Advances in Nano Research, *Vol. 10, No. 1 (2021) 59-69*
DOI: https://doi.org/10.12989/anr.2021.10.1.059

Using Taguchi design of experiments for the optimization of electrospun thermoplastic polyurethane scaffolds

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(*Received November 1, 2019, Revised August 4, 2020, Accepted November 9, 2020*)

Abstract. Electrospinning is a cost-effective and versatile method for producing submicron fibers. Although this method is relatively simple, at the theoretical level the interactions between process parameters and their influence on the fiber morphology are not yet fully understood. In this paper, the aim was finding optimal electrospinning parameters in order to obtain the smallest fiber diameter by using Taguchi's methodology. The nanofibers produced by electrospinning a solution of Thermoplastic Polyurethane (TPU) in Dimethylformamide (DMF). Polymer concentration and process parameters were considered as the effective factors. Taguchi's L9 orthogonal design (4 parameters, 3 levels) was applied to the experiential design. Optimal electrospinning conditions were determined using the signal-to-noise (S/N) ratio with Minitab 17 software. The morphology of the nanofibers was studied by a Scanning Electron Microscope (SEM). Thereafter, a tensile tester machine was used to assess mechanical properties of nanofibrous scaffolds. The analysis of DoE experiments showed that TPU concentration was the most significant parameter. An optimum combination to reach smallest diameters was yielded at 12 wt% polymer concentration, 16 kV of the supply voltage, 0.1 ml/h feed rate and 15 cm tip-to-distance. An empirical model was extracted and verified using confirmation test. The average diameter of nanofibers at the optimum conditions was in the range of 242.10 to 257.92 nm at a confidence level 95% which was in close agreement with the predicted value by the Taguchi technique. Also, the mechanical properties increased with decreasing fibers diameter. This study demonstrated Taguchi method was successfully applied to the optimization of electrospinning conditions for TPU nanofibers and the presented scaffold can mimic the structure of Extracellular Matrix (ECM).

Keywords: electrospinning; nanofibers; thermoplastic polyurethane; Taguchi's orthogonal design; optimization

1. Introduction

Electrospinning is a unique and versatile process to produce polymeric fibres in the submicron range (Kucinska-Lipka *et al*. 2015, Ye *et al*. 2019). Electrospun fibrous mats have numerous applications, such as protective clothing, drug delivery, wound dressing, tissue scaffolds, nanocatalysis, optical electronics, filtration, personal care, composite, insulation, energy storage and sound absorption (Ceylan and Bölgen 2016, Celep and Dincer 2017, Yanilmaz *et al*. 2012). The nanofibers prepared by electrospinning generally exhibit high surface area-to-volume ratios, high porosity, nanosized effects and enhanced physico-mechanical properties (Albetran *et al*. 2015, Horuz and Belibağlı 2017).

In a typical electrospinning process, the polymer solution is forced through a syringe, and then a solution drop is formed at the tip of the needle, at a sufficient voltage to overcome surface tension forces, fine jets of polymer solution jet out toward a grounded collector. The jets are then stretched and attenuated prior to reaching the collector; thereafter, they are dried and collected as an interconnected web of ultrafine fibers with diameters ranging from the nanometer to micrometer scale (Amini *et al*. 2013, Dufresne 2017, Hamed *et al*. 2017, Bhattarai *et al*. 2019). Fig. 1 shows a schematic illustration of an electrospinning setup.

In general, electrospun nanofiber diameters depend on the three working parameter sets such as solution parameters, processing parameters and ambient parameters (Fallahiarezoudar *et al*. 2017, Li and Wang 2013a, Albetran *et al*. 2015). Viscosity, concentration, surface tension, molecular weight, conductivity and dielectric of polymer solution are solution parameters of electrospinning (Tarus *et al*. 2016). The polymer concentration is one of the most significant factors in controlling beads and fiber diameters (Albetran *et al*. 2015). Process parameters are the second set of parameters, which consist of the gap distance between the capillary tip and the collector, the applied voltage, and flow rate (Tarus *et al*. 2016). Within the electrospinning process, applied voltage is the crucial factor (Li and Wang 2013a). Aspects of the atmospheric environment, such as humidity, pressure, and temperature, belong to the last set of parameters (Albetran *et al*. 2015). Parameters in each category affect the morphology of the fibers (Elkasaby *et al*.

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ISSN: 2287-237X (Print), 2287-2388 (Online)

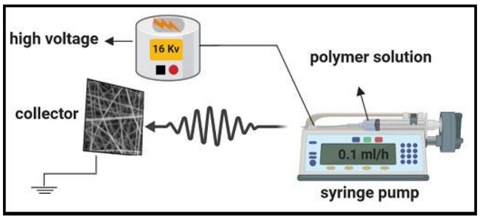


Fig. 1 Electrospinning setup

2017). Under the same electrospinning conditions, an increase in polymer concentration causes an increase in diameters of electrospun nanofibers. However, there are different observations about the effects of process parameters (Yanilmaz *et al*. 2012); combinations of these factors determine fiber diameter, uniformity, and alignment (Elkasaby *et al*. 2017, Anindyajati *et al*. 2018).

Different achievements have been reported from previous works in terms of fiber diameter, fiber properties and the effect of individual parameters on the fiber properties (Jing *et al*. 2015, Ballarin *et al*. 2014, Zhuo *et al*. 2008, Jia *et al*. 2014, Banuškevičiūtė *et al*. 2011, Karakaş *et al*. 2013, Tetteh *et al*. 2014). Zhuo *et al*. (2008) prepared polyurethane nanofibers and investigated the effects of some process parameters on electrospinning. They concluded that diameters of nanofibers increased with increasing concentration. In another study, Karakaş *et al*. (2013) observed that the electrospinning properties (i.e., solution concentration, nozzle-collector distance, applied voltage and the solution flow rate) were important factors in the final fiber diameter and fiber morphology. Among these properties, solution concentration was found to have the strongest and the solution flow rate to have the weakest effect.

The interaction between these parameters is complex, with the variation of one factor often altering another. It is, therefore, challenging to investigate each individual parameter experimentally and the resultant procedure is time-consuming; for reproducible electrospinning to occur, the key parameters must be identified and stably controlled (Ruiter *et al*. 2017). However, all of these parameters must be adjusted specifically depending on the types of polymer-solvent systems. Therefore, optimization of the conditions for each polymer-solvent system becomes a challenging task in order to get the best results (Horuz and Belibağlı 2017).

An appropriate model can be utilized for the electrospinning process to evaluate the effects of the parameters on the fiber morphology (Mohammad Khanlou *et al*. 2015). Design of Experiment (DOE) method seems a vital and reasonable way to study the effect of simultaneously changing a wide range of parameters (Amini *et al.* 2013). There are several techniques in the DOE, including factorial, response surface method (RSM), and the robust parameter design (Taguchi's method) (Anindyajati *et al*. 2018, Douglasc 2009); this paper will be focused on the latter.

Taguchi experimental design approach is a very simple technique by which one can optimize device parameters by very less number of experiments (Amini *et al.* 2013, Aydin and Gundogdu 2018). It has been widely used in recent engineering statistics (Amini *et al*. 2013, Albetran *et al*. 2015, Mohammad Khanlou *et al*. 2015, Horuz and Belibağlı 2017, Celep and Dincer 2017). The Taguchi method differs from the classical methods by using orthogonal arrays. Orthogonal arrays reduce the number of samples and result in easy to handle experimental designs. In addition, Taguchi methods use different types of signal to noise ratios (S/N ratio) to measure variability around the target performance (Tascan 2014, Pirsalami *et al*. 2016, Sayed *et al*. 2017).

Polyurethane (PU) is one of the most common thermoplastic polymers having superior mechanical, thermal and chemical properties with a high elasticity (Zhuo *et al*. 2008). Polyurethanes can be used in the textile industry, medicine, environmental fields and so on (Karakaş *et al*. 2013).

Thermoplastic Polyurethane (TPU) as a class of PU has linear segmented molecular chains, good processability, high elongation, and excellent abrasion and tear resistance (Jing *et al*. 2015). TPU has good biocompatibility and recent studies have shown that electrospun thermoplastic polyurethane fibers is a proper candidate in bone tissue engineering (Drupitha *et al*. 2018), skin replacements (Li *et al*. 2018) tissue engineering heart valve (Fallahiarezoudar *et al*. 2017) and vascular graft (Jing *et al*. 2015). Therefore, its application to the field of tissue engineering scaffolds warrants further investigation.

Any scaffold material must be able to interact with cells in three dimensions and facilitate communication. In the native tissues, the structural ECM proteins (50-500 nm diameter fibers) are 1 to 2 orders of magnitude smaller than the cell itself; this allows the cell to be in direct contact with many ECM fibers, thereby defining its three dimensional orientation. This property may be a crucial factor in determining the success or failure of a tissue engineering scaffold (Barnes *et al*. 2007, Ethier and Simmons 2007). Usage of electrospinning is motivated by the capability to generate fibrous structures with fibre diameters in this range (Rüder *et al*. 2013). Christopherson *et al*. (2009) investigated the effect of nanofiber diameter on cell growth and differentiation. They prepared nanofibers with diameters of 283 ± 45, 749 ± 153 and 1452 ± 312 nm from Polyether Sulfone (PES). The results showed that the highest degree of differentiation of neural precursor cells was reported in the smallest fiber diameter of 283 ± 45 nm. Lower adhesion and limited migratory ability of neural stem/progenitor cells on larger fibers (749 nm and 1452 nm) have significantly reduced the survival of these cells in comparison with 283 nm fibers (Christopherson *et al*. 2009). Therefore, it seems that using the smallest diameter is effective to improve cell behaviors. Also, studies show that reducing the diameter of the fibers can increase the mechanical properties (Fallahiarezoudar *et al*. 2017, Doustgani 2016, Baji *et al*. 2010).

In this article, the robust statistical Taguchi DoE is applied during the TPU nanofiber production using the electrospinning process. The aim of this paper is to understand how the morphology and diameter of produced electrospun nanofibers from a solution of thermoplastic polyurethane in Dimethylformamide (DMF) are affected by

Table 1 Four factors and their levels selected in Taguchi's design

Factor	Symbol	Level		
		1	2	3
Polymer concentration (wt%)	C	12	16	20
Voltage supplied (kV)	V	12	16	20
Distance between collector and tip (cm)	D	12	15	18
Flow rate (ml/h)	F	0.1	0.2	0.3

solvent concentration and process parameters consisted of applied voltage, the distance between the capillary tip and the collector and flow rate. In order to create scaffolds or ECM analogues, which are truly bio-mimicking at 50 to 500 nm scale (nearly identical to that of natural collagen in the ECM), small-diameter fibers must be used. Thus, this research was carried out to optimize the fabrication process to obtain thin, bead-free, strong and homogeneous distributed thermoplastic polyurethane nanofibers.

2. Experimental

2.1 Materials

A commercial grade of thermoplastic polyurethane (Desmopan, 3485A-polyester based, ρ = 1200 kg/m^3) was supplied from Bayer material science AG, Germany and N, N-Dimethylformamide (DMF, M = 10/73 g/mol) was received from Merck, Germany was used as a solvent.

2.2 Preparation of solutions

Polymer solution samples were prepared through dissolving 12, 16 and 20 wt% TPU in a DMF solvent. The solutions were then stirred for about 24 h using a magnetic stirrer at 25°C for the complete dissolving of thermoplastic polyurethane until homogeneous TPU-DMF solutions were obtained.

2.3 Electrospinning experiments

Thermoplastic polyurethane and DMF were used to make a polymer solution. The electrospinning equipment used in this study consisted of a syringe pump, a syringe needle, a high voltage power supply and a collector plate covered in non-stick aluminum foil. The key parameters of the electrospinning process were the polymer solution concentration (wt%), the applied voltage (kV), the feed rate of the polymer solution (ml/h) and the tip-to-collector distance in centimetres (Xue *et al*. 2019). The solutions were placed in 1 ml syringes fixed horizontally on the syringe pump delivering the solution to the tip of a metal needle where the voltage was applied. Fibers were then collected on the aluminium foil. Most of the solvent evaporated rapidly in the jet region. As they arrived at the collector plate, the collected nanofibers were almost dry. The electrospinning experiments were performed at a temperature of 25°C.

Table 2 L9 orthogonal array for selected factors and levels

Run	Factors			
	TPU (wt%)	Voltage (kV)	Distance (cm)	Flow rate (ml/h)
1	12	12	12	0.1
2	12	16	15	0.2
3	12	20	18	0.3
4	16	12	15	0.3
5	16	16	18	0.1
6	16	20	12	0.2
7	20	12	18	0.2
8	20	16	12	0.3
9	20	20	15	0.1

2.4 Design and analysis of experiments

The production of TPU nanofibers was achieved by implementing the Taguchi method in order to estimate the optimal production conditions. The Taguchi method takes in arranging an orthogonal array to order the parameters affecting the process and the levels they should be assorted. It determines the factors affecting the performance quality with the least number of experiments, thus this method greatly improves the engineering productivity and saves time and resources (Amini *et al*. 2013, Chaudhari *et al*. 2011). It works by changing the number of target attributes to a signal-to-noise (S/N) ratio for measuring the performance of the level of controlling parameters in conflict to these parameters. There are three categories of S/N ratios to select from: the "smaller is better" type, the "larger is better" type and the "nominal is better" type. The selected type of S/N ratio is based on the design target (Celep and Dincer 2017). In addition, analysis of variance (ANOVA) utilizes to conclude the statistical significance of the electrospinning factors (Mohammad Khanlou *et al*. 2015).

In our study, the first step was to investigate the influences of three levels of four factors (Albetran *et al*. 2015, Mohammad Khanlou *et al*. 2015, Horuz and Belibağlı 2017, Shahavi *et al*. 2016) on the diameter of electrospun TPU fibers. Each of these factors was considered to be varying at three levels as summarized in Table 1. The next step was to optimize these parameters to get thinner fibers. The L9 design was chosen using a factorial design of four parameters with three levels. A total of nine experimental runs were planned and performed. Table 2 shows the L9 orthogonal array with the independent factors.

In the current research, the objective was to minimize the nanofiber diameter. Therefore, the "smaller is better" quality methodology was studied for obtaining the optimal electrospinning conditions. The S/N ratio was calculated as follows (Eq. (1))

$$\frac{S}{N} = -10\log\left(\frac{1}{n}\sum_{i=1}^{n} y_i^2\right) \qquad (1)$$

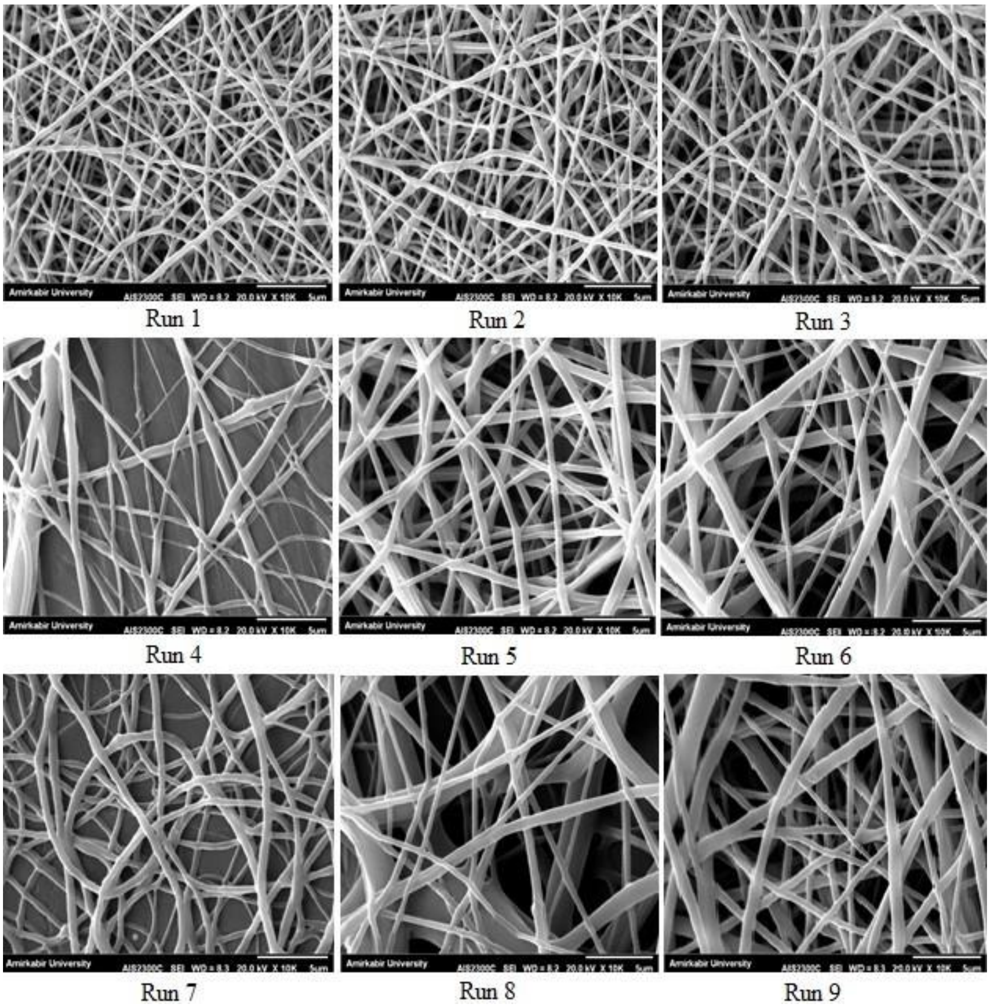


Fig. 2 SEM micrographs of electrospun TPU nanofibers used in DoE study. All scale bars represent 5 µm

where S/N is the signal-to-noise ratio, *n* is the number of observations, and *y* is the diameter of TPU nanofibers measured (Andrzej *et al*. 2015, Saligheh *et al*. 2015, Dong *et al*. 2013).

2.5 Morphological characterization

Diameter and morphology of the obtained nanofibrous mats were assessed using scanning electron microscopy (SEM, AIS 2100, Seron, South Korea). The samples were gold coated and imaged at an operating voltage of 80 kV for 80 seconds to reduce the variations and to produce a completely conductive surface. Using SEM images, 100 random measurements of the fiber diameter were performed for each sample using Fiji Image J (1.46v) software (Hotaling *et al*. 2015).

2.6 Mechanical properties

Tensile tests were performed on a mechanical testing machine (Instron 5566) equipped with a 30 N loaded cell at ambient temperature (25°C). Electrospun membranes were cut into 5 mm × 30 mm rectangular shapes and 0.06 ± 0.01 µm in thickness, then stretched at a crosshead speed of 5 mm/min until the sample fractured. Tensile modulus, tensile strength and strain at break were measured and considered in comparison study. Statistical results were the average of three samples.

2.7 Statistical analysis and optimization

Minitab 17 software (Minitab Ltd., UK) was used to optimize the nanofiber production process using the Taguchi approach (Horuz and Belibağlı 2017, Mohammad Khanlou *et al*. 2015). The mean diameter and standard deviation were calculated as the responses. The significance level of the variables for the fiber diameter was determined using the 95% confidence level of the ANOVA. For the confirmation, one more experiment was carried out at the determined conditions.

3. Results and discussions

3.1 Nanofiber morphology and diameter SEM

Diameter SEM micrographs of electrospun nanofiber morphology for the L9 DoE are illustrated in Table 2. Electrospun TPU nanofibers showed bead-free and smooth morphology (Fig. 2) and Fig. 3 shows the frequency

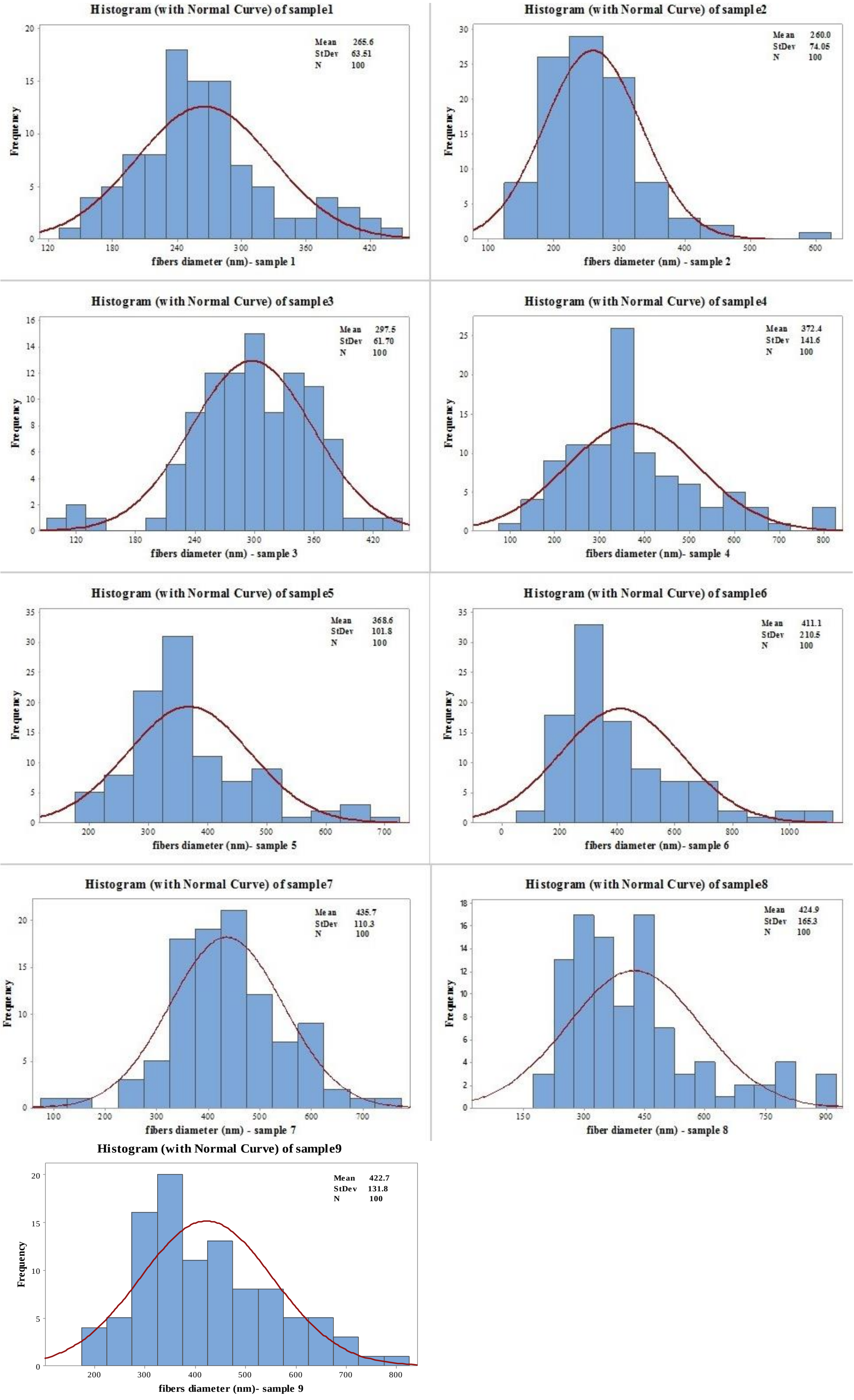


Fig. 3 Frequency contribution of fiber diameter range in the DoE study

contribution diagrams for the DoE study in the diameter range of 260-435 nm. The corresponding average fiber diameters and standard deviations are illustrated in Table 3.

At first glance to the SEM images, a random fiber

Table 3 Thermoplastic polyurethane fiber diameter with standard deviation and their corresponding signal-to-noise (S/N) ratios based on “smaller is better”

Run	Combination of factors	Average nanofiber diameter and standard deviation (nm)	S/N
1	C1V1D1F1	265 ± 63	−48.48
2	C1V2D2F2	260 ± 74	−48.29
3	C1V3D3F3	297 ± 61	−49.46
4	C2V1D2F3	372 ± 141	−51.42
5	C2V2D3F1	368 ± 101	−51.33
6	C2V3D1F2	411 ± 210	−52.27
7	C3V1D3F2	435 ± 110	−52.78
8	C3V2D1F3	429 ± 165	−52.56
9	C3V3D2F1	422 ± 131	−52.52

Table 4 Response table for means of TPU fiber diameters and S/N values

	Means of fiber diameters (nm)				Means of S/N values			
Level	C	V	D	F	C	V	D	F
1	274.36	357.9	367.2	352.36	−48.75	−50.89	−51.10	−50.78
2	384.1	351.23	351.7	368.93	−67.51	−50.73	−50.74	−51.12
3	427.76	377.1	367.33	364.93	−62.52	−42.51	−51.19	−51.15
Range	153.4	25.87	15.63	16.57	18.76	8.38	0.45	0.37
Rank	1	2	4	3	1	2	3	4

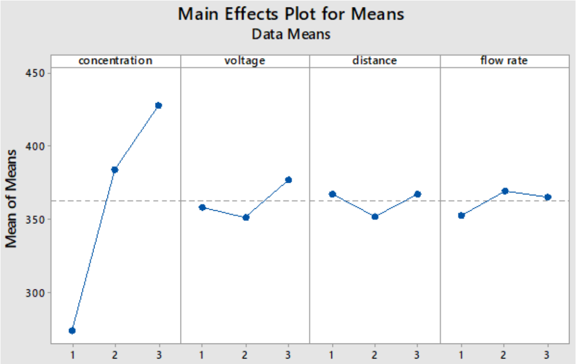


Fig. 4 Main effects plot for means of electrospun TPU fiber diameter

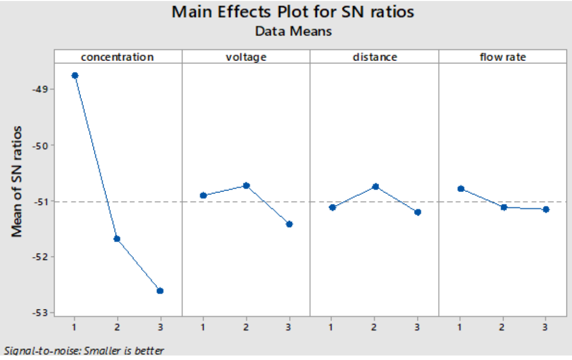


Fig. 5 Main effects plot for signal-to-noise (S/N) ratios of electrospun TPU fiber diameter

distribution was evident in most mat samples and it can be easily seen that TPU nanofibers obtained in Run 1 to Run 3 had smaller diameters than others. The common parameter used in these runs was TPU concentration with the lowest level. However, bead-free and smooth nanofibers with larger diameter were produced by electrospinning of the TPU solutions at higher TPU concentrations.

Albetran *et al*. (2015) also produced electrospun TiO_2/PVP nanofibers using Taguchi design of experiment method. The analysis of DoE experiments for nanofiber diameters demonstrated that TiO_2 concentration was the most significant factor. Elkasaby *et al*. (2017) designed a mathematical model of the polymer fiber diameter as a function of significant process parameters have been built using Response Surface Methodology (RSM). It is observed that the lower diameters are obtained in the lowest concentration used; and the dimensions ranged from 0.51 to 0.59 µm. It is also observed that the middle values of the studied parameter generally resulted in higher diameters.

3.2 Analyzing and evaluating the results of the experiments using the Taguchi method

Orthogonal arrays are utilized in the Taguchi method to organize the factors that influence the process and the levels where they should vary. As an alternative, the Taguchi design examines a pair of combinations rather than having to investigate every possible combination, suchlike the full factorial design. By determining the relation of these process parameters to fiber characteristics, it may then be feasible to optimize the design factors to get smooth nonbeaded fibers with the smaller diameter (Abdelhakim *et al*. 2019). In this method, the parameters that influence product quality could be indicated with a minimal number of trials (Douglasc 2009, Ballarin *et al*. 2014, Horuz and Belibağlı 2017).

In our work, the S/N ratio should be at maximum to get optimum combination of factors in Taguchi method. S/N ratio values calculated by reorganizing the results by ‘Minitab-17’ statistical software agreement with the “smaller is better” characteristic formula and it has been used to reduce both the fiber diameter and its variation in electrospun TPU nanofibers (Patra *et al*. 2009, Dong *et al*. 2013, Horuz and Belibağlı 2017) (Table 3).

Table 3, showing the thinnest nanofibers (260 ± 74 nm) were obtained in Run 2 containing lowest level of TPU concentration and middle levels of voltage applied, distance between collector and tip and flow rate. In contrast, the highest levels of TPU concentration and distance with the lowest level of voltage applied yielded the highest diameter of TPU nanofiber (435 ± 110 nm) and the lowest value of S/N ratio (Run 7). In order to understand the effects of each factor and level on the response, the average fiber diameter and S/N ratio value for three levels of four parameters were calculated as outlined in Table 4. As seen in this table, the delta value (maximum - minimum) of the three levels were calculated and the degree of importance of each factor on the fiber diameter was determined in a way that the factor with larger range had the more significant effect on the fiber diameter. This table suggests that polymer concentration (factor C) and voltage (factor V) are more significant for modifying fiber diameters. Feed rate (factor F) and the distance between the needle and the collector (factor D) are proportionately low significance.

Other researchers confirm our results. Tan *et al*. (2005) indicated the morphology of the electrospun nanofibers is primarily affected by polymer concentration, its molecular weight and electrical conductivity of the solvent, followed by the voltage and feed rate. Mohammadian and Haghi (2014) in another study concluded increasing polymer concentration will result in greater polymer chain entanglements. This causes the viscoelastic force to increase enabling the charged jet to withstand a larger electrostatic stretching force leading to a larger diameter of fibers.

The applied voltage was found as the second influential factor on the TPU fiber diameter. The fiber diameters were seen as smaller when the applied voltage was 16 kV. Generally with an increase in the applied voltage beyond a critical value, the TPU fiber diameter was decreased but in Run 3 and Run 6 with an increase in applied voltage, the TPU fiber diameter was increased too. In literature, the effect of voltage on the fiber diameter is also crucial and still controversial (Horuz and Belibağlı 2017).

Some research showed increasing the voltage, i.e., increasing the electric field strength will increase the electrostatic repulsive force on the fluid jet; therefore, thinner fibers will be formed. Simultaneously, the solution will be removed from the capillary tip more quickly as a jet is ejected from the Taylor cone that making the control of the process more difficult. Also, this resulting in the increase of the fiber diameter (Zhang *et al*. 2005, Vigani 2017). Demir *et al*. (2002) also in their research indicated the morphology of polyurethaneurea fibers was strongly correlated with viscosity, equivalently concentration and temperature. As concentration, or equivalently, the viscosity increases, higher electrical forces are required to overcome both the surface tension and the viscoelastic force for stretching the fiber.

Very high levels of voltage applied are caused a greater volume of polymer solution to be drawn from the needle and the jet diameter is seemed to increase in a sigmoidal manner with increasing voltage.

In another study, Şener *et al*. (2011) indicated there was no clear correlation between the applied voltage and diameters of fibers, and suggested the effect of voltage may depend on other parameters such as gap distance and eventually the shape of the electric field. In result, the applied voltage is the crucial factor but the level of significances varies with the polymer solution concentration, on the distance between the tip and the collector and other parameters (Li and Wang 2013a).

Our results showed the distance between the collector and the tip and the flow rate were the least important among the parameters. In most cases, if the feed rate is very high, bead fibers with thick diameter will form rather than the smooth fiber with thin diameter, Due to the short drying time before fiber reaching the collector and also low stretching forces (Kyzas and Mitropoulos 2018, Li and Wang 2013b).

Zhang *et al*. (2005) also indicated the morphological specifications can be a bit changed by changing the solution feed rate. When the feed rate exceeded a critical value, the delivery rate of the solution jet to the capillary tip exceeded the rate at which the solution was removed from the tip by the electric forces. This shift in the mass-balance leaded to formation of fibers with big beads and different diameters.

Even though the distance between the collector and the tip is considered to be the least effective factor, its effect is approximately equal to voltage changes (Horuz and Belibağlı 2017). If the distance is too long, the bead fibers will form, while if the distance is too short, the the fibers will not have enough time to consolidate before reaching distance between the collector and the tip and the feed rate both increased and decreased the diameter of the fiber, this difference can be attributed to the dependence of these factors on the main parameters (TPU concentration and applied voltage).

3.3 Optimum electrospinning parameter condition and parameters

The optimized combination of factors by which fibers with a minimum diameter were obtained was found by the Taguchi method. Fig. 4 shows the graphs given to illustrate the relationships between the fiber diameter and the main effects of the electrospinning parameters. The contribution of each factor on the improvement of average nanofiber diameter can be found from the lowest point of the mean effect plots to obtain the optimum condition of finest fiber diameter achievement.

Fig. 5 demonstrates the S/N ratios of the nanofiber diameter data obtained from the experiment results, calculated using Eq. (1), that are evaluated for assigning the optimal levels for each parameter. The larger the S/N ratio, the smaller the variance of the nanofiber diameter from the required value.

Therefore, the optimum production conditions of the electrospun TPU nanofibers were determined to be as follows: 12 wt% for the polymer concentration (C1), 16 kV for the voltage (V2), 0.1 ml/h for the feed rate (F1) and 15 cm for the distance between the collector and the tip (D2), respectively.

3.4 Regression model for fibers diameter

According to the analysis an empirical regression model was obtained. In statistical modeling, regression analysis is a set of statistical processes for estimating the relationships between a dependent variable (often called the 'outcome variable') and one or more independent variables (Fallahiarezoudar *et al*. 2017). The Minitab software regression analysis tab was used to explore the equation. In this case, the regression was expressed by means of all controllable factors as (Eq. (2))

$$\begin{aligned}&\text{Fiber diameter}\\&= 176.8 + 76.7\,(C) + 9.6\,(V) + 0.1\,(D) + 6.3\,(F)\end{aligned} \tag{2}$$

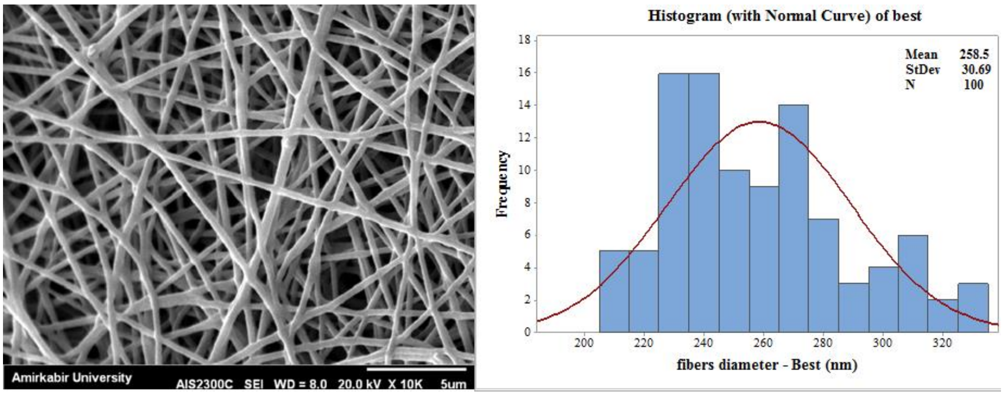
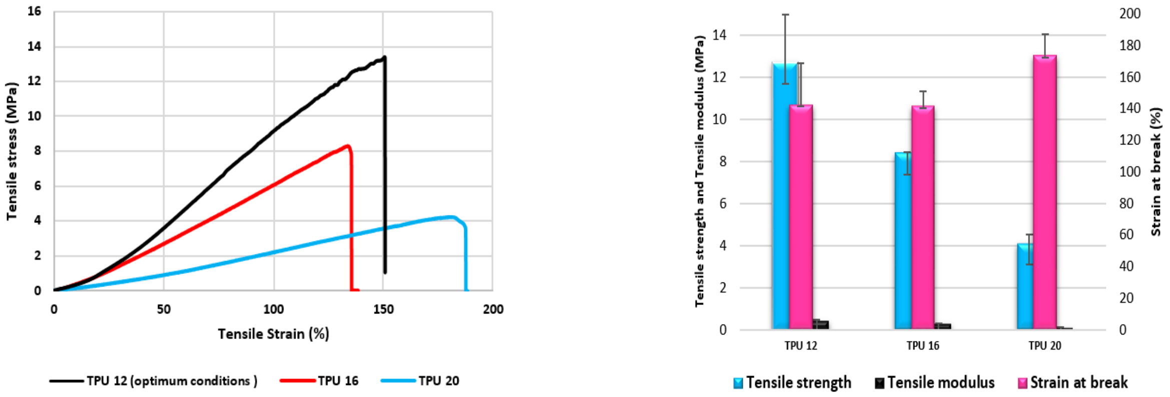


Fig. 6 SEM image and bar graph of diameter ranges of electrospun TPU nanofibers obtained at optimized conditions (12% TPU; 16 kV; 0.1 ml/h; 15 cm)



(a) (b)

Fig. 7 Tensile test results of TPU scaffolds: (a) representative strain vs. stress curves; (b) statistical results of tensile modulus, tensile strength and strain at break

3.5 Confirmation of Taguchi design

The predicted result (S/N ratio) at optimum conditions was −47.959 ± 0.273 at a confidence level 95%. Using the Taguchi method, the average diameter of fibers at the optimum conditions can be predicted (Y_{exp}) without running any experiment; it is calculated as follows (Eq. (3)) (Saligheh *et al*. 2015)

$$Y_{exp} = (MSD)^{\frac{1}{2}}$$
$$MSD = 10^{-\left[\text{expected result}\left(\frac{S}{N}\text{ ratio}\right)\text{ at optimum conditions}\right]/10} \quad (3)$$

As the expected result (S/N ratio) at optimum conditions was −47.959 ± 0.273 at confidence level 95% (low value = −48.232 and high value = −47.686), thus the related mean standard deviation (MSD) would be 66527.31 and 58631.81, respectively, from the maximum and minimum S/N. Therefore, in this study, Y_{exp} at the 95% confidence level should be in the range of 242.10 to 257.92 nm.

Also, the estimated fiber diameter can be calculated with the help following predictive (Eq. (4))

$$\eta = \bar{T} + (\overline{C1} - \bar{T}) + (\overline{V2} - \bar{T}) + (\overline{D2} - \bar{T}) + (\overline{F1} - \bar{T}) \quad (4)$$

where η is the predicted average diameter, T is the average result of 9 runs and C1V2D2F1 is the mean response for factors at designated levels. Accordingly, the diameter of the optimum conditions is calculated to be about 242.99 nm, which is the same as the predicted value of (Eq. (3)).

The confirmation experiment is the final step in the design of experiment process. The confirmation experiment is conducted to validate the interference drawn during the analysis phase. The confirmation experiment is performed by considering the new set of factor settings C1V2D2F1 to predict the fiber diameters. Fig. 6 shows the SEM images with the distribution of fiber diameters of actual electrospun nanofibers obtained with optimized conditions. The average fiber diameter was achieved at 258 ± 30 nm which showed a good consistency. That means that the experimental fiber diameter value was very close to the predicted value; therefore, the resulting model seems to be capable of predicting TPU fiber diameter to a reasonable accuracy.

3.6 Mechanical properties

Tensile test was carried out to distinguish different mechanical behavior of optimal fibers compared to larger diameter fibers of TPU. The representative stress versus strain curves and statistical resulting from the tensile tests of the electrospun scaffolds are shown in Figs. 7(a)-(b). It is obvious that the tensile modulus and tensile strength of the scaffolds increased as the diameter of the fibers decreases. Statistical analysis of the samples shows that the difference in the reported mechanical properties between the 3 groups is significant ($P < 0.05$).

Doustgani (2016) in a study to investigate the optimization of mechanical and structural properties of PVA nanofibers. According to the results, solution concentration was found to be the most significant parameters affecting nanofiber diameter. The fibers diameter increased, but tensile strength decreased by increasing the concentration of the polymer solution. The fibers with the lowest diameter (284 nm) had a tensile strength of 2.87 MPa and the fibers with the highest diameter (522.6 nm) had a tensile strength of 0.55 MPa (Doustgani 2016), which is consistent with our findings. In addition, Baji *et al*. (2010) have considered the mechanical properties of fibers to be influenced by the diameter of the fibers. Upon increasing the fibers size, both tensile strength and tensile modulus decreases and the larger diameter fibers tend to display bulk-like properties. This observation is extremely important for conceivable applications of eletrospun nanofibers (Baji *et al*. 2010).

4. Conclusions

TPU nanofibers were produced by using electrospinning technique and the effects of the most important process parameters (polymer concentration, applied voltage, tip to collector distance and flow rate) on the morphologies of nanofibers were evaluated statistically. Taguchi method as one the most prominent methods of experimental design was employed to optimize the crucial electrospinning factors to obtain the smallest nanofiber diameter. The results achieved from this investigation are as below:

- The TPU concentration was found as the most influential factor on the diameter of electrospun fibers. The smaller diameters were produced by electrospinning of the thermoplastic polyurethane solutions at lower polymer concentration (12 wt%). The applied voltage was the second most influential factor on the diameter of the fibers.
- The feed rate and the distance between the collector and the tip were found to have fewer effects on the fiber diameter compared to other factors.
- The optimum electrospinning conditions were determined to be as follows: 12 wt% for the polymer concentration, 16 kV for the voltage, 0.1 ml/h for the feed rate and 15 cm for the tip-to-distance.
- Using the Taguchi method, the average diameter of fibers at the optimum conditions can be predicted be in the range of 242.10 to 257.92 nm at a confidence level 95%.
- The nanofiber diameter at the optimum conditions experimentally was found to be 258 ± 30 nm, which showed a good consistency with the estimated value.
- Ultimate tensile stress and Young's modulus of TPU at the optimum conditions was 12.66 ± 2.3 MPa and 0.39 ± 0.06 MPa, respectively. The fiber diameter increased, but tensile strength decreased by increasing the concentration of the polymer solution.

In conclusion, the Taguchi method was successfully applied to the optimization of electrospinning conditions for TPU nanofibers. In addition, the optimum conditions of the parameters for electrospun TPU nanofibers are economical for nanofiber production and the presented scaffold can mimic the structure of Extracellular Matrix (ECM).

Acknowledgments

The authors acknowledge the Nanofibers and Electrospinning Lab and Amirkabir University of Technology for the support to do this work.

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