

Properties of Electrospun Poly(vinyl alcohol) Hydrogel Nanofibers Crosslinked with 1,2,3,4-Butanetetracarboxylic Acid

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ABSTRACT: Electrospun nanofibrous hydrogel membranes have been gaining significant importance due to the combination of unique physical properties of nanofibers and biocompatibility of hydrogels. Thus, they are considered as potential candidates for medical textile applications. This study deals with electrospinning of poly(vinyl alcohol) (PVA) hydrogel nanofibrous membranes. The chemical crosslinking of PVA with proportionate quantities of 1,2,3,4 butanetetracarboxylic acid (BTCA) was undertaken to form hydrogel structures. Cross-linked membranes were characterized by scanning electron microscopy, FT-IR and thermogravimetric analysis, water swelling, and durability tests. FT-IR analysis demonstrated the formation of ester linkages between PVA and BTCA and thermogravimetric analysis showed that crosslinking improved the thermal stability of the nanofibrous structure. Furthermore, the results indicated that crosslinking with BTCA improved water stability of PVA membranes and the nanofibrous structure was preserved after water treatment. It is envisaged that use of BTCA as a cross-linker to form hydrogel nanofibers could be a practical and a promising method for medical textile applications, especially for wound dressings given its nontoxicity and immiscibility with polymer solutions. © 2013 Wiley Periodicals, Inc. *J. Appl. Polym. Sci.* 129: 3140–3149, 2013

KEYWORDS: electrospinning; crosslinking; fibers; hydrophilic polymers; properties and characterization

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INTRODUCTION

Hydrogels are three-dimensional hydrophilic polymer networks that can absorb large amounts of water^{1,2} while maintaining their dimensional stability in their swollen state,³ which is achieved by several crosslinking methods. Because of their high water absorption characteristics, hydrogels exhibit similar properties to biological tissues^{4,5} and thus they are of interest in terms of tissue engineering applications.^{6,7} Hydrogels can be based upon natural polymers such as chitosan, alginate, gelatine, and collagen; as well as synthetic polymers including; poly(ethylene oxide), poly(vinyl alcohol), poly acrylates, methacrylates; and their derivatives and blends.^{1,3,8} Special properties and diverse raw material selection possibilities allows hydrogels to be used in a wide range of applications and research areas such as wound dressings, drug delivery systems, pads, dental materials, contact lenses, polymeric implants, filtration, separation, etc.⁸ Among these applications, the use of polymeric hydrogels as wound dressings have received the greatest attention and are currently available in the market.⁹ They possess excellent tissue compatibility and provide rapid wound healing by creating moist environment and maintaining high humidity in the wound area,^{10,11} while reducing the pain by cooling the surface of the wound.¹²

In recent years, in the area of medical textiles and especially in tissue engineering, nanotechnology and nanofibers have received the greatest attention due to their unique structure and hence specific properties. Because in any polymeric solids and hydrogels, the diffusion kinetics is proportional to the specific surface area,¹³ nanofibers are ideal candidates for wound dressings due to their high surface area to volume or mass ratio and small interfiber pore sizes with high porosity. Electrospinning is the most versatile process for producing nanofibers through an electrically charged jet of polymer solution or polymer melt.¹⁴ Electrospinning requires mainly a high voltage supply, a capillary tube and a grounded collector. By applying the high voltage to the fluid droplet at the capillary tube, it deforms the droplet into a conical shape (Taylor cone¹⁵) and when the electrical potential is increased to a sufficiently high value to overcome surface tension, an electrically charged jet of fluid is created. The solvent within the solution begins to evaporate or if a polymer melt is used, the melt begins to solidify. As a result, nano-scaled polymer fibers are deposited on the grounded collector.^{16–19} The appearance of the collected fibers depends upon many factors including; polymer solution parameters, processing conditions which include the applied voltage, temperature and

effects of collector and ambient conditions. The detailed principles of electrospinning process and the effects of process parameters on the resultant fiber properties have been extensively researched by many researchers and can be found elsewhere.^{14,17–24}

Electrospun poly(vinyl alcohol) (PVA) hydrogel nanofibers have been one of the most extensively studied topics due to biocompatibility, nontoxicity and ease of processability of PVA.^{25–29} PVA is considered as an ideal candidate for nanofibrous medical textiles such as wound dressings, drug delivery systems and artificial skins. It is a highly hydrophilic polymer and polymer solutions can be prepared by dissolving PVA in water and be easily electrospun into nanofibers. To make PVA water insoluble and to form PVA hydrogels, several crosslinking methods have been used such as freezing/thawing, methanol treatment, chemical crosslinking, and irradiation.^{28,30,31} For electrospun PVA hydrogel nanofibers, methanol treatment and chemical crosslinking with glutaraldehyde are found to be most used treatments adopted in the literature. It has been reported that the addition of glutaraldehyde into the polymer solution is problematic due to an increase in the solution viscosity.³² Thus generally immersion of nanofibrous PVA membranes into a glutaraldehyde solution (in acetone, etc)^{33,34} or treatment with glutaraldehyde vapor^{35–37} have been applied. Correspondingly, methanol treatment has been carried out by immersion into pure methanol for 8–24 h.^{38,39} Both of these methods have been applied as a post treatment and are reported to require long processing times. More to the point, treatment with glutaraldehyde has potential toxicity problems,²⁸ which is not acceptable for tissue engineering applications. Thus in this study, the crosslinking of PVA with BTCA (1,2,3,4 butanetetracarboxylic acid) was selected and the properties of the resultant fibers were investigated. To the best of authors' knowledge, stabilization of PVA with BTCA has been carried out for the first time in this study. BTCA is a nontoxic, formaldehyde-free⁴⁰ crosslinking agent (Figure 1)⁴¹ and could directly be added into the spinning solutions, which creates the prime condition for crosslinking in the present work. BTCA with four carboxylic acid groups can form ester bonds with hydroxyl groups. Esterification can be achieved by heat treatment and generally salts of weak acids are used as catalysts for acceleration of the reaction.⁴² BTCA is extensively researched for imparting crease resistance to cotton fabrics⁴³ and enhancing the durability of several functional agents such as chitosan,⁴⁴ cyclodextrins,⁴⁵ microcapsules,⁴⁶ etc. on textiles. Combination of BTCA with PVA has only appeared in the study of Zhu et al.⁴⁷ where the abrasion resistance of durable press finished cotton fabrics were improved by the addition of PVA.

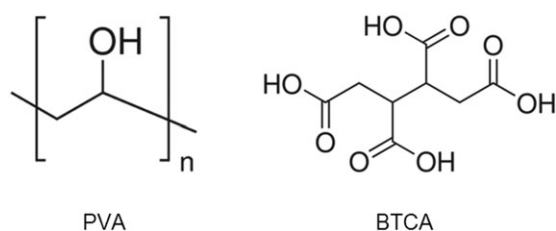


Figure 1. Schematic representation of PVA and BTCA.

It was reported that PVA esterifies with BTCA and improves the abrasion resistance by decreasing the amount of crosslinkages between cotton and BTCA.

In this study, crosslinking of PVA hydrogel nanofibers by BTCA and its effects on the resultant fiber morphology, as well as water/artificial serum absorption capabilities were investigated. Furthermore, crosslinked PVA hydrogel nanofiber structures were characterized by means of FT-IR spectroscopy and TGA.

EXPERIMENTAL

Materials

Poly (vinyl alcohol), (PVA) with molecular weight of 89,000–98,000 g mol⁻¹ (99% hydrolyzed), BTCA (1,2,3,4-butanetetracarboxylic acid) and sodium hypophosphite monohydrate (NaPO₂H₂·H₂O) were obtained from Sigma Aldrich. A polyoxyethylene (20) sorbitan monooleate-based nonionic surfactant (Tween 80) was also used.

Electrospinning

A 12.5% PVA stock solution was prepared by dissolving PVA powder in distilled water at room temperature and stirred for at least 2 h at 80°C. After allowing the solution to cool down to room temperature, 0.06 mL g_{polymer}⁻¹ (v/w) nonionic surfactant was added to decrease the surface tension of the spinning solution and stirred for further 15 min. BTCA, as a crosslinking agent, was directly added into the spinning solution with sodium hypophosphite monohydrate as a catalyst in ratio of 2 : 1 (w/w) followed by stirring for 15 min. To examine the effects of amounts of the crosslinking agent, 1, 2, 3, and 5% BTCA (w/w polymer) concentrations were used and are encoded throughout the article as B1, B2, B3, and B5, respectively.

Electrospinning of the polymer solutions was carried out by a set-up consisting of a syringe (10 mL) and needle (3-cm long, 22 gauges, and flat tip), a ground electrode and a high voltage supply (Spellman High Voltage DC Supply). Polymer solutions were electrospun at a voltage of 12 kV, a tip-to-collector distance of 10 cm with a feeding rate of 0.2 mL h⁻¹. A grounded stationary rectangular metal collector covered by a piece of aluminum foil was used for the nanofiber deposition.

After electrospinning, PVA/BTCA nanofibrous mats were heat set at 180°C for 2 min in an oven to enhance the esterification reaction. To compare the performance of BTCA crosslinked PVA membranes, a widely used crosslinking method by methanol was also used for pure PVA nanofibers. To do this, pure PVA nanofibers were immersed into pure methanol and treated for 8 h at room temperature. Then the methanol-treated PVA membranes were dried under ventilation at room temperature for 24 h. Methanol treated samples are encoded as M throughout the article.

Characterization

Viscosity of the polymer solutions was measured by using Brookfield DV-III Rheometer with the spindle type SC4-27 at 30 rpm. Surface tension measurements were carried out by a Krüss Easy Dyne Analyser by Plate Method. Conductivity measurements were carried out using a J.P. Selecta Conductivity

Table I. Parameters of PVA and PVA/BTCA Polymer Solutions and Diameters of Resultant Submicron Fibers

	pH	Viscosity (cp)	Conductivity ($\mu\text{S cm}^{-1}$)	Surface tension (mN m^{-1})	Mean fiber diameter (nm)	Standard deviation of mean fiber diameter
PVA	5.73	666	650	63.2	203.8	36.3
B1	4.04	600	972	61.3	303.9	59.9
B2	3.61	600	1230	61.4	314.5	83.9
B3	3.30	600	1558	61.0	346.0	99.2
B5	2.99	600	2140	60.4	375.0	123.7

meter, CD-2004 and pH tests by Hanna HI 8424 pHmeter, at room temperature.

The morphology of the electrospun PVA nanofibers was characterized using scanning electron microscopy (SEM, Hitachi S-3400N). Each sample was coated with thin film of gold using a Polaron SC7620 ion sputtering device for 60 s. Fiber diameters were determined by using Image J software. Fiber diameters were measured by using SEM images by drawing straight lines perpendicular to the fiber axis. The pixel values of the lines were converted to diameter values. Twenty measurements were carried out from the different parts of each sample.

Fourier transform infrared spectroscopy (FT-IR) analysis were carried out to identify the esterification of PVA and BTCA using a Thermo Scientific Nicolet iS10 FT-IR spectrometer. Additionally, to eliminate ambiguity in interpretation of FT-IR spectrometer i.e., an ester carbonyl band or a carboxyl carbonyl band,⁴⁵ a post alkaline treatment with 0.1M NaOH solution at room temperature for 2 min,⁴⁸ was also applied to PVA/BTCA samples to convert the carboxyl groups to carboxylate groups before carrying out further FT-IR test and analysis.

The thermal behavior of PVA and crosslinked PVA samples was investigated by thermogravimetric analysis (TGA) (SDT 2960 simultaneous DTA-TGA instrument) by heating samples from room temperature to 600°C under continuous nitrogen purge at the rate of 10 mL min⁻¹.

Swelling, Absorptivity, and Weight Loss Tests

Swelling behavior of crosslinked PVA membranes were tested by measuring the initial weight of the dry samples and subsequently after they were immersed into distilled water (pH = 6.2) for 24 h. Each test was repeated three times. Before measuring the weight of the swollen samples, the excess surface water was removed by filter papers. The swelling ratio was calculated using the following equation:

$$\text{Swelling ratio (g/g)} = \frac{W_s - W_0}{W_0} \quad (1)$$

where, W_0 is the initial dry weight and W_s the weight of swollen samples.

Because swelling test method involves manual removal of excess water and thus possible inaccuracy in the recorded results, an additional absorptivity test using the centrifuge method were carried out to reinforce the findings and allow to unbiased discussion of the results. In this method, nanofibrous membranes

were immersed in distilled water for 30 min and centrifuged at 1600 rpm for 15 min using Thermo Scientific Heraeus Labofuge 200 centrifuge. The wet weights (W_s) of the samples were recorded after centrifuging and they were then dried in an oven until a constant dry weight was obtained. The dry weight (W_0) was then recorded and absorptivity (g/g) of the hydrogel fibers was calculated using the same equation as in the swelling test [eq. (1)]. This process was repeated with the fibers immersed in Solution A which is a closer match to artificial serum for wounds. Solution A consists of 8.298 g of NaCl and 0.368 g of CaCl₂ in 1 L of distilled water.⁴⁹

To address the durability of the samples in water, nanofibrous membranes were immersed in water at room temperature for 24 h and in boiling water for 1 h. Then they were dried at room temperature and weight loss of the samples was calculated as follows:

$$\text{Weight loss (\%)} = \frac{W_0 - W_1}{W_0} \times 100 \quad (2)$$

where W_0 is the initial weight and W_1 the dry weight after water treatment.

RESULTS AND DISCUSSION

Crosslinking of PVA nanofibers to form hydrogel structures are generally carried out by post treatments of several chemicals such as glutaraldehyde and methanol requiring long processing times. These methods have also toxicity issues and associated health problems. Thus in this study, cross-linking of PVA nanofibers with nontoxic BTCA was investigated. BTCA and a selected catalyst were directly added into the polymer solution and after electrospinning a short period of heat treatment was applied. Because the composition of the spinning solution is directly related to the resultant fiber morphology, parameters governing the behavior of the spin solution need to be taken into account. Table I displays changes in some of the most important solution parameters after the addition of BTCA. The pH of the solutions was noted to decrease with increase in BTCA amounts, as expected due to the acidic nature of BTCA. Correspondingly, the electrical conductivity of the solutions increased by a large extent with the increase in BTCA concentration. Solutions with BTCA had slightly lower viscosity values compared to pure PVA solution, however no change was observed in the viscosity of the polymer solutions due to the increase in BTCA concentration. The surface tension of the

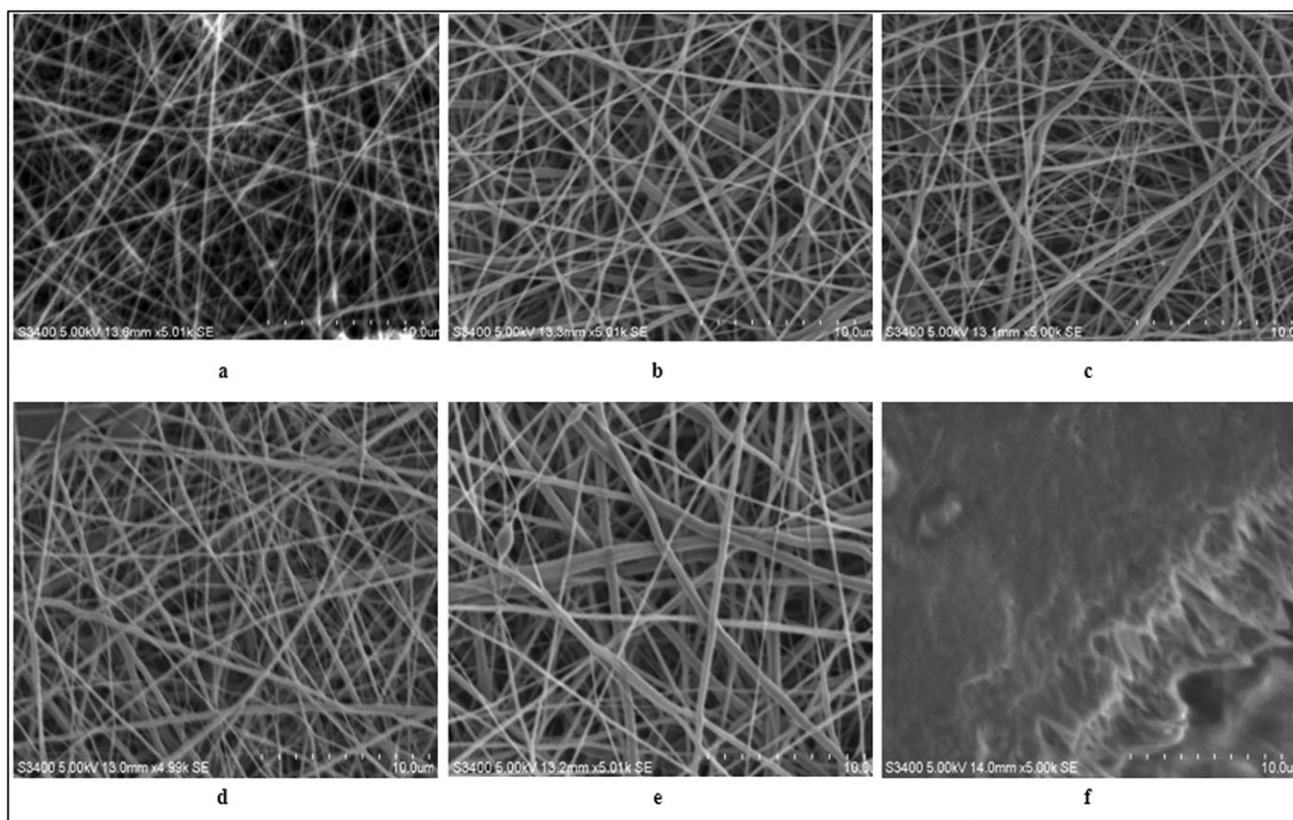


Figure 2. SEM images of (a) pure PVA nanofibers, PVA/BTCA crosslinked nanofibers with different BTCA concentrations of (b) 1% (c) 2% (d) 3% (e) 5% and (f) methanol treated PVA nanofibers.

polymer solutions were not affected significantly by the addition of BTCA either.

Figure 2 represents the scanning electron micrographs of PVA nanofibers [Figure 2(a)] and PVA/BTCA crosslinked hydrogel nanofibers [Figure 2(b–e)]. The fiber diameters were expected to decrease by the addition of BTCA due to the higher conductivity of the polymer solution. On the contrary, the resultant fiber diameters increased and this increase was more pronounced at higher concentrations of BTCA (Table I) although the increase in diameter was not quite universal. Fiber diameter distribution histograms shown in Figure 3, highlights these variations with increasing addition of BTCA. More importantly, when the standard deviations of mean fiber diameters were taken into account (Table I), it is quite clear that the variation range in fiber diameter increases with the increase in BTCA concentration. This means that increase in BTCA concentration leads to the production of more heterogeneous nanofibrous structures. In the study made by Hayati et al.,⁵⁰ in which the effects of conductivity were investigated, it has been illustrated that high conducting fluids produced highly unstable streams, resulting in a broader diameter distribution. In confirmation of this study, the heterogeneity in fiber diameter observed in our research with the increase in the BTCA concentration (especially for 5% BTCA concentration) could be connected to high conductivity of the polymer solutions. Alternatively, Son et al.⁵¹ proposed that the protonation of PVA under acidic conditions

leads to lower mobility under an external electric field, and the repulsive forces between the protonated PVA backbones partially inhibit the formation of continuous jets during electrospinning. In fact, in our work, with the increase in the BTCA concentration, same difficulties in electrospinning process occurred (especially for 5% BTCA concentration). Thus, these variations in fiber diameter could be as a result of both the high conductivity and the difficulties in the electrospinning at higher BTCA concentrations due to the highly acidic state of the solution at the tip of the needle.

To compare BTCA crosslinking, popularly used methanol treatment technique was also applied to PVA nanofibers. It is claimed that methanol treatment increases the number of physical crosslinks by removal of residual water within the fibers and allows intermolecular hydrogen bonding.³⁸ However, in our trials after 8 h treatment, the nanofibrous structure of the membrane was totally destroyed and a film-like structure occurred as shown in Figure 2(f). The handle of the membranes became harsh and fragile, with a semitransparent appearance. This is thought to be due to the lower molecular weight of the PVA studied in the current work compared to those used for methanol treatment in the literature. Thus as a further study, on optimization of methanol treatment is recommended with respect to polymer type and solution parameters.

When BTCA including PVA nanofiber membranes were subjected to heat treatment, an esterification reaction was expected

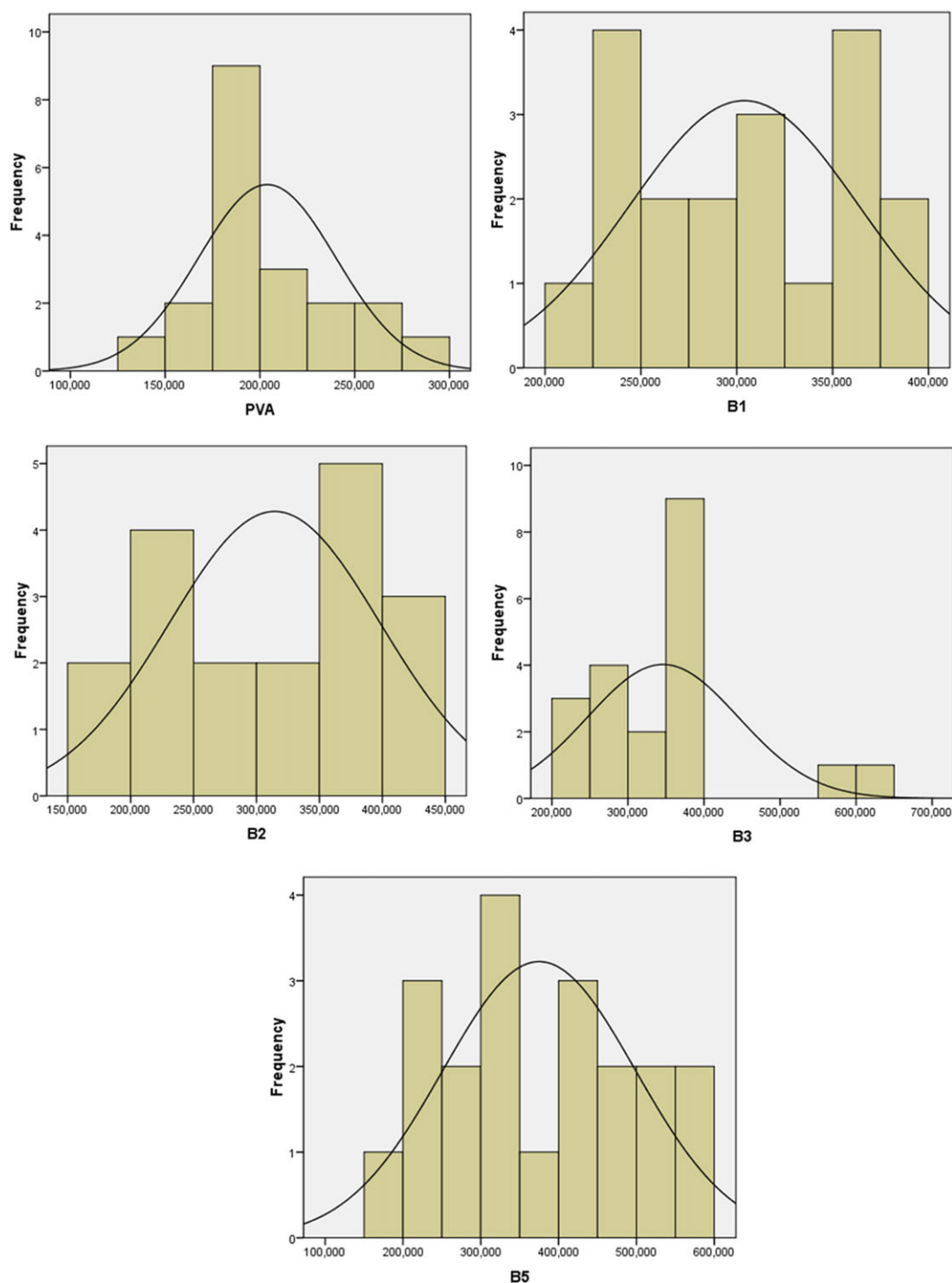


Figure 3. Fiber diameter distribution histograms of pure PVA nanofibers, PVA/BTCA crosslinked nanofibers with different BTCA concentrations. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

to form between carboxyl groups of BTCA and hydroxyl groups of PVA. Figure 4 illustrates the FT-IR spectra of pure PVA nanofibers and PVA/BTCA hydrogel nanofibers after heat treatment. New vibration bands were observed for PVA/BTCA nanofibers (B1, B2, B3, and B5) around $1700\text{--}1710\text{ cm}^{-1}$ which can be due to the formation of ester C=O groups. Additionally, a double

peak formation was observed at 1135 and 1154 cm^{-1} which could be assigned to the C—O stretching of esters. It is known that the bands around $1700\text{--}1750\text{ cm}^{-1}$ could be as a result of either ester carbonyl band or a carboxyl carbonyl band.^{41,45,46} Therefore, a post alkaline treatment was applied to PVA/BTCA samples to convert the carboxyl groups to carboxylate groups.

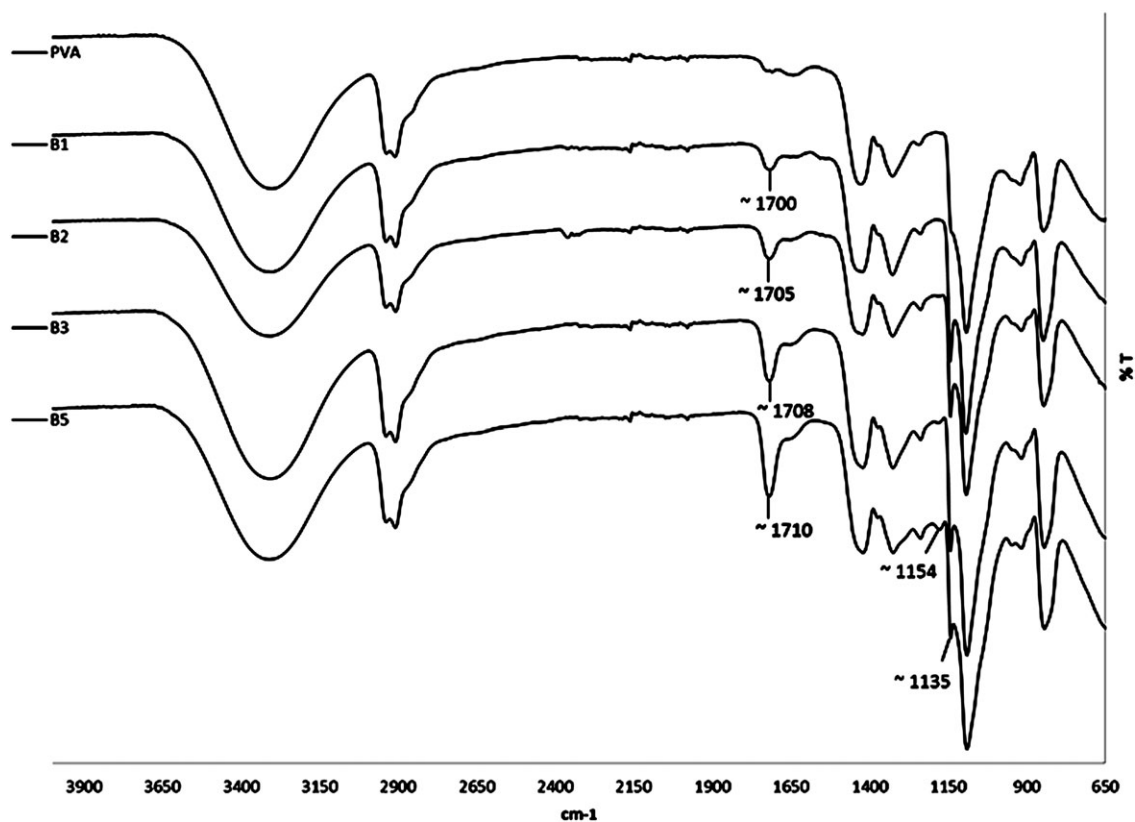


Figure 4. FT-IR spectra of pure PVA nanofibers and BTCA crosslinked PVA hydrogel nanofibers.

Figure 5 shows the FT-IR spectra of PVA/BTCA (5% BTCA, w/w) after heat treatment and after post alkaline treatment. A new band emerged at 1556 cm^{-1} attributing to carboxylate anions af-

ter alkaline treatment, and the ester carbonyl band was left unchanged with a lower intensity, which further confirms the validation of ester link formation between PVA and BTCA.

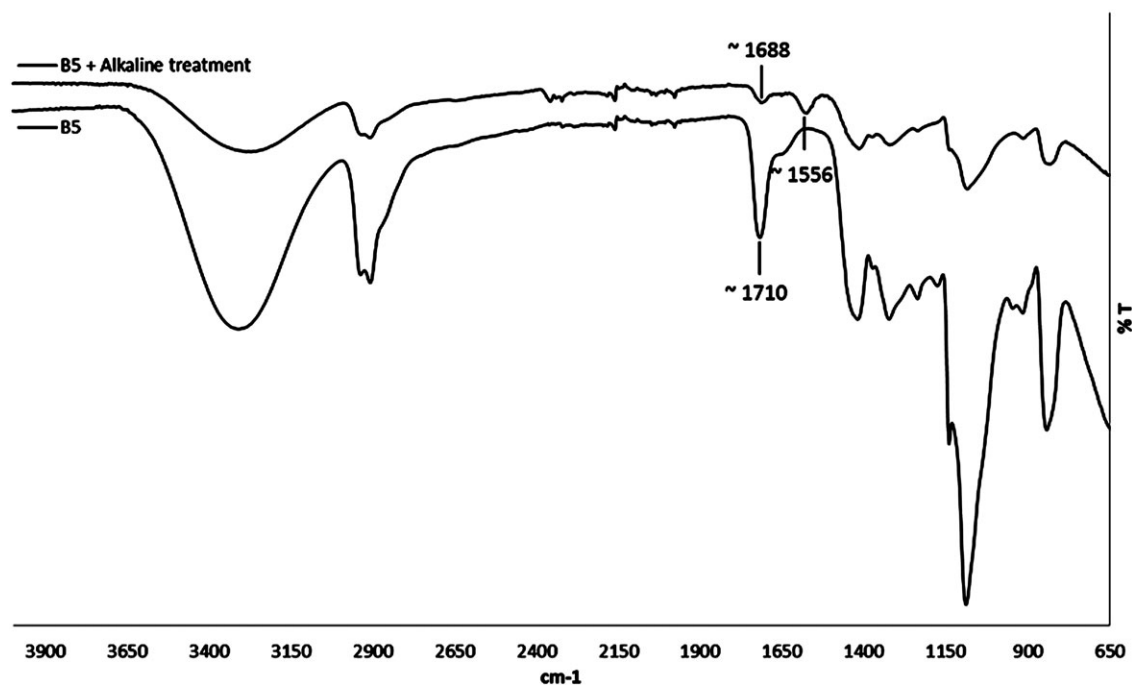


Figure 5. FT-IR spectra of PVA hydrogel nanofibers crosslinked with 5% BTCA before and after alkaline treatment.

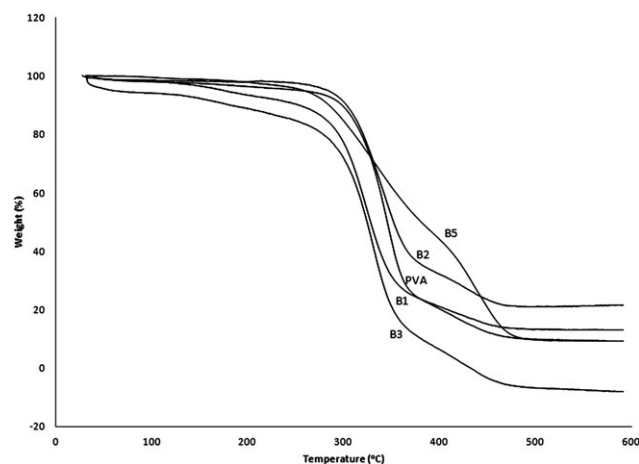


Figure 6. TGA curves of PVA nanofibers and crosslinked PVA hydrogel nanofibers.

Thermal stability of the electrospun PVA and PVA/BTCA cross-linked nanofibers was measured using thermogravimetric analysis (TGA) in nitrogen atmosphere. TG and DTG (differential thermogravimetry) curves are shown in Figures 6 and 7, respectively. It is clear that pure PVA nanofibers had two degradation steps, the elimination reactions^{34,52} started at around 305°C and the breakdown of the polymer backbone (mostly chain-scission reactions⁵²) started at around 375°C as a second stage. Pure PVA nanofibers lost half of its weight at around 345°C. The thermal degradation properties of the crosslinked PVA nanofibers with

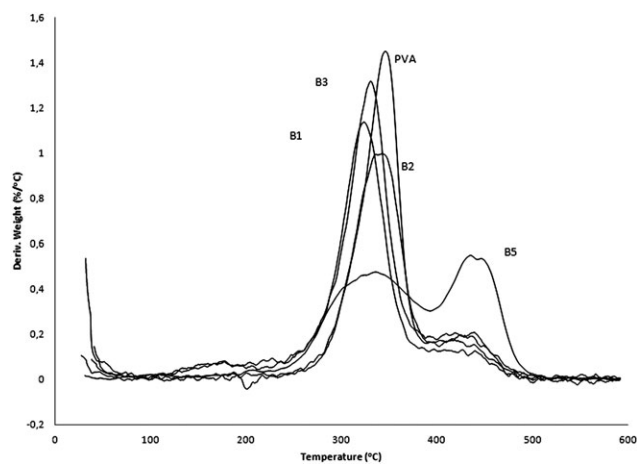


Figure 7. DTG curves of PVA nanofibers and crosslinked PVA hydrogel nanofibers.

BTCA of 1–3% showed similar tendencies to pure PVA nanofibers and the differences were not significantly clear. But in general, the peak degradation temperatures with maximum weight loss rates were lower for the first stage (around 320–335°C) and higher for the second stage (around 430–440°C) compared to pure PVA nanofibers (~345°C and 416°C for the first and the second stage, respectively). These differences give some provision about the crosslinking of the polymer. On the other hand, 5% BTCA cross-linked PVA nanofibers were characterized by a different thermal curve and the difference in the degradation

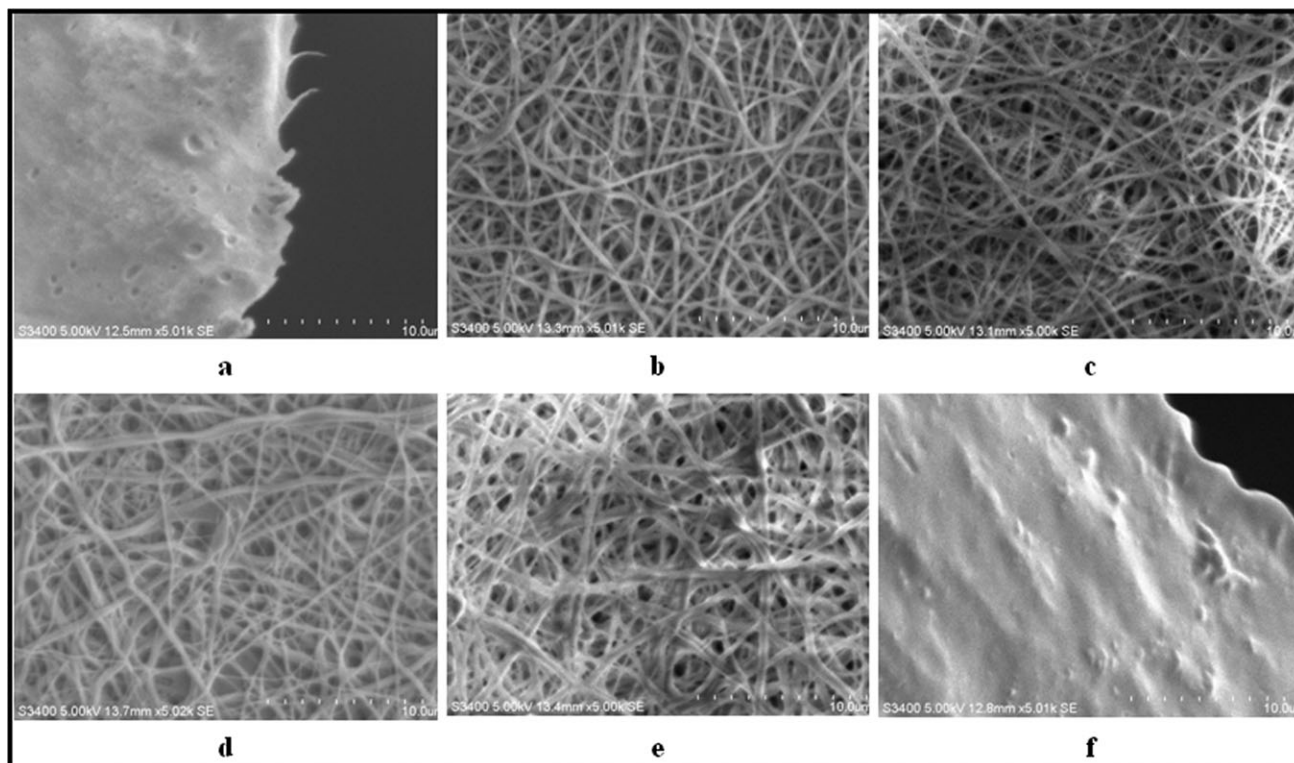


Figure 8. SEM images of nanofibers after immersion of water for 24 h (a) pure PVA nanofibers, PVA/BTCA crosslinked nanofibers with different BTCA concentrations of (b) 1% (c) 2% (d) 3% (e) 5% and (f) methanol treated PVA nanofibers.

Table II. Weight Loss Percentage of Pure PVA Nanofibers and Crosslinked PVA Hydrogel Nanofibers

	Weight loss (%)	
	24 h in water at room temperature	1 h in boiling water
PVA	94.1	100.0
B1	6.1	22.2
B2	6.4	16.7
B3	3.2	5.2
B5	3.0	3.8
M	18.4	100.0

process is quite clear. The relatively wider DTG curves observed for B5 is most likely to be due to the prolonged degradation time resulting from better and possibly higher crosslinking density. Additionally, B5 sample lost half of its weight around 380°C, which is higher compared to pure PVA nanofibers. Pure PVA nanofibers' weight loss was around 15% for the second stage whereas weight loss percentage of B5 in the second stage increased to as much as ~36%. This categorically confirms that increase in thermal stability is as a direct consequence of crosslinking with BTCA.

Water resistance of the samples was measured by immersing the membranes into distilled water for 24 h and boiling water for 1 h (Figure 8 and Table II). When pure PVA nanofiber membranes were immersed in water, they shrunk immediately and became fully transparent. On the other hand, BTCA crosslinked nanofibers became bulky and no change in color was observed. Figure 8 shows the scanning electron micrographs of the samples after 24 h water treatment and drying. The nanofibrous structure of pure PVA nanofibers was totally destroyed by water due to high solubility [Figure 8(a)]. They lost ~94% of their weights after the treatment in water for 24 h at room temperature. With the immersion into boiling water, an immediate disintegration of the structure was observed followed by fast dissolution of the remains. Methanol treated PVA nanofibers were also totally dissolved in boiling water. Interestingly though,

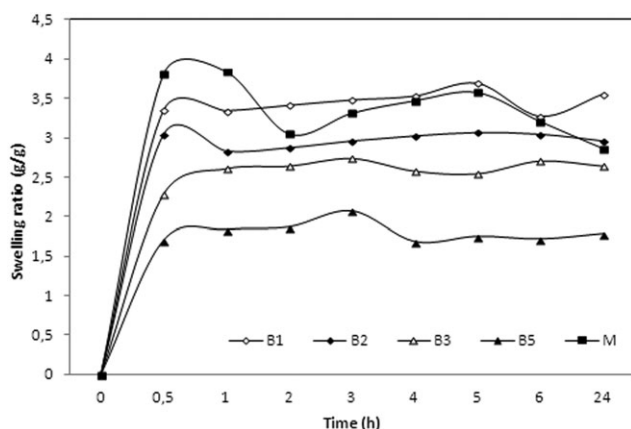


Figure 9. Swelling ratio of crosslinked PVA hydrogel nanofiber membranes as a function of time.

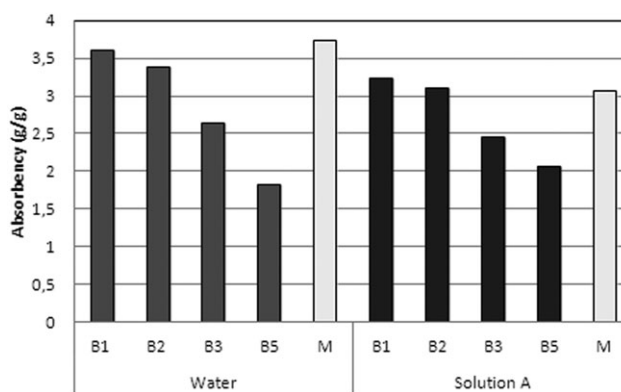


Figure 10. Water and Solution A absorbency of crosslinked PVA hydrogel nanofibers. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

water resistance of PVA nanofibers was significantly improved by crosslinking with BTCA as shown in Table II. Nanofibrous structure of the membranes was observed to be preserved after water treatment [Figure 8(b–e)]. Even the weight loss of the crosslinked samples with BTCA concentration of 1% was calculated to be around 6% after 24 h water treatment. With the increase in BTCA concentration, the weight loss percentage of the samples reduced further, as expected.

Swelling tests indicated that (Figure 9) BTCA crosslinked PVA samples could swell between 150 and 350% of their initial dry weight. Swelling ratio decreased with the increase in the BTCA concentration. It was observed that, after 30 min treatment with water, the swelling ratio did not change significantly for all concentrations of BTCA. The swelling behavior of methanol treated PVA was found to be similar to PVA/BTCA (1% concentration, B1).

Swelling test includes a manual surface water removal by filter paper, which could result in inaccurate conclusions. To verify the swelling results, water and artificial serum (Solution A) absorbency tests were also carried out, which is a common test for wound dressings. The results of these tests (Figure 10) were found to be similar to the swelling tests. Both water and solution A absorbency decreased with the increase in crosslinking concentration. Solution A absorbency of the samples were found to be slightly lower compared to water absorbency due to the ionic effect. Overall, swelling results of the crosslinked PVA were not very high. This could be due to the lower molecular weight of the PVA polymer. Further research using high molecular weight PVA crosslinked with BTCA as well as including other highly hygroscopic natural polymers such as alginates are planned to be investigated at a later date.

CONCLUSIONS

Crosslinking of PVA nanofibers with BTCA was proven to be effective for production of water stable hydrophilic PVA nanofibrous hydrogels. It was observed that BTCA crosslinked PVA hydrogel nanofibers had higher fiber diameters compared to pure PVA nanofibers. The use of BTCA led to the formation of heterogeneous nanofibrous structures and the variation range in fiber diameter increased with the increase in BTCA

concentration. Crosslink formation between BTCA and PVA was confirmed by FT-IR and TGA analysis. BTCA crosslinker was shown to be a better choice given its nontoxic nature and better miscibility with PVA spinning solution prior to electrospinning. It was established that BTCA crosslinked nanofibers preserved their nanofibrous structure after cold and hot water treatments. The weight loss in water was found to be quite low and swelling ratios differed depending on the crosslinking density. BTCA crosslinked PVA hydrogel nanofibers are believed to have good potentials for biotechnological and medical textile applications.

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