RESEARCH ARTICLE

Evaluation of factors affecting bead formation on electrospun PU/PEG nanofibers

Pouyan Shakouri[1], Fatemeh Oroojalian[2,3], Amir Amani[3,4,*]

[1] Sankhast Community Health Center, North Khorasan University of Medical Sciences, Bojnurd, Iran

[2] Cell Therapy and Regenerative Medicine Innovation Center, North Khorasan University of Medical Sciences, Bojnurd, Iran

[3] Department of Medical Nanothecnology, School of Medicine, North Khorasan University of Medical Sciences, Bojnurd, Iran

[4] Natural Products and Medicinal Plants Research Center, North Khorasan University of Medical Sciences, Bojnurd, Iran

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ABSTRACT

The formation of beads on electrospun nanofibers is commonly considered as a defect; therefore, researchers typically aim to produce bead-free nanofibers. Although several studies have investigated the parameters influencing bead formation, most have employed a one-factor-at-a-time approach, which is not ideal for capturing interaction effects among variables. In the present study, a Box–Behnken design was used to investigate the effects of solution concentration, applied voltage, and feed rate on bead formation. A total of 17 samples were prepared according to the design generated by the software, and bead formation on the samples was analyzed using scanning electron microscopy (SEM). The resulting data were subsequently used to develop a predictive model. The findings indicated that feed rate and applied voltage are the dominant factors, each exhibiting an optimal range required for the fabrication of bead-free fibers. In conclusion, bead-free nanofibers can be obtained through appropriate optimization of the applied voltage and feed rate.

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INTRODUCTION

Electrospinning and electrospray are electrohydrodynamic techniques which are controlled by electromechanical and fluid-dynamic forces. In both methods, a strong electric field is applied to a liquid at a capillary nozzle which charges and deforms the droplet at the tip of the nozzle. Once the field exceeds a critical value, the droplet makes a Taylor cone that emits a fine, charged jet. In electrospray, Rayleigh–Plateau instability occurs that breaks the jet into fine charged particles (due to Coulomb repulsion), while in electrospinning, sufficient viscoelasticity of the polymer solution suppresses the breakup, thus, ends in formation of fibers [1]. Between these extremes, intermediate conditions can end in formation of beaded fibers, a morphology which combines features of both methods [2].

In the fabrication of polymer fibers, the formation of beads is typically considered a defect that compromises the structural integrity and uniformity of the material [3]. Although beaded morphologies are desirable in specific applications (e.g. controlled drug release systems) [4], they are predominantly regarded as detrimental by-products. A major drawback of beading is the reduction of effective surface area, which diminishes the performance of nanofibrous mats. This is particularly important in filtration, where beads impair filtration efficiency [5]. Also, in tissue engineering applications, beads can reduce cell adhesion and growth [6]. In a report, straight nanofibers from solution of polyacrylonitrile (PAN) in dimethylformamide (DMF) were prepared via electrospinning by adding potassium iodide to the solution. The submicron fibers (below 300 nm in diameter) were aimed for improved aerosol

* Corresponding Author Email: *a.amani@nkums.ac.ir*

filtration [7].

Reviewing the literature, several parameters have been suggested that can affect beading on fibers: nozzle to collector distance, polymer flow rate, solution conductivity, applied voltage [5] and the surface tension of the solution [8] are examples of these parameters. However, the majority of works in this field are using one-factor-at-a-time approach. The tendency to converge on local rather than global optima, along with the restriction of the factor space inherent to this approach, are two major limitations that justify the use of alternative methods when it is required to obtain a deeper understanding of the phenomenon [9]. To fully exploit the potential of electrospinning, one should have precise control over the morphology of the produced nanofibers. Here in, we investigated the influence of some processing and solution properties (i.e. applied voltage, feed rate and polymer concentration) on formation of beads in polyurethane/ polyethylene glycol nanofibers. These three parameters have been investigated in our previous studies, where their significant effects on the electrospray process were demonstrated [10].

MATERIALS AND METHODS

Materials

Polyurethane (PU), Polyethylene glycol (PEG, 1000 kDa) and Ploylactic acid (PLA) were from Sigma (USA). Dimethylformamide (DMF) was from Neutron co (Iran). Tetrahydrofuran (THF) and chloroform were purchased from Dr Mojallali co (Iran).

Methods

Preparation and characterization of PU/PEG nanofibers

DMF and THF (1:1) were mixed, then, 9 % PU was added and stirred overnight. Subsequently, different concentrations of PEG were added and stirred for 1 h. The solution was then electrospun using Electroris ® (Fanavarn Nano Meghyas co, Iran) as detailed earlier ([11]). In brief, using a 5 mL plastic syringe, having a 21G needle, the solution was sprayed on the grounded drum of the device (i.e. collector). The needle to collector distance was 20.0 cm. A high voltage device was connected to the needle. The rotation speed of the drum was 20 rpm and the electrospinning time was ~ 10 min. The electrospinning process was performed at ambient temperature and humidity. The obtained mat was collected on the drum was investigated for formation of bead and fiber on the mat using scanning electron microscopy (SEM, model S-3000N, Hitachi, Japan). The SEM images were analyzed using ImageJ (National Institute of Health, USA) to find the area occupied by formed fibers and beads. Then, the ratio of bead/fiber was calculated for each sample.

Statistical analyzes

Here in, the influence of three experimental factors on the formation fiber and bead from PU/PEG mixture was assessed. The independent factors included feed rate (injection rate, mL/h), PEG concentration (% W/V) and voltage (kV). The ratio of bead/fiber area was taken as the dependent variable.

To model the relation between the independent and dependent variables, we used Box–Behnken experimental design which is a response surface methodology [12]. This design requires lesser experiments compared with commonly used designs such as central composite design (CCD). The modeling process was done using Design-Expert (Version 7.0.0, Stat-Ease, Inc., USA). The independent (input) factors were defined in low, basal and high levels, coded as -1, 0 and +1, respectively (see Table 1).

17 experiments were designed having 12 factorial points and 5 replicates (at the center point to estimate the pure error sum of squares). The details of the variables have been given in Table 2.

The relations of the outputs with the inputs were modeled by the equation (1) :

$$Y = \beta_0 + \beta_1 X_1 + \beta_2 X_2 + \beta_3 X_3 + \beta_{11} X_1^2 + \beta_{22} X_2^2 + \beta_{33} X_3^2 + \beta_{12} X_1 X_2 + \beta_{13} X_1 X_3 + \beta_{23} X_2 X_3 \quad (1)$$

Table 1. Independent variables used in Box-Behnken design

Independent variable	Coded levels		
	-1	0	1
Concentration (% W/V)	1	5	9
Voltage (kV)	10	17	24
Feed rate (mL/h)	0.4	1.2	2.0

Table 2.

Sample No.	Concentration (% W/V)	Voltage (kV)	Feed rate (mL/h)	Bead Area (%)	Fiber Area (%)	Bead/Fiber ratio
1	5.0	17.0	1.2	5.41	42.84	0.17
2	9.0	24.0	1.2	8.24	46.63	0.19
3	5.0	17.0	1.2	8.65	43.98	0.20
4	5.0	17.0	1.2	9.84	25.24	0.28
5	5.0	10.0	0.4	6.62	34.83	0.14
6	5.0	24.0	0.4	20.27	34.89	0.59
7	9.0	17.0	2.0	16.15	34.09	0.51
8	9.0	17.0	0.4	8.77	32.58	0.26
9	5.0	24.0	2.0	10.41	27.29	0.28
10	1.0	10.0	1.2	5.87	31.76	0.17
11	5.0	10.0	2.0	14.89	31.66	0.43
12	9.0	10.0	1.2	6.25	35.02	0.23
13	1.0	17.0	0.4	5.85	47.55	0.12
14	1.0	17.0	2.0	6.79	46.80	0.15
15	5.0	17.0	1.2	18.21	36.95	0.58
16	5.0	17.0	1.2	9.41	39.90	0.26
17	1.0	24.0	1.2	12.31	35.79	0.31

Where Y is the predicted response (bead/fiber ratio), β_0, intercept, β_1 to β_3, linear coefficients, β_{11}, β_{22} and β_{33}, squared coefficients, β_{12} to β_{23}, the interaction coefficients and X_1, X_2 and X_3 are the independent variables (concentration, voltage and feed rate). The equation enables the evaluation of the linear, quadratic and interactive effects of the independent variables on the dependent variable. Using the software, the relations and interactions between the independent and the dependent variables were visualized using the response surfaces (3D graphs). To find the optimized preparation, constraints for bead/fiber ratio were set to minimum. Subsequently, the suggested preparation was experimentally prepared and characterized.

RESULTS AND DISCUSSION

Our work comprised of formation of PU/PEG nanofibers using electrospinning. Nanofibers with mean diameter, bead area and fiber area of 274 to 519 nm, 5.4 to 20.3 (%) and 25.2 (%) to 47.6 (%) were obtained (see Figure 1). We then used response surfaces to study the effects of independent variables on the bead/fiber ratio and find the optimum values for each independent variable to minimize the bead/fiber ratio. This will lead to prepare "bead-less nanofibers".

To find the best matching model, analysis of variance was performed (i.e. F-value). Quadratic second-order polynomial equation was fitted:

Bead/Fiber = +0.027544 × Voltage - 0.088834 × Feed rate - 5.56607×10^{-4} Voltage^2 + 0.055497 × Feed rate^2 (equation 2)

The F-value of the model was 4.31, indicating a significant model and the lack of fit F-value was calculated as 2.73, which shows a not significance relative to the pure error. Table 3 briefs the results of ANOVA study.

The software was then used to visualize the effect of independent variables on the dependent variable using the response surfaces (see Figures 1-3). In each plot, the effect of two interacting independent variables has been illustrated when the third variable has been fixed in a mid-level value.

Fig. 2 shows the effects of concentration and voltage on the bead/fiber ratio. From the details, concentration of the polymer does not appear to influence the bead/fiber ratio, a fact which can be determined from equation 2. Also, a value of ~ 17 kV is required for the voltage as the optimum value, above or below which the bead/fiber ratio tends to increase.

Figure 3 shows the effect of concentration and feed rate on the bead/fiber ratio. The findings show that concentration is not influencing the ratio while feed rate has an optimal value (~ 1.1 mL/h), above or below which the bead/fiber ratio tends to increase.

From Figure 4 which shows the effect voltage and feed rate, to obtain bead/fiber ratio close to 0, the two independent parameters should be fixed at their optimum values.

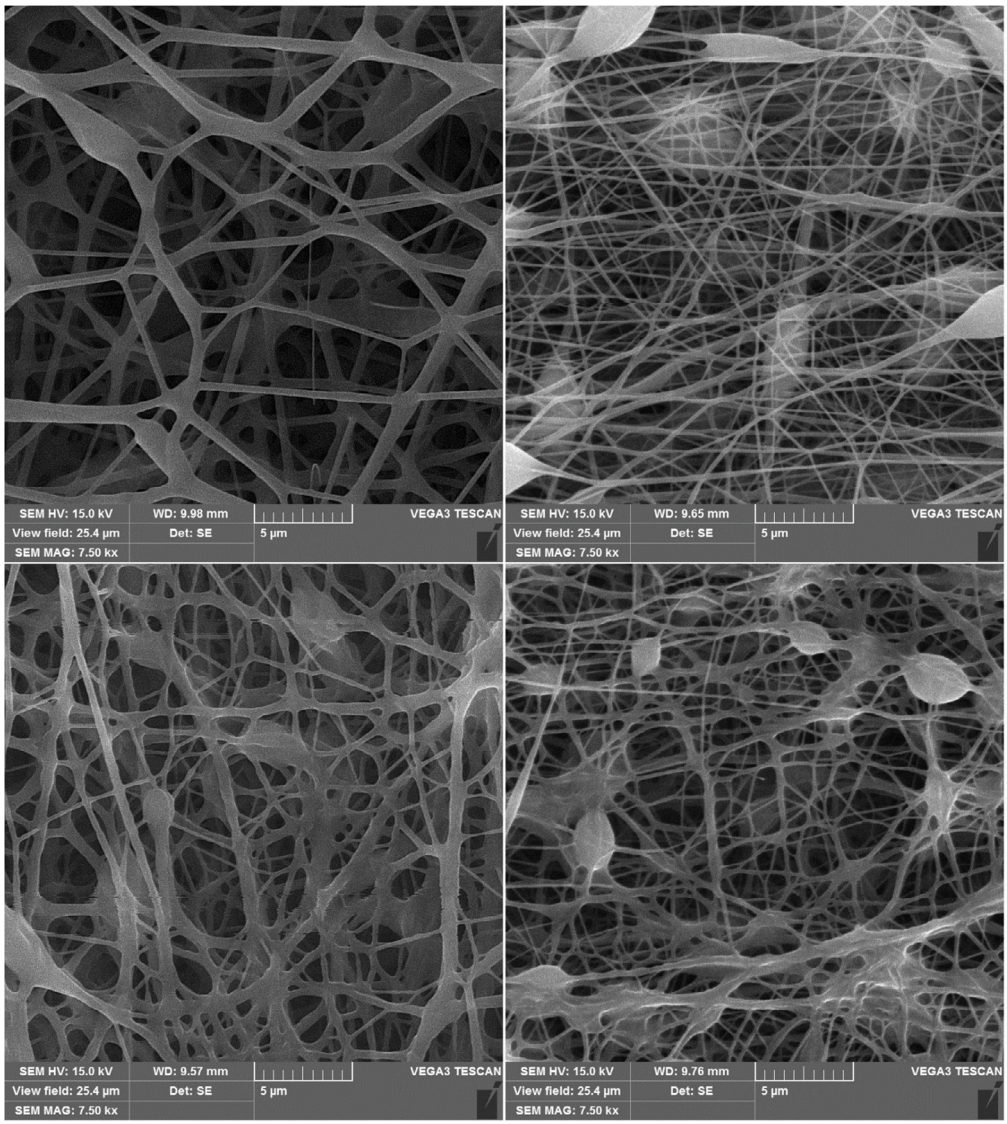

Fig. 1. Examples of the samples analyzed by SEM: Top left: sample No. 1 (concentration: 5.0 % W/V, voltage: 17.0 kV, feed rate: 1.2 mL/h), Top right: sample No. 7 (concentration: 9.0 % W/V, voltage: 17.0 kV, feed rate: 2.0 mL/h), Bottom left: Sample No. 9 (concentration: 5.0 % W/V, voltage: 24.0 kV, feed rate: 2.0 mL/h), Bottom right: sample No. 15 (concentration: 5.0 % W/V, voltage: 17.0 kV, feed rate: 1.2 mL/h), scale bar = 5 µm.

Table 3. ANOVA results for bead/fiber ratio.

Source	Sum of Squares	df	Mean Square	F value	p-value Prob>F
Model	1.00	4	0.25	4.31	0.0195*
Voltage	0.021	1	0.021	0.36	0.5569
Feed rate	7.189×10^{-3}	1	7.189×10^{-3}	0.12	0.7308
Voltage^2	0.20	1	0.20	3.46	0.0855
Feed rate^2	0.29	1	0.29	4.96	0.0443
Residual	0.76	13	0.058		
Lack of Fit	0.65	9	0.072	2.73	0.1735**
Pure Error	0.11	4	0.026		
Total	1.76	17			

*: significant, **: not significant

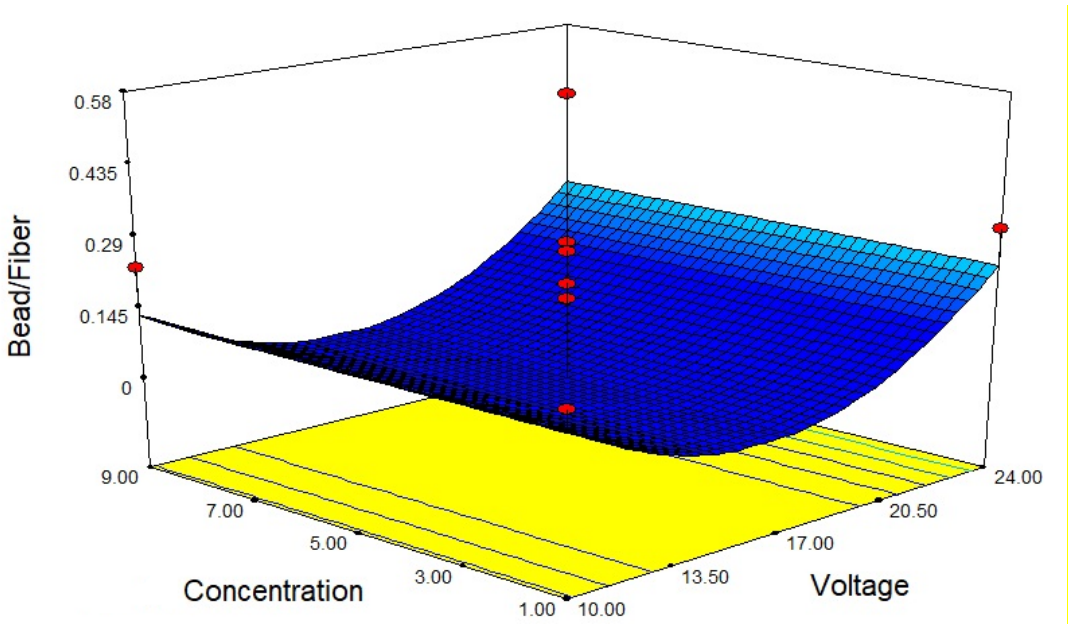

Fig. 2. Response surface generated by the software to illustrate the effect of variation of concentration and voltage on bead/fiber ratio.

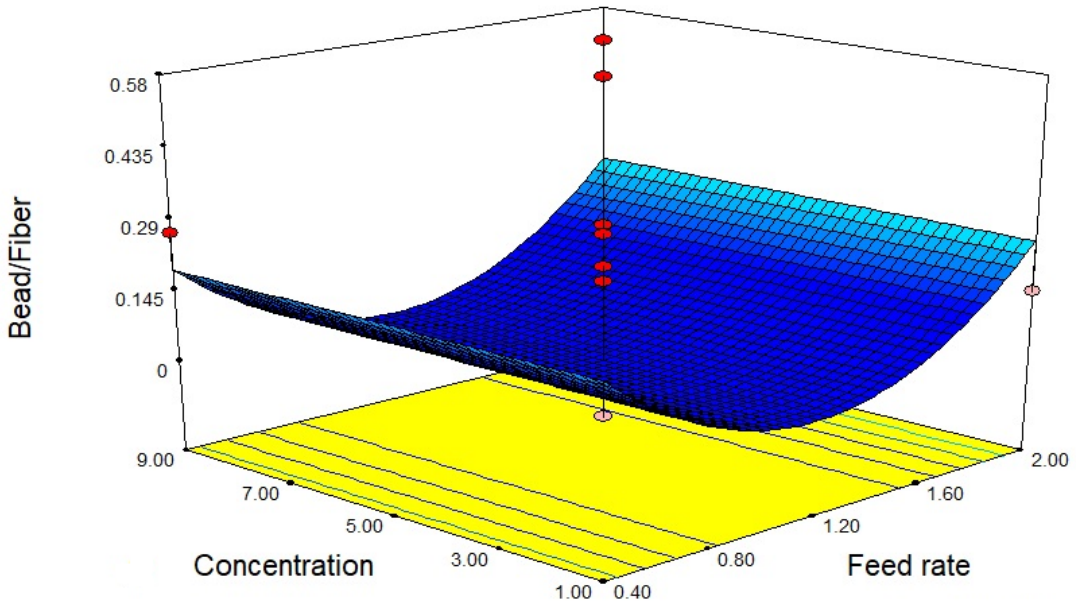

Fig. 3. Response surface generated by the software to illustrate the effect of variation of concentration and feed rate on bead/fiber ratio.

Optimization

Following to generation of the response surfaces, the model was used to suggest the optimum values for the dependent variables. The goal was to obtain nanofibers with minimum beads (preferably no bead). The model suggested voltage and feed rate values of 14.84 (kV) and 1.14 (mL/h), respectively. The model predicted bead/fiber ratio of 0.0005, which can be considered as zero.

To validate the generated model, the suggested sample was prepared and analyzed using SEM. As the Figure 5 shows, the bead is hardly detectable,

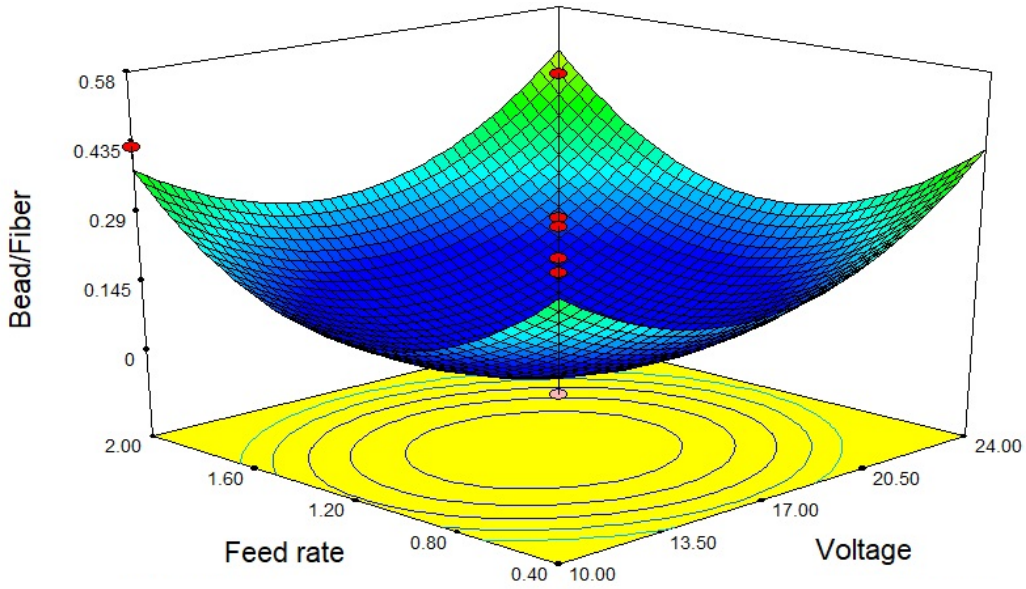

Fig. 4. Response surface generated by the software to illustrate the effect of variation of voltage and feed rate on bead/fiber ratio.

confirming the capability of the generated model in predicting the optimum conditions.

DISCUSSION

A prevalent challenge in electrospinning is the formation of beads which is commonly considered as morphological defects. Various parameters have been reported to affect the bead formation during an electrospinning process. Concentration of the polymer solution appears to be important: In an SEM-based study, it was indicated that indicated that bead-on-string nanofibers could be successfully produced only within a specific range of PLGA solution concentrations [4]. Polyethylene oxide (PEO) solutions (3.0% and 3.5% (W/V), with viscosities of 617 ± 6 cP and 995 ± 6 cP, respectively) yielded beaded nanofibers, while increasing the concentration to 4.0%, resulted in formation of bead-free morphology [13]. The effect of polymer concentration on size of nanoparticles has also been highlighted in electrospray [14]. High viscosity (due to high polymer concentration) is a critical requirement for the production of continuous, bead-free PEO nanofibers. In our study, concentration demonstrated no significant effect on formation of bead on electrospun nanofibers. This is likely because the concentration ranges investigated (i.e. > 1%) were sufficient to provide the viscosity required for forming defect-free fibers. Consequently, further increases in concentration (up to 9%) did not yield a measurable reduction in beads number.

Applied voltage can also influence the bead formation. In a PEO/water system, increasing the voltage beyond 5.5 kV transformed the fiber morphology from defect-free to high density beaded fibers. When the voltage is low, a stable Taylor cone forms, which produces cylindrical, defect-free fibers. By increasing the voltage, the droplet recedes, and the jet initiates from within the syringe tip, which leads to formation of bead defects [15]. On the other hand, bead formation is not exclusive to high voltage values: low voltages can also cause beaded fibers, indicating a non-monotonic relationship. For instance, in a polystyrene/THF system, beaded fibers were produced at both low (5 kV) and high (12 kV) voltages, whereas mid-range voltages (7.5 and 10 kV) yielded bead-free morphologies [16]. In our study, an optimum value for applied voltage was obtained for preparation of bead-free fibers, which agrees with the above findings.

Flow rate has been reported to directly increase the bead density on fibers: polystyrene fibers demonstrated beading when the flow rate was 0.10 mL/min and higher [16]. In another report, PLGA electrospun nanofibers showed controversial effects from voltage: The bead number initially

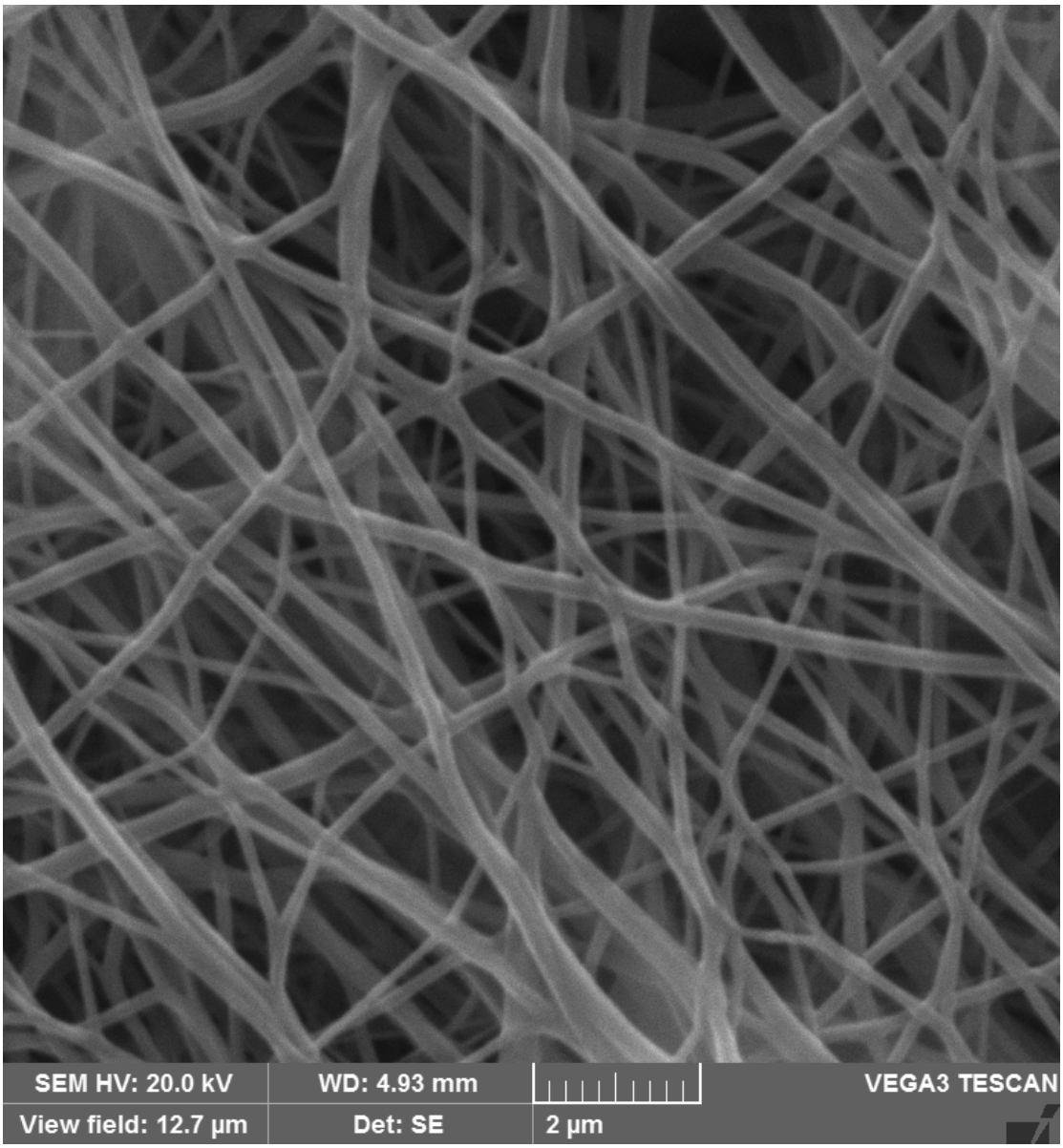

Fig. 5. the result of SEM analysis of the optimum sample, scale bar = 2 µm.

increased and then decreased with increasing flow rate from 0.5 mL/h to 1.5 mL/h. The increase in flow rate enhances the net charge density, which suppresses bead formation. Conversely, high flow rate may result in a larger volume of solution being ejected within the same time period. The excess solution that cannot be adequately stretched by the electric field may form beads due to surface tension [17]. Therefore, the flow rate can affect the bead formation through different approaches, a possible explanation for our finding (i.e. decrease, followed by increase, in bead count when the flow rate increased).

CONCLUSION

Although several previous studies have reported some types of linear relationships between applied voltage or feed rate and bead formation, the present study revealed a more complex influence of these parameters on bead development. Optimal values of each parameter are required to achieve bead-free fiber formation.

ACKNOWLEDGMENT

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CONFLICT OF INTEREST STATEMENT

Authors declare that no competing financial interests exist.

The artificial intelligence–based chatbot ChatGPT (OpenAI, USA) was used to assist in proofreading the manuscript. All suggested corrections were carefully reviewed/revised by the authors, and only the selected modifications were incorporated into the final version.

REFERENCES

1. Luo C, Edirisinghe M. Core-liquid-induced transition from coaxial electrospray to electrospinning of low-viscosity poly (lactide-co-glycolide) sheath solution. Macromolecules. 2014;47(22):7930-8. https://doi.org/10.1021/ma5016616
2. Eda G, Shivkumar S. Bead-to-fiber transition in electrospun polystyrene. J Appl Polym Sci. 2007;106(1):475-87. https://doi.org/10.1002/app.25907
3. Jacobs V, Anandjiwala RD, Maaza M. The influence of electrospinning parameters on the structural morphology and diameter of electrospun nanofibers. J Appl Polym Sci. 2010;115(5):3130-6. https://doi.org/10.1002/app.31396
4. Li T, Ding X, Tian L, Hu J, Yang X, Ramakrishna S. The control of beads diameter of bead-on-string electrospun nanofibers and the corresponding release behaviors of embedded drugs. Mater Sci Eng C Mater Biol Appl. 2017;74:471-7. https://doi.org/10.1016/j.msec.2016.12.050
5. Subbiah T, Bhat GS, Tock RW, Parameswaran S, Ramkumar SS. Electrospinning of nanofibers. J Appl Polym Sci. 2005;96(2):557-69. https://doi.org/10.1002/app.21481
6. Chen M, Patra PK, Warner SB, Bhowmick S. Role of fiber diameter in adhesion and proliferation of NIH 3T3 fibroblast on electrospun polycaprolactone scaffolds. Tissue Eng. 2007;13(3):579-87. https://doi.org/10.1089/ten.2006.0205
7. Balgis R, Kartikowati CW, Ogi T, Gradon L, Bao L, Seki K, et al. Synthesis and evaluation of straight and bead-free nanofibers for improved aerosol filtration. Chem Eng Sci. 2015;137:947-54. https://doi.org/10.1016/j.ces.2015.07.038
8. Fong H, Chun I, Reneker DH. Beaded nanofibers formed during electrospinning. Polymer. 1999;40(16):4585-92. https://doi.org/10.1016/S0032-3861(99)00068-3
9. Dayhoff JE, DeLeo JM. Artificial neural networks: opening the black box. Cancer. 2001;91(S8):1615-35. https://doi.org/10.1002/1097-0142(20010415)91:8+<1615::AID-CNCR1175>3.0.CO;2-L
10. Abyadeh M, Karimi Zarchi AA, Faramarzi MA, Amani A. Evaluation of factors affecting size and size distribution of chitosan-electrosprayed nanoparticles. Avicenna J Med Biotechnol. 2017;9(3):126-32.
11. Mirzaei E, Amani A, Sarkar S, Saber R, Mohammadyani D, Faridi-Majidi R. Artificial neural networks modeling of electrospinning of polyethylene oxide from aqueous acid acetic solution. J Appl Polym Sci. 2012;125(3):1910-21. https://doi.org/10.1002/app.36319
12. Esnaashari SS, Amani A. Optimization of noscapine-loaded mPEG-PLGA nanoparticles and release study: a response surface methodology approach. J Pharm Innov. 2018;13(3):237-46. https://doi.org/10.1007/s12247-018-9318-0
13. Uyar T, Besenbacher F. Electrospinning of cyclodextrin functionalized polyethylene oxide (PEO) nanofibers. Eur Polym J. 2009;45(4):1032-7. https://doi.org/10.1016/j.eurpolymj.2008.12.024
14. Esmaeili F, Aghajani M, Rashti A, Abdollahi M, Faridi-Majidi R, Ghanbari H, et al. Parameters influencing size of electrosprayed chitosan/HPMC/TPP nanoparticles containing alendronate by an artificial neural networks model. J Electrostat. 2021;112:103598. https://doi.org/10.1016/j.elstat.2021.103598
15. Deitzel JM, Kleinmeyer J, Harris D, Tan NB. The effect of processing variables on the morphology of electrospun nanofibers and textiles. Polymer. 2001;42(1):261-72. https://doi.org/10.1016/S0032-3861(00)00250-0
16. Megelski S, Stephens JS, Chase DB, Rabolt JF. Micro- and nanostructured surface morphology on electrospun polymer fibers. Macromolecules. 2002;35(22):8456-66. https://doi.org/10.1021/ma020444a
17. Li T, Liu L, Wang L, Ding X. Solid drug particles encapsulated bead-on-string nanofibers: The control of bead number and its corresponding release profile. J Biomater Sci Polym Ed. 2019;30(15):1454-69. https://doi.org/10.1080/09205063.2019.1643984