Preparation and Performance Evaluation of Tetracycline Hydrochloride Loaded Wound Dressing Mats Based on Electrospun Nanofibrous Poly(lactic acid)/Poly(ϵ-caprolactone) Blends

Payam Zahedi,[1] Zeinab Karami,[1] Iraj Rezaeian,[1] Seyed-Hassan Jafari,[1] Parvin Mahdaviani,[2] Amir Hossein Abdolghaffari,[3,4] Mohammad Abdollahi[2]

[1]*Department of Polymer, School of Chemical Engineering, College of Engineering, University of Tehran, P. O. Box 11155-4563, Tehran, Iran*
[2]*Faculty of Pharmacy and Pharmaceutical Sciences Research Center and Endocrinology & Metabolism Research Center, Tehran University of Medical Sciences, Tehran, Iran*
[3]*Department of Pharmacology, Research Institute of Medical Plants, ACECR, Tehran, Iran*
[4]*Departmnet of Pharmacology, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran*

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ABSTRACT: In this article, we present the drug-release rate, water uptake, water permeability, morphology, and mechanical properties of a series of active wound dressing nanofibrous mats prepared via an electrospinning process of poly(lactic acid) (PLA), poly(ε-caprolactone) (PCL), and their (50/50) blends loaded with different doses of tetracycline hydrochloride antibiotic. The performance of these active wound dressings in terms of a sustained and suitable drug-release rate, adequate water uptake and water permeability, and antibacterial activities were compared with those of a commercial wound dressing (Comfeel Plus). The results show that the dressings made from PCL and PLA/PCL blends showed better performance compared with the commercial wound dressing sample as far as these properties were concerned. The improved performance could be explained on the basis of the nanofibrous structure of the mats and the hydrophilicity of PCL and PLA. © 2011 Wiley Periodicals, Inc. J Appl Polym Sci 124: 4174–4183, 2012

Key words: biomaterials; biopolymers; drug delivery systems; nanofiber; polyesters

INTRODUCTION

Modern wound dressings are replacing conventional bandages such as gauze and tulles. Commercial products, such as Comfeel Plus and Tegaderm,[1,2] are biopolymeric films with suitable moisture control on the wound surface and suitable healing of the wound area. Over the last decade, many research works have focused on polymeric nanofibrous wound dressings produced by electrospinning because of their high aspect ratio and porosity. Electrospinning is a simple process for producing fibers with submicrometer diameters (Scheme 1). In this process, a polymer solution from a reservoir is ejected through a syringe needle by means of Coulombic repulsion of charges that are accumulated at the tip of a pendant droplet as soon as a high electrical potential (10–30 kV) is applied between the needle and a collecting device.[3,4]

There have been many reports in the field of polymeric wound dressings with an emphasis on nanofibers.[5] A literature review revealed that the following polymers have been used as wound dressings: glucan/poly(vinyl alcohol) (PVA),[6] collagen/chitosan,[7] carboxyethyl chitosan/PVA,[8] poly(ε-caprolactone) (PCL)/gelatin,[9] poly(vinyl pyrrolidone)–iodine complex,[10] poly(lactide–glycolide),[11] and polyurethane.[12] Kang et al.[13] studied the water-uptake capacity and wound healing properties of wound dressings based on PVA nanofibers coated with chitosan. The PVA nanofibers were prepared from a 10 wt % solution and stabilized against water by heat treatment (H-PVA) and by coating with 1 wt % chitosan (C-PVA), respectively. Open-wound healing and histology tests showed that C-PVA was more effective than H-PVA.

To increase the efficiency of polymeric nanofibrous wound dressings and to convert them from interactive to bioactive materials, some essential wound healing additives are included. Some commonly used additives are nanosilver particles,[14] antibiotics,[15,16] vitamins,[17,18] and cellular growth agents

Correspondence to: I. Rezaeian (rezaeian@ut.ac.ir) or S.-H. Jafari (shjafari@ut.ac.ir).
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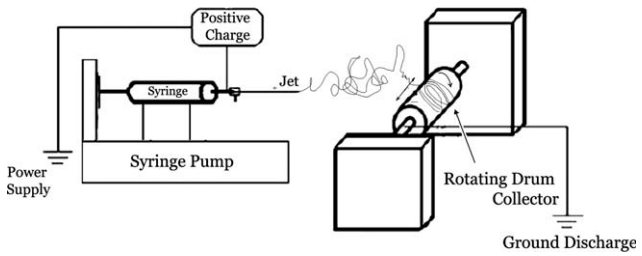


Scheme 1 Schematic presentation of the electrospinning process.

for activating fibroblasts.[19,20] Rojitanaroj et al.[21] examined the antibacterial activity of gelatin containing $AgNO_3$ on aerobic bacteria that usually grows on burned wounds. They used vancomycin drug for *Staphylococcus aureus* and methicilin-resistant *S. aureus* and antibiotics such as gentamicin for *Escherichia coli* and *Pseudomonas aeroginosa* bacteria. They found that polymeric electrospun nanofibers containing silver nanoparticles were more effective in stopping bacterial growth compared to the samples without silver.

In a recent study by Liu and Huang,[22] wound dressings based on nonwoven mats mixed with chitosan and herbal extract membrane were used. They found that using a two-layered composite containing nonwoven fibers from soybean protein blended with chitosan and herbal extract of *Bletilla striata* led to the growth of fibroblast L929 cells. Tetracycline hydrochloride (Scheme 2) was used by Kenawy et al.[23] on electrospun nanofibers from poly(ethylene-*co*-vinyl acetate), poly(lactic acid) (PLA), and their polyblend. From their studies on morphological and antibiotic release rate, they concluded that poly(ethylene-*co*-vinyl acetate) samples containing 5% tetracycline hydrochloride relative to a blank polymer solution had the highest drug-release rate (60%). They did not examine the antibacterial activity, water uptake, and water permeability, which are some essential characteristics for effective wound dressing materials.

In this work, a systematic study was carried out on electrospun nanofibrous wound dressing materials made from PLA, PCL, and 50/50 PCL/PLA blends loaded with high doses of tetracycline hydrochloride. The morphology and mechanical properties and the antibacterial activity, drug-release rate, water permeability, and water uptake of these samples were evaluated. The properties of the wound dressing samples were compared with that of a commercial wound dressing, Comfeel Plus.

The use of PLA/PCL blends as potential wound dressing materials can be justified on the basis of the following reasons: although PLA and its copolymers are the most widely used biomedical polymers, it is known that the drug-release rate from pure PLA is relatively lower than that of pure PCL.[23] Moreover, the spinnability of PLA is weaker than that of PCL. On the other hand, PLA is considered a more appropriate biomedical polymer compared to PCL as far as the biomedical properties are concerned. By blending these two polymers, one can expect to develop a more suitable system for wound dressing applications with balanced properties.

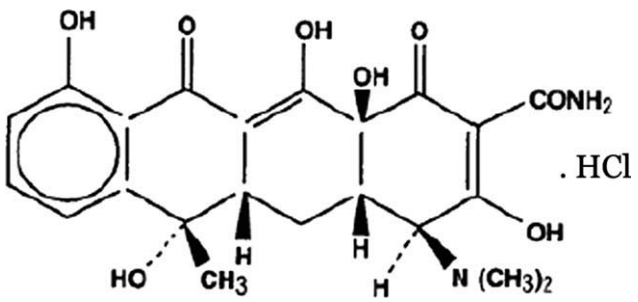
EXPERIMENTAL

Materials

PCL (biodegradable, weight-average molecular weight = 80,000 g/mol) was purchased from Sigma-Aldrich Corp. (Pilsburg, The Netherlands). PLA (4042 D grade, density = 1.24 g/cm^3) was obtained from NatureWorks LLC (Bobingen, Germany). The commercial polyurethane hydrocolloidal coating (with the trade name Comfeel Plus) was received from Coloplast Co., Ltd. (Denmark). Tetracycline hydrochloride antibiotic with a purity of 99.99% was obtained from Merck (Germany). All of the other chemicals were analytical-reagent grade and were used without further purification.

Preparation of electrospun samples containing tetracycline hydrochloride

The preparation of electrospun nanofibers were carried out for PCL, PLA, and 50/50 PCL/PLA with concentrations of 6, 9, 12, and 15% (w/v) in a 9/1 solvent mixture of chloroform and dimethylformamide (DMF), and the mixture was stirred for 1 h. At the next stage, these samples containing tetracycline hydrochloride at 250 and 500 μg/mL concentrations were prepared.[23] First, the drug was weighed and dissolved in 1 mL of DMF, and then, it was added to polymer solution samples with known concentrations containing 9 mL of chloroform. Then, the mixture was stirred for 1 h. The operation conditions of the electrospinning device (model eSpinner NF-CO EN/II, Asian Nanostructures Technology Co., Tehran, Iran) for the preparation of the samples were as



Scheme 2 Chemical structure of tetracycline hydrochloride.

follows: solution flow rate = 0.7 mL/h, voltage = 15 kV, gauge needle = 0.7 mm, and distance between the needle tip and rotational collector = 12 cm. The electrospun nanofibers as nonwoven mats were collected on sterile aluminum foil. To achieve fully dried electrospun nanofiber samples and to ensure evaporation of the organic solvents from the spun fibers, the samples were dried at room temperature for about 12 h at a relative humidity of 32% until a constant weight was attained.

Because the thickness of the spun nanofiber mats is an important parameter in controlling the drug-release rate, we tried to keep the thickness of the obtained samples constant by maintaining the fixed processing conditions. Under the aforementioned processing conditions, the average thickness of the obtained nanofiber samples was about 0.6 ±0.05 mm.

It is to be noted that during the electrospinning process for the production of nanofibers mats, a small amount of the polymer solution containing the drug can be lost on the rotating drum and so on. However, because all of the electrospinning was performed under similar conditions, the drug lost remained almost constant for all samples. On the other hand, high doses of drug loadings (250 and 500 μg/mL) were used to compensate for drug lost during the spinning process.

Characterizations of the samples

Scanning electron microscopy (SEM) analysis

Electrospun nanofibers on aluminum foil were coated with a thin layer of gold by a Bio-Rad E5200 auto sputter coater (England). For morphological observations of the samples, a scanning electron microscope (CamScan MV2300 model, Oxford) with 1000× magnification was used. The mean values of the nanofiber diameters from five different sections were measured and recorded.

Water vapor permeability (WVP) and water-uptake capacity

WVP tests for the samples were carried out according to the British Standard test 7209–1990. Circular samples with 10-cm diameters were cut from nonwoven mat samples. They were placed on special plates inside a small room with 65 ± 3% relative humidity at 32 ± 2°C. Every 1 h, the weight variations (ΔW's) of the samples were determined with the following equation:

$$\mathrm{WVP(mg.cm^{-2}.h^{-1})} = \Delta W/(A \times \Delta t), \quad (1)$$

where Δt is the time interval and is equal to 1 h and A is the effective surface area of nanofibers in contact with water vapor and a humid environment. The overall WVP test time was about 6 h. Three measurements were performed for each sample, and the standard deviation was ±0.3 mg cm^{-2} h^{-1}.

The water-uptake capacity of the samples immersed in distilled water for 24 h was determined as 200 mg. The water-uptake capacity of each sample could be calculated from the following equation:

$$\text{Water} - \text{uptake capacity}(\%) = (W - W_0)/W_0 \times 100, \quad (2)$$

where W_0 and W are the weights of the samples before and after 24 h of immersion in water, respectively.

Fourier transform infrared (FTIR) spectroscopy

FTIR spectroscopy of the samples carried out with an EQUINOX X55 model by Bruker Corp. (Billerica, MA, USA) with an attenuated total reflection technique at room temperature. The wave-number range used in FTIR spectroscopy was 1000–4000 cm^{-1}.

Tetracycline hydrochloride release rate measurements

An ultraviolet–visible spectrometer (UNICAM series 8700 model, Philips Co., Amsterdam, The Netherlands) was used for the determination of the antibiotic (tetracycline hydrochloride) release rate. The maximum wavelength for tetracycline hydrochloride in DMF solution was 364.8 nm. The calibration curve, with an r^2 value of 0.9966, was plotted with Beer–Lambert law according to the following linear equation:

$$A = \varepsilon \times 1 \times c = 0.037 \times c, \quad (3)$$

where A is the absorption percentage, c is the concentration of the antibiotic, l is the distance the light travels through the material and ε is the extinction coefficient of the antibiotic.

The molar extinction coefficient for the antibiotic (tetracycline hydrochloride) in DMF was found to be 17,793.3 (L/mol) for 1 cm of the linear Beer–Lambert curve. Absorption took place at 364.8 nm on the basis of concentration.

Antibacterial evaluations

The antibacterial activity of the electrospun nanofibers samples of PCL, PLA, and the 50/50 blend of PCL and PLA containing tetracycline hydrochloride with 250 and 500 μg/mL, along with the commercial sample Comfeel Plus, for the usual bacteria on wounds, such as *E. coli* (Gram negative, ATCC 25922) and *S. aureus* (Gram positive, ATCC 25023),

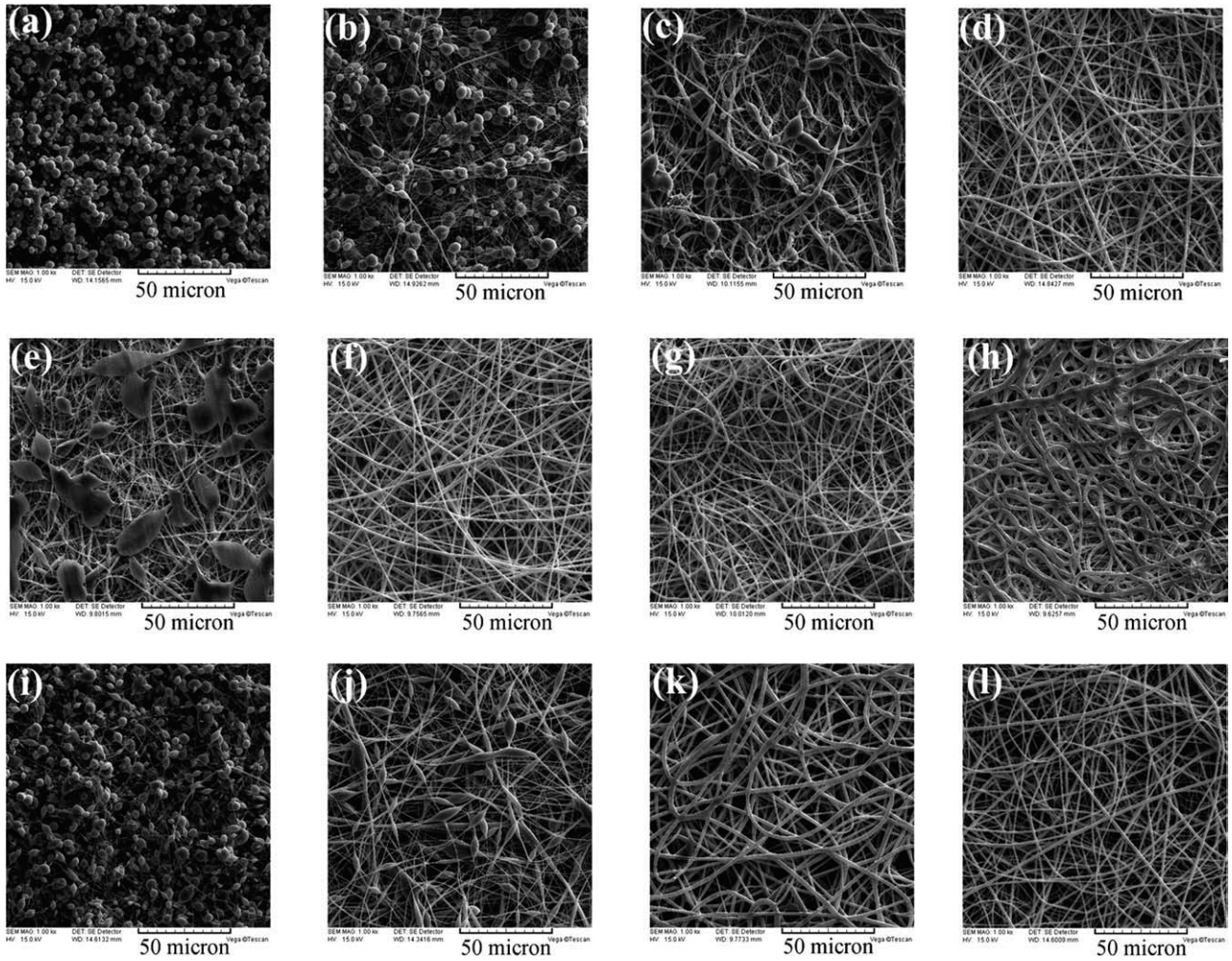


Figure 1 SEM micrographs of the nanofibrous mats prepared from PCL solutions with different concentrations [(a) 6, (b) 9, (c) 12, and (d) 15% w/v], PLA solutions with different concentrations [(e) 6, (f) 9, (g) 12, and (h) 15% w/v], and 50/50 PCL/PLA blend solutions with different concentrations [(i) 6, (j) 9, (k) 12, and (l) 15% w/v]. The operation conditions of the electrospinning were as follows: applied potential = 15 kV, tip-to collector distance = 12 cm, and flow rate = 0.7 mL/h.

were tested after 48 h. The assessments were conducted on the basis of the disc diffusion method of the U.S. Clinical and Laboratory Standards Institute. Nanofiber samples with the drug and without the drug and commercial samples were cut as circular discs with 7-mm diameters. The total amount of drug in the 7-mm disc of the electrospun patch was about 1 mg. The samples containing the drug and the other samples were placed on Difco^{TM}Mueller Hinton agar and then incubated at 37°C for 48 h. At inhibitory concentration, there should have been no growth of microbes; this was seen as a clear zone around the disc specimens. These were photographed for further evaluation.

Mechanical properties of the samples

The mechanical properties of the electrospun nanofiber samples of PCL, PLA, and the 50/50 PCL/PLA blend were tested for tensile strength and Young's modulus with an Instron model 5566 (Amersham, England) according to ASTM D 882-02. The crosshead speed for the sample extensions was 10 mm/min, and the gauge distance was 40 mm. The tests were carried out at a relative humidity of about 32 ± 1% and a temperature of 24°C. For each sample, three measurements were done, and the standard deviation was less than 5%.

RESULTS AND DISCUSSION

Selection of optimized electrospun samples from SEM analysis

Figure 1(a–l) and Table I show the morphology and mean diameter values for electrospun PCL, PLA, and 50/50 PCL/PLA nanofiber samples at 6, 9, 12, and 15% (w/v) concentrations without the tetracycline hydrochloride drug. The purpose of this test

TABLE I
Average Diameters of Electrospun Nanofibrous PCL, PLA, and Their 50/50 Blends for Different Polymer Solution Concentrations

Sample	Diameter (nm)	Sample	Diameter (nm)	Sample	Diameter (nm)
PCL (6% w/v)	159 ± 6.4	PLA (6% w/v)	744.3 ± 28	50/50 PCL/PLA (6% w/v)	271.3 ± 16.7
PCL (9% w/v)	433.6 ± 31.1	PLA (9% w/v)	842 ± 47.9	50/50 PCL/PLA (9% w/v)	799.3 ± 34.3
PCL (12% w/v)	557.3 ± 31.3	PLA (12% w/v)	741 ± 41.6	50/50 PCL/PLA (12% w/v)	1708 ± 72.9
PCL (15% w/v)	863 ± 61.7	PLA (15% w/v)	1551.6 ± 85.4	50/50 PCL/PLA (15% w/v)	885.3 ± 53.7

was to choose the best samples from each material at a definite concentration for injecting the drug. The results show that the PCL nanofibers with 15% (w/v) [Fig. 1(d)], PLA with 12% (w/v) [Fig. 1(g)], and 50/50 PCL/PLA with 15% (w/v) [Fig. 1(l)] concentrations had morphologies with smooth nanofibers, suitable diameters, and without any bead formation. The average diameters of the PCL, PLA, and 50/50 PCL/PLA nanofiber samples were 863, 741, and 885.3 nm, respectively (Table I). The formation of spherical beads observed in the SEM micrographs was due to incomplete vaporization of the solvent before the arrival of the polymer solution to the surface of the collector and also to agglomerate formation.

For constant electrospinning process parameters such as the constant distance between the needle head and the collector, the breakdown of the jet flow to droplets can be due to a low molecular weight or a low concentration of polymer solutions.[24]

To have a better control of the drug-release rate, a lack of the beads in the sample morphology is more important than the diameter of the nanofibers because the beads can trap some portion of the drug. Therefore, in view of the SEM observations, the best nanofiber samples selected for a known drug load were PCL, PLA, and 50/50 PCL/PLA with 15, 12, and 15% (w/v) concentrations, respectively.

It is to be noted that the porosity, diffusion, density, thickness, and degradation were the main factors controlling the drug-release rate in the nanofibrous mats. In this work, constant process variables (applied voltage, flow rate, distance between the needle tip to collector, etc.) were maintained to prevent large changes in the morphology and porosity of the obtained nanofiber mats due to process parameters.

Evaluation of the water-uptake capacity and WVP of the samples

The water uptake or fluid retention is a gravimetric test for determining the maximum fluid absorption of the wound surface for a wound dressing.

Because of the great importance of water loss control for an open and wet wound, controlling this factor is a very critical property for wound dressing materials. Figure 2 shows the water-uptake capacity for the electrospun nanofibrous PCL, PLA, 50/50 PCL/PLA, and commercial Comfeel Plus samples. From the results, we concluded that the rate of water uptake had a direct relation with the hydrophilic properties of the samples. The wettability and contact angle for PCL and PLA with water at 22°C were reported to be 70.7 and 67.7°, respectively, in the literature.[25] Also, the percentages of water absorption for PLA, PCL, and 50/50 PCL/PLA were 610, 500, and 520%, respectively (Fig. 2). The very high relative water-uptake percentages for these nanofibers were due to the high surface area-to-volume ratio compared with the Comfeel wound dressing from a polyurethane film (ca. 130%). Commercial Comfeel is a hydrocolloidal wound dressing, which is designed for high water absorption from the surface of exudate wounds.

Usually, for a normal skin, WVP is about 0.85 mg cm^{-2} h^{-1} and, for a damaged skin, is about 1.16–21.41 mg cm^{-2} h^{-1}. Normally, it is very important that a wound dressing must have a suitable WVP of about 8.3–10.4 mg cm^{-2} h^{-1}.[26] At these WVP values, additional dehydration reactions are prevented. Table II shows that the WVPs for the nanofiber samples were about 3–4 mg cm^{-2} h^{-1}; this was about 40% of the WVP optimum value for a suitable wound dressing. The relatively crystalline structure of the aliphatic polyester nanofibers reduced the WVP compared with an amorphous polymeric nanofiber structure. Considering the formulation design

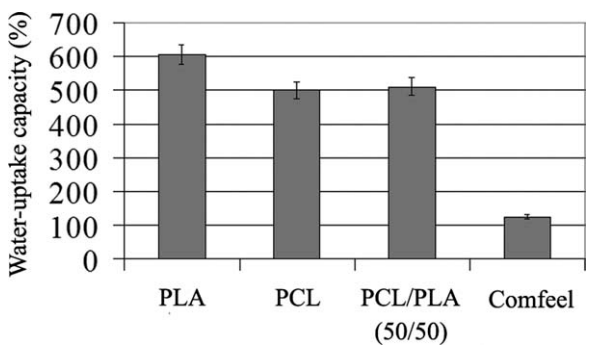


Figure 2 Water-uptake capacities of PCL, PLA, and 50/50 PCL/PLA blend nanofibrous mats and Comfeel Plus as a commercial wound dressing.

TABLE II
WVP of the PLA, PCL, and PLA/PCL Nanofiber Samples and the Well-Known Commercial Sample Comfeel Plus

Sample	PLA nanofibrous mats	PCL nanofibrous mats	PLA/PCL nanofibrous mats	Comfeel Plus (a commercial wound dressing)
WVP (mg cm^{-2} h^{-1})	3.17 ± 0.12	3.63 ± 0.22	3.7 ± 0.19	Nonpermeable

to get the most suitable WVP for these biodegradable aliphatic polyesters and also the water absorption abilities can make them suitable materials for wound dressings.

Biodegradable polymers can be hydrolyzed by water molecules. In the hydrolytic degradation mechanism of the polyesters, the water molecules attack the polyester bond —CO—O at a 1190-cm^{-1} wave number and break it down. Figure 3(a–f) shows the FTIR–attenuated total reflection spectra for the PCL, PLA, and (50/50) PCL/PLA blend samples without any drug loading before and after the WVP test. The ester group peak in PLA sample before the WVP test was about 1186.87 cm^{-1}

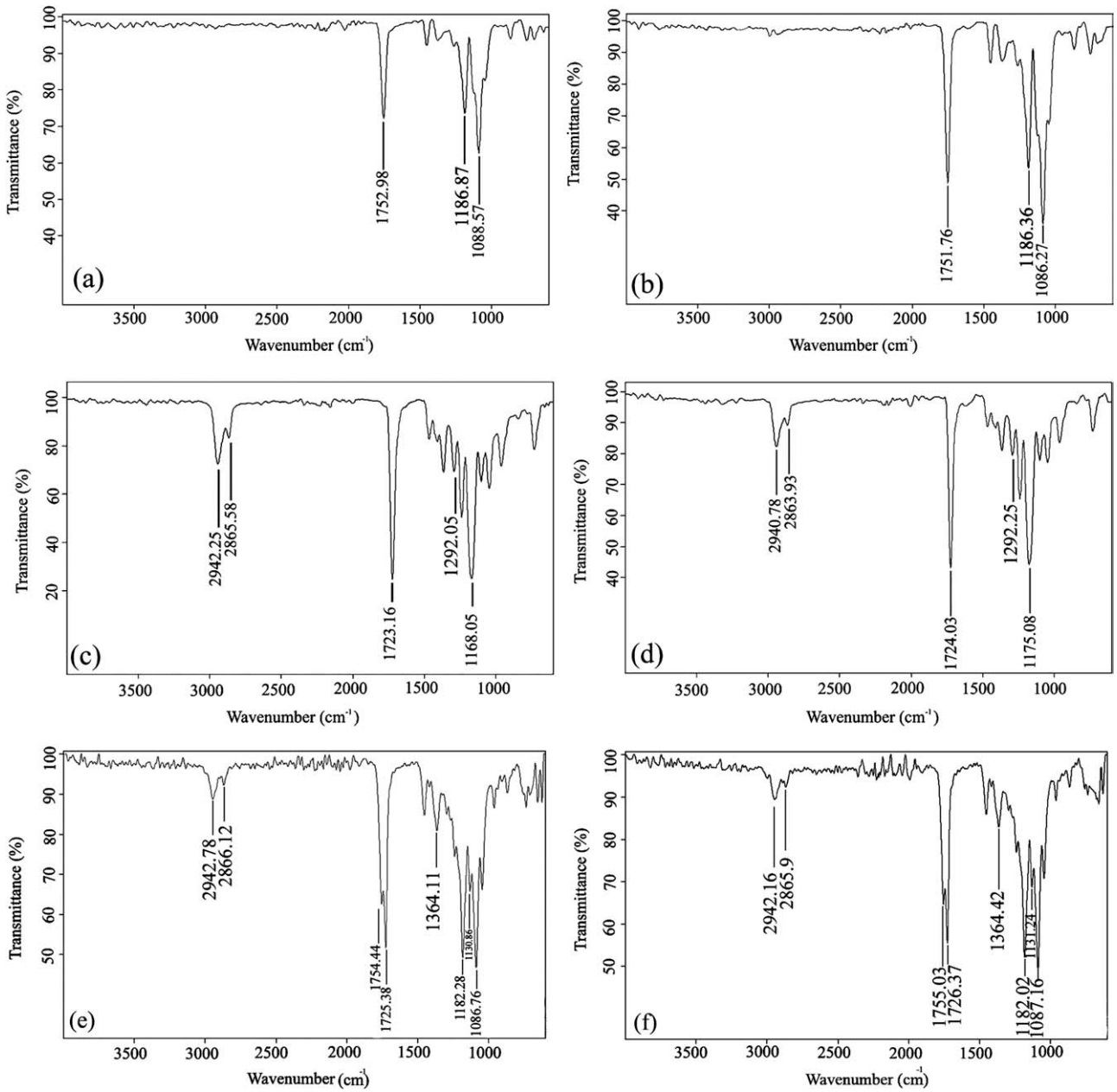


Figure 3 FTIR spectra of the PLA nanofibers (a) before and (b) after WVP testing, PCL nanofibers (c) before and (d) after WVP testing, and 50/50 PCL/PLA blends (e) before and (f) after WVP testing.

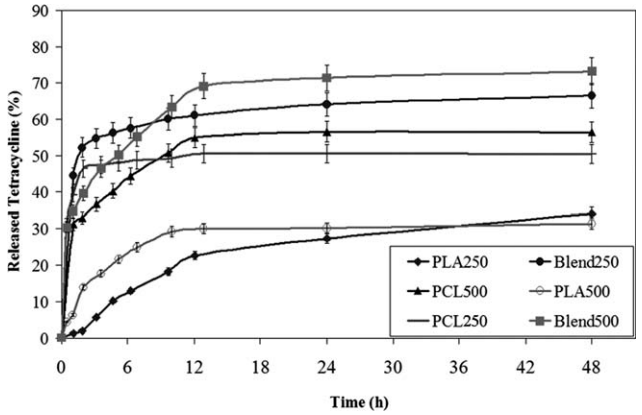


Figure 4 Release profiles of tetracycline hydrochloride drug from (◆) PLA with 250 μg/mL drug, (○) PLA with 500 μg/mL drug, (—) PCL with 250 μg/mL drug, (▲) PCL with 500 μg/mL drug, (○) 50/50 PCL/PLA blend with 250 μg/mL drug, and (■) 50/50 PCL/PLA blend with 500 μg/mL drug.

[Fig. 3(a)], and after the WVP test, it was 1186.36 cm^{-1} [Fig. 3(b)]. Also, for PCL nanofibers, the values were 1168.05 cm^{-1} [Fig. 3(c)] and 1175.08 cm^{-1} [Fig. 3(d)], respectively. These variations in the FTIR peaks for the blend samples were negligible, and the location of ester bonds before and after WVP test were 1182.28 and 1182.02 cm^{-1}, respectively [Fig. 3(e,f)]. These results show that the extent of nanofiber degradation due to hydrolysis during the WVP test was nonsignificant.

Tetracycline hydrochloride release rate and antibacterial evaluation

Figure 4 shows the profiles of the tetracycline hydrochloride release rate for the PCL, PLA, and 50/50 PCL/PLA blend samples containing 250 and 500 μg/mL drug. The results were obtained in the presence of a phosphate buffer solution at pH 7.4 for 48 h. It was seen that all of the samples showed a two-stage (bimodal) drug-release pattern. Moreover, the 50/50 PCL/PLA sample containing 500 μg/mL tetracycline hydrochloride had the highest drug-release rate (ca. 70%), followed by 250 μg/mL drug-loaded blend sample and PCL nanofiber containing 500 μg/mL drug with the highest drug-release rates of 65 and 60%, respectively. The PLA nanomats with 250 and 500 μg/mL drug loadings had the lowest release rate (ca. 30%). This slow release rate of PLA could be attributed to its partial crystallinity, which limited the diffusion of the aqueous environment into the polymer layers and, consequently, limited the diffusion of the drug from the nanofibers.

The bimodal drug-release pattern could be explained on the basis of a two-release mechanism, as proposed by Jannesari et al.[27] They attributed the bimodal release behavior to a diffusion mechanism, best described by the Higuchi model, during the initial stage of release and to an erosion mechanism, described by the Hixson–Crowell model, during the final stage of the release process.

The antigrowth region for *S. aureus* bacteria in different nanofiber samples was evaluated, and the results are presented in Figure 5(a–e). The following sample coding was used to distinguish the specimens.

The blend samples loaded with 250 and 500 μg/mL drug were denoted as 1 and 2, the PCL samples containing 250 and 500 μg/mL drug were denoted as 3 and 4, the PLA samples containing 250 and

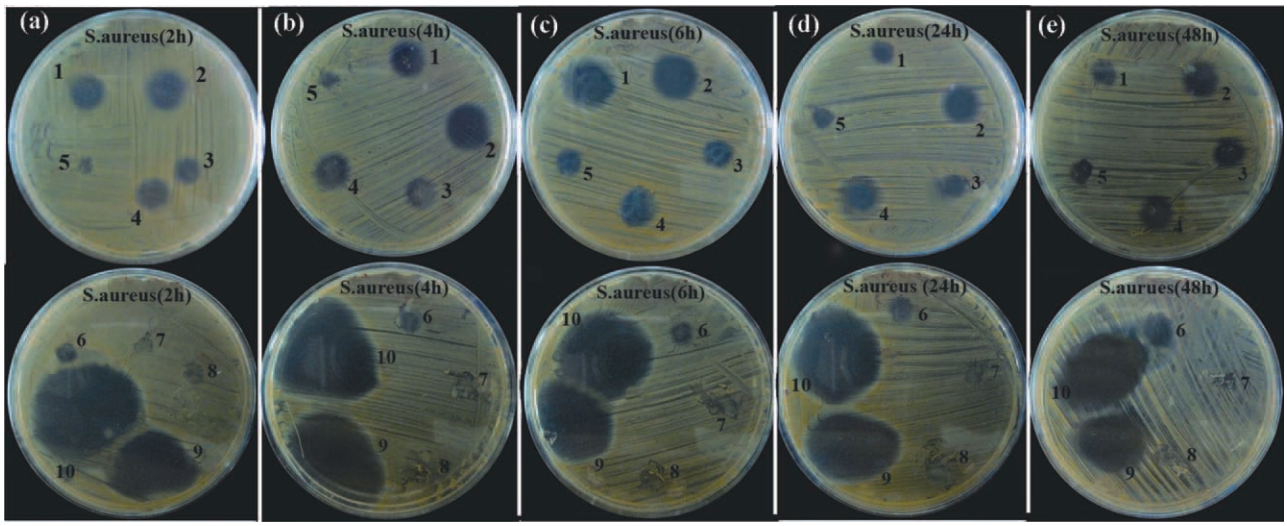


Figure 5 Antibacterial activities of (1) 50/50 PCL/PLA blend with 250 μg/mL drug, (2) 50/50 PCL/PLA blend with 500 μg/mL drug, (3) PCL with 250 μg/mL drug, (4) PCL with 500 μg/mL drug, (5) PLA with 250 μg/mL drug, (6) PLA with 500 μg/mL drug, (7) 50/50 PCL/PLA blend without drug, (8) Comfeel Plus, (9) tetracycline hydrochloride drug solution (250 μg/mL), and (10) tetracycline hydrochloride drug solution (500 μg/mL) against *S. aureus* after (a) 2, (b) 4, (c) 6, (d) 24, and (e) 48 h. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

TABLE III
Antibacterial Activity of the Electrospun Fiber Mats from the PCL and 50/50 PCL/PLA Solutions

	Antibacterial activity in terms of disc diffusion method reported as inhibition zone diameter (cm)/sample diameter (cm)						
	S. aureus					*E. coli*	
Sample no.	2 h	4 h	6 h	24 h	48 h	4 h	24 h
1	1.5/0.7	1.7/0.7	1.9/0.7	0.8/0.7	0.8/0.7	0.7/0.7	1/0.7
2	1.7/0.7	1.9/0.7	1.7/0.7	1.4/0.7	1.4/0.7	0.9/0.7	0.7/0.7
3	0.8/0.7	1.2/0.7	0.1/0.7	0.9/0.7	0.9/0.7	0.7/0.7	0.7/0.7
4	1.3/0.7	1.7/0.7	1.4/0.7	1.6/0.7	1/0.7	1.1/0.7	1.2/0.7

1, PCL/PLA + 250 μg/mL tetracycline; 2, PCL/PLA + 500 μg/mL tetracycline; 3, PCL + 250 μg/mL tetracycline; 4, PCL + 500 μg/mL tetracycline.

500 μg/mL drug were denoted as 5 and 6, and the unloaded blend and the commercial sample (negative controls) were denoted as 7 and 8, respectively. The tetracycline hydrochloride solutions with 250 and 500 μg/mL concentrations (positive controls) were denoted as 9 and 10, respectively.

Figure 5(a) shows no significant bacterial inhibition zone formation changes for samples 6–8. PLA samples containing the drug, Comfeel, and the polyblend sample without the drug did not show any activity against the bacteria. On the other hand, the observations from Figure 5(a–e) for samples 1–5 were remarkable for 2–48 h; the diameter for the lack of bacterial growth zone was variable for different samples. The results represented in Table III show that, as shown in Figure 5(a), the diameter of bacterial growth inhibition for samples 2, 1, and 4 were 1.7, 1.5, and 1.3 cm, respectively. This process was reduced after 48 h, and for these samples, 1.4-, 0.8-, and 1-cm diameters, respectively, were observed. Sample 1 showed

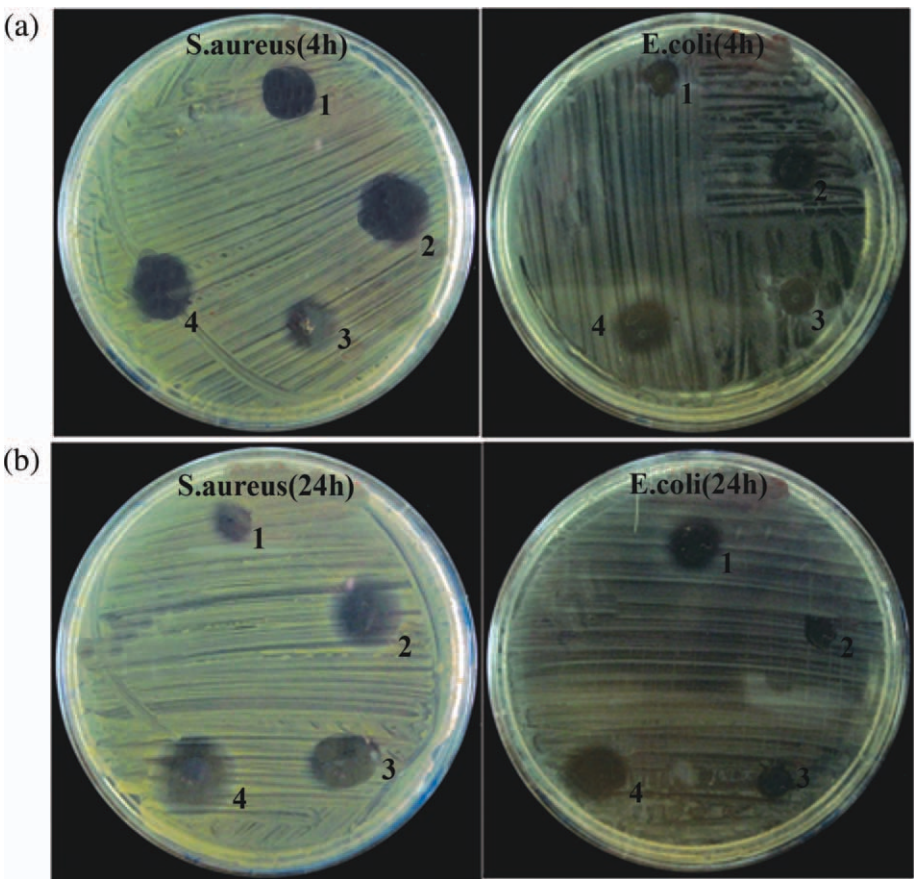


Figure 6 Comparison of (1) 50/50 PCL/PLA blend with 250 μg/mL drug, (2) 50/50 PCL/PLA blend with 500 μg/mL drug, (3) PCL with 250 μg/mL drug, (4) PCL with 500 μg/mL drug, and (5) PLA with 250 μg/mL drug between *S. aureus* and *E. coli* after (a) 4 and (b) 24 h. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

the most reduction because of the plateau profile of tetracycline hydrochloride release, which will bring about the release of drug in a bacterial cultivation environment; as a result, bacteria will grow again, and the bacterial inhibition zone is reduced.

Figure 6(a,b) shows the performance of the samples containing the drug in 4 and 24 h for *E. coli* and *S. aureus* bacteria, respectively. Generally, the effect of tetracycline hydrochloride antibiotic for *S. aureus* bacteria is stronger than that for *E. coli* because *E. coli* is a Gram-negative bacterium and *S. aureus* is a Gram-positive bacterium, and their cellular wall structures are different from each other.[28] Also, the results presented in Table III and a comparison between the bacterial inhibition zone diameters for 4 and 24 h for the samples confirmed these conclusions.

Mechanical properties of the electrospun nanofibers samples

Although the use of nanofibrous wound dressings do not require high mechanical properties, to have easy application and for a better situated wound dressing on a wound, the mechanical properties of the different samples were compared with each other. Figure 7 and Table IV show the stress–strain curves, modulus, tensile stress at maximum load, and elongation at break for the samples. For each experimental result, we concluded that the structure of elastomeric nanofibers led to a higher toughness and flexibility compared with the PLA and 50/50 PCL/PLA samples (elongation at break = 300%). This behavior was attributed to semielastomeric property and the presence of a methyl group in the chemical structure of this polymer.[29] The mechanical property behavior of the 50/50 PCL/PLA sample was due to unsuitable blending properties of the blend components and probably the phase separation in this sample during the electrospinning process. The result of possible phase separation for the blended sample (50/50 PCL/PLA) led to a weak interaction between the polymer chains of the blended components, and therefore, failure occurred in these regions.

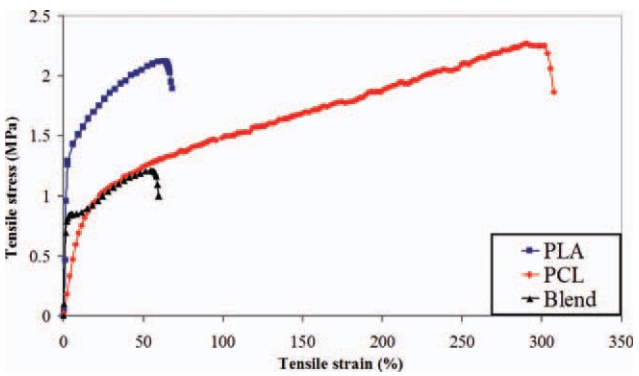


Figure 7 Stress–strain curves of the nonwoven nanofibrous samples (■) PLA, (○) PCL, and (▲) 50/50 PCL/PLA blend. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

TABLE IV
Mechanical Data for the PLA, PCL, and PLA/PCL (50/50) Samples

Sample	Modulus (MPa)	Tensile stress at maximum load (MPa)	Elongation at break (%)
PLA	42.01 ± 23.20	2.12 ± 0.12	67.57 ± 12.33
PCL	7.86 ± 0.74	2.26 ± 0.25	277.01 ± 48.37
Blend (50/50 PLA/PCL)	23.43 ± 11.01	1.24 ± 0.16	47.5 ± 6.38

The results of this study show that the nanofiber mats made from PCL and PLA/PCL blends showed better performance compared to the commercial wound dressing material as far as the water uptake, water permeability, drug-release rate, and antibacterial activity were concerned. It is to be noted that for a suitable wound dressing with an optimized performance, besides these characteristics, the biocompatibility and biodegradability are also important parameters for ideal therapeutic effects. These issues will be considered in our next studies.

CONCLUSIONS

Optimized electrospun nanofibers of PCL, PLA, and 50/50 PCL/PLA blend samples containing tetracycline hydrochloride with polymer solutions having concentrations of 6, 9, 12, and 15% (w/v) and tetracycline hydrochloride concentrations of 250 and 500 μg/mL were investigated, and the results were compared with those of a well-known commercial sample, Comfeel Plus. The SEM micrographs showed that PCL, PLA, and 50/50 PCL/PLA samples with 15, 12, and 15% (w/v) concentrations had the best morphologies. Water absorption and WVP results obtained for PLA, PCL, and 50/50 PCL/PLA had the highest values. These results had a direct relation with the hydrophilic properties of these polymers. The 50/50 PCL/PLA blend loaded with 500 μg/mL drug had the highest drug-release rate of about 70% in phosphate buffer solution and the most effective antibiotic activity against *S. aureus* bacteria among all of the investigated samples. The results show that the nanofiber mats made from PCL and the PLA/PCL blends had better performance compared to the commercial wound dressing material as far as the water uptake, water permeability, drug-release rate, and antibacterial activity were concerned.

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