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A REVIEW OF ELECTROSPINNING PROCESS AND MICROSTRUCTURE MORPHOLOGY CONTROL

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ABSTRACT

Electrospinning can be used to produce nanoscale polymeric fibers. The fibrous structure inherent in the electrospun scaffolds provides large surface area and high porosity that allow the scaffolds to be potentially used for various applications including tissue engineering, wound dressing and filtration. However, it is difficult to control microstructure morphology of electrospun scaffolds, which is sensitive to various parameters. This paper reviews ways to control three important microstructure morphologies including fiber diameter, the formation of beads and pores. The review shows that electrospinning parameters including polymer solution concentration, voltage, tip-collector distance, solution feed rate, solvent selection, addition of salt, polymer molecular weight and humidity affect the scaffold morphology. Knowledge of complex interactions of these interrelated variables is still lacking. The review gives insight for the robust production of fibrous scaffolds with controlled microstructure morphology by using an electrospinning technique.

Keywords: electrospinning, electrospinning process, microstructure morphology control.

INTRODUCTION

Over the past decade, electrospinning technique has been widely used in fabricating fibrous materials for various applications, such as hard and soft tissue engineering scaffolds, wound healing, drug delivery and pharmaceutical composition, nanofibers composite, filtration and optical devices [1 - 4]. For biomedical applications, the concept of electrospun scaffolding was first emerged in 1978 where researchers fabricated grafts from thermoplastic polyetherurethane elastomer (PU) by electrospinning process [5].

Electrospinning has been found to be a promising method in a wide range of biomedical applications especially tissue engineering due to its ability in fabricating fibrous structures which mimic natural extracellular matrix (ECM), and further it is also capable to spin biocompatible and biodegradable polymers. In term of flexibility, electrospinning is able to control fiber size and generates fibrous mats with either random or aligned configurations. The polymeric fibers with diameters ranging from 3 nm to 5 µm can be produced by this technique [2, 6]. As the diameters of polymeric fibers are in small scales, the surface area to volume ratio of electrospun scaffolds becomes high. This promotes biological responses of seeded cells in vitro including cell adhesion, proliferation, drug loading and mass transfer properties [3]. Scaffolds produced by electrospinning indicate higher adsorption of cell-adhesive proteins included vitronectin and fibronectin as compared to scaffolds with solid surface [7, 8].

One of the advantages of electrospinning is its ability to spin small scaled fibers from a variety of polymer solution. These polymers included synthetic polymers, *e.g.* polystyrene (PS), polyethylene oxide (PEO), polycaprolactone (PCL) and polymethyl methacrylate (PMMA), and natural polymer, *e.g.* chitin, chitosan, gelatin and silk. In recent years, researchers not only electrospun single type of polymer but also fabricate composite polymeric fibers such as PCL/gelatin [9, 10], chitosan/polylactic acid (PLA) [11] and chitosan/gelatin/polyvinyl alcohol (PVA) [12]. These electrospun composite fibers can enhance the mechanical and chemical properties of polymeric fibers.

Although electrospinning process is able to produce continuous eletrospun fibers from various polymers, it is hard to control the microstructure morphology of resultant fibrous mats. The morphology of final electrospun fiber is highly dependent on setting of the electrospinning process. Therefore, this paper is aimed to review electrospinning process in particular on how electrospinning parameters can affect the morphology fibrous mat. The paper focuses on three important microstructure morphologies, including fiber diameter, the formation of beads and pores. The review shows that any slight variation of electrospinning parameters including polymer concentration, solution feed rate and tip-collector distance can result to significant effect on the microstructures. Such review providing useful insight in optimizing the eletrospinning process and suggesting ways to control the microstructure morphology of electrospun fibrous scaffolds, which make them potential candidates in tissue engineering applications.

ELECTROSPINNING PROCESS

The setup of a typical electrospinning process is simple. The setup consists of three major components (Figure-1): a conductive syringe needle of small diameter with feed pump, a high voltage power supply with positive or negative polarity and a conducting collector. In the electrospinning process, electrostatic forces are utilized to generate electrospun fibers. The grounded collector is used to collect the resultant fibers either in the form of non-woven or aligned fibrous mat, depending on types of collectors.

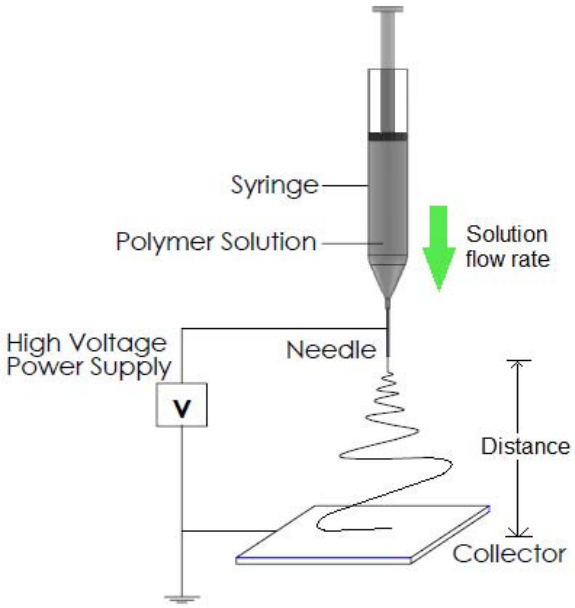

Figure-1. Basic setup of vertical electrospinning apparatus.

In order to start the electrospinning process, solid polymer is firstly dissolved in single or mixture of solvents to produce polymer solution. Continuous stirring and homogenous mixing are necessary to produce well mix polymer solution. The polymer solution is then poured into a capillary tube or a syringe for electrospinning. Polymer solution is fed through the syringe pump to form a pendant drop of the polymer at the tip of capillary. The formation of pendant drop is due to high surface tension which exists in polymer solution. Typically the electrode of high voltage source is attached to the capillary tube in case a metal needle is used. Otherwise, the electrode is immersed in the polymer solution.

As the high voltage is supplied to the polymer solution inside the syringe through the metallic needle, the pendant drop of polymer is then highly electrified. As a result, the pendant drop at the tip of metal needle elongates and deforms into a conical shape, which is commonly known as the Taylor cone. The formation of Taylor cone is illustrated in Figure-2. The distortion of pendant drop into Taylor cone is caused by the repulsive force between the like charges in the polymer solution and attractive force between the charged liquid and grounding collector.

Once the strength of electric field has reached a threshold value, the electrostatic force overcomes the surface tension of polymer solution, and the solution is ejected from the tip of the Taylor cone towards the grounded collector. As the fiber jet is fed towards the collector, it undergoes a chaotic bending instability and elongation process. This process leads to increment of travel time and distance of fiber jet to the collector and thus aiding the formation of long and thin fiber and evaporation of solvent. This bending instability process, alternatively referred to whipping instability process, is due to the repulsive force between like charges in the polymer jet.

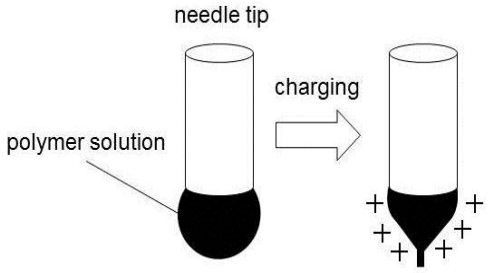

Figure-2. The formation of Taylor cone of polymer solution at the needle tip when high voltage is supplied.

A nonwoven solid polymer fiber is then deposited on the grounded collector plate. Depending on the application and requirements, a variety of collector configurations such as a stationary flat plate, rotating drum, rotating disc collector can be employed during electrospinning process. Generally, stationary grounded collector generates randomly oriented electrospun fibers while the rotating drum forms aligned electrospun fibers.

THREE IMPORTANT MICROSTRUCTURE MORPHOLOGIES OF ELECTROSPUN FIBROUS SCAFFOLDS

Electrospinning parameters highly affect the microstructure morphologies of electrospun fibrous scaffolds, which are fiber diameter, beads formation and pores formation on fiber surface. The variation in microstructure morphologies may significantly influence the mechanical properties of fibrous scaffolds [13, 14]. Therefore, reviewing the ways to control the electrospinning parameters on microstructure morphologies is essential in preparing fibrous scaffolds with desired mechanical properties.

Control of electrospun fiber diameter

Figure-3a illustrates microstructures of a random fibrous scaffold. The fiber diameter of fibrous scaffold is highly dependent on numerous parameters including types of polymers, polymer concentration in solvent system, and processing parameters. Review shows that polymer concentration significantly influences resultant fiber diameters (Table-1). Solution with higher polymer concentration has higher viscosity and tends to increase fiber diameters and produces uniform electrospun fibers [15 - 18]. However, most of the polymer concentration in precursor solution is less than 30 wt. % (Table-1). In particular, 10 wt. % is the most frequently reported.

Besides of polymer concentration, processing parameters such as applied voltage, solution feed rate and distance between capillary tube and grounded collector also control fiber diameters. Increase of applied voltage and solution feeding rate can result increment of polymer jet velocity towards the grounded collector. The effect of voltage on the fiber diameter is not consistent. The applied

voltage was found to reduce fiber diameter [19, 23], and increase fiber diameter [6, 21, 24]. These larger fibers were spun at higher solution feed rate. Longer distance between tip and collector results in reduction of fiber diameters. In the case of electrospinning polyacrylonitrile (PAN), Gomes and coworkers noted that upon a critical tip-collector distance, there is no significant variation in fiber diameter [6].

Instead of varying processing parameters, electrospun with smaller fiber diameter can be achieved by the addition of salt. The salt increases solution conductivity and electric charges. This causes the jet to stretch, elongate and deposit on the collector. The reduction of fiber diameter depends on types of salt and their concentration. In the case of electrospinning poly (D, L-lactic acid) (PDLA) solution, it was found that solution with the addition of sodium chloride (NaCl) produced the smallest fiber diameter compared to monosodium phosphate (NaH_2PO_4) and monopotassium phosphate (KH_2PO_4) [24].

It was found that electrospinning PCL fibers with a binary solvent system yielded fibers with smaller diameters (Table-1). Lee and coworkers also reported that the changes of fiber diameters when they varied solvent composition of methylene chloride/dimethylformamide (MC/DMF) at fixed polymer concentration [25]. In MC solvent only, larger fiber diameters in the range of 5000 to 7000 nm were generated. By increasing DMF volume fraction into MC solvent, fibers with diameter less than 400 nm is reported.

Several studies have been carried out to discover relationship between relative humidity and fiber diameter. Increase of relative humidity from 10% RH to 50% RH tends to slightly decrease PCL fiber diameter at fixed polymer concentration [17]. Similar observations were obtained in electrospinning single polymer solution, PVA and PEO fibers [26] and PS/DMF fibers [27]. When the polymer jet was spun at higher relative humidity condition, fibers took longer time to solidify as it came from the end of the capillary and consequently it was subjected to more stretching. This resulted thinner fibers depositing on collector. In contrary, De Vrieze and coworkers reported cellulose acetate solution in acetone: dimethylacetamide (acetone:DMAc) solvent possessed of larger fiber diameter as humidity in atmosphere increased [28].

Control of beads formation

One of the problems encountered in electrospinning is the formation of beads (Figure-3b). The formation of beads in electrospun fibers is due to insufficient time and path length for polymer jet to travel before reaching the collector. Longer travel time and path length are necessary in spinning process in order to accelerate the evaporation of solvent in polymer jet and then allow completely dry fiber deposited on collector. As polymer solution is spun at high feed rate, fibers with beads were deposited on collector [3, 4, 23]. In addition, short distance between nozzle and collector results beads formation. This is due to the fact that the longer gap distance allows the polymer jet to elongate further and thus causes solvent to have more time to evaporate before reaching grounded collector [6, 19, 29]. In contrast, in the case of spinning gelatin fibers, a lot of droplets have been observed at long tip-collector distance [16].

The other factor that causes the formation of beads is low polymer concentration [9, 22, 24, 30]. The dilute polymer solution has low solution viscosity which prevents fiber to maintain its shape at the end of needle (Table-2). Moreover, high surface tension also converts the polymer jet into droplets before reaching the collector. Beads connected poly (carbonate urethane) (PCU) electrospun thin fibers were observed when PCU/DMAc solution was spun at relatively low humidity, 5 % RH. The humidity was adjusted the relative humidity to 50 % to produce bead-free scaffolds [32]. Similar observations were obtained in the case of electrospinning PS in DMF solvent [33]. In other study carried out by Pelipenko and coworkers, they noticed that bead-free PEO fibers were occurred at relative humidity, 70% [26].

Reduction of beads on fibers can also be achieved by controlling polymer molecular weight. At constant polymer concentration, solution with lower molecular weight tends to produce bead in electrospun scaffolds. This is due to insufficient of polymer chain entanglements in the polymer solution. However, in the case of electrospinning chitin with relatively high molecular weight, it hinders solubility in solvents and limits the spinablity [22, 34].

In some cases, the addition of salt into polymer solution can result in significant increment of solution conductivity and reduction of beads formation in fibrous structure [24, 35, 36].

Control of pores formation on fiber surface

For many applications, include filtration and solar cells, porous surface structure which inherent higher surface area is more favourable rather than smooth surface structure. In biomedical applications such as tissue engineering and wound dressing, porous fiber surface is more efficient for cell adhesion, nutrient transportation and tissue growth [37 - 39]. The formation of pores on electrospun fiber surface, as depicted in Figure-3c, provides larger surface area which would beneficial for cells attachment, proliferation and migration when compared to non-porous structure [40, 41].

Table-1. The diameters of electrospun polymeric fibers under various electrospinning conditions.

No.	Polymers	Polymer molecular weight, M_w (*g/mol*)	Polymer concentration (%)	Solvent	Processing parameters			Fiber diameter (μm)	References
					Solution feed rate (*ml/min*)	Tip-collector distance (*cm*)	Applied voltage (*kV*)		
1	PS	190,000	30 wt.	THF/DMF	0.07	35	10	~ 10	[19]
				carbon disulfide	0.1	12	20	4 – 25	
				toluene	0.07	15	14	~ 5	
2	PEO	300,000	10 wt.	water	0.0025	15	7	0.2 – 0.8	
				chloroform	0.19	25	8	~ 10	
				acetone	0.24	20	8	0.800 – 14	
3	PMMA	540,000	10 wt.	THF	0.07	35	10	10 – 35	
				acetone	0.07	35	10	~ 0.750	
				chloroform	0.09	35	10	0.750 – 13	
4	PCL	--	10 wt.	chloroform	0.033	10	10	3.886 – 4.460	[17]
				formic acid/chloroform	0.017	10	12	0.183 – 0.261	
				formic acid/acetic acid	0.017	12.5	12	0.227 – 0.305	
5	PCL	80,000	8 wt.	MC/DMF	0.033	20	18	0.760 – 3	[20]
6	PCL	80,000	10 wt.	glacial acetic acid	0.5	20	15	0.080 – 0.144	[21]
				90 % acetic acid	0.5	20	15	0.099 – 0.195	
				MC/DMF	0.5	20	15	0.295 – 0.911	
				glacial formic acid	0.5	20	15	0.122 – 0.170	
				formic acid/acetone	0.5	20	15	0.077 – 0.123	
7	PCL	80,000	23 wt.	glacial acetic acid	0.005	25	12	1.464 - 2.202	[18]
8	Gelatin	60,000	25 wt.	glacial acetic acid/water	0.005	25	15	0.762 – 0.954	
9	Gelatin	--	7 wt.	formic acid	--	10	--	0.074	[16]
			8 wt.					0.076	
			10 wt.					0.131	
			12 wt.					0.169	
10	Chitin	91,000	1 – 6 wt.	HFIP	--	7	15	0.040 – 0.600	[22]

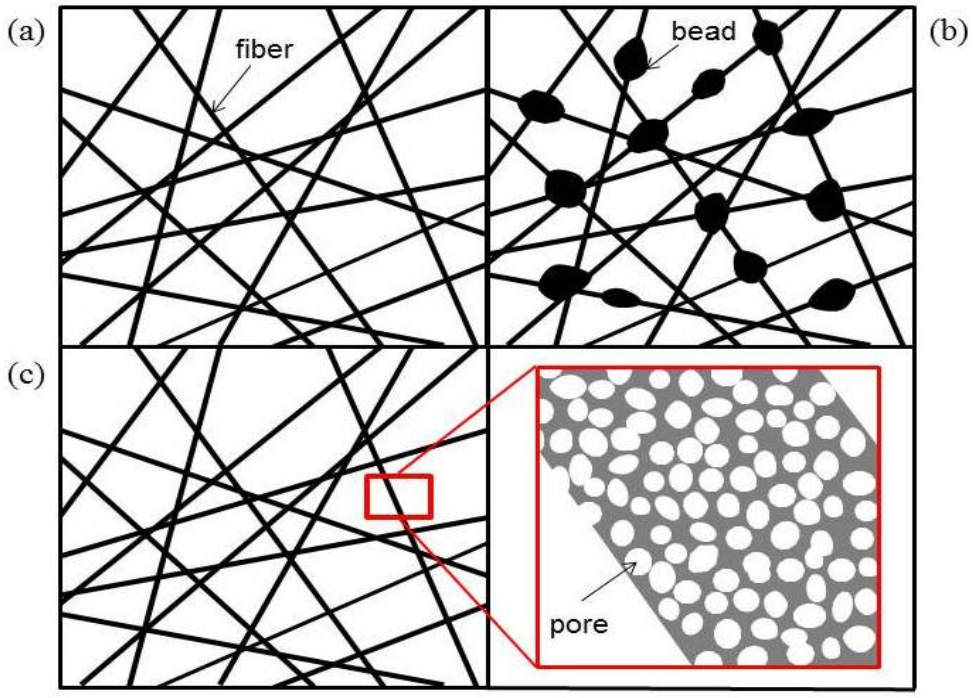

Figure-3. Illustration of the microstructures of (a) a random fibrous scaffold, (b) the formation of beads on the scaffold and (c) the formation of pores on fiber surface.

In addition, the wettability and absorption behaviour were found to increase in PCL fibrous mats with high porous surface [42]. In electrospinning process, factors that have been reported for introducing pore formation on electrospun fiber surface include relative humidity conditions in electrrospinning chamber and solvent vapor pressure.

In electrospinning process, humidity has been found to be one of the determinants of pore formation on fibers surface [19, 32, 33, 43]. In the case of electrospinning PS fiber at low relative humidity (less than 25%), fibers with smooth surface were observed. As relative humidity is increased which is higher than 25%, pores were formed along the electrospun fibers. Further increase of relative humidity resulted bigger pores on fiber surface. This phenomenon can be explained as the amount of water vapor present in air become higher when relative humidity increase and thus water.

Droplets are tend to condense on fiber surface. It is noteworthy that not all of electrospun fibers are porous at relative humidity higher than 25%, it varied between polymers. The formation of pores for PVC is 60% RH while for PMMA is 80% [27].

Solvent vapor pressure also affects the pore formation on fiber surface. Pores diminished and the fiber surface area decreased as solvent with lower volatility was used. Solvent with higher volatility evaporates more rapidly as polymer jets towards target. The water in air condensed and the water droplets left an imprint on the surface after drying, causing the pore formed on fiber surface. The solvent vapor pressure can be controlled by mixing solvents with different vapor pressure. Solvents, e.g. DMF, tetrahydrofuran (THF) and toluene which have various vapor pressures used for electrospinning of different polymers, e. g. PVC, PCL, PS, PMMA. The use of various solvent affects the solvent vapor pressure and pore formation on surface structure of fibers [19, 32, 43].

SUMMARY

Electrospinning is a cost effective technique in fabricating uniform electrospun fibers with continuous length for various applications. Besides its ability to produce electrospun fibers in nanoscale, this innovative technique is able to adjust fiber orientation with controllable diameters. Although a lot of improvements have been proposed, controlling the morphology of electrospun scaffolds remains a challenge. Three important morphology features, which are fiber diameter, beads formation and pores formation on fiber surface, have been reviewed. The review shows that any slight changes in any electrospinning parameters can significantly affect the morphology. Current literature shows that electrospinning technique is still used in laboratory level and most of the parameters optimization was done through repeated testing without a complete comprehension of the process.

Table-2. The formation of beads on electrospun scaffolds.

No.	Polymers	Polymer molecular weight, M_w (*g/mol*)	Polymer concentration (%)	Solvent	Processing parameters			The formation of beads	References
					Solution feed rate (*ml/min*)	Tip-collector distance (*cm*)	Applied voltage (*kV*)		
1	PS	--	23 w/v	THF	--	10	15	No	[29]
				DMF	--	10	15	Yes	
				toluene	--	10	15	No	
2	PCL	80,000	10 wt.	glacial acetic acid	0.5	20	15	Yes	[19]
				90 % acetic acid	0.5	20	15	Yes	
				MC/DMF	0.5	20	15	No	
				glacial formic acid	0.5	20	15	No	
				formic acid/acetone	0.5	20	15	No	
3	PDLA	109,000	20 – 30 wt.	DMF	0.02	15	20	Yes	[22]
			35 wt.		0.02	15	20	No	
4	PCU	217,000	15 – 20 wt.	DMAc	0.017	40	15	Yes	[30]
5	Gelatin	--	5 – 7.5 w/v	TFE	--	--	--	Yes	[9]
			10 – 12.5 w/v		--	--	--	No	
6	Chitin	91,000	1 - 6 wt.	HFIP	--	7	15	Yes	[20]

Knowledge of complex interactions of the interrelated variables is still incomplete. Hence, a delicate balance and optimization of electrospinning conditions must be achieved in order to produce uniform yet beads free eletrospun fibers that make them favorable candidates to robust production.

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