives, chitosan, alginate; synthetic polymers such as polyvinyl pyrrolidone, polyvinyl alcohol, poly-L-lactic acid, poly (ε-caprolactone), or their blends (Pillay et al., 2013; Paaver et al., 2014).

Hydrophobic polymers such as poly (ε-caploractone) (PCL) and poly (urethane) (PU) are easy to electrospin and exhibit high mechanical strength and elastic properties after electrospinning.However, the hydrophobicity of electrospun nanofibers is not good for cell attachment and the nanofibers must be further modified to add hydrophilicity. Natural polymers are hydrophilic and provide sites for cell adhesion while synthetic polymers have better mechanical properties and slower degradation rate (Gomes et al., 2015).

Drugs can be simply blended with the polymer solution, physically or chemically surface immobilized. The development of single nozzle to co-axial nozzle electrospinning could support the fabrication of a solid

nanofiber that can control the initial burst release, overall release kinetics, and multi-drug loading properties (Sebe et al., 2015).

This review focuses on various electrospinning methods to produce drug loaded nanofibers, used polymers, electrospinning process parameters, their advantages and limitations for topical/transdermal drug delivery applications.

Electrospinning method

There are various methods to produce nanofibers, for example, self-assembly of polymers, template synthesis, phase separation, and electrospinning. Electrospinning is the most frequently chosen because it is a simple, cost-effective, and versatile process to produce large volumes of nanofibers (Abrigo et al., 2014; Heunis et al., 2010).

After being discovered in the late 16th century by William Gilbert that an electric field can effect fluid dynamics, electrospinning technique was first observed by Rayleigh in 1897 and investigated in detail by Zeleny in the early 1900s and then patented in 1934 by Formhals (Chen et al., 2014; Pillay et al., 2013).

There are four elementary components to complete the electrospinning process: (1) a syringe pump, which controls the flow rate of polymer solution, (2) a voltage power supply, which provides the force to stretch the charged polymer solution into a fiber form, (3) a needle, which shifts the solution into the high electric field and (4) a collector, such as a stationary or rotating metal screen, plate, or wheel, on which electrospun nanofibers are collected (Rim et al., 2013; Kai et al., 2014). One electrode is placed on the syringe needle of a polymer solution and the other electrode is linked to a metal collector. When a sufficiently high voltage, usually between 1 and 30 kV is applied to a liquid droplet, the liquid becomes charged. When the applied electric field is strong enough to overcome the surface tension, charged polymer forms a "Taylor cone" at the tip of the needle and tiny jet is ejected from the surface of the droplet. As the polymer solution accelerates, the solvent evaporates in the air and nanofibers are formed on the collector (Heunis et al., 2010; Chen et al., 2014; Hu et al., 2014; Rim et al., 2013) (Figure 1).
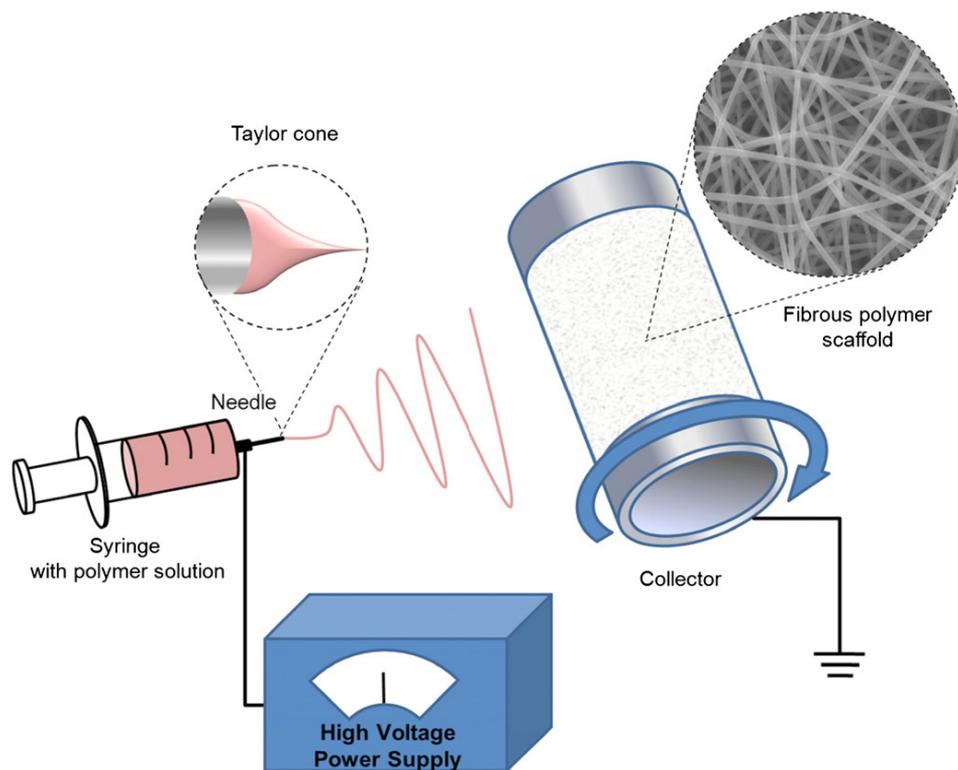
Figure 1. Scheme of electrospinning method (Rim et al., 2013)

Polymers used in nanofiber production

Polymer selection is important for the production of nanofibers and their interaction with cells. The ideal polymer is not only biocompatible and biodegradable, but also non-toxic, moderately hydrophilic, and has appropriate mechanical strength. Nanofiber can be produced with polymers alone or in blends. Since the use of natural polymers have certain disadvantages like low stability, toxic degradation products which can be harmful to the cells, the natural polymers are often blended with synthetic polymers. Composite nanofibers composed of natural and synthetic polymers express the ideal biological properties of the natural polymers and the mechanical strength of the synthetic polymers. Polymers used in nanofiber production have variety of mechanical properties, degradation rates, and cell-material interactions (Pelipenko et al., 2015).Electrospun

drug-loaded nanofibers in skin drug delivery applications based on different polymers are listed in Table 1.

Natural polymers

Proteins

Collagen has excellent biocompatibility, non-immunogenicity and biodegradability. Collagen has molecular structure similar to glycosaminoglycans (GAGs), which is an important component of extracellular matrix. Collagen is abundant in the dermal layer of skin and recognized by cell surface receptors. Therefore, it has the ability to crosslink and appropriate mechanical strenght to the skin tissue (Zulkifli et al., 2015).

Gelatin is a non-immunogenic protein, obtained from the partial hydrolysis of collagen, the main structural protein of the dermal extracellular matrix(Gomes et al., 2015).Due to its polyelectrolyte nature and strong hydrogen bonding, it is difficult to be electrospun alone(Pelipenko et al., 2015). Gelatin nanofibers have the regeneration ability of a variety of tissues and organs, such as skin, bone, muscle and nerve(Gomes et al., 2015).

Elastin is a naturally occurring extracellular protein that possesses crosslinking molecules between the amino acid chains and is responsible for tissue elasticity. Due to its polyelectrolyte nature, it is difficult to be electrospun alone. Elastin is added to nanofiber formulations to improve cell adhesion (Swindle-Reilly et al., 2014).

Fibrinogen is a natural polymer that is present in blood plasma. It has great healing advantages, as it provides a favorable surface for cellular attachment and proliferation. Especially in tissue engineering, fibrinogen based scaffolds induce extracellular matrix production that renders support to connective tissues, such as skin, cartilage, ligament, bones, tendons, nerves, and blood vessels. It can be electrospun alone (Rajangam et al., 2013).

Table 1. Electrospun drug-loaded nanofibers in skin drug delivery applications.

Polymer	Drug	Solvent	Aim	Reference
Poly (ε-caprolactone)	Cyanocobalamin	Chloroform/methnol	Transdermal delivery	Madhaiyan et al., 2013
Poly vinyl alcohol/ sodium alginate	Ciprofloxacin	Distilled water	Wound healing	Kataria et al., 2014
Poly vinyl alcohol/ sodium alginate	Voriconazole	Distilled water	Topical delivery	Esenturk et al., 2016
Poly vinyl alcohol	Prazosin HCl	Distilled water	Transdermal delivery	Shen et al., 2014
Gelatin	Amphotericin B, natamycin, terbinafine, fluconazole, itraconazole	Trifluoroethanol	Topical delivery	Lakshminarayanan et al., 2014
Polyvinyl caprolactam-polyvinyl acetate-PEG graft copolymer	Piroxicam	Acetone	Wound healing	Paaver et al., 2014
Poly (L-lactic acid)	Cyclosporine A	Chloroform/ 1,2-dichlorethane/ ethyl acetate	Topical delivery	Holan et al., 2011
Poly vinyl alcohol/ poly-N-isopropylacrylamide	Levothyroxine	Water or ethanol	Topical delivery	Azarbayjani et al., 2010
Polyvinyl alcohol or cellulose acetate	cellulose acetate	Distilled water or acetone/dimethylacetamide	Topical delivery	Opanasopit et al., 2013
Cellulose acetate	Vitamin A or Vitamin E	Acetone/dimethylacetamide	Transdermal delivery	Taepaiboon et al., 2007
Polyurethane/ hydroxypropyl cellulose	Donepezil hydrochloride	Dimethylformamide	Transdermal delivery	Gencturk et al., 2016
Poly(N-isopropyl acrylamide)/egg albumen/ poly(ε-caprolactone)	Gatifloxacin hydrochloride	Trifluoroethanol	Wound healing	Pawar et al., 2015

Polysaccharides

Hyaluronic acid is a major glycosaminoglycan found in the extracellular matrix of many soft tissues in higher animals. It is a linear natural polysaccharide and has good biocompatibility and biodegradability. Some complications arise when working with charged polymer solutions due to their long-range electrostatic interactions and the presence of counter ions. Since hyaluronic acid is charged in solution, it is blended with uncharged carrier polymers(Brenner et al., 2012). However, electrospinning method using hyaluronic acid can be difficult because of its high viscosity and surface tension, even in low concentrations, and its hydrophobic nature that may not be favorable for some applications (Fischer et al., 2012).

Alginate is a natural polymer composed of (1, 4)-linked *b*–D-mannuronic acid and α– L-glucuronic acid. It has good biocompatibility, biodegradability, and ease of chemical derivatization. Alginate-based beads demonstrate pH sensitivity and stability, and have been developed for controlled delivery systems. Due to its high rigidity and fragility like most of the natural polymers, alginate is usually used as a co-polymer, and is blended with synthetic polymerslike poly vinyl alcohol and poly (ethylene oxide) (Arthanari et al., 2014). Alginates have antibacterial properties and are usedin tissue engineering for the treatment and regeneration of skin (Bogun et al., 2013).

Chitin and chitosan have been used as nanofiber scaffolds due to their biodegradability, hydrophilicity, nonantigenicity, non-toxicity, antimicrobial activity, bioadherence and cell affinity (Shalumon et al., 2011). Chitosan is the N-deacetylated derivative of chitin and very similar to the glycosaminoglycans (GAGs) found in the extracellular matrix. It is known for adhering to wounds and for its antimicrobial and immunostimulating activity. All derivatives of chitosan have antimicrobial activity of plain chitosan(Gomes et al., 2015).It is difficult to directly spin pure chitosan. In order to form nanofiber, chitosan is commonly blended with other polymers that possess fiber forming capabilities such as polyethylene oxide, polyvinyl alcohol, polylactic acid, silk fibroin, and collagen (Xu et al., 2015). Chitosan has a positive effect both on the re-epithelialization and regeneration of the granular layer of the skin (Gomes et al., 2015).

Cellulose is the most abundant renewable polysaccharide and has been utilized as wound dressings for many years. But the processability of cellulose is extremely restricted due to its limited solubility in common organic solvents (Vatankhah et al., 2014). Instead, soluble derivatives of cellulose, which are the cellulose acetate, hydroxy ethyl cellulose, and ethyl cellulose and hydroxypropyl methylcellulose are most commonly used as nanofiber scaffolds in skin tissue engineering applications(Zulkifli et al., 2015; Zulkifli et al., 2014; Lim et al., 2010).

Synthetic polymers

Polyethylene oxide (PEO) and poly (vinyl alcohol) (PVA), water-soluble polymers, are often used in the preparation of nanofiber mats from their blend solutions and have good spinnability. Therefore, they are often added to chitosan, alginate, hyaluronic acid, and other polyelectrolytes that are difficult to be electrospun alone (Pelipenko et al., 2015). PEO and PVA are non-toxic, hydrophilic polymers with biodegradation and adhesive properties and were used as wound healing scaffolds (Shen et al., 2014).

Poly (ε-caprolactone) (PCL), polylactic acid (PLA), and poly (lactic-co-glycolic acid) (PLGA) nanofibers are all stable in an aqueous environment, but organic solvents are needed for their production. These nanofibers are widely studied as drug delivery systems because the drug release can be controlled (Pelipenko et al., 2015). PCL is biodegradable hydrophobic polyester characterized by a high plasticity, and a slow degradation rate resulting from the hydrolysis of its ester linkages (Gomes et al., 2015).PLAand PLGA are not only mechanically strong, but also has biocompatibility and good cell attachment and proliferation. They also have good electrospinning ability features (Jang et al., 2012; Ajalloueian et al., 2014).

Poly-vinylpyrrolidone (PVP) has excellent biocompatibility and can be used easily electrospinning procedure. It has been used as the main component of wound dressings (Quiros et al., 2015).

Polyurethane is a soft and hydrophobic polymer commonly used for wound dressing and sustained drug delivery applications. It is used in wound dressings because of its good barrier properties and oxygen permeability (Unnithan et al., 2014).

Solvents used in nanofiber production

Water is the most commonly used solvent due to its safety and biocompatibility. However, its use is limited to hydrophilic polymers. In addition to this limitation, the solubility of polymers inwater is often low, or water-based solutions have high viscosity at low concentrations, resulting in a small amount of electrospun product per large volume of polymer dispersion(Pelipenko et al., 2015).Most of the natural polymers are soluble in water, as example; alginate and cellulose.

The commonly used organic solvents in electrospinning areacetone, dichloromethane, methanol, ethanol, acetic acid, dimethylformamide,ethyl acetate, trifluoroethanol, tetrahydrofuran, andformic acid.The major disadvantages of organicsolvents are their toxicity, price, and oftentoohighvolatility. Inorderto achieve optimal solution viscosity, surface tension, and solventvolatility, a combination of two or more solvents is often used(Pelipenko et al., 2015).As an example, for electrospinning of polylactic acid chloroform, 1,2-dichlorethane, and ethyl acetate are usually used as solvents (Holan et al., 2011).

Other excipients used in nanofiber production

In order to achieve spinnability of natural and semi-synthetic polymers, improve the production process reproducibility, or change the product morphology from beads on fibers to homogeneous, surfactants and salts are added to the polymer solution. As salts, sodium chloride or tetramethyl ammonium chloride has been used to increase the charge density on the liquid jet and thus prevent the formation of beads and obtain uniform thin fibers. Surfactants are amphiphilic molecules that readily absorb at surfaces and thereby lower the interfacial tension; a key parameter that influences electrospinning.Nonionic Tween 20, Tween 80, Triton X-100, Triton X-15, polyoxyethylene glycol lauryl ether (Brij 35), anionic sodium dodecyl sulfate (SDS), and cationic dodecyltrimethylammonium bromide (DTAB) can be used as surfactants (Zheng et al., 2014; Shanet al., 2014; Araujo et al., 2013; Ziani et al., 2011).

Parameters that influence nanofiber formation and the electrospinning process

Although the electrospinning process is simple, a number of processing variables need to be regulated in order to generate nanofibers instead of droplets or beaded morphologies. The major challenge of the electrospinning process lies in the optimization of these parameters to achieve desirable nanofiber morphology and properties(Pillay et al., 2013).

Polymer solution parameters

Polymer type selection has an important effect on nanofiber production. Polymers with high molecular weights (higher degrees of polymerization) are preferable for electrospinning in order to enable a sufficient number of intermolecular entanglements. Polymers with low molecular weight, nonlinear and polyelectrolyte nature are very difficult to electrospin (Gupta et al., 2005; Rosic et al., 2012).

At lower polymeric concentrations, due to the effect of the applied voltage and surface tension of the polymeric solution, droplets occur before reaching the collector (Pillay et al., 2013).At an increased polymeric concentration, solution viscosity increases and more uniform nanofibers in higher fiber diameters are formed(Haghi & Akbari, 2007; Cramariuc et al., 2013).

Surface tension of the solution depends on the characteristics of the solvent and solute. Usually, low surface tension values result in the formation of fibers without beads and low voltages can be applied in electrospinning. Surface tension can be changed by the addition of surface active substances(Bhardwaj & Kundu, 2010; Pillay et al., 2013).

Viscosity and viscoelastic properties of a polymer solution greatly affect jet formation and its stability, and therefore nanofiber morphology (Rošic et al., 2012). There is need to be a balance between the elastic and plastic moduli of the polymer solution. When elasticity is higher than plasticity droplet formation occurs (Pelipenko et al, 2012).

Polymer solutions with low conductivity cannot be electrospun due to the absence of a surface charge on the fluid droplet, which is needed for Taylor cone formation. Generally higher solution conductivities result in

thinner nanofibers. In case of uncharged polymers, the problem of low conductivity can be solved by adding salts(Bhardwaj & Kundu, 2010; Cramariuc et al., 2013).

Another solution parameter is dielectric constant of the solvent. Solvents with higher dielectric constants result in thinner nanofiber formation (Son et al., 2004).

Process parameters

Generally, voltages between 1 and 30 kV are used. Solutions with low conductivity, high surface tension, and high viscosity require higher voltages, and therefore thinner fibers occur(Cremariuc et al., 2013; Heunis et al., 2010).

The nozzle tip to collector distance influences the size and morphology of the nanofibers formed. If the distance between the capillary and collector is not optimized properly, bead formatio and electrospraying may be observed. Generally when the distance increases, thinner fibers occur (Bhardwaj &Kundu et al., 2010).

When the flow rate of the solution increases thicker nanofibers form due to thicker jet formulation but also may result in generation of beads (Bhardwaj & Kundu, 2010; Cramariuc et al., 2013).

Another factor affecting nanofiber morphology is nozzle design. A single-channel nozzle allows formation of uniform nanofibers, whereas a coaxial nozzle enables formation of core– shell or even multilayered nanofibers (Maleki et al., 2013).

Collector type affects the orientation and morphology of the electrospun nanofibers. Randomly-oriented nanofiber mats can be produced when a conductive flat collector is used, but aligned nanofibers can be obtained if the collector is a rotating cylinder or a wheel-like disk(Bhardwaj & Kundu et al., 2010).

Ambient parameters

Environmental temperature and relative humidity are the ambient parameters affecting nanofiber formation. When environmental temperature

is high, solvent evaporation rate increases and thicker nanofibers occur. The effect of temperature on the solution viscosity is opposite i.e. higher temperatures result in lower viscosity and the formation of thinner nanofibers (De Vrieze et al., 2009).

When hydrophobic polymers dissolved in organic solvents, water acts as a non-solvent and higher relative humidity values lead to the formation of porous nanofibers (Medeiros et al., 2008). In the case of aqueous polymer solutions, at low relative humidity values, rapid solvent evaporation causes thicker nanofiber formation (Pelipenko et al., 2013).

Drug loading methods into nanofibers for skin applications

The aim of designing a drug delivery system is to enable drug release at a controlled rate over a desired period. Nanofibers, with their large specific surface areas, can improve the solubility and dissolution rates of drugs, thereby resulting in fast release of poorly soluble active drugs. Drug release from nanofiber in terms of processing setup and modulate the release kinetics, there are three methods in drug loading intonanofibers: blend electrospinning, coaxial electrospinning and immobilizing after electrospinning (Figure 2) (Goh et al., 2013).

Blend electrospinning

If the drug and polymer are soluble in the same solvent, the drug can be dissolved directly into the polymer solution, or in the case where the drug and polymer are not soluble in the same solvent, the drug can be solubilized in a small quantity of another solvent before being added to the polymer solution. According to this method, the drug is embedded in the produced nanofiber (Pillay et al., 2013).

Holan and coworkers prepared cyclosporine A, a potent immunosuppressive drug with low water solubility, loaded electrospun poly (L-lactic acid) nanofibers for investigation as topical drug delivery carriers. Poly (L-lactic acid) was dissolved in chloroform (7 wt.%), and two other solvents, 1,2-dichlorethane (29 wt.%) and ethyl acetate (10 wt.%). The drug was added to this solution and the resulting solution was electrospun. Study of cyclosporine A release behavior in culture

medium showed a release for at least 96 h. After the topical application of cyclosporine A loaded nanofibers on skin allografts in vivo, the release was significantly slower and about 35% of the drug was still retained in the nanofibers on day 8 (Holan et al., 2011).

Arthanari and coworkers electrospun gatifloxacin-loaded nanofibers for wound healing. Sodium alginate (2 wt %) and polyvinyl alcohol (10 wt %) solutions were prepared separately in water. Gatifloxacin (1% w/v) was dissolved in PVA and then, the SA solution was mixed into this solution and the resulting solution was electrospun. As much as 90% of the GH was released from the electrospun nanofibers within 6 h of incubation. Beyond this, the release was sustained for 24 h. Moreover, GH-loaded sodium alginate/PVA composite nanofibers exhibited a useful and convenient method for electrospinning in order to control the rate and period of drug release in wound-healing applications (Arthanari et al., 2014).

In another study, Lakshminarayanan and coworkers compared antifungal-loaded (amphotericin B, natamycin, terbinafine, fluconazole, and itraconazole) electrospun gelatin nanofiber mats. Gelatin was dissolved in trifluoroethanol at a concentration of 10% weight/volume (w/v). The drugs were added to the gelatin solution so that the final antifungal:gelatin ratio was maintained at 0.25 %. The antifungal-loaded nanofibers had improved elasticity, an important requirement for wound dressing (Lakshminarayanan et al., 2014).

If the drug and polymer are not soluble in a common solvent, the drug can be dissolved in a solvent that is immiscible with that in which the polymer is dissolved and the two solutions could be blended, resulting in an emulsion that can be electrospun. According to this method, the drug is encapsulated in the polymeric matrix (Pillay et al., 2013).

Qi and coworkers produced PLLA composite electrospun nanofibers. Alginatewas dissolved in water and bovine serum albumin (BSA) was taken as the model drug and added to the alginatesolution in water. The aqueous solution was then slowly added to dichloromethane comprising the surfactant sodium bis(2-ethylhexyl) sulfosuccinate.A calcium chloride solution was added to the mixture in order to cross-link the alginate to form calciumalginate gel beads. PLLA was then added to the emulsionand

dissolved in the DCM phase and then, the resulting mixture was electrospuninto nanofibers. After an initial burst release, a slow release over a period of 120 hours was observed (Qi et al., 2006).

Coaxial electrospinning

Coaxial electrospinning is an easy method to electrospin two immiscible polymer solutions containing drugs in the core and sheath because the two components are simultaneously electrospun from separate capillaries. Multiple drugs can be loaded into the nanofibers and their release kinetics can be controlled individually. A co-axial needle is a horizontal arrangementof outer and inner needles that separate two differentsolutions. In comparison to blend electrospinning, the drug loading efficiency is higher and the initial burst release property is decreased. Drug release occurs after swelling or dissolving of the core polymer resulting in the formation of pores in the shell after dissolution of hydrophilic portion in the core (Son et al., 2014; Choi et al., 2015).

Jin and coworkers prepared multiple epidermal induction factors (EIF) such as the epidermal growth factor (EGF), insulin, hydrocortisone, and retinoic acid (RA) with gelatin and poly (L-lactic acid)-co-poly-(ε-caprolactone) (PLLCL) solutions and performed electrospinning by two different approaches: blend spinning and core–shell spinning as a graft for skin regeneration. No burst release was observed from EIF encapsulated core–shell nanofibers; however, an initial 44.9% burst release from EIF blended nanofibers was observed over a period of 15 days (Jin et al., 2013).

Immobilizing after electrospinning

The sustained diffusion-controlled release of a delivery system can be prolonged by immobilizing the active drugs on the polymeric chains. In this method, the drug is absorbed into the electrospun nanofibers by immersing the nanofibers in a drug solution (Sebe et al., 2015; Pillay et al., 2013).

Jiang and coworkers prepared a PEG–CS–ibuprofen conjugate to decrease the release rate of ibuprofen from PLGA and PLGA/PEG–CS blend nanofibers. In the case of the covalently immobilized ibuprofen, the

released amount of drug was lower (only 40% over 16 days) compared with the complete 12-day drug release from the PLGA fibers and the nearly 70% drug release from the blend fibers (Jiang et al., 2004).
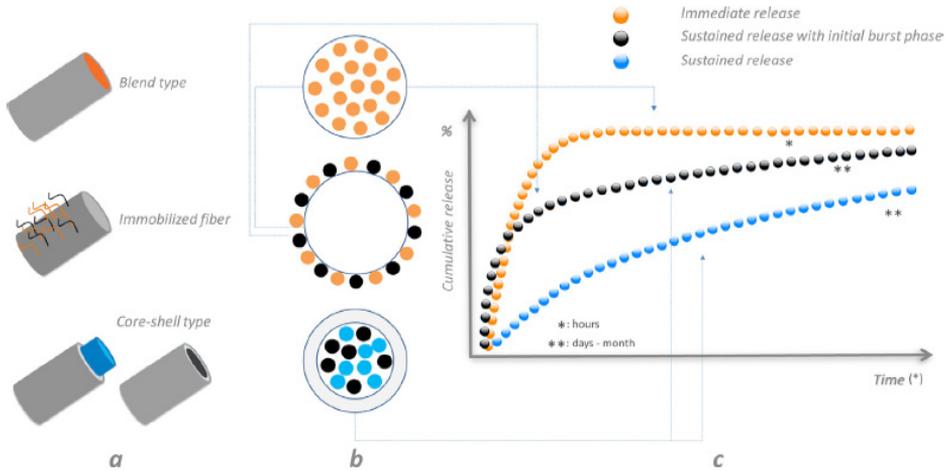
Figure 2: Relationship between the most relevant structural parameters of fibers and their drug release profiles (a)fiber structure; (b)fiber cross section; (c)corresponding drug release (Sebe et al., 2015).

Conclusions

Nanofibers have many advantages, such as large surface area to volume ratio, high drug loading capacity, and extracellular matrix mimicking structure. Therefore, numereous applications of nanofibers have been achieved in drug delivery. As described in this review, the successful production of nanofibers starts with the selection of suitable polymers and solvents. Many desirable properties can be achieved by blending multiple polymers during electrospinning processes. Moreover, the design of core-shell structured or immobilized drug-loaded electrospun nanofibers can present a controlled and prolonged release. Electrospinning technology holds great potential in topical/transdermal drug delivery applications because it is simple and cost-effective. Although new drug delivery systems based on electrospinning are being formulated, there is still need for much extensive research on different electrospinning parameters and to develop methods for electrospinning new polymer combinations and drug loading.

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