

Preparation and Characterization of Polycaprolactone/ Diclofenac Sodium and Poly(vinyl alcohol)/Tetracycline Hydrochloride Fiber Mats and Their Release of the Model Drugs

Kamonrat KANAWUNG,¹ Kanokwan PANITCHANAPAN,¹ Siri-orn PUANGMALEE,¹
Witchuporn UTOK,¹ Narumol KREUA-ONGARJNUKOL,¹ Ratthapol RANGKUPAN,²
Chidchanok MEECHASUE,³ and Pitt SUPAPHOL^{4,†}

¹*Department of Industrial Chemistry, Faculty of Applied Science, King Mongkut's Institute
of Technology North Bangkok, Bangkok 10800, THAILAND*

²*Metallurgy and Materials Science Research Institute, Chulalongkorn University, Bangkok 10330, THAILAND*

³*Department of Materials Technology, Faculty of Science, Ramkhamhaeng University, Bangkok 10240, THAILAND*

⁴*Technological Center for Electrospun Fibers and The Petroleum and Petrochemical College,
Chulalongkorn University, Bangkok 10330, THAILAND*

(Received April 17, 2006; Accepted January 24, 2007; Published March 5, 2007)

ABSTRACT: In the present contribution, electrospinning was used to fabricate ultrafine fiber mats from neat polycaprolactone (PCL) and poly(vinyl alcohol) (PVA) solutions as well as PVA/sodium alginate (SA) blend solutions and the PCL and PVA solutions that contained diclofenac sodium (DS) and tetracycline hydrochloride (TH) as the model drugs. The effects of solution and process parameters (*i.e.*, solution concentration, applied electrical potential, and collection distance) on morphological appearance and size of the as-spun PCL, PVA, and PVA/SA fibers were investigated. Generally, the average fiber diameter increased with increasing solution concentration and decreased with increasing both the applied electrical potential and the collection distance. Incorporation of the model drugs caused the resulting as-spun fibers to be larger in their diameters. The cumulative release of the model drugs from drug-loaded as-spun PCL and PVA fiber mats increased monotonically with increasing immersion time and became practically constant at long immersion times. Finally, a thin layer of PVA/SA fibers that were coated on TH-loaded PVA fiber mats caused the total amount of the drug released to decrease appreciably. [doi:10.1295/polymj.PJ2006011]

KEY WORDS Electrospinning / Polycaprolactone / Poly(vinyl alcohol) / Sodium Alginate / Drug Delivery /

Electrostatic spinning or electrospinning is a process by which a mat of ultrafine fibers with diameters of the individual fibers in sub-micrometer down to nanometer range can be fabricated. These ultrafine fibers exhibit several interesting characteristics, *e.g.*, high surface area to mass or volume ratio and flexibility for surface functionalization; while the as-spun fiber mat exhibits a high porosity with pore size being in sub-micrometer length scale.^{1,2} These unique properties render electrospun ultrafine fiber mats as excellent candidates for potential use in various biomedical applications, *e.g.*, tissue engineering scaffolds,^{3–6} DNA delivery systems,⁷ and drug delivery systems.^{8–12}

Fabrication of ultrafine fibers by electrospinning process concerns with the application of a high electrical potential from an emitting electrode of a high-voltage power supply to a polymer liquid across a finite distance between a conductive nozzle and a grounded collector.¹³ The Coulombic repulsion force between charges of the same polarity generated in the polymer liquid destabilizes the partially-spherical droplet of the polymer liquid located at the tip of the nozzle to finally form a droplet of a conical shape (*i.e.*, the

Taylor cone). Further increase in the electrostatic field strength beyond a critical value causes the Coulombic repulsion force to finally exceed that of the surface tension, resulting in an ejection of a charged stream of the polymer liquid (*i.e.*, the charged jet) from the apex of the cone. The charged jet travels in a linear manner for a short distance before undergoing a bending instability, resulting in a looping trajectory of the jet.¹⁴ During its flight to the collector, the charged jet elongates and, simultaneously, dries out or solidifies, leaving ultrafine fibers on the collector.

Electrospun fiber mats from a good number of polymers have been developed as the matrix materials for delivery of drugs. Poly(lactic acid) (PLA) and poly(ethylene-*co*-vinyl acetate) (PEVA) were successfully electrospun with tetracycline hydrochloride (TH) (an antibiotic drug) by Kenawy *et al.*⁸ It appeared that the total amount of TH released from corresponding cast films was lower than that from the as-spun fiber mats, due possibly to the much lower surface area.⁸ Zong *et al.*⁹ also used PLA as the matrix for delivery of mefoxin (an antibiotic drug). They arrived at a similar finding to that reported by Kenawy *et al.*⁸ For

[†]To whom correspondence should be addressed (E-mail: pitt.s@chula.ac.th).

poorly water-soluble drugs, such as itraconazole (an anti-fungal drug) and ketanserlin (a drug for ischemic acute renal failure), polyurethane, a non-biodegradable polymer, was used as the matrix.¹¹ It was concluded that the release of poorly water-soluble drugs could be achieved using a water-insoluble polymer and the rate of release could be tailored by varying the drug to polymer ratio.¹¹

Over the past few years, many researchers have investigated various parameters affecting morphology and diameters of electrospun polycaprolactone (PCL) fibers, *e.g.*, solution concentration, solvent system, applied electrical potential,^{15,16} and rotational speed of the rotating collection device.¹⁵ Potential uses of the as-spun PCL fiber mats are, for examples, artificial tissue grafts/scaffolds for engineered myocardium,¹⁷ cartilage,¹⁸ and bone,⁶ and delivery vehicles for heparin.¹⁹ Likewise, many researchers have investigated various parameters affecting morphology and diameters of electrospun poly(vinyl alcohol) (PVA) fibers, *e.g.*, solution concentration, solution flow rate, degree of hydrolysis, applied electrical potential, collection distance, ionic salt addition,²⁰ molecular weight of PVA,^{21–23} pH,²⁴ surfactant addition,²⁵ and type of collector.²⁶ Potential uses of the as-spun PVA fiber mats are, for examples, immobilization membranes for cellulase²⁷ and delivery membranes of bovine serum albumin (BSA),²⁸ and sodium salicylate, diclofenac sodium, naproxen, and indomethacin.¹²

In the present contribution, electrospun PCL and PVA fiber mats were fabricated as carriers for delivery of model drugs. These materials were chosen due to its biocompatibility, non-toxicity, good water permeability, and, particularly, good electro-spinnability. Various parameters (*i.e.*, solution concentration, applied electrical potential, and collection distance) affecting morphological appearance and size of the as-spun fibers were investigated using scanning electron microscopy (SEM). The optimal conditions producing uniform and smooth fibers were chosen to prepare electrospun fiber mats that contained diclofenac sodium (DS) or tetracycline hydrochloride (TH) in various amounts. The release characteristics of the drugs from the as-spun fiber mats were investigated using UV-visible spectrophotometry.

EXPERIMENTAL

Materials

Polycaprolactone (PCL; $M_w \approx 65,000$ g/mol) was purchased from Sigma-Aldrich (USA). Poly(vinyl alcohol) (PVA; $M_w \approx 70,000$ g/mol; degree of hydrolysis ≈ 98 mol. %) was purchased from BDH (England). Sodium alginate (SA) was purchased from Fluka (Switzerland). Dichloromethane (Fisher Scientific,

England) and chloroform [Labscan (Asia), Thailand] were of analytical reagent grade and used as solvents for PCL without further purification. Sodium acetate (Fluka, Switzerland) and acetic acid (BDH, England) were of analytical reagent grade and used without further purification for the preparation of the acetate buffer solution.

Preparation and Characterization of Spinning Solutions

To elucidate the effect of solution concentration on morphological appearance and size of the obtained fibers, PCL solutions in various concentrations (*i.e.*, 5, 10, 13, 15, and 17% w/v) were prepared in either dichloromethane or chloroform. PVA solutions of varying concentration ranging between 8 and 16% w/v were prepared in distilled water, while PVA/SA blend solutions were prepared by mixing SA solutions of varying concentration ranging between 1 and 5% w/v with 10% w/v PVA solution at an equal weight ratio. Slight stirring was used to expedite the dissolution. Prior to electrospinning, the as-prepared solutions were measured for their viscosity, surface tension, and conductivity using a Brookfield LVDL-II+ viscometer, a Krüss DSA10 Mk2 drop shape analyzer, and a Orion 160 conductivity meter, respectively.

Electrospinning Process

Electrospinning of the as-prepared solutions was carried out by stocking each solution in a 5 mL glass syringe. A 1 cm-long blunt-ended gauge-20 stainless steel needle, used as the nozzle, was attached to the open end of the syringe. A piece of aluminum sheet, wrapped around a thick plastic sheet, was used as the collector. A Gamma High Voltage Research UC-30P DC power supply (Florida, USA) was used to generate high electrical potentials. The emitting electrode of positive polarity was connected to the needle and the grounding electrode was connected to the aluminum sheet. The distance between the tip of the needle and the collector defined the collection distance. In this particular work, the applied electrical potential was fixed at 7.5 kV for the spinning of PCL solutions, 8 kV for the spinning of PVA solutions, and 10 kV for the spinning of PVA/SA blend solutions, while the collection distance was fixed at 10 cm. To elucidate the effect of the applied electrical potential on morphological appearance and size of the as-spun fibers, the electrical potential was varied (*i.e.*, 7.5, 8.5, and 9.5 kV for PCL solutions and 10 and 15 kV for PVA/SA solutions for a fixed collection distance of 10 cm). The collection distance was also varied (*i.e.*, 10, 15 and 20 cm) during the spinning of 10% w/v PVA solution under a fixed electrical potential of 8 kV to investigate the effect of the collection distance on

morphological appearance and size of the as-spun fibers.

Preparation of Drug-Loaded Electrospun Fiber Mats

Diclofenac sodium (DS) in various amounts (*i.e.*, 10, 30, and 50 mg) was loaded in 10 mL of 15% w/v PCL solution, while tetracycline hydrochloride (TH) in various amounts (*i.e.*, 0.2, 0.3, 0.4, and 0.5 g) was loaded in 10 mL of 10% w/v PVA solution. The solutions were electrospun into fiber mats under an electrical potential of 7.5 kV that was applied over a collection distance of 10 cm for DS-loaded PCL solutions and an electrical potential of 8 kV that was applied over a collection distance of 10 cm for TH-loaded PVA solutions. In addition, a thin layer of PVA/SA fibers was coated on TH-loaded as-spun PVA fiber mats to investigate the effect of such a coating on the release of the drug from these coated mats.

Morphological Observation

Morphological appearance and size of both the neat and the drug-loaded electrospun fibers was observed by a JEOL JSM-5200 scanning electron microscope (SEM). The specimens for SEM observation were prepared by cutting an Al sheet covered with an electrospun mat and the cut sections were carefully affixed on SEM stubs. Each specimen, prior to SEM observation, was gold-coated using a JEOL JFC-1100E sputtering device. Diameters of the as-spun fibers were measured directly from the SEM images, from which a histogram from at least 50 readings for each specimen was constructed and an average value and a standard deviation were reported.

Determination of Drug Released from Drug-Loaded Electrospun Fiber Mats

Each drug-loaded electrospun fiber mat was cut into specimens of a square shape (about 2×2 cm²). Each of these specimens was immersed in an exact amount of acetate buffer aqueous solution (pH = 5.5) at 37 °C under a constant mechanical stirring. At a specified immersion period ranging between 0 and 465 min for drug-loaded PCL fiber mats or 0 and 390 min for drug-loaded PVA fiber mats, a small amount of the buffer solution was taken out. The amount of the drug dissolved in the withdrawn buffer solution was quantified against a calibration curve (specific to each type of drugs investigated) using a UV-visible spectrophotometer at a wavelength of 275 nm for DS and 355 nm for TH, respectively. These data were carefully calculated to determine the cumulative amount of drug released from the specimens for each specified immersion period, based on an assumption that the distribution of drug within the fibers was uniform and directly proportional to the initial loaded amount.

Table I. Some properties of the as-prepared PCL, PVA, and PVA/SA solutions

Polymer	Solution concentration (% w/v)	Viscosity (cP)	Surface tension (mN/m)	Conductivity (μ S/cm)
PCL	5	7	20.0	—
	10	31	21.0	—
	13	67	21.0	—
	15	90	22.0	—
	17	125	22.0	—
PVA	8	454	41.6	153
	9	676	42.0	163
	10	1996	42.0	174
	11	2353	42.5	176
	12	4156	43.0	179
	13	5362	43.2	185
	14	8415	43.9	192
	15	—	44.1	198
10% w/v PVA/SA	16	—	44.2	217
	1	185	44.4	1340
	2	363	44.5	1620
	3	684	44.6	2200
	4	888	45.0	2880
	5	2134	45.7	3870

RESULTS AND DISCUSSION

Effect of Solution Concentration

The as-prepared solutions of PCL in dichloromethane at various concentrations (*i.e.*, 5, 10, 13, 15, and 17% w/v), PVA in distilled water at various concentrations ranging between 8 and 16% w/v, and PVA/SA in distilled water at various concentrations of SA ranging between 1 and 5% w/v for a fixed PVA concentration of 10% w/v in an equal weight ratio between the two solutions were characterized for their viscosity, surface tension, and conductivity, prior to electrospinning, and the results are summarized in Table I. For PCL and PVA solutions, the viscosity was found to increase significantly, while the surface tension increased slightly, with increasing concentration of the solutions. The increased viscosity was obviously due to the increased molecular entanglements. For PVA/SA blend solutions, addition of an equal weight of SA solutions with 10% w/v PVA solution caused the actual concentration of PVA solution to decrease by about half, thus reducing the viscosity of the resulting blend solutions significantly (see Table I). The increase in the SA concentration also caused the viscosity of the resulting blend solutions to increase. In term of the conductivity, an increase in the PVA concentration caused the conductivity to increase slightly. On the contrary, the addition and an increase in the SA concentration in the PVA/SA blend solutions caused the conductivity of the blend solutions to increase

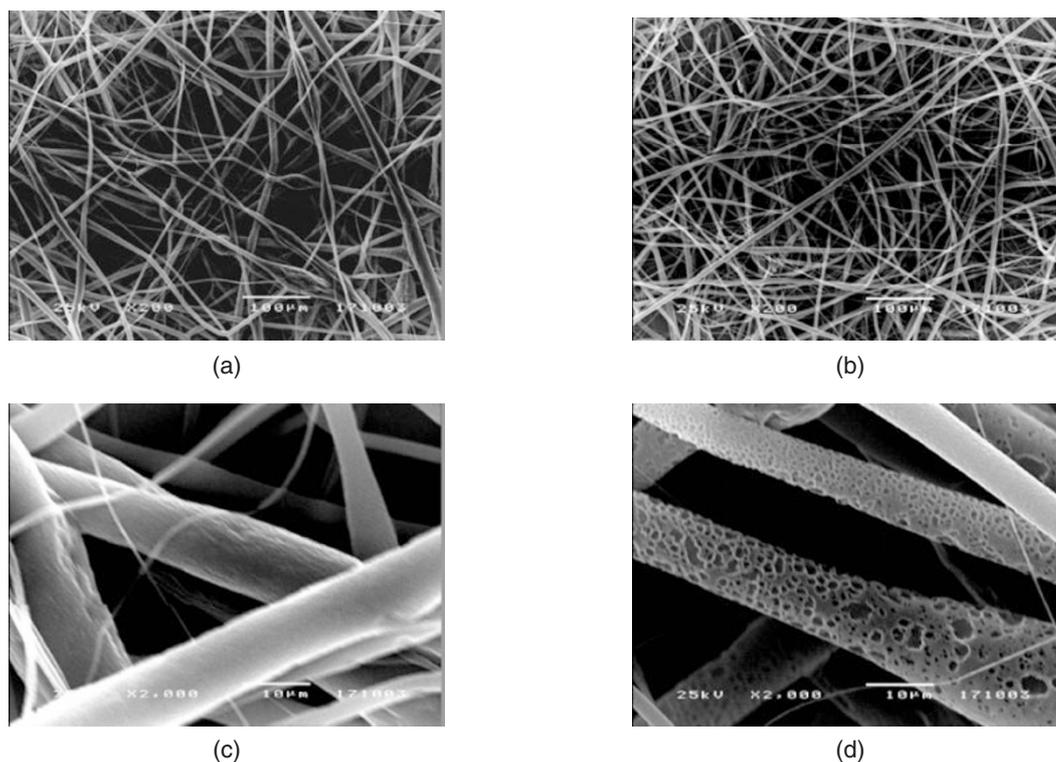


Figure 1. Selected SEM images of electrospun fibers from (a,c) 15 and (b,d) 17% w/v PCL solutions in dichloromethane at (a,b) 200x (scale bar = 100 μm) and (c,d) 1000x (scale bar = 10 μm). The applied electrostatic field strength was 7.5 kV/10 cm.

significantly, likely a result of the dissolution products of SA (*i.e.*, Na⁺ and alginate⁻ ions).

Electrospinning of the PCL solutions was carried out at a fixed applied electrostatic field strength of 7.5 kV/10 cm. For PCL solutions in dichloromethane, only droplets were obtained at the concentrations of 5, 10, and 13% w/v. At such low concentrations, the viscoelastic force (*i.e.*, a result of the low degree of chain entanglements) in a given jet segment was not large enough to counter the higher Coulombic repulsion force, resulting in the break-up of the charged jet into many smaller jet segments, which later rounded up, as a result of the surface tension, to form droplets. When the concentration increased to 15 and 17% w/v, electrospun fibers were obtained (see Figure 1a and b), which attributed to the increased chain entanglements that were sufficient to prevent the break-up of the charged jet and to allow the Coulombic stress to further elongate the charged jet during its flight to the grounded collector.^{29,30} The average diameter of the as-spun PCL fibers ranged between about 2.6 and 4.5 μm. A high magnification of the SEM images (see Figure 1c and d) revealed rough surface topography of the fibers, possibly a result of the rapid evaporation of the solvent (*i.e.*, boiling point of dichloromethane = 40 °C) prior to solidification. On the other hand, electrospinning of the PCL solutions in chloroform at all concentrations investigated (*i.e.*, 5, 10, 13, 15 and 17% w/v) only resulted in the formation of

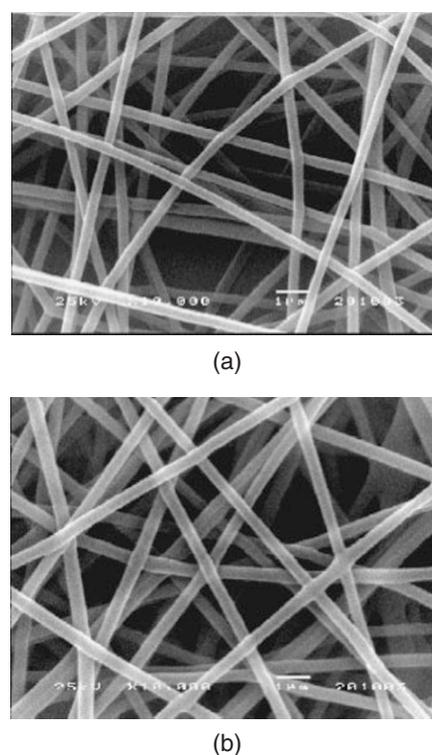


Figure 2. Selected SEM images (scale bar = 1 μm) of electrospun fibers from (a) 10 and (b) 12% w/v PVA solutions in distilled water. The applied electrostatic field strength was 8 kV/10 cm.

droplets.

Electrospinning of the PVA solutions in distilled water was carried out at a fixed applied electrostatic

field strength of 8 kV/10 cm. Within the concentration range investigated (*i.e.*, from 8 to 16% w/v), all of the PVA solutions produced uniform and smooth fibers (see Figure 2). The average diameter of the obtained PVA fibers ranged from about 244 nm at a concentration of 8% w/v to about 549 nm at a concentration of 16% w/v (see Figure 3). The increased concentration (*i.e.*, increased viscoelastic force) enabled the charged jet to withstand larger Coulombic repulsion force, resulting in the observed larger diameters of the charged jet (ultimately, the as-spun fibers).³⁰ The increased viscoelastic force also caused the onset for the bending instability to occur further away from the tip of the nozzle, causing the total path length that a jet segment traveled to the collector to decrease. The shorter path length decreased the probability for the charged jet to be elongated by the Coulombic repulsion force,

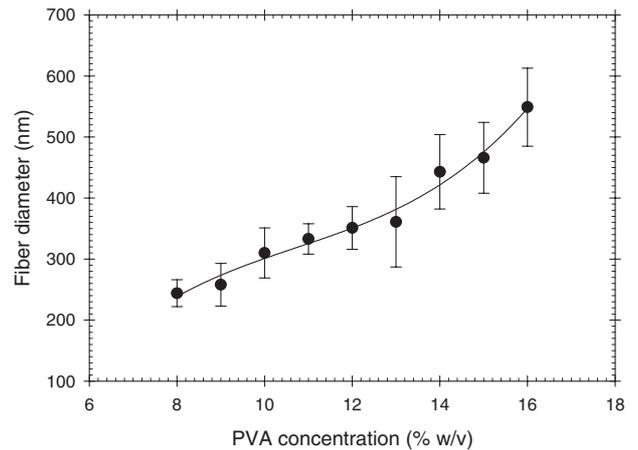


Figure 3. Average diameter of electrospun PVA fibers plotted as a function of PVA solution concentration.

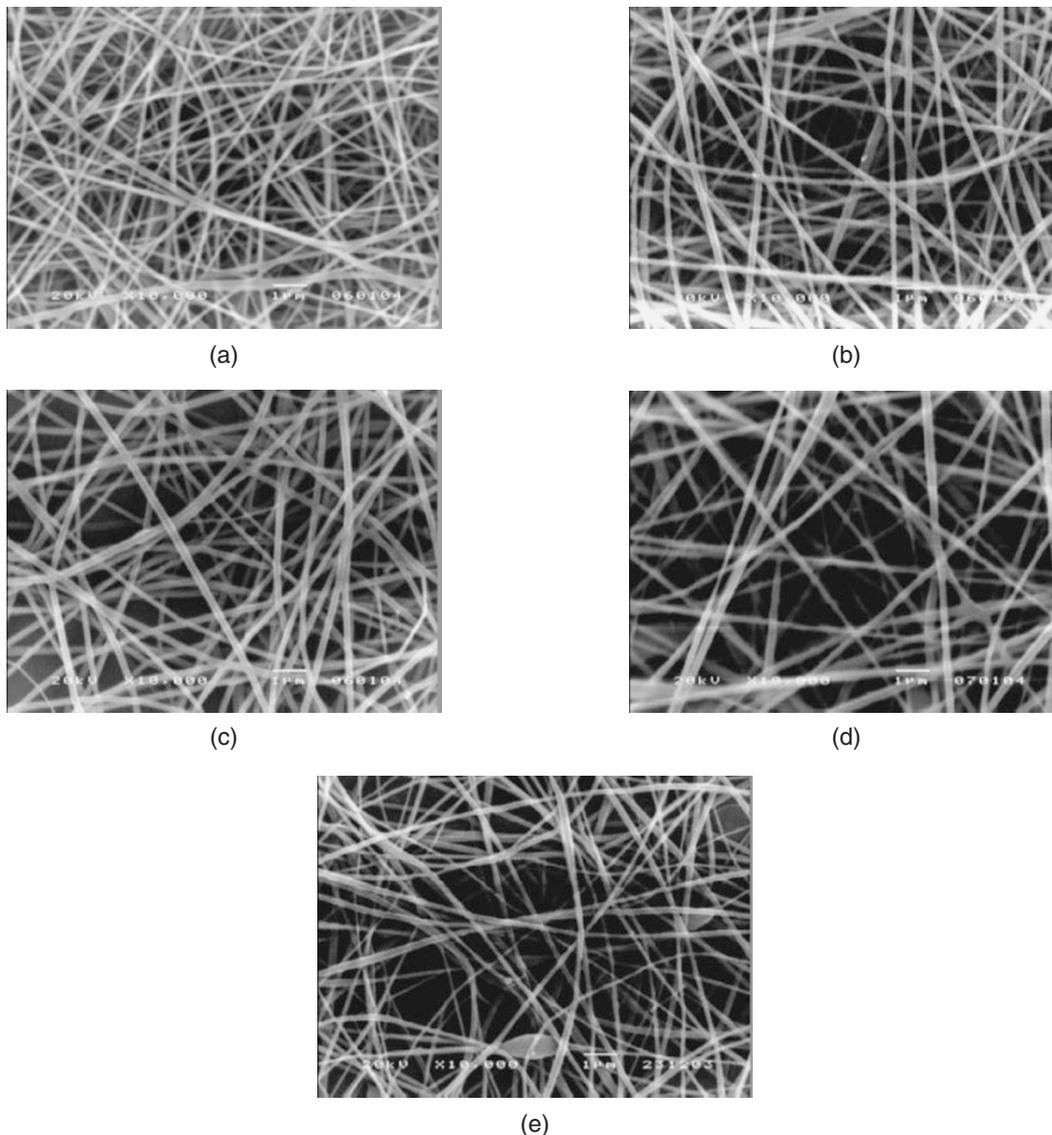


Figure 4. Selected SEM images (scale bar = 1 μm) of electrospun fibers from blend solutions of 10% w/v PVA solution and SA solution of varying concentration [*i.e.*, (a) 1, (b) 2, (c) 3, (d) 4, and (e) 5% w/v] in an equal weight ratio between the two solutions. The applied electrostatic field strength was 10 kV/10 cm.

hence the observed increase in the diameters of the fibers with increasing concentration.³⁰

Figure 4 shows selected SEM images of the as-spun fibers from the blend solutions of 10% w/v PVA solution and SA solutions of varying concentration between 1 and 5% w/v in an equal weight ratio. Electrospinning of these blend solutions was carried out at a fixed applied electrostatic field strength of 10 kV/10 cm. As previously mentioned, the addition of an equal weight of SA solutions with 10% w/v PVA solution caused the actual concentration of PVA solution to decrease by about half, but the resulting blend solutions still produced uniform and smooth as-spun fibers. The average diameter of these fibers increased from about 119 nm at the concentration of the SA solution of 1% w/v to about 182 nm at the concentration of the SA solution of 5% w/v (see Table II). Clearly, these obtained fibers were much smaller than those obtained from 8% w/v PVA solution (*i.e.*, 244 nm), as normally would obtain.

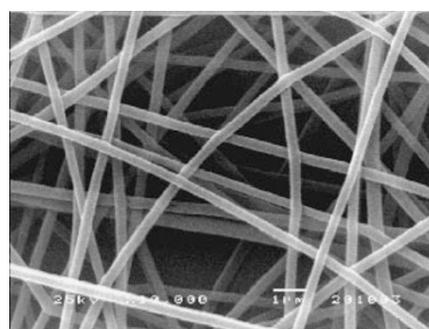
Effect of Applied Electrical Potential

To illustrate the effect of applied electrical potential on morphological appearance and size of the obtained PCL fibers, 17% w/v PCL solution in dichloromethane was electrospun under various electrical potentials (*i.e.*, 7.5, 8.5 and 9.5 kV) that were applied over a fixed collection distance of 10 cm. Similar to what have been shown in Figure 1, the obtained PCL fibers were not uniform, possibly due to the high volatility of the solvent. Specifically, the diameters of the as-spun fibers were in the range of 4.5–4.7 μm at 7.5 kV, 3.4–4.2 μm at 8.5 kV, and 3.0–3.9 μm at 9.5 kV. Apparently, the fiber diameters decreased with increasing applied electrical potential. The effect of applied electrical potential was also investigated on the as-spun fibers from PVA/SA blend solutions. In such studies, the applied electrical potential was increased from 10 to 15 kV over a fixed collection distance of 10 cm. Evidently from Table II, the average diameter of the as-spun PVA/SA fibers for any given concentration

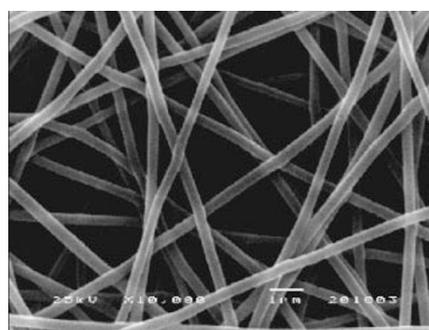
of the SA solutions was found to decrease with increasing applied electrical potential. The observed decrease in the diameters of the obtained fibers with increasing applied electrical potential, in both cases, could be due to the increase in the electrostatic force.³¹ Nonetheless, conflicting results have also been observed and reported.^{32,33}

Effect of Collection Distance

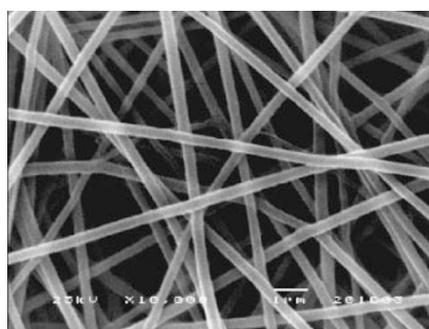
Figure 5 shows selected SEM images of the as-spun fibers from 10% w/v PVA solution under a fixed electrical potential of 8 kV that was applied over a collection distance of 10, 15, or 20 cm. Clearly, the as-spun fibers were uniform and smooth, with the average diameter decreasing from about 310 nm at a collection distance of 10 cm to about 269 nm at a collection dis-



(a)



(b)



(c)

Table II. Diameters of electrospun fibers obtained from blend solutions of 10% w/v PVA solution and SA solution of varying concentration ranging from 1 to 5% w/v in an equal weight ratio under an electrical potential of either 10 or 15 kV across a collection distance of 10 cm

Solution	Fiber diameters (nm)	
	10 kV	15 kV
10% w/v PVA/1% w/v SA	119 ± 20	116 ± 15
10% w/v PVA/2% w/v SA	131 ± 15	123 ± 21
10% w/v PVA/3% w/v SA	134 ± 22	131 ± 22
10% w/v PVA/4% w/v SA	178 ± 38	150 ± 34
10% w/v PVA/5% w/v SA	182 ± 35	152 ± 41

Figure 5. Selected SEM images (scale bar = 1 μm) of electrospun fibers from 10% w/v PVA solutions in distilled water under an electrical potential of 8 kV applied across a collection distance of (a) 10, (b) 15, or (c) 20 cm.

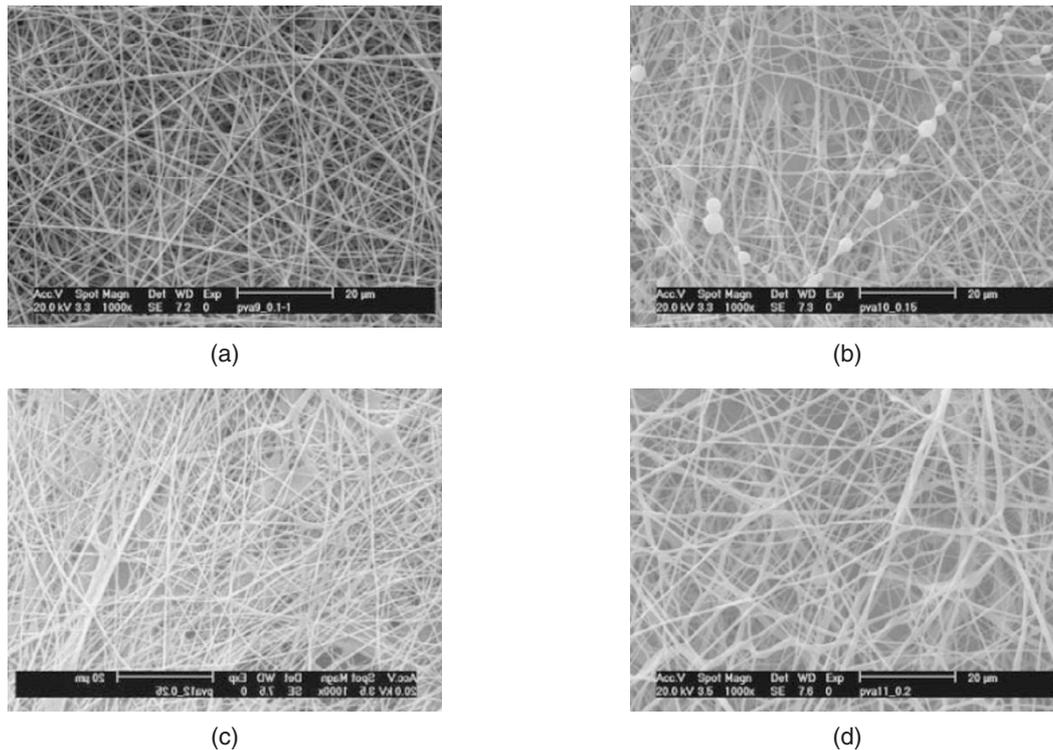


Figure 6. Selected SEM images (scale bar = 20 μm) of drug-loaded electrospun fiber mats from 10% w/v PVA solutions loaded with the initial amount of TH of (a) 0.2, (b) 0.3, (c) 0.4, and (d) 0.5 g, respectively. The applied electrostatic field strength was 8 kV/10 cm.

tance of 20 cm. The observed decrease in the average fiber diameter with increasing collection distance was likely a result of the increased total path length that a jet segment travelled to the collector, thus increasing the likelihood for the charged jet to be further elongated by the Coulombic repulsion force.³⁴

Release of Model Drugs from Drug-Loaded Electrospun Fiber Mats

Drug-loaded as-spun PVA fiber mats were prepared from 10% w/v PVA solutions loaded with tetracycline hydrochloride (TH) in various amounts (*i.e.*, 0.2, 0.3, 0.4, and 0.5 g) under an applied electrostatic field strength of 8 kV/10 cm. Figure 6 shows selected SEM images of TH-loaded as-spun PVA fiber mats. Obviously, the addition of TH within the PVA solution affected the morphological appearance and size of the resulting fibers. Noticeably, the obtained fibers were not uniform, and the average fiber diameter was found to increase with increasing amount of TH. Specifically, it increased from about 300 nm for neat as-spun fibers to 330 nm for the PVA solution having 0.2 g of TH and, finally, to 560 nm for the PVA solution containing 0.5 g of TH. In a similar manner, drug-loaded as-spun PCL fiber mats were prepared from 15% w/v PCL solutions incorporated with diclofenac sodium (DS) in various amounts (*i.e.*, 10, 30, and 50 mg) under an applied electrostatic field strength of 7.5 kV/10 cm. Figure 7 shows selected SEM im-

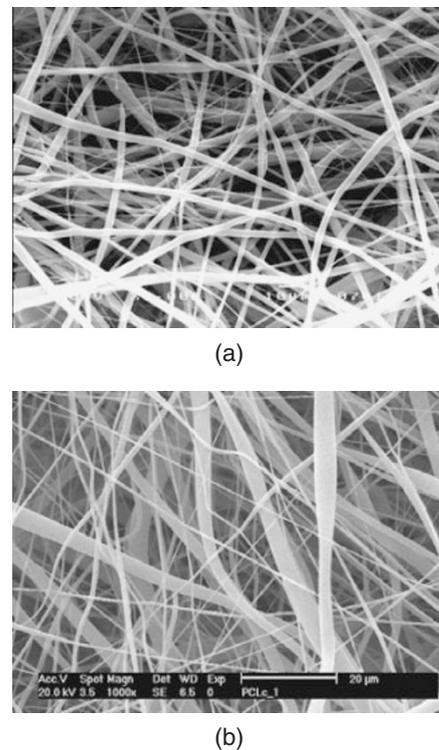


Figure 7. Selected SEM images of (a) neat electrospun PCL fiber mat (scale bar = 10 μm) and (b) DS-loaded electrospun PCL fiber mat (scale bar = 20 μm) from neat and drug-loaded PCL solutions. The concentration of the PCL solution was 15% w/v; the initial drug content was 10 mg; and the applied electrostatic field strength was 7.5 kV/10 cm.

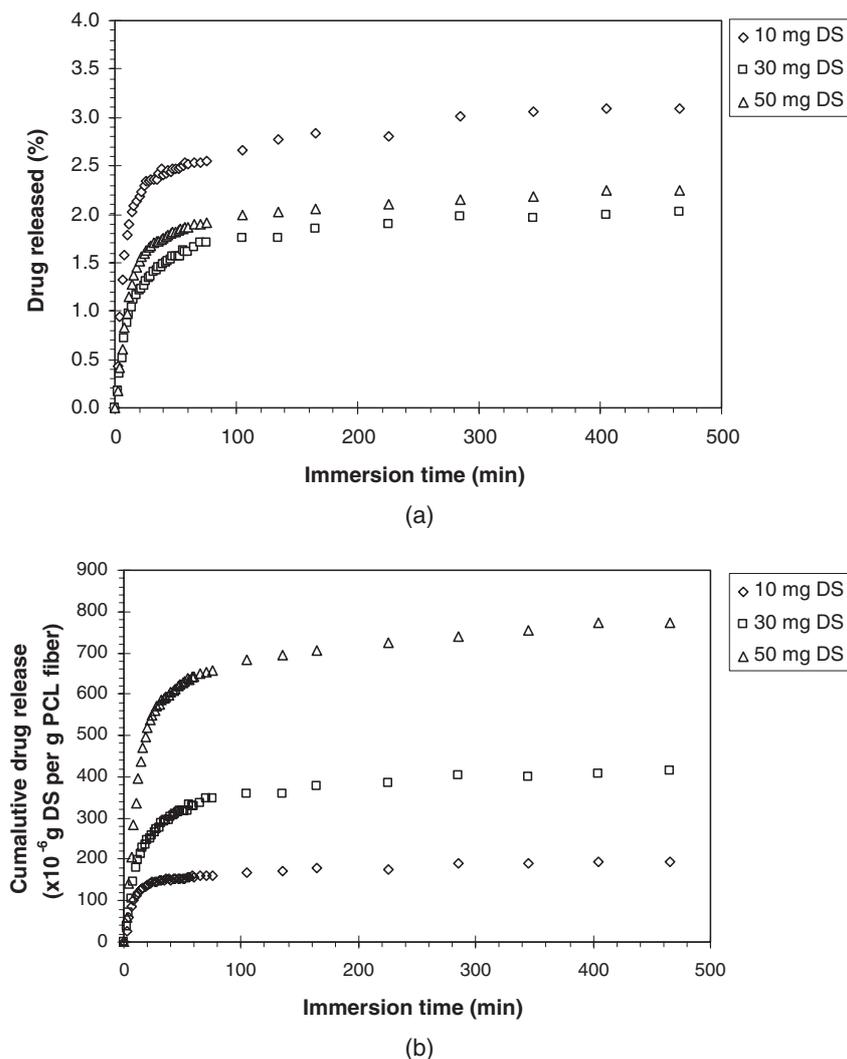


Figure 8. Cumulative amount of DS released from DS-loaded PCL fiber mats that were electrospun from PCL solutions loaded with (\diamond) 10, (\square) 30 and (\triangle) 50 mg of DS over an immersion period of 465 min: expressing in terms of (a) percentage of initial drug loaded and (b) weight of DS released (μg) per 1 g of drug-loaded PCL fiber mat.

ages of neat and DS-loaded as-spun PCL fiber mats. Evidently, the addition of the drug caused the fibers to become larger and less uniform. Similarly, the diameters of the resulting fibers were also found to increase with increasing amount of DS.

The release characteristics of the model drugs from DS-loaded electrospun PCL and TH-loaded electrospun PVA fiber mats were carried out by the total immersion method, using acetate buffer solution as the transfer medium at a controlled temperature of 37°C . The cumulative amount of drugs released from the DS-loaded electrospun PCL fiber mats and TH-loaded electrospun PVA fiber mats with or without a thin coating layer of electrospun PVA/SA fibers is respectively shown in Figures 8 and 9. The cumulative amount of drugs released was reported both as the percentage of the calculated amount of drugs being present in the specimens and as the weight of the drugs released normalized over 1 g of the drug-loaded

fiber mat specimens.

For the release of DS from DS-loaded electrospun PCL fiber mats, the cumulative amount of DS increased rapidly in the first 20 to 30 min and became practically constant at long immersion times. Interestingly, the total amount of DS released after long immersion times (*i.e.*, at 465 min) was found to decrease with increasing the initial amount of DS loaded in the PCL solution. Specifically, such values were only about 3.09, 2.03, and 2.25% (see Figure 8a) for the initial amount of DS of 10, 30, and 50 mg, respectively. Intuitively, the DS-loaded as-spun PCL fiber mat from the solution that contained the highest amount of the drug should exhibit the highest rate of release and the highest amount of drug released. Such an order was not observed in Figure 8a, which is a result of the difference in the thickness of the fiber mat samples, hence the difference in the weight of the samples. However, when the cumulative amount of the

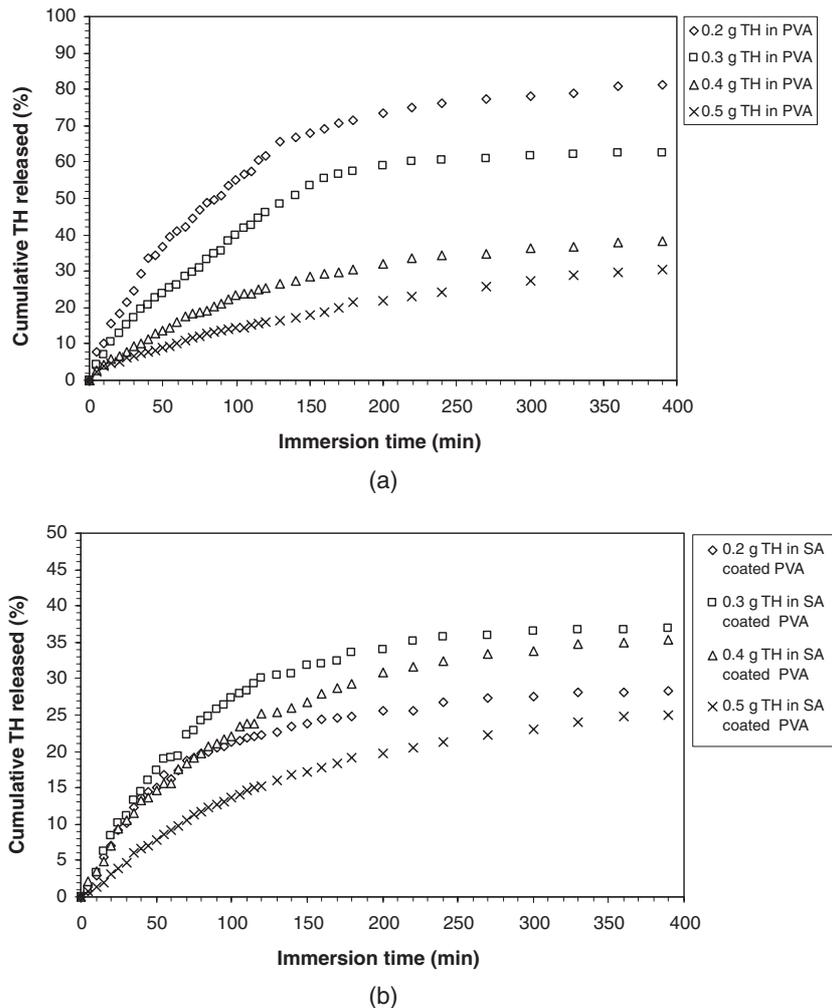


Figure 9. Cumulative amount of TH released from TH-loaded PVA fiber mats that were electrospun from PVA solutions loaded with (\diamond) 0.2, (\square) 0.3, (\triangle) 0.4, and (\times) 0.5 g over an immersion period of 390 min: (a) for the drug-loaded mats without a thin layer of as-spun PVA/SA fibers and (b) for the drug-loaded mats covered with a thin layer of as-spun PVA/SA fibers.

drug released was expressed as the weight of DS released per gram of the PCL fiber mats (see Figure 8b), the total amount of DS release after 465 min increased with increasing the initial amount of DS loaded in the PCL solution, which was found to be about 194, 413, and 774 μg per 1 g of the PCL fiber mats for the initial amount of DS of 10, 30, and 50 mg, respectively.

A similar behavior was also observed for the release of TH from TH-loaded electrospun PVA fiber mats. Particularly, the total amount of TH released at long immersion times (*i.e.*, at 390 min) was about 81.4, 62.6, 38.2, and 30.4% (see Figure 9a) for the initial amount of TH of 0.2, 0.3, 0.4, and 0.5 g, respectively. However, when a thin layer of as-spun PVA/SA fibers were coated on the TH-loaded electrospun PVA fiber mats, the total amount of the drug released was reduced to about 28.3, 36.9, 35.4, and 24.9% (see Figure 9b), respectively. Comparing with the total amount of drug released from the drug-loaded PCL fiber mats, the drug-loaded PVA fiber mats were able to

release the drug in a much greater amount, most likely a result of the main difference between the two matrices in which PVA was able to swell and partially dissolve in the aqueous medium, while PCL was not.

CONCLUSION

In the present contribution, the effects of solution and process parameters (*i.e.*, solution concentration, applied electrical potential, and collection distance) on morphological appearance and size of electrospun polycaprolactone (PCL), poly(vinyl alcohol) (PVA), and PVA-sodium alginate (PVA/SA) fibers were investigated using scanning electron microscopy (SEM). Generally, the spinnability and the average fiber diameter were found to increase with increasing solution concentration. For PCL fibers, the average fiber diameter ranged between 2.6 and 4.5 μm . For PVA fibers, it ranged between 244 and 549 nm, while, for PVA/SA fibers, it ranged between 119 and 182 nm.

In addition, the diameters of the obtained fibers decreased with the increase in both of the applied electrical potential and the collection distance. Incorporation of tetracycline hydrochloride (TH) in various amounts in 10% w/v PVA solution caused the resulting as-spun fibers to be non-uniform and the average fiber diameter was found to increase from about 330 nm for the PVA solution containing 0.2 g of TH to about 560 nm for the solution containing 0.5 g of TH. Incorporation of diclofenac sodium (DS) in 15% w/v PCL solution also resulted in larger as-spun fibers. The release characteristics of the drugs from these drug-loaded as-spun PCL and PVA fiber mats, by the total immersion method, showed that the cumulative release of the model drugs increased monotonically with increasing immersion time and became practically constant at long immersion times. The total amount of the drugs released for these drug-loaded fiber mats at long immersion times was generally found to decrease with increasing the initial amount of the drugs loaded in the spinning solutions, a direct result of the discrepancy in the weight of the samples. Finally, a thin layer of PVA/SA fibers that were electrospun directly on TH-loaded PVA fiber mats caused the total amount of the drug released to decrease appreciably.

Acknowledgment. The authors acknowledge partial support received from 1) the Faculty of Applied Science, King Mongkut's Institute of Technology North Bangkok and 2) the National Research Council of Thailand (NRCT).

REFERENCES

- Z. M. Huang, Y. Z. Zhang, M. Kotaki, and S. Ramakrishna, *Compos. Sci. Technol.*, **63**, 2223 (2003).
- J. Doshi and D. H. Reneker, *J. Electrostat.*, **35**, 151 (1995).
- H. Yoshimoto, Y. M. Shin, H. Terai, and J. P. Vacanti, *Biomaterials*, **24**, 2077 (2003).
- S. A. Riboldi, M. Sampaolesi, P. Neuenschwander, G. Cossu, and S. Mantero, *Biomaterials*, **26**, 4606 (2005).
- X. Zong, H. Bien, C. Y. Chung, L. Yin, D. Fang, B. S. Hsiao, B. Chu, and E. Entcheva, *Biomaterials*, **26**, 5330 (2005).
- P. Wutticharoenmongkol, N. Sanchavanakit, P. Pavasant, and P. Supaphol, *J. Nanosci. Nanotechnol.*, **6**, 514 (2006).
- Y. K. Luu, K. Kim, B. S. Hsiao, B. Chu, and M. Hadjiargyrou, *J. Controlled Release*, **89**, 341 (2003).
- E. R. Kenawy, G. L. Bowlin, K. Mansfield, J. Layman, D. G. Simpson, E. H. Sanders, and G. E. Wnek, *J. Controlled Release*, **81**, 57 (2002).
- X. Zong, K. Kim, D. Fang, S. Ran, B. S. Hsiao, and B. Chu, *Polymer*, **43**, 4403 (2002).
- J. Zeng, X. Xu, X. Chen, Q. Liang, X. Bian, L. Yang, and X. Jing, *J. Controlled Release*, **92**, 227 (2003).
- G. Verreck, I. Chun, J. Rosenblatt, J. Peeters, A. V. Dijck, J. Mensch, M. Noppe, and M. E. Brewster, *J. Controlled Release*, **92**, 349 (2003).
- P. Taepaiboon, U. Rungsardthong, and P. Supaphol, *Nanotechnology*, **17**, 2317 (2006).
- D. H. Reneker and I. Chun, *Nanotechnology*, **7**, 216 (1996).
- D. H. Reneker, A. L. Yarin, H. Fong, and S. Koombhongse, *J. Appl. Phys.*, **87**, 4531 (2000).
- K. H. Lee, H. Y. Kim, M. S. Khil, Y. M. Ra, and D. R. Lee, *Polymer*, **44**, 1287 (2003).
- S. A. Theron, E. Zussman, and A. L. Yarin, *Polymer*, **45**, 2017 (2004).
- M. Shin, O. Ishii, T. Sueda, and J. P. Vacanti, *Biomaterials*, **25**, 3717 (2004).
- W. J. Li, R. Tuli, C. Okafor, A. Derfoul, K. G. Danielson, D. J. Hall, and R. S. Tuan, *Biomaterials*, **26**, 599 (2005).
- E. Luong-Van, L. Grøndahl, K. N. Chua, K. W. Leong, V. Nurcombe, and S. M. Cool, *Biomaterials*, **27**, 2042 (2006).
- C. Zhang, X. Yuan, L. Wu, Y. Han, and J. Sheng, *Eur. Polym. J.*, **41**, 423 (2005).
- A. Koski, K. Yim, and S. Shivkumar, *Mater. Lett.*, **58**, 493 (2004).
- J. S. Lee, K. H. Choi, H. D. Ghim, S. S. Kim, D. H. Chun, H. Y. Kim, and W. S. Lyoo, *J. Appl. Polym. Sci.*, **93**, 1638 (2004).
- Z. Jun, H. Hou, H. J. Wendorff, and A. Greiner, *e-Polymer*, article no. 038 (2005).
- W. K. Son, J. H. Youk, T. S. Lee, and W. H. Park, *Mater. Lett.*, **59**, 1571 (2005).
- L. Yao, T. W. Haas, A. Guiseppi-Elie, D. G. Simpson, G. L. Bowlin, and G. E. Wnek, *Chem. Mater.*, **15**, 1860 (2003).
- S. Chuangchote and P. Supaphol, *J. Nanosci. Nanotechnol.*, **6**, 125 (2006).
- L. Wu, X. Yuan, and J. Sheng, *J. Membr. Sci.*, **250**, 167 (2005).
- J. Zeng, A. Aliger, F. Czubayko, T. Kissel, J. H. Wendorff, and A. Greiner, *Biomacromolecules*, **6**, 1484 (2004).
- C. J. Buchko, L. C. Chen, Y. Shen, and D. C. Martin, *Polymer*, **40**, 7397 (1999).
- C. Mit-uppatham, M. Nithitanakul, and P. Supaphol, *Macromol. Chem. Phys.*, **205**, 2327 (2004).
- L. Larrondfo and J. Manley, *J. Polym. Sci., Part B: Polym. Phys.*, **19**, 909 (1981).
- J. M. Deitzel, J. Kleinmeyer, D. Harris, and N. C. Bectan, *Polymer*, **42**, 261 (2001).
- V. Pornsopone, P. Supaphol, R. Rangkupan, and S. Tantayanon, *Polym. Eng. Sci.*, **45**, 1073 (2005).
- P. K. Baumgarten, *J. Colloid Interface Sci.*, **36**, 71 (1971).