Optimization of chitosan-polyvinylalcohol electrospinning process by response surface methodology (RSM)

A. Gholipour, S. H. Bahrami, M. Nouri

1 Department of Textile Engineering, Textile Research & Excellence Center, Amirkabir University of Technology, Tehran, Iran; e-mail: hajirb@aut.ac.ir
2 Department of Engineering and Technology, Textile group, Gilan University, Rasht, Iran.

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Abstract: Response Surface Methodology (RSM) is a collection of statistical and mathematical techniques useful for developing, improving, and optimizing processes. RSM was used to model and optimize the electrospinning parameters for the spinning of blend CS/PVA nanofibers. In this study, chitosan (CS)/polyvinyl alcohol (PVA) blend solutions (CS ($M_w=1 \times 10^6$) in 2% acetic acid and PVA ($M_w=12 \times 10^3$) in deionized water) with different blend ratio ranging from 10/90 to 50/50 were electrospun. CS/PVA (25/75) blend ratio was chosen as base and optimum ratio due to its suitable morphological properties and diameter. In a constant ratio of blend SEM analysis shows that the diameter of nanofibers changed by varying the voltage and extrusion rate in the electrospinning process. Voltage (10-25 KV) and polymer solutions extrusion rate of (0.2-1 ml/hr) from the nozzle were chosen as variables to control the fiber diameter at similar spinning distances (10 cm). Fiber diameter was correlated to production variables by using a second order polynomial function. The predicted fiber diameters were in good agreement with the experimental results.

Keywords: RSM, Chitosan, Electrospinning, Nanofibers, Optimization

Introduction

In the recent years, nanotechnology has attracted a lot of attention. The nanotechnology is used in several research fields such as nanophotocatalysis, electrospinning, etc. [1-3]. A variety of processes exist to fabricate nano-scale materials. The electrospinning process can be considered a variation of the better-known electrospray process [3]. It has received a dramatic revival of interests because of its potential to produce ultra fine fibers with diameter in the range of nanometer to sub-micrometer. This process produces continuous polymer fibers with diameters in the sub-micron range through the action of an external electric field imposed on a polymer solution or melt. Briefly, a high voltage is applied to overcome the surface tension of polymer solution or polymer melt, and then a charged jet is ejected. The jet extends on a straight line for a certain distance and then bends and follows a looping and spiraling path. These jets get dried to form nanofibers which are collected on a target (an electrically grounded metal sheet or a winder) as a nonwoven fabric. Non-woven textiles, composed of electrospun fibers, have a large specific surface area and small pore size compared to commercial textiles, making them excellent candidates for use in filtration and membrane applications [3, 4].

Response Surface Methodology (RSM) is a collection of statistical and mathematical techniques useful for developing, improving, and optimizing processes [5].
technique is an interesting method for optimization in several variable parameter systems. Yordem [6] investigated the effects of material and process parameters on the diameter of electrospun polyacrylonitrile fibers experimentally.

Response surface methodology (RSM) was utilized to design the experiments at the settings of solution concentration, voltage and the collector distance. It also imparted the evaluation of the significance of each parameter on the resultant fiber diameter. The investigations were carried out in the two-variable process domains of several collector distances as applied voltage and the solution concentration varied at a fixed polymer molecular weight [6].

Sukigaraa and coworkers [7] used the response surface methodology to model and optimize the electrospinning parameters for the spinning of regenerated nanoscale silk fibers from domestic silkworm, Bombyx mori. Electric field and silk concentrations were chosen as variables to control fiber diameter at different spinning distances. Fiber diameter was correlated to these variables by using a second order polynomial function.

Gu and coworkers [8] reported that polyacrylonitrile (PAN)/N,N-dimethyl formamide (DMF) solution as a precursor of carbon nanofibers was electrospun and fibers with diameters ranging from 200 to 1200 nm were obtained. A more systematic understanding of process parameters was obtained and a quantitative relationship between electrospinning parameters and average fiber diameter was established by response surface methodology (RSM). They found that the concentration of solution played an important role in the diameter of fibers and standard deviation of the fiber diameter. Whereas, applied voltage had no significant impact on the PAN fiber diameter and the standard deviation of the fiber diameter.

RSM is used in situations where several variables influence a feature (called the response) of the system [7]. The steps in the procedure are described briefly as follows:

1. Identification of variables \( \zeta_1, \zeta_2, \zeta_3, \ldots \) for response \( \eta \).
2. Calculation of corresponding coded variables \( x_1; x_2; x_3 \ldots \) by using the following equation.

\[
x_i = \frac{\zeta_i - \zeta_{Ai}}{\zeta_{Bi} - \zeta_{Ai}} / 2
\]

(1)

where \( \zeta_{Ai} \), \( \zeta_{Bi} \) refer to the high and low levels of the variables \( \zeta_i \); respectively.

3. Determining the empirical model by multiple regression analysis to generate theoretical responses (\( \hat{y} \)). The second-order model is widely used in RSM. The general equation for response \( \eta \) of the second-order model is given by:

\[
\eta = \beta_0 + \sum_{i=1}^{k} \beta_i x_i + \sum_{i=1}^{k} \beta_{ii} x_i^2 + \sum_{i<j=2}^{k} \beta_{ij} x_i x_j
\]

(2)

where \( k \) is the number of factors, \( x_i \) is the coded variables and \( \beta_{ij} \) are the coefficients.
4. Calculating the coefficients $\beta$ to fit the experimental data as close as possible. The relationship between the response and the variables is visualized by a response surface or contour plot to see the relative influence of the parameters, to find an optimum parameter combination and to predict experimental results for other parameter combinations. The electric fields and concentrations are the two variables identified in our study.

When $k=2$; the empirical model from the general Eq. (2) becomes

$$y = \beta_0 + \beta_1x_1 + \beta_2x_2 + \beta_{11}x_1^2 + \beta_{22}x_2^2 + \beta_{12}x_1x_2 + \varepsilon$$

(3)

where $y$ is the natural logarithm of the fiber diameter, $x_1$ is the coded electric field variable, $x_2$ is the coded concentration variable and $\varepsilon$ is the random error term [9].

The literature review showed that the response surface methodology was not used to model and optimize the electrospinning parameters for the spinning of blend Chitosan/PVA Nanofibers. In this paper, Response Surface Methodology (RSM) was used to model and optimize the electrospinning parameters for the spinning of blends CS/PVA blends. Chitosan (CS)/polyvinylalcohol (PVA) blend solutions with different blend ratio ranging between 10/90 and 50/50 were electrospun. CS/PVA (25/75) blend ratio was chosen as the base and optimum ratio due to its well morphological properties and diameter. Voltage (10-25 KV) and extrusion rate of polymer solutions (0.2-1 ml/hr) from the nozzle were chosen as variables to control fiber diameter at same spinning distances (10 cm). Fiber diameter was correlated to production variables by using a second order polynomial function.

**Results and discussion**

**Morphological study**

Chitosan is a cationic polysaccharide with amino groups at the C2 position, which are ionizable under acidic or neutral pH conditions. Therefore, the morphology and diameter of electrospun fibers will be seriously influenced by the weight ratio of PVA/CS. Fig. 1 shows SEM images of Cs/PVA blend fibers with different weight ratios of Cs to PVA under the same processing condition [19]. It shows that finer fibers were produced with increasing the chitosan content in the blend solution; on the other hand fibers became more fragile (Fig.1e). Although the 50/50 ratio of Cs/PVA produces the finest fiber, the fibers have got some micro cracks on the surface. With decreasing the PVA content the plasticizing effect reduces hence the brittleness of produced fibers increases. With increasing chitosan content in the blend, the number of amino groups which can be protonated in acidic media, increases and, therefore, the density of electrical charges on the surface of the jet increases and the jet is more affected by the electrical field. Thus, it draws the jet more and produces fiber with finer diameter. Pure chitosan (Fig.1f) due to its high viscosity cannot be electrospun.

Changing voltage will result in change in the diameter of the produced nanofibers at a constant extrusion rate. The voltage has been changed from 10KV to 25KV and the nanofibers obtained are shown in Fig. 2. As it can be seen from Fig. 6 with increasing the voltage, the diameter of the nanofibers is reduced. This may be due to change in electrostatic forces resulting in faster extrusion of the solution from needle.
**Fig. 1.** SEM photographs of nanofibrous mat with different weight ratio of CS to PVA: a) pure PVA, b) 10/90, c) 20/80, d) 25/75, e) 50/50, f) pure Chitosan; d=10 cm, V=15 KV; 10000×.

**Fig. 2.** SEM photographs of nanofibers that have been prepared in constant extrusion rate (R=1 ml/hr): a) 10 KV, b) 15 KV, c) 20 KV, d) 25 KV; d=10 cm, 10000 x.
By increasing the voltage the ejected jet is affected by higher electric field, so that the jet gets more and more extended in its path from the nozzle to the collector. Finally, the nanofibers become finer.

![Fig. 3](image)

**Fig. 3.** SEM photographs of nanofibers that have been prepared A) V=10KV, B) 20KV, C) 25 KV; a) 0.2 ml/hr, b) 0.5 ml/hr, c) 1 ml/hr; d=10 cm,10000 x.

**Tab. 1.** Change in diameter of nanofibers with changing the voltage or extrusion rate.

<table>
<thead>
<tr>
<th>Voltage (KV)</th>
<th>Extrusion Rate (ml/hr)</th>
<th>Diameter (nm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>10</td>
<td>0.2</td>
<td>481.0</td>
</tr>
<tr>
<td></td>
<td>0.5</td>
<td>461.5</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>326.0</td>
</tr>
<tr>
<td>15</td>
<td>0.2</td>
<td>480.5</td>
</tr>
<tr>
<td></td>
<td>0.5</td>
<td>402.1</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>300.0</td>
</tr>
<tr>
<td>20</td>
<td>0.2</td>
<td>461.4</td>
</tr>
<tr>
<td></td>
<td>0.5</td>
<td>384.7</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>296.7</td>
</tr>
<tr>
<td>25</td>
<td>0.2</td>
<td>454.6</td>
</tr>
<tr>
<td></td>
<td>0.5</td>
<td>373.2</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>291.0</td>
</tr>
</tbody>
</table>

The extrusion rate is a parameter of electrospinning process that has a different effect on nanofibers with different polymer (i.e. It causes less or more finesse in diameter or no significant effect). In this study, when the voltage was kept constant
and the extrusion rate varied, it was observed that with increasing the extrusion rate
the nanofibers diameter decreased (Fig. 3). This effect is shown in 3 different
voltages, in each constant voltage with increasing the extrusion rate (R=0.2) to (R=1)
the average diameter of nanofibers becomes finer (Table1).

Optimization and modeling the process by RSM

-Response function

This resulted in an uneven spacing of the levels as can be seen in Fig. 4. Coded and
Natural variables are listed in Table 2.

Tab. 2. Design of experiments (variables and levels).

<table>
<thead>
<tr>
<th>Experiment</th>
<th>Coded Variables x1</th>
<th>Coded Variables x2</th>
<th>Voltage (KV) ξ₁</th>
<th>Extrusion Rate (ml/hr) ξ₂</th>
<th>Diameter (nm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>-1</td>
<td>-1</td>
<td>10</td>
<td>0.2</td>
<td>481.0</td>
</tr>
<tr>
<td>2</td>
<td>-1</td>
<td>-0.25</td>
<td>10</td>
<td>0.5</td>
<td>461.5</td>
</tr>
<tr>
<td>3</td>
<td>-1</td>
<td>1</td>
<td>10</td>
<td>1</td>
<td>326.0</td>
</tr>
<tr>
<td>4</td>
<td>-0.33</td>
<td>-1</td>
<td>15</td>
<td>0.2</td>
<td>480.5</td>
</tr>
<tr>
<td>5</td>
<td>-0.33</td>
<td>-0.25</td>
<td>15</td>
<td>0.5</td>
<td>402.1</td>
</tr>
<tr>
<td>6</td>
<td>-0.33</td>
<td>1</td>
<td>15</td>
<td>1</td>
<td>300.0</td>
</tr>
<tr>
<td>7</td>
<td>0.33</td>
<td>-1</td>
<td>20</td>
<td>0.2</td>
<td>461.4</td>
</tr>
<tr>
<td>8</td>
<td>0.33</td>
<td>-0.25</td>
<td>20</td>
<td>0.5</td>
<td>384.7</td>
</tr>
<tr>
<td>9</td>
<td>0.33</td>
<td>1</td>
<td>20</td>
<td>1</td>
<td>296.7</td>
</tr>
<tr>
<td>10</td>
<td>1</td>
<td>-1</td>
<td>25</td>
<td>0.2</td>
<td>454.6</td>
</tr>
<tr>
<td>11</td>
<td>1</td>
<td>-0.25</td>
<td>25</td>
<td>0.5</td>
<td>373.2</td>
</tr>
<tr>
<td>12</td>
<td>1</td>
<td>1</td>
<td>25</td>
<td>1</td>
<td>291.0</td>
</tr>
</tbody>
</table>

By linear regression analysis of Eq. (3) the numerical values for coefficients (b₀; b₁; b₂; b₁₁; b₂₂; b₁₂) were obtained. The fitted second-order equation for the natural logarithmic fiber diameter is given by

\[ y = 378.065 - 24.324 x_1 - 82.975 x_2 + 11.606 x_1^2 + 1.887 x_2^2 + 1.457 x_1 x_2 \]  

(4)

P-values (a measure of the statistical significance) and R² (a measure of the percent of the response being represented by the variables) for regression model (Eq. (4)) are shown in Table 3. P-value is less than the significance level of 0.05, validating the adequacy of this model. The value of R² is 0.953. The model predicts a variability of 95%.
**Fig. 4.** (Experimental design) the values at the coordinate points show the mean fiber diameter (nm) measurements and coded values are shown in the brackets (voltage and extrusion rate).

**Tab. 3.** Significance probability (P-value) and correlation coefficient of linear regression for response surface equation.

<table>
<thead>
<tr>
<th>spinning distance (cm)</th>
<th>P_value</th>
<th>R</th>
<th>Adjusted R Square</th>
</tr>
</thead>
<tbody>
<tr>
<td>10</td>
<td>0.000</td>
<td>0.987</td>
<td>0.953</td>
</tr>
</tbody>
</table>

-Response surfaces of fiber diameter as a function of voltage and extrusion rate

**Fig. 5.** Contour plots of fiber diameters (nm) as a function of voltage and extrusion rate for 10 cm spinning distance. The corresponding experimental mean fiber diameters (nm) are placed in the contour plot (symbol + at experimental design).
Fig. 5 shows contour plots in the case of 10 cm spinning distance. The response indicates that changes in fiber diameter are more responsive to extrusion rate at the low voltage. High voltage of process gives low diameter of chitosan/PVA fibers. A voltage of 10 gives fiber diameters ranging from 326 to 481 nm while voltage of 25 gives fiber diameters ranging from 291 to 454 nm. The contour plot for the 10 cm spinning distance shows that the fiber diameter decreases as the extrusion rate is increased at a given or fixed voltage. The interaction effect of the voltage can also be observed.

The corresponding experimental mean fiber diameters used to build this function are shown in Fig. 5 (symbol +). The residual (difference between the experimental fiber diameters and the predicted fiber diameter) is less than the standard deviation of the predicted fiber diameters. However, this result follows the direction obtained from contour plots suggesting that the higher extrusion rate gives lower fiber diameter.

**The optimum processing window for nanofibers**

The center of the response surface system called the stationary point is a point representing minimum values of the response or the smallest fiber diameter. The stationary point is mathematically described by the following Eqs. (5) and (6). The fitted regression model, Eq. (4), in the matrix notation:

\[ \hat{y} = b_0 + X'\hat{b} + X'\hat{B}X \]  

where \( b_0\); \( \hat{b} \) are estimates of the intercept, the linear, and the second-order coefficients, respectively. \( X=[x_1, x_2] \) and \( \hat{B} = 2\times2 \) symmetric matrix.

The stationary point \( X_s \) is obtained by

\[ X_s = -\hat{B}^{-1}b / 2 \]

The stationary points were calculated using Eq. (6). For spinning distance of 10 cm the coded values are \( X_s= [-0.1929, 4.0756] \). The corresponding physical values are 16 kV (voltage), 2.23 ml/hr (extrusion rate). In the case of 10 cm spinning distance, higher extrusion rate with higher voltage produces smaller fiber diameter.

**Conclusions**

In this study, the Cs-PVA nanofibers were fabricated by electrospinning. Voltage ranging 10-25 KV, extrusion rate 0.2-1 ml/hr and 10 cm tip-to-collector distance were the basic process parameters. The 25/75 Cs/PVA is the best ratio in this condition. The average diameter changes with changing the voltage and the extrusion rate of polymer. With increasing the voltage, the diameter of the nanofibers is reduced but with increasing the extrusion rate the nanofibers diameter decreased. The response of the RSM method indicates that changes in fiber diameter are more responsive to extrusion rate at the low voltage. High voltage of the process gives low diameter of chitosan_PVA fibers. Voltage of 10 gives fiber diameters ranging from 326 to 481 nm while voltage of 25 gives fiber diameters ranging 291 to 454 nm. The contour plot for the 10 cm spinning distance shows that the fiber diameter decreases as the extrusion rate is increased at a given or fixed voltage. The stationary points were \( X_s= [-0.1929, 4.0756] \). The corresponding physical values are 16 kV (voltage), 2.23 ml/hr (extrusion rate).
rate). In the case of 10 cm spinning distance, higher extrusion rate with higher voltage produces smaller fiber diameter.

**Experimental**

**Materials**

Chitosan (Mw = 1000 kDa, 85% DD), poly(vinyl alcohol) (M_w = 94–120 kDa) and acetic acid (AA) were purchased from MERK, Co.

**Electrospinning procedures**

A high voltage power supply (10-25 kv) was employed to generate the electric field. At first chitosan solutions (3wt %) were prepared in acetic acid at 2-90% v/v concentrations. Then PVA was used to moderate the repelling interaction between polycationic chitosan molecules and to enhance the molecular entanglement. PVA was dissolved in distilled water (DW) at a concentration of 20 wt%, and CS was dissolved in AA-water solution (2 wt %) at a concentration of 3 wt%. A PVA-DW solution (20 wt %) was mixed with a CS-AA solution (3 wt %) in weight ratios of (Cs/PVA) 0/100(pure PVA), 10/90, 20/80, 25/85, 50/50 and 100/0(pure Chitosan), respectively [10]. Then, the mixed solutions were subjected to the electrospinning experiment. The applied voltage was 15 KV and the electrospinning distance (tip-to-collector distance: TCD) was 10 cm.

**References**