Investigation on Process Parameters of Electrospinning System through Orthogonal Experimental Design

Wenguo Cui, Xiaohong Li, Shaobing Zhou, Jie Weng

Key Laboratory of Advanced Technologies of Materials, School of Materials Science and Engineering, Southwest Jiaotong University, Chengdu 610031, China

Received 4 May 2006; accepted 6 September 2006
DOI 10.1002/app.25464
Published online in Wiley InterScience (www.interscience.wiley.com).

ABSTRACT: Electrospinning is a very simple and versatile method of creating polymer-based high-functional and high-performance nanofibers. But most of the investigations are not systematic and describe the electrospinning process without quantitative accuracy. Inconsistent and even opposite results have been reported, which has hindered the consistent interpretation of the experiments. Orthogonal experimental method was used to investigate qualitative and quantitative correlations between fiber characteristics (diameters and morphologies) and the processing and materials parameters. Uniform fibers can be obtained without any beads by proper selection of the processing parameters, and a lower glass transition temperature was observed for electrospun fibers than that of native polymer. Results of statistical analysis showed that significant influences were observed for polymer molecular weight and solution concentration on fiber diameters, and there were significant effects of polymer molecular weight, solution concentration, and solvent system on fiber morphologies. Meanwhile, solution concentration and polymer molecular weight, and polymer molecular weight and solvent system had obvious interaction effects. Regression analysis revealed quantitative relations of fiber diameters and beads percent, that is, $Y_1 = 72.8X_1 - 8.1X_2 + 138.8$, $Y_2 = -3.2X_1 + 0.4X_2 + 60.5$, where Y_1 is fiber diameter (nm), Y_2 beads percent (%), X_1 solution concentration (%, w/w), and X_2 polymer molecular weight (kDa). Validation test showed that the experimental values of fiber size and beads percent were in good agreement with the calculated ones. Based on these results, optimal conditions could be obtained for predetermined diameters and morphologies for electrospun fibers. © 2006 Wiley Periodicals, Inc. J Appl Polym Sci 103: 3105–3112, 2007

Key words: fiber; nanotechnology; processing; thermal properties; morphology

INTRODUCTION

The past decade has seen considerable efforts in the use of polymer nanofibers for biomedical, biotechnological, protective textiles, and filtration applications, which is mainly due to its high surface area and nanostructure surface morphologies that enable a myriad of advanced applications.[1] Electrospinning is a very simple and versatile method of creating polymer-based high functional and high performance nanofibers that can revolutionize the world of structural materials. Electrospinning has gained much attention not only because of its versatility in spinning a wide variety of polymeric fibers but also because of its consistency in producing fibers in the submicron range.[2] Electrospun fibers, with the diameter between 50 nm and 5 μm, has shown many outstanding properties, such as large surface area, high length–diameter ratio, flexible surface functionalities, tunable surface morphologies, and superior mechanical performance. Current emphasis of research is to exploit such properties and focus on determining appropriate conditions for electrospinning various polymers and biopolymers for eventual applications including multifunctional membranes, biomedical structural elements (scaffolds used in tissue engineering, wound dressing, drug delivery, artificial organs, vascular grafts), protective shields in special fabrics, filter media for submicron particles in separation industry, composite reinforcement, and structures for nanoelectronic machines among others.[3–5]

The electrospinning process involved use of a polymer solution that is contained in a syringe and held at

Correspondence to: X. Li (xhli@home.swjtu.edu.cn).

Contract grant sponsor: National Natural Science Foundation of China; contract grant number: 30570501.
Contract grant sponsor: Specialized Research Fund for the Doctoral Program of Higher Education, Ministry of Education of China; contract grant number: 20050613025.
Contract grant sponsor: Fok Ying Tong Education Foundation, Ministry of Education of China; contract grant number: 104032.
Contract grant sponsor: Cultivation Fund of the Key Scientific and Technical Innovation Project, Ministry of Education of China; contract grant number: 704039.
Contract grant sponsor: The Basic Research Program of Sichuan Province of China; contract grant number: 05JY029-100-1.
Contract grant sponsor: Cultivation Fund of Scientific and Technological Leaders of Sichuan Province of China; contract grant number: 2006S26003.

the end of the needle by its surface tension. Charge is induced on the solution by an external electric field. As the applied electric field is increased, charges create directly opposed the surface tension. Beyond a critical value the electric field causes the charges to overcome the surface tension and form a charged jet of solution. During the electrospinning process the surface tension of the polymer solution, the aligning effect of the elongational flow under the electrostatic force, and rapid solidification are believed to have some effects on the diameter and surface morphologies. With enormous research interests and both fundamental and applied research opportunities in nanofibers, process parameters, like solution feed rate, applied voltage, nozzle-collector distance, and spinning environment, and material properties, like solution concentration, viscosity, surface tension, conductivity, and solvent vapor pressure, influence the structure and properties of electrospun nanofibers.[6,7] But most of the investigations are not systematic and describe the electrospinning process without quantitative accuracy. Inconsistent, even opposite results have been reported, which has hindered the consistent interpretation of the experiments. Zong et al. confirmed that an increase in the electrospinning voltage could alter the shape of the initial droplet. Consequently, the resulting fiber morphology could be changed from a typical cylindrical shape to a beaded or string-of-pearls structure.[8] But Nair et al. found that an increase in the electric field from 27 to 33 kV altered the shape of the fibers from a curly or distorted shape with dimples or nanoindentations on the surface to a more cylindrical and rod-like structure. And increasing the applied potential to 36 kV further improved the shape of the fibers, and distinct cylindrical fibers were formed.[9] Although significant work has been done to characterize the properties of fibers as a function of process and material parameters, thus far, there is not a substantial amount of research carried out on the fundamental aspects of electrospinning. Especially, there has been no reliable model simulating the influences of so many parameters on the characteristics of electrospun fibers. Additional efforts should be made on controlling processing variables so as to obtain defect-free and uniform diameter nanofibers, as well as on improving throughput of the nanofibers. On the other hand, electrospun fibers often had beads as by ''products.'' But beads on the fibers could be used as reservoir for drug or cell inclusion, and should have quite different degradation properties from the fibers. The optimization of bead percent was also necessary to extend fibers application in biomedical, biotechnological, and other industrial fields.

Orthogonal experimental design is one way to qualitatively analyze the correlations among the relevant variables at different levels through designing orthogonal table and statistic analysis. Regressive analysis can be used to get the parameters optimized, to achieve the predetermined features, and to uncover the statistic principle based on the hidden or equivocal factors.[10] The orthogonal table $L_{18}(3)^7$ was used in the experiment, and the fiber diameter and beads percent of obtained fibers were set as the investigation target. Six influential factors of electrical voltage, solution concentration, polymer molecular weight, solvent system, flow velocity, and the needle size of syringe were chosen, and three levels were set for each factor. Biodegradable poly(DL-lactide) (PDLLA) was chosen as the materials in this experiment because its safety in clinical use has been well established, initially as a biomaterial in Vicryl sutures and later as excipients for sustained release of parenteral drugs.[11] Furthermore, the biocompatibility and flexibility they offer in terms of their degradation profiles, hydrophilicity, and mechanical properties enable researchers to tailor these polymers to other specific applications.[12] In the current study, through the range analysis, analysis of variance, interaction effects between factors and regression analysis, the qualitative and quantitative analysis of the correlations between fiber characteristics (diameters and beads percent) and the process and materials parameters were demonstrated.

EXPERIMENTAL

Materials

Poly(DL-lactide) (PDLLA) was synthesized in our lab. The molecular weight was determined by gel permeation chromatography (GPC, waters 2695 and 2414, Milford, MA) using polystyrene as standard. The column used was a Styragel HT 4 (7.8×300 mm^2). The mobile phase consisted of tetrahydrofuran (THF) using a regularity elution at a flow rate of 1.0 mL/min.

Electrospinning experiment

The electrospinning apparatus was equipped with a high-voltage statitron (Tianjing High Voltage Power Supply Co., Tianjing, China) of maximal voltage of 50 kV. The polymer was dissolved in a mixture of acetone and chloroform and added in a 5-mL syringe attached to a circular-shaped metal syringe needle as nozzle. An oblong counter electrode was located about 15 cm from the capillary tip. The flow rate of the polymer solution was controlled by a precision pump (Zhejiang University Medical Instrument, Hangzhou, China) to maintain a steady flow from the capillary outlet. The experiment of temperature was controlled at 25°C, and the environment humidity was controlled between 45% and 50%. All the nonwoven fiber mats were vacuum dried at room temperature for 3 days to completely remove any solvent residue prior to further characterization.

Orthogonal experiments designing

The quantitative evaluation and statistic analysis of the effects of solution properties and processing parameters were investigated on the fiber diameter and morphologies through orthogonal experiments designing.[10] Six relevant factors were investigated: the concentration of polymer solution, applied voltage, molecular weight (MW) of matrix polymer, flow velocity of polymer solution, solvent system, and nozzle size. The orthogonal table $L_{18}(3)^7$ was designed, in which a blank column was designated for the error evaluation. Three levels were set for each factor, and the boundary values for the levels were determined in pilot experiments to ensure continuous fibers instead of particles or bubbles were formed. The boundary values of molecular weight were set at 50 and 165 kDa, and nozzle sizes were 0.45 and 0.80 mm, which were used as the primary conditions for pilot study. And the boundary values of applied voltage, solution concentration, solvent system, and flow velocity can be obtained to form continuous fibers without breaking up into droplets. Solution concentrations of 10.0%, 20.0%, and 30.0% were used in the current investigation, and three levels of 15, 20, and 25 kV were set for the applied voltage. Acetone and mixture of acetone and chloroform with the ratios of 4 : 1 and 3 : 1 (v/v) were chosen as the solvent of matrix polymer, and the flow velocities of 1.8, 5.4, and 9.0 mL/h were applied, respectively. Based on the investigation factors, the corresponding levels, and the designated boundary values, the orthogonal experimental table is shown in Table I.

Fiber characteristics and statistic analysis

The diameters and morphologies of the electrospun fibers were investigated by a scanning electron microscope (SEM, FEI Quanta 200, the Netherlands) equipped with field-emission gun (20 kV) and Robinson detector after 2 min of gold coating to minimize charging effect. The fiber diameter was measured from the SEM images with the magnification of 10,000×, and five images were used for each fibrous sample. From each image, at least 20 different fibers and 200 different segments were randomly selected, and their diameter was measured to generate an average fiber diameter by using the tool of Photoshop 8.0 edition.[13] The beads percents of the obtained fibers were also evaluated using the SEM images with the magnification of 2000× through the similar process. The software of orthogonal designing assistant II V3.1 was used in the orthogonal table design and data analysis. The DSC measurements had been performed by differential scanning calorimeter (Netzsch STA 449C, Bavaria, Germany). The samples were analyzed in perforated and covered aluminum pans under a nitrogen purge. Approximately 10 mg of polymer or fiber sample was heated from 20 to 100°C with a heating rate of 10°C/min.

RESULTS AND DISCUSSION

Fiber diameter and morphology

In the electrospinning fiber system, polymer solution drops were kept in nozzle because of the surface ten-

TABLE I
Design of Orthogonal Table $L_{18}(3)^7$ and Characteristics of Obtained Fibers

Exp. No.	Voltage (kV)	Concentration (%)	MW (kDa)	Solvent[a]	Flow velocity (mL/h)	Nozzle size (mm)	Diameter (nm)	Beads percent (%)
1	15.0	10.0	50	1	1.8	0.45	187 ± 23	60.0 ± 9.0
2	15.0	20.0	100	2	5.4	0.60	468 ± 140	15.0 ± 4.3
3	15.0	30.0	165	3	9.0	0.80	1000 ± 221	10.0 ± 2.1
4	20.0	10.0	50	2	5.4	0.80	118 ± 30	60.0 ± 6.9
5	20.0	20.0	100	3	9.0	0.45	803 ± 193	5.0 ± 1.4
6	20.0	30.0	165	1	1.8	0.60	238 ± 87	50.0 ± 7.8
7	25.0	10.0	100	1	9.0	0.60	86 ± 29	90.0 ± 4.5
8	25.0	20.0	165	2	1.8	0.80	223 ± 69	60.0 ± 6.2
9	25.0	30.0	50	3	5.4	0.45	2500 ± 338	1.0 ± 0.5
10	15.0	10.0	165	3	5.4	0.60	0	99.0 ± 1.0
11	15.0	20.0	50	1	9.0	0.80	1000 ± 267	10.0 ± 2.5
12	15.0	30.0	100	2	1.8	0.45	1500 ± 304	1.0 ± 0.5
13	20.0	10.0	100	3	1.8	0.80	217 ± 81	40.0 ± 5.1
14	20.0	20.0	165	1	5.4	0.45	152 ± 54	80.0 ± 6.8
15	20.0	30.0	50	2	9.0	0.60	2550 ± 353	5.0 ± 1.3
16	25.0	10.0	165	2	9.0	0.45	0	99.0 ± 0.5
17	25.0	20.0	50	3	1.8	0.60	845 ± 202	1.0 ± 0.5
18	25.0	30.0	100	1	5.4	0.80	1560 ± 238	1.0 ± 0.5

[a] Solvent 1 was acetone; solvents 2 and 3 were mixtures of acetone and chloroform of 4 : 1 and 3 : 1, respectively.

sion, while also attracted by the coulomb forces against the surface tension. According to these observations, under coulomb forces, a cone, called the Taylor cone, was formed at the nozzle. When the electric field force was increased to the edge of force, it would overcome the surface tension and made the solution drops shaking and splitting, which were jetted to opposite electric field, and the solvent quickly volatilized from the polymer solution. So, the solution properties, electric field, and equipment parameters should influence the diameter and morphologies of electrospun fibers to some extent. Table I shows the orthogonal experimental designing, and summarizes the diameter and beads percent of obtained fibers. Fibers with wide ranges of diameters from 80 nm to 2.5 μm can be obtained through parameters optimization, and all the electrospun fiber mats were opaque due to light scattering by the fine fibers.

Figure 1 shows the typical SEM photographs of electrospun PDLLA fibers. It can be found that uniform fibers can be obtained without any beads by proper selection of the processing parameters [Fig. 1(a)]. Also during the process of fiber forming, the electric force made the fiber thinner, but the surface tension resulted in decreasing the liquid surface area,[14] and therefore, the structure of beads in the fibers might be formed as the liquid flowing turn to solid in some experiments [Fig. 1(b–d)]. As shown in Table I, lower solution concentration would result in higher degree of beads formation. It indicated that there was almost no fiber but all beads formed under these conditions shown in experiment number 10 and

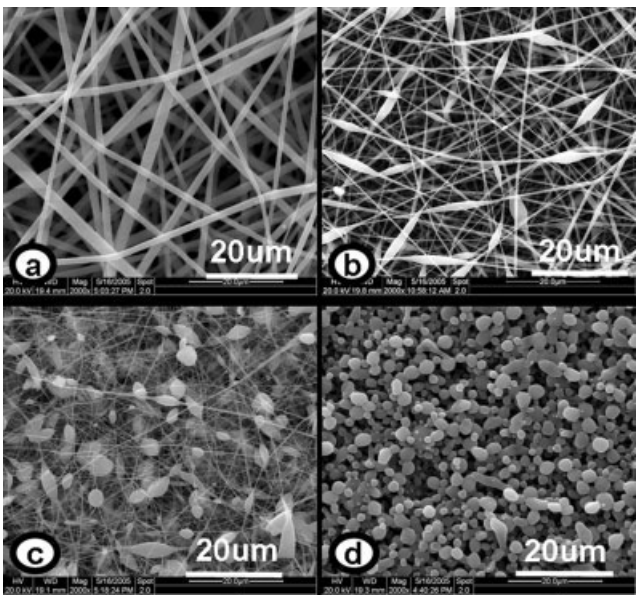

Figure 1 SEM observations of electrospun mat containing: (a) only fibers, exp. no. 12; (b) fibers and small amount of beads, exp. no. 3; (c) fiber and large amount of beads, exp. no. 8; (d) beads with few fibers, exp. no. 10.

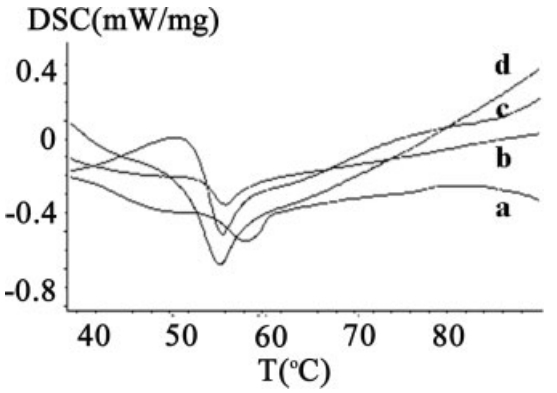

Figure 2 DSC thermograms of native polymer (a) and electrospun fibers with the average diameters of 803 nm (b), 2500 nm (c) and 217 nm (d).

16 of Table I. At lower concentrations electrospun fibers were harder to dry before they reach the collector. The presence of junctions and bundles in the fibers electrospun from lower concentrations solutions provided the evidence that the polymer fibers were still wet at the time that they reach the collector. As the wet fibers were no longer strained by the electric field when they were laid on the collector, they could undergo a solidification process as a result of the surface tension and the relaxation process controlled by the viscoelastic property of the wet fibers. Above a critical concentration, the electrospun fibers were mostly dried by the time they were collected, a continuous fibrous structure was obtained, and the number of beads along the fibers was found to decrease and their shape appeared to be more elongated. And the increase in the polymer concentration also resulted in increased chain entanglement, and the break-up of charged jet into smaller droplets was sufficient to be hindered, which led to form fibers of larger size. But if the concentration was further increase above certain values, electrospinning should be prohibited because of the instability of flow caused by the high cohesiveness of the solution.

DSC analysis of nonwoven electrospun fiber mats

Up to now, few reports have been focusing on the effect of electrospinning process on the thermodynamic behaviors of obtained fibers.[6] To determine the effect of electrospinning on the thermodynamic behaviors, DSC experiments of the obtained electrospun fiber mat with different fiber diameters were recorded and shown in Figure 2. A lower glass transition temperature (T_g) was observed for electrospun nonwoven mat than that of native polymer (58.3°C). These results were ascribed to the very large surface to volume ratio of the electrospun membranes having air as the plasticizer, and the inner-stress and the high degree of alignment and orientation of polymer chains

caused by the electrospinning process. With the temperature rising, the movement of polymer chains driven by the inner-stress occurred at a lower T_g. To clarify the driven force of inner-stress, DSC analysis of electrospun mats with diameters of 2500 nm (sample c), 803 nm (sample b), and 217 nm (sample d) was performed, and T_g of 55.0, 55.2, and 55.8°C were observed, respectively. The smaller diameter of fiber, the more energy could be restocked to lead to falling glass state temperature. The glass transition enthalpy was 7.55 and 2.84 J/g for electrospun mat and native polymer, respectively. The inner stress of polymer chain of electrospun fibers resulted in significantly higher transition enthalpy than that of native polymer.

Range analysis

The range analysis was aimed to clarify the significance levels of different influencing factors on the diameter and morphology of obtained fibers. And those most significant factors could be disclosed basing on the result of range analysis.[10] Table II summarizes the statistics analysis of the effect of different factors on the diameter and beads percent of electrospun fibers. The K value for each level of a parameter was the average of six values shown in Table I, and the range value (R) for each factor was the difference between the maximal and minimal value of the three levels. And the square of deviation (S) of three levels for each factor was also obtained accordingly.[10] Based on the results of range analysis and the square of deviation, the significance sequence of all the investigated influencing factors was lined. For the fiber diameter, the order of significance levels was as follows: solution concentration, polymer molecular weight, solution flow velocity, solvent system, applied voltage, and nozzle size, and that of the factors influencing beads percent: solution concentration, polymer molecular weight, solvent system, nozzle size, applied voltage, and solution flow velocity.

Therefore, it could be concluded that solution concentration and polymer molecular weight had significant influences on both the diameter and beads percent of the obtained fibers. The formation of this continuous fiber was attributed to the extensive chain entanglements of matrix polymer. At lower concentration, the wet fibers were no longer strained by the electric field when they were laid on the ground, they could undergo a solidification process as a result of the surface tension and the relaxation process controlled by the viscoelastic property of the wet fibers, which would result in beaded fibers. A viscosity high enough could prevent the jet from collapsing into droplets before the solvent has evaporated. As seen from Table I, the fibers with smallest diameter of 86 nm could be got in the 10.0% (w/w) concentration of matrix polymer of 100 kDa (exp. no. 7). But fiber with lowest beads percent could be obtained when mixture of acetone and chloroform (3/1, v/v) was used as solvent with the solution concentration of 30.0% (w/w) and matrix polymer of 50 kDa (exp. no. 9). Compared with the exp. nos. 9 and 18, solvent mixture of acetone and chloroform (3/1, v/v) resulted in fibers with good morphology, even the concentration of polymer decreased from 30.0% to 20.0%. The tendency for the observation of beaded fibers was found to decrease, while the diameters of the smooth fibers obtained were found to increase with increasing the solution concentration. It was indicated that solution parameters, such as solution concentration and polymer molecular weight had shown different influencing tendencies on the fiber diameter and the amount of beads. The polymer solution must be optimized to have a concentration high enough to cause polymer entanglements yet not so high that the viscosity prevents polymer motion induced by the electric field, which achieved smaller fibers with bead-free morphologies.

Previous studies have shown that the electrospinning voltage had a significant influence on the diameter and shape of the resulting nanofibers, but inconsis-

TABLE II
Statistics Analysis for Diameter and Beads Percent of Electrospun Fibers

Factors	Voltage	Concentration	MW	Solvent	Flow velocity	Nozzle size
Fiber diameter						
K_1	692.5	101.3	1200.0	537.2	535.0	857.0
K_2	679.7	581.8	772.3	809.8	799.7	697.8
K_3	869.0	1558.0	268.8	894.2	906.5	686.3
R	189.3	1456.7	931.2	357.0	371.5	170.7
S (10^3)	22.4	1101.9	434.5	69.6	73.2	18.2
Beads percent						
K_1	32.5	74.7	22.9	48.5	35.4	41.0
K_2	40.0	28.5	25.3	40.0	42.7	43.3
K_3	42.0	11.3	66.3	26.0	36.5	30.2
R	9.5	63.3	43.5	22.5	7.3	13.2
S	41.5	2150.0	1193.2	258.2	31.6	97.9

tent, even opposite results have been reported. During the electrospinning system, once an electric field was applied on the droplet of the polymer solution at the tip of the spinneret, the surface of the liquid became charged via the motion of ions through the liquid. When the electric field is high enough so that the electric force overcame the forces associated with the surface tension, a quasi-stable, straight and electrically charged jet was ejected. The balance between the surface tension and the electric force was critical to determine the initial cone shape of the polymer solution at the tip of the spinneret. Typically, a larger applied voltage increases the net charge experienced by the jet, thereby increasing the electrostatic stress on the jet, resulting in enhanced fiber drawing to smaller diameters.[15] However, Demir et al. showed an increase in polymer jet diameter in a sigmoidal manner with increasing voltage resulting in an increase in diameter of the resulting fibers.[16] And Nair et al. showed that an increase in applied voltage did not show any increase in fiber diameter in the range of voltage studied.[9] Also, there were controversial reports on the effect of applied voltage on the fiber morphologies. Deitzel et al. have evaluated the effects of spinning voltage on the morphology of the fibers formed. They found that spinning voltage is strongly correlated with the formation of beads defects in the fibers.[17] On the contrary, Nair et al. found that an increase in the electric field improved the shape of the fibers, and distinct cylindrical fibers were formed.[9] Through the statistic analysis in the current investigation, it was indicated that much less significant effects of applied voltage were detected on both the fiber diameter and the beads percent compare with those of solution concentration, polymer molecular weight and solvent system. One possible reason is that the liquid drop was split and fibers were formed after the electric force went beyond the surface tension. And the increase in the voltage led to the increase in the net charge of the fibers and moving speed of the electric ions to the opposite electrode, which would not greatly affect the diameter and shape of the resulting fibers.

Analysis of variance

In our experiments, a blank column was set in the orthogonal table for error estimate; thus, it was unnecessary to repeat the experiments for each protocol.[10] The sum of squares of deviation (SS), degree of freedom (DF), and mean squared deviation (MS) of fiber diameter and beads percent were determined[10] and summarized in Table III. The F value of a factor is the ratio of the MS value of the factor to that of error line. Through comparing the obtained F value with the theoretical one of specific level and DF, the significance level can be determined for each factor. As shown in Table III, the polymer solution concentration and polymer molecular weight had shown significant influences on the fiber diameter ($P < 0.01$). In comparison, all six studied factors showed significant influence on the beads percent ($P < 0.05$), and solution concentration, polymer molecular weight and solvent system had greatly significant influences on fiber morphologies ($P < 0.01$).

TABLE III
Analysis of Variance for Diameter and Beads Percent of Electrospun Fibers

Factors	SS	DF	MS	F[a]
Fiber diameter				
Voltage	7461	2	3731	1.53
Concentration	367314	2	183657	75.1[b]
Molecular weight	144836	2	72418	29.6[b]
Solvent	23209	2	11605	4.74
Flow Velocity	23224	2	11612	4.75
Nozzle Size	24387	2	12194	4.98
error	12235	5	2447	
Beads percent				
Voltage	13.8	2	6.9	10.2[c]
Concentration	716.7	2	358.3	527[b]
Molecular weight	397.7	2	198.9	292[b]
Solvent	86.1	2	43.0	63.3[b]
Flow Velocity	10.5	2	5.3	7.74[c]
Nozzle Size	31.6	2	15.8	23.3[b]
error	3.4	5	0.68	

[a] $F_{0.05}(2,5) = 5.79$, $F_{0.01}(2,5) = 13.3$.
[b] $P < 0.01$.
[c] $P < 0.05$.

Interaction effects of investigated factors

When the influencing factors in orthogonal analysis interacted with each other, the trend-lines would cross each other or had such a trend.[10] In the light of the above analysis, we could find that solution concentration and polymer molecular weight had simultaneity significant influence on the fiber diameter and beads percent. To test whether there were interactions among the parameters, the influencing tendencies of factors on fiber diameter and beads percent were clarified using the software of orthogonal designing assistant II V3.1, which was shown in Figure 3. It can be seen that the lines of solution concentration and polymer molecular weight, and the lines of polymer molecular weight and solvent system had obvious crossing tendency, which indicated the interaction among these factors would have more significant effects on the results of fiber diameter and beads percent.

Regression analysis

Based on above analysis, solution concentration and polymer molecular weight were the most significant factors that influenced the fiber diameter and beads

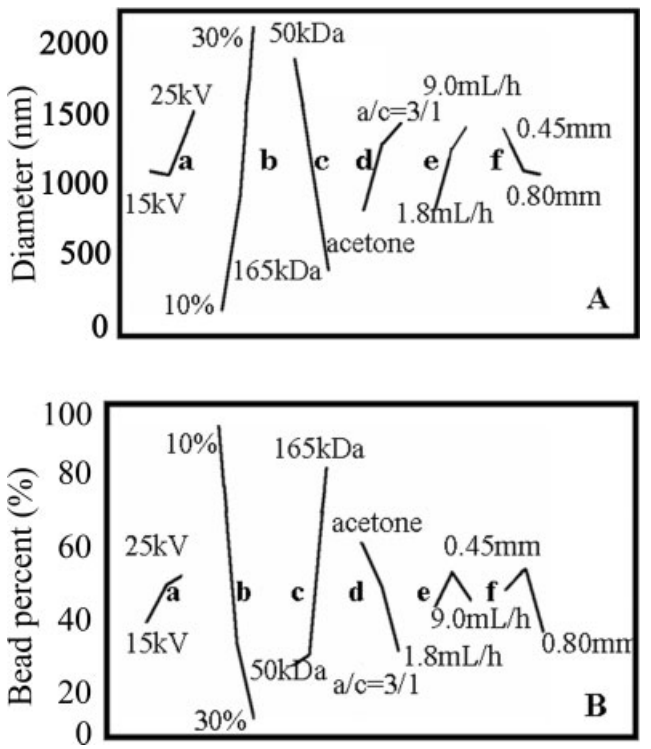

Figure 3 The influencing tendency of factors on diameters (A) and beads percent (B) of electrospun fibers (a, electric voltage; b, solution concentration; c, polymer molecular weight; d, solvent system; e, flow velocity; f, nozzle size; a/c, acetone/chloroform).

percent. Statistic software of SPSS 12.0 was adopted for the regressive analysis. The solution concentration (X_1, % w/w) and polymer molecular weight (X_2, kDa) were set as variables, and dependent variables were fiber diameter (Y_1, nm) and beads percent (Y_2, %). The linear dependence regression equation for fiber diameter was

$$Y_1 = 72.8X_1 - 8.1X_2 + 138.8 \quad \text{(regression coefficient: 0.895)}, \quad (1)$$

and that for beads percent of obtained fibers was

$$Y_2 = -3.2X_1 + 0.4X_2 + 60.5 \quad \text{(regression coefficient: 0.883)}. \quad (2)$$

Coefficients of correlation of the above two regression equation were relatively high, which was in agreement with the requirements of statistic analysis. It was suggested that solution concentration and polymer molecular weight had regular effect on fiber diameter and beads percent.[10]

To validate the results of regression analysis, several experiments were carried out to clarify the differences between the predicted and experimental values of fiber diameter and beads percent, and the results are summarized in Table IV. It should be noted that when the value of fiber diameter was predicted to be negative (exp. no. 4 of Table IV), there was almost no fiber found in electrospun mat, as shown in Figure 1(d), and this was the same as the calculated value of beads percent (exp. no. 8 of Table IV); there was no bead found in the electrospun mat. Through the obtained regression equations, the exp. nos. 1–4 were to validate the predicted value of exp. nos. 12, 3, 8, and 10 of the orthogonal design table (Table I), respec-

TABLE IV
Validation Tests of Regression Equations

	Process parameter		Diameter (nm)		Beads percent (%)	
Exp. No.	Concentration (%)	MW (kDa)	Exp.	Cal.	Exp.	Cal.
1[a]	30.0	100	1500 ± 304	1513	1.0 ± 0.5	4.5
2[b]	30.0	165	1000 ± 221	986	10.0 ± 2.1	30.5
3[c]	20.0	165	223 ± 69	258	60.0 ± 6.2	62.5
4[d]	10.0	165	0	−470	99.0 ± 1.0	94.5
5[e]	25.0	165	552 ± 32	622	63.1 ± 4.9	46.5
6[f]	25.0	165	580 ± 48	622	51.7 ± 2.8	46.5
7[g]	25.0	165	678 ± 92	622	38.9 ± 6.1	46.5
8[h]	30.0	78	1724 ± 136	1691	0	−4.3
9[h]	26.0	120	1124 ± 75	1060	17.0 ± 4.3	25.3
10[h]	25.0	50	1584 ± 213	1554	1.0 ± 0.5	0.5

[a] Exp. no. 12 of Table I, shown in Figure 1(a).
[b] Exp. no. 3 of Table I, shown in Figure 1(b).
[c] Exp. no. 8 of Table I, shown in Figure 1(c).
[d] Exp. no. 10 of Table I, shown in Figure 1(d).
[e] Voltage: 15.0 kV, flow velocity: 5.4 mL/h, nozzle size: 0.6 mm, solvent: acetone/chloroform 4 : 1 (v/v).
[f] Voltage: 20.0 kV, flow velocity: 5.4 mL/h, nozzle size: 0.6 mm, solvent: acetone/chloroform 3 : 1 (v/v).
[g] Voltage: 25.0 kV, flow velocity: 1.8 mL/h, nozzle size: 0.8 mm, solvent: acetone.
[h] Voltage: 20.0 kV, flow velocity 5.4 mL/h, nozzle size: 0.6 mm, solvent: acetone.

tively. The morphologies of electrospun mats are shown in Figure 1. The difference between the calculated and experimental values of beads percent was larger than that of fiber size in some sort. When the solution concentration and molecular weight was the same, as indicated in the exp. nos. 5–7 of Table IV, the fiber size and beads percent stayed closely to calculated values, and other process parameters would result in some variations of the observed values against the predicted ones. Process parameters of other molecular weight and solution concentrations were also tested, as shown in the exp. nos. 8–10 of Table IV; the experimental values of fiber size and beads percent were in good agreement with the calculated values. When the regression equation was set up for the electrospinning system, fibers with a certain range of diameter and specific morphologies can be obtained through designing the process parameters. Thus, the optimization process would greatly be simplified, which was essential for scale-up of the electrospinning system to meet the wide applications.

CONCLUSIONS

Orthogonal analysis is introduced in the current study to investigate effect of the process parameters on the fiber properties of PDLLA, which is also referential to other systems. The results showed that significant influences were observed for polymer molecular weight and solution concentration on fiber diameters, and there were significant effects of polymer molecular weight, solution concentration, and solvent system on fiber morphologies. Meanwhile, solution concentration and polymer molecular weight, and polymer molecular weight and solvent system had obvious interaction effects. Regression analysis revealed quantitative relations between fiber properties (diameters and beads percent) and electrospinning parameters (polymer molecular weight and solution concentration). Validation test showed that the experimental values of fiber size and beads percent were in good agreement with the calculated values. Based on these results, quantitative equations of regression analysis could be used to prepare electrospun fibers with predetermined diameters and surface morphologies.

References

1. Zhang, Y. Z.; Lim, C. T.; Ramakrishna, S.; Huang, Z. M. J Mater Sci: Mater Med 2005, 16, 933.
2. Subbiah, T.; Bhat, G. S.; Tock, R. W.; Parameswaran, S.; Ramkumar, S. S. J Appl Polym Sci 2005, 96, 557.
3. Lia, M.; Mondrinosa, M. J.; Gandhia, M. R.; Kob, F. K.; Weissc, A. S.; Lelkes, P. I. Biomaterials 2005, 26, 5999.
4. Frenot, A.; Chronakis, I. S. Curr Opin Colloid Interf Sci 2003, 8, 64.
5. Zong, X. H.; Li, S.; Chen, E.; Garlick, B.; Kim, K.; Fang, D. F.; Chiu, J.; Zimmerman, T.; Brathwaite, C.; Hsiao, B. S.; Chu, B. Ann Surg 2004, 240, 910.
6. Huang, Z. M.; Zhang, Y. Z.; Kotaki, M.; Ramakrishna, S. Compos Sci Technol 2003, 63, 2223.
7. Zeng, J.; Chen, X.; Xu, X.; Liang, Q.; Bian, X.; Yang, L.; Jing, X. J Appl Polym Sci 2003, 89, 1085.
8. Zong, X.; Kim, K.; Fang, D.; Ran, S.; Hsiao, B. S.; Chu, B. Polymer 2002, 43, 4403.
9. Nair, L. S.; Bhattacharyya, S.; Bender, J. D.; Greish, Y. E.; Brown, P. W.; Allcock, H. R.; Laurencin, C. T. Biomacromolecules 2004, 5, 2212.
10. Fan, D. Y.; Chen, Y. H. Probability Theory and Mathematical Statistics; Zhejiang University Press: China, 1996; p 215.
11. Hans, M. L.; Lowman, A. M. Curr Opin Solid State Mater Sci 2002, 6, 319.
12. Leiggener, C. S.; Curtis, R.; Muller, A. A.; Pfluger, D.; Gogolewski, S.; Rahn, B. A. Biomaterials 2006, 27, 202.
13. Yuan, X.; Zhang, Y.; Dong, C.; Sheng, J. Polym Int 2004, 53, 1704.
14. Fong, H.; Chun, I.; Reneker, D. H. Polymer 1999, 40, 4585.
15. Buchko, C. J.; Chen, L. C.; Shen, Y.; Martin, D. C. Polymer 1999, 40, 7397.
16. Demir, M. M.; Yilgor, I.; Yilgor, E.; Erman, B. Polymer 2002, 43, 3303.
17. Deitzel, J. M.; Kleinmeyer, J.; Harris, D.; Beck Tan, N. C. Polymer 2001, 42, 261.