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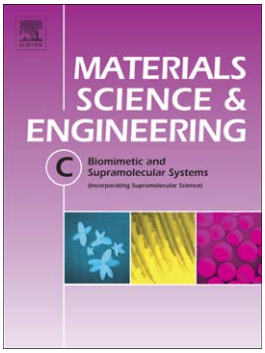

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A Novel Multifunctional Biomedical Material Based on Polyacrylonitrile：Preparation and Characterization

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ABSTRACT

Wet spun microfibers have great potential in the design of multifunctional controlled release materials. Curcumin (Cur) and vitamin E acetate (Vit. E Ac) were used as a model drug system to evaluate the potential application of the drug-loaded microfiber system for enhanced delivery. The drugs and polyacrylonitrile (PAN) were blended together and spun to produce the target drug-loaded microfiber using an improved wet-spinning method and then the microfibers were successfully woven into fabrics. Morphological, mechanical properties, thermal behavior, drug release performance characteristics, and cytocompatibility were determined. The drug-loaded microfiber had a lobed "kidney" shape with a height of 50~100 μm and width of 100~200 μm. The addition of Cur and Vit. E Ac had a great influence on the surface and cross section structure of the microfiber, leading to a rough surface having microvoids. X-ray diffraction and Fourier transform infrared spectroscopy indicated that the drugs were successfully encapsulated and dispersed evenly in the microfilament fiber. After drug loading, the mechanical performance of the microfilament changed, with the breaking strength improved slightly, but the tensile elongation increased significantly. Thermogravimetric results showed that the drug load had no apparent adverse effect on the thermal properties of the microfibers. However, drug release from the fiber, as determined through *in-vitro* experiments, is relatively low and this property is maintained over time. Furthermore, *in-vitro* cytocompatibility testing showed that no cytotoxicty on the L929 cells was found up to 5% and 10% respectively of the theoretical drug loading content (TDLC) of curcumin and vitamin E acetate. This study provides reference data to aid the development of multifunctional textiles and to explore their use in the biomedical material field.

Keywords: biomedical materials, drug delivery system, wet spinning, polyacrylonitrile

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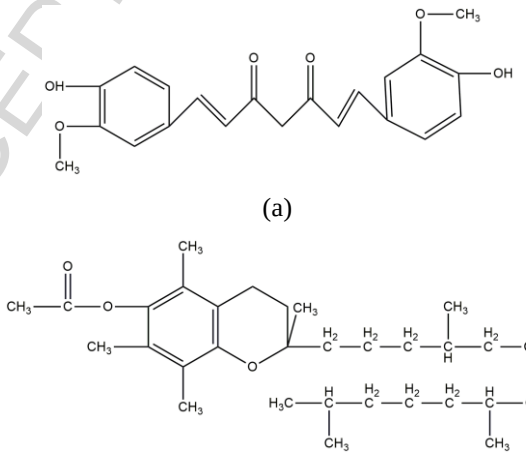
1. Introduction

Multifunctional drug-loaded fibers [1-3] have attracted extensive attention because of their unique properties which offer the ability of drug controlled release and a set of functionalities, such as antibacterial, therapeutic effects and morphological changes. Thus, their functional activity is mainly attributed to their gradual and persistent release from the fibers into the moist environment. On the other hand, one of the difficulties of drug release whether *in vivo or in vitro* is the uncontrollable release rate [4] with usually a burst release phenomenon [5,6] which results in a lower utilization of a drug. Thus, the drug delivery system（DDS）has become a very important topic in current pharmaceutics and consequently drug-loaded fibers have received considerable attention [7, 8] and play a crucial role.

Along with living standard improvements, people have begun to pay more attention to physical health resulting in an increased demand for a variety of healthcare clothing and textiles incorporating natural dyes [9]. Natural products of plant origin have been used for years in medicine and pharmacy for the prevention and treatment of different diseases [10,11] and one of the most extensively studied representatives is curcumin (Cur) [Fig. 1(a)]. It is a low molecular weight natural yellow-orange polyphenol compound [12] which exhibits a wide spectrum of antibacterial, antiviral and antitumor therapeutic properties [9] and is also well known for its anticoagulant [13], antioxidant and anti-inflammatory activity and is used in wound treatment [14]. In the field of textile dyeing, curcumin it has been widely studied since it is a natural pigment, [9,15] and it has high color stability and good fastness due to its structure [16]. One concern, however, is that the mechanical properties of the fibers after drug loading will decrease, but on the contrary, studies have indicated that the addition of curcumin to the fiber is beneficial [17,18].



(a)

(b)

Figure 1. Chemical structure of (a) curcumin and (b) vitamin E acetate.

Vitamin E (α-tocopherol; Vit. E), having anti-aging properties and the ability to improve immunity, is a natural biological anti-inflammatory and antioxidant agent protecting cells from damaging effects [19,20]. At present, it is extensively used in the pharmaceutical, health care, food and cosmetics industries. Vitamin E acetate (Vit. E Ac, tocopheryl acetate) [Fig. 1(b)] is the semi-synthetic esterified form of Vit. E, which is commonly used as a more stable alternative to tocopherol. Moreover, it is believed that this molecule, when absorbed through the skin, undergoes hydrolysis, regenerating α-tocopherol [21] and several studies have shown that it has a positive

effect on biomaterials such as in textile finishing [22], bone tissue [21], orthopedic engineering [23] and dialysis membranes [24-27] by maintaining or enhancing mechanical properties, improving biocompatibility and increasing of antioxidative performance.

Wet spinning is now considered to be a mature technology having emerged from the textile industry in the 1930s as a means of producing synthetic fibers such as viscose, polyvinyl alcohol and polyacrylonitrile (PAN) [28]. In general, fibers such as PAN which cannot be processed using the melt spinning process are more suitable for wet spinning because their melting point is higher than their decomposition temperature. At present, research on fibers such as polylactic acid [29], chitin [30], chitosan [31], silk fibroin [32], collagen [33], bacterial cellulose [34], sodium alginate [6] and fibers produced as composites/blends，known as novel functional materials or biodegradable wet spun polymers, have become a topic of great interest due to their potential application as biomedical materials.

Recently, the flexible technique of physical blending technology has become popular and by utilizing this technology, drugs may be dissolved or dispersed in a spinning dope matrix, then wet spun blended to produce drug-loaded fibers. The resulting product allows for slow drug release due to decomposition of the polymer or by diffusion of the drug from the fiber channel. Drug loaded wet spun fiber technology has been widely studied in the last 10 years and has mainly focused on two areas: tissue engineering [3,35,36] and medical textiles such as surgical sutures, drug dressings [6,7] and clothing textiles [37-39].

Based on previous work, more advanced equipment and an enhanced preparation process was employed to prepare a new fiber with potential commercial application. In this paper, vitamin E acetate (a lipid soluble antioxidant) and curcumin (a water insoluble yellow-orange compound with multiple therapeutic properties) were blended with polyacrylonitrile（PAN）via a wet spinning process in order to obtain multifunctional microfibers. PAN, a well-known polymer exhibiting excellent thermal and mechanical stabilities and processability, is widely utilized as ultrafiltration and hemodialysis membranes and in the preparation of textile, flame retardant and carbon fibers [40,41]. The spun-dyed [42-45] drug-loaded fibers with a bright yellow color have the advantages of having environmentally friendly processing, evenness of dyeing and offer microvoid structures with better capillary suction effects and biomedical properties for DDS, and have enhance stability, uniformity and functionality. Furthermore, for the first time we report the preparation of the wet-spun fibers loaded with two drugs, curcumin and vitamin E acetate which exhibit various functions, such as anti-aging, biocompatibility, antitumor, anti-inflammatory effects. Besides, the curcumin and vitamin E acetate are all relatively stable and they can be used as models to analyze the release behaviors of two drugs from wet-spun fibers and may provide reference for the development of multifunctional textiles in the biomedical material field and could find potential applications in health care underwear, surgical dressings and dialysis materials [46,47].

2. Materials and methods

2.1. Materials

PAN (Mw≈80,000) was provided by Jinshan Petrochemistry Co., Ltd. (Shanghai, China). Pharmaceutical grade curcumin and vitamin E acetate and analytical quality chemicals were purchased from Sinopharm Chemical Reagent Co., Ltd. L929 cells (mouse fibroblast cells) were provided by the Institute of Biochemistry and Cell Biology (Chinese Academy of Sciences, China).

2.2. Preparation of spinning dope and microfiber fabrication

It is well known that the properties of fabricated fibers obtained from a homogeneous spinning dope are superior to those made from a dispersion system, so dimethylacetamide (DMAc) was utilized as solvent since it can readily dissolve PAN, curcumin and vitamin E acetate. In order to obtain homogeneity, four methods of preparing the spinning solutions were investigated: (i) PAN powder (25.0g) was added into DMAc (100 mL) and dissolved by stirring at 65 ^{o}C for 5 h and then Cur (1.25g) and Vit A acetate (2.5g) were added into the PAN/DMAc solution maintained at 65 ^{o}C; (ii) Cur (1.25g) and Vit A acetate (2.5g) were added into DMAc and dissolved by stirring at 65 ^{o}C for 1 h. PAN powder (25.0g) was then added into the DMAc/drug solution and dissolved by stirring at 65 ^{o}C for another 5 h; (iii) PAN powder (25.0g), Cur (1.25g) and Vit A acetate (2.5g) were added simultaneously with stirring to DMAc and kept at 65 ^{o}C for 5 h; (iv) PAN powder (25.0g) and the drugs were separately dissolved in DMAc (50 mL) with stirring at 65 ^{o}C and then stirred together before spinning.

Microfibers were spun on a custom-made wet-spinning device (Fig. 2) using the spinning process parameters shown in Table 1. A nitrogen pressure of 0–0.3 MPa controlled by a pressure regulator was used to extrude the aqueous solutions (20% w/w) at 1.0 mL/min through a commercial spinneret plate with thirty 0.1 mm diameter orifices. The spinning dope was extruded directly into an aqueous DMAc (50% v/v) coagulant solution kept below 15 ^{o}C using ice. The effective length of the coagulation bath, the second and the third bath was 60 cm and after passing though the baths and the three rollers, the resulting microfibers were wound onto spools, dried at 50 ^{o}C for 2–3h and then woven into fabrics.

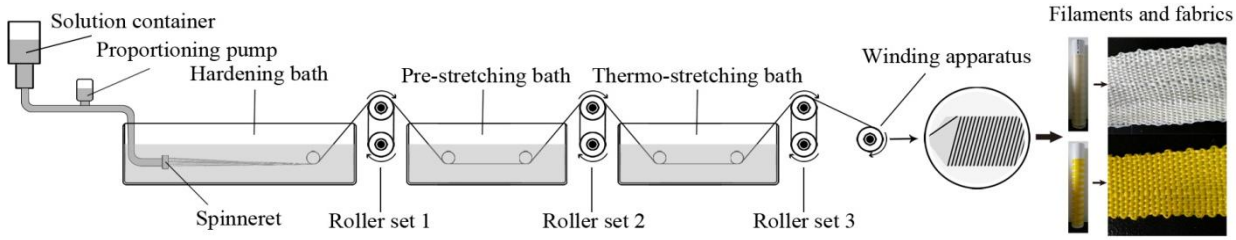


Figure 2. Wet spinning line, spun filaments and woven fabrics.

Table 1.
The wet spinning process parameters.

Spinning bath	Hardening bath	Pre-stretching bath	Thermo-stretching bath
Composition	50% DMAc	Water	Water
Temperature (◦C)	15	55	90
Rollers	Roller 1	Roller 2	Roller 3
Diameter of rollers (cm)	25	25	25
Speed of rollers (rpm)	1.0	2.0	4.0
Winding speed (m/min)		100	

2.3. Determination of drug content

An appropriate weight of microfibers was cut up into very small pieces (ca. 0.5 mm) and loaded into a dialysis tube (MWCO: 10–12 kDa) against a 60% (v/v) aqueous solution of DMAc at 30 °C for 1 day. Thus, any drugs that were dissolved and passed out of the dialysis tube into the aqueous solution were determined using a spectrophotometric method (Unico UV-2102PC Shanghai, China) at a wavelength of 430 nm for Cur and 286 nm for Vit. E Ac. The amount of drug in the microfibers was back-calculated from the obtained data against

predetermined calibration curves. Drug loading content (DLC) was defined as follows:

$$DLC(\%) = \frac{\text{actual content of drug}(mg)}{\text{fiber sample weight}(mg)} \times 100\% \quad (1)$$

The theoretical drug loading content (TDLC) was also calculated:

$$TDLC(\%) = \frac{\text{added amount of drug}(mg)}{\text{added amount of drug and PAN}(mg)} \times 100\% \quad (2)$$

2.4. Viscosity testing

The viscosity of the spinning solution was measured using a NDJ-8S Digital Viscometer (Sunny Hengping Scientific Instrument Co. Ltd., Shanghai, China) at different temperatures.

2.5. Mechanical properties

The mechanical properties of microfibers were measured with a XQ-2 Fiber Tension Meter (Shanghai S&CI, Shanghai, China) using a gauge length of 20 mm and crosshead speed of 50 mm/min. All samples were preconditioned at 20 °C and 65% relative humidity for 24 h prior to mechanical testing. The tensile strength and breaking elongation were calculated and the mean and standard deviation reported for n = 20.

2.6. Color strength (K/S).

The color strength (K/S) value of the fabric prepared from the spun-dyed microfiber containing Cur was measured using a Datacolor 650 spectrophotometer (Datacolor, USA) under illuminant D65 and 10° standard observers. The color strength was calculated from the reflectance at 430 nm using the Kubelka–Munk equation as given in Eq. (3) where R and R_0 are the reflectance of the colored and uncolored fabrics made from the spun-dyed microfiber:

$$K/S = \frac{(1-R)^2}{2R} - \frac{(1-R_0)^2}{2R_0} \quad (3)$$

2.7. In vitro drug release

Experiments were conducted at 37 ^{o}C and 100 rpm in a thermostatic shaking incubator (Jintan Instrument Co. Ltd., Jiangsu, China) in the release medium (20 mL; pH 7.2 phosphate buffer with 10% ethanol and 0.5% (v/v) Tween 80). A volume (1mL) of release media was removed at regular intervals and the remaining volume was kept constant by the addition of fresh buffer. The sample solutions were analyzed at a wavelength of 430 nm for Cur and 286 nm for Vit. E Ac on a UV spectrophotometer (UV-2102, Unico Instrument Co., Ltd., Shanghai, China). The amount of drug release was determined using a standard curve of Cur and Vit. E Ac. and plotted as the percentage released versus time. All measurements were carried out in triplicate and the results reported as average values ± S.D.

2.8. Cell culture and cytocompatibility assay

L929 cells were selected as a model cell line for the cytocompatibility assay. Wet spun fibers were first woven into fabrics and then four groups of woven fabric pieces (drug loaded and unloaded) with a circular shape (diameter = 14mm) were placed in 24-well plates and another group without fabric was set as the control. A stainless steel ring was placed on the top of each fabric sample prevent it from floating [48]. The culture plates

were sterilized by alcohol steam for 4 h and PBS solution was used for washing away any residual alcohol. After being soaked with DMEM, all the culture plates were put in an incubator for 24 h (37 °C, 5% CO_2). After this time, a suspension of L929 cells (200 μL; with a cell density of 1.0×10^4 cells/mL) was seeded into each well with DMEM (containing10% FBS) and then incubated (37 °C, 5% CO_2). The time points of the test were set as 1, 3 and 5 days and at each point, the culture plates were taken out of the incubator and the DMEM in every well was replaced by fresh DMEM (360 μL) and MTT (40 μL) solutions. After incubation for 4 h, DMSO (400μL) was added to each well and the plates shaken for 30 min at room temperature. Afterwards, the solutions in each well were transferred into 96-well plates and the OD values of the resulting purple solutions were measured at 570 nm with a Microplate Reader (Multiskan, ThermoFisher, USA).

2.9. Statistical analysis

Statistical analysis was carried out using the unpaired Student's t-test on SAS software (version 9.0). A value of $p < 0.05$ was considered statistically significant. Data are annotated with * for $p < 0.05$, ** for $p < 0.01$, and *** for $p < 0.001$.

2.10. Further characterization

Scanning Electron Microscopy (SEM). The morphology of the microfiber was characterized with a JSM-5600LV scanning electron microscope (JEOL, Tokyo, Japan) and the samples were prepared by the epoxy resin embedding method.

Fourier Transform Infrared (FTIR). The FTIR spectra of the blank and drug-loaded PAN were recorded on a Nicolet-Nexus 670 FTIR spectrometer (Nicolet Instrument Corp., Madison, WI) in the wavenumber range 500–3000 cm^{-1}.

X-ray Diffraction (XRD). XRD measurements were performed on a Bruker D Advance Xray powder diffractometer with a graphite monochromatized Cu Ka electrode (k50.15406 nm). A scanning rate of 0.058/s was applied to record the pattern in the 2θ range of 10–70°.

Thermogravimetric Analysis (TGA). Thermogravimetric data were recorded on a TG209F1 thermogravimetric analyzer (TA Instruments Corp., Delaware, USA) from 20 to 900 °C at a heating rate of 20 °C /min under a nitrogen atmosphere. Differential thermal gravity (DTG) is a differential obtained from the TG curve.

Prior to XRD, FTIR and TGA characterization, the microfibers were cut up into very small pieces (ca. 0.5 mm) using scissors since a homogenizer may cause a decrease in crystallinity.

3. Results and discussion

3.1. Wet-spinning of drug−loaded microfibers

In the spinning process, the dissolution properties and the added sequence of drugs were considered carefully and four methods of adding drugs and PAN into DMAc were selected (Section 2.2). In the first and third methods, PAN was found to be completely dissolved whereas the drugs were only partly soluble. For the second and the fourth methods, both PAN and drugs easily dissolved but drugs in the second approach are more likely lose efficacy because the DMAc/drug solution system needed extended time (ca.5h) to dissolve the PAN powder. Therefore, the fourth method was considered the most suitable for further studies. In order to

achieve favorable double diffusion during coagulation of the polymer, several other factors such as the components and temperature of the coagulation bath, draw ratio and heat setting conditions were considered. Furthermore, the whole process was kept very dry by exclusion of air as any moisture would lead to poor quality of the spinning solution.

3.2. Fiber properties

In this study, four different types of fibers were prepared: blank PAN fiber (S_0); Cur / PAN fiber (S_1); Vit. E Ac /PAN fiber (S_2); and Cur /Vit. E Ac / PAN fiber (S_3) and the properties are listed in Table 2.

Table 2.
Composition of spinning solution and properties of the drug-loaded PAN fibers.

Samples	Spinning solution		Properties of fibers							
	TDLC (%)	Viscosity at 65℃ (Pa·s)	DLC (%)	linear density (dtex)	Breaking strength (cN/dtex)	SD	Tensile elongation (%)	SD	Moisture regain（%）	K/S at λmax=430nm
S_0	0	21.16×10^3	0	18.21	2.45	0.13	12.27	1.37	2.64	
S_1	Curcumin 5%	18.24×10^3	3.86	13.87	2.68	0.17	18.74	2.05	2.23	15.16
S_2	Vit. E Ac 10%	16.65×10^3	7.09	14.33	2.53	0.14	19.25	2.26	2.26	
S_3	Curcumin 2% ; Vit. E Ac 10%	17.08×10^3		15.26	2.60	0.16	21.58	2.53	1.82	9.42

In Table 2, it can be seen that the DLC is lower than TDLC because some of the drugs diffuse into coagulation bath during spinning. Also, the four samples had different viscosities at 65 °C and it appears that the viscosity of the spinning solution decreased after addition of the drugs probably due to the molecular weight of curcumin (368.39) and vitamin E acetate(472.75) being very low compared to the PAN (n≈70 kDa) thus causing a decrease in viscosity of the spinning dope. Table 2 also shows that there are considerable differences in properties between the four microfibers and such information on the mechanical properties could be used as a guide for selection or modification for further applications. After drug loading, linear density decreased, signifying that the fibers were thinner. The breaking strength increased slightly and the tensile elongation increased significantly probably because the addition of small molecules can facilitate molecular chain slip in the fiber; and the moisture regain decreased probably due to the hydrophobic character of the drugs. Hence, compared to the blank PAN, blended spun fibers containing curcumin and vitamin E acetate can enhance the mechanical properties of the composite materials as also observed in previous studies [17,18,23]. By contrast, the standard deviations (SD) showed low values of 0.13, 0.17, 0.14, 0.16 for breaking strength and 1.37, 2.05, 2.26, 2.53 for tensile elongation reflecting relatively good accuracy and stability during manufacturing process. In addition, the spun filaments showed that the K/S value of curcumin 5% / PAN fiber and curcumin 2% / vitamin E acetate 10% / PAN fiber were 15.16 and 9.42, respectively, indicating that curcumin can be considered as a very excellent colorant [15,16,49].

3.3. Fiber morphology

The surface and cross-sectional morphology of wet spun microfibers, shown in Fig. 3 and Fig. 4, were analyzed with a JSM-5600LV scanning electron microscope.

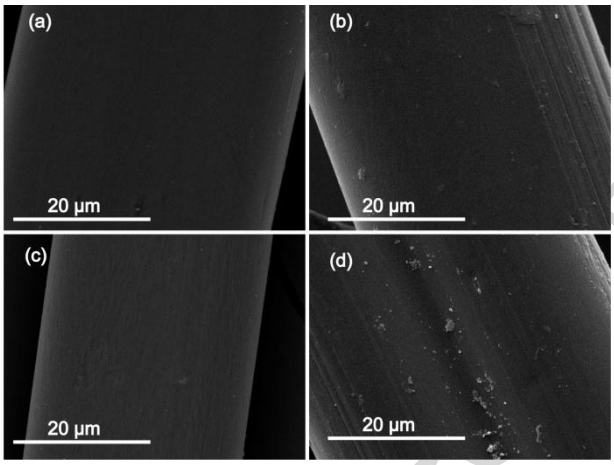


Figure 3. SEM images at 3000x magnification of the surface morphology of (a) blank PAN, (b) curcumin / PAN, (c) Vit. E Ac / PAN, and (d) curcumin / Vit. E Ac / PAN.

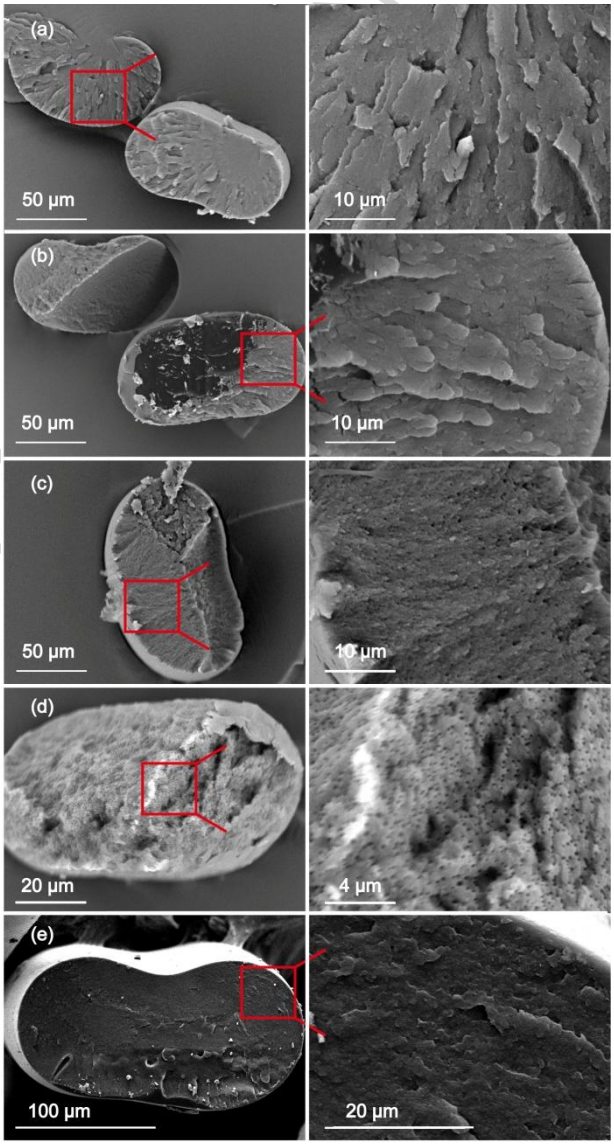


Figure 4. SEM images at 1000~5000x magnification of the cross-sectional morphology of (a) blank PAN; (b) curcumin / PAN; (c) Vit. E Ac / PAN; (d) curcumin / Vit. E Ac / PAN; and (e) nascent blank PAN (i.e. passed through the spinneret but was not drawn).

It can be seen from the images in Fig. 3 that the blank PAN shown in Fig. 3(a) has a smooth surface whereas the curcumin / PAN (b) and curcumin / Vit. E Ac / PAN (d) have obvious groove structures and are covered by granular material, which are probably drug aggregates, and the Vit. E Ac /PAN (c) appears to have a relative rough surface. Hence, it can be concluded that the rough surface is caused by Vit. E Ac while the granular material is due to the curcumin.

The SEM images in Fig. 4 show the cross-sectional morphology of the fibers and they all exhibit a lobed "kidney" shape with a height of 50~100 μm and width of 100~200 μm. The fiber shape can be explained by the solvent and non-solvent (water) counter-diffusion. If the rate of solvent diffusing out is higher than the rate of non-solvent diffusing in then the fiber structure collapses and a non-circular "kidney" shape is obtained [50]. The images shown in Fig. 4(a-b,e) possess a similar cross-sectional structure whereas Fig. 4(c and d) display porous structures which differ in the size and distribution of the holes caused by the presence of Vit. E Ac. Therefore, the addition of drugs has a great influence on the structure of the fibers both in terms of surface and cross section morphology. The porous structure is formed during the process of fiber preparation when rapid surface coagulation during phase inversion leads to entrapment of solvent and non-solvent within the precipitating microfilament [51] and a porous structure is formed once solvent and non-solvent are evaporated after microfilament solidification [29].

3.4. XRD analysis

XRD experiments were used to determine the crystalline structure of PAN microfibers and X-ray scattering patterns of blank and drug-loaded microfibers and are presented in Fig. 5. Pure curcumin exists in a crystalline state, displaying a number of characteristic reflections between 10° and 30° 2θ. For PAN microfibers, one large peak (16.8) and one small peak (28.4) is observed and it can be seen that 2θ and the diffraction intensity of drug loaded fibers are virtually identical to blank PAN fibers suggesting that the drug content has negligible influence on the crystal phase of the drug loaded spun-dyed fibers [43]. In addition, the peaks for curcumin are absent in the curcumin / PAN and curcumin / Vit. E Ac/PAN microfibers indicating that curcumin is evenly dispersed in the fiber in an amorphous state.

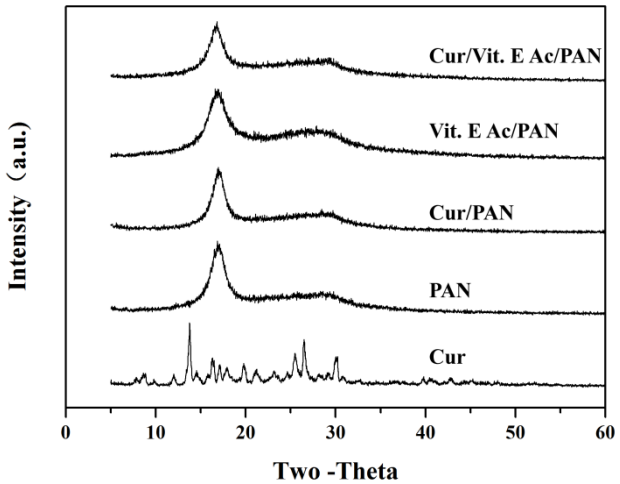


Figure 5. XRD diffractograms of the blank PAN; curcumin / PAN; Vit. E Ac / PAN; and curcumin / Vit. E Ac / PAN microfibers.

3.5. FTIR Spectroscopy

The blank and drug-loaded PAN microfibers were characterized by FTIR (Fig. 6) performed in order to elucidate the combination of drugs with PAN. Compared to blank PAN fibers, the FT-IR spectra of the drug-loaded fibers show both characteristic peaks of PAN and the drugs. For PAN, an absorption band at 2243 cm^{-1} is due to the stretching vibration of nitrile groups (–C≡N), the bands at 2926 cm^{-1} and 1453 cm^{-1} correspond to the methylene stretching vibrations and bending vibrations respectively [37,52]. Sharp peaks at 1514 cm^{-1} and 1453 cm^{-1} are typical of aromatic C=C str of the phenyl ring and olefinic bending vibrations of C–H bound to the phenyl ring of curcumin [53,54]. A further peak at 806 cm^{-1}, generated in curcumin was also observed in the curcumin / Vit. E Ac /PAN fiber and the C=O stretch at 1588 cm^{-1} from both curcumin and Vit. E Ac is seen in the curcumin / Vit. E Ac / PAN spectrum. Additionally, the peak at 1207 cm^{-1} reflects the contribution of the CO–O peak mainly donated by Vit. E Ac [55]. Of particular note is the peak at 2926 cm^{-1} which is sharper and relatively stronger after drug loading owing to the Vit. E Ac. All these results indicate that curcumin, Vit. E Ac and PAN have bound together to form a drug-loading system.

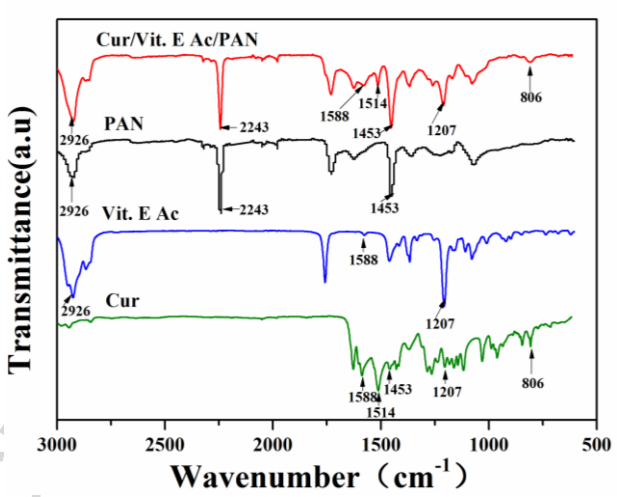


Figure 6. FTIR spectra of the curcumin; Vit. E Ac; blank PAN microfibers; and curcumin / Vit. E Ac /PAN microfibers.

3.6. Thermal analysis

The thermal gravimetric (TG) and the differential thermal gravimetric (DTG) curves of the blank PAN, curcumin / PAN, Vit. E Ac / PAN, and curcumin / Vit. E Ac / PAN microfibers are shown in Fig. 7. The decomposition process starts at around 300 °C and continues to about 500 °C, as a result of the thermal degradation of PAN, curcumin and Vit. E Ac. The onset of thermal degradation of the four fibers is very similar although there are different weight losses, with the curcumin / Vit. E Ac / PAN particularly prominent. The reason for this result may be due to its porous structure. Heat can penetrate from the surface to the interior of the fiber more easily so that it can be degraded from the interior and the exterior simultaneously, which can accelerate the degradation of the curcumin / Vit. E Ac / PAN microfiber. However, these results signify that the drug content does not cause any evident adverse effects on the thermal properties of fibers up to about 450 °C.

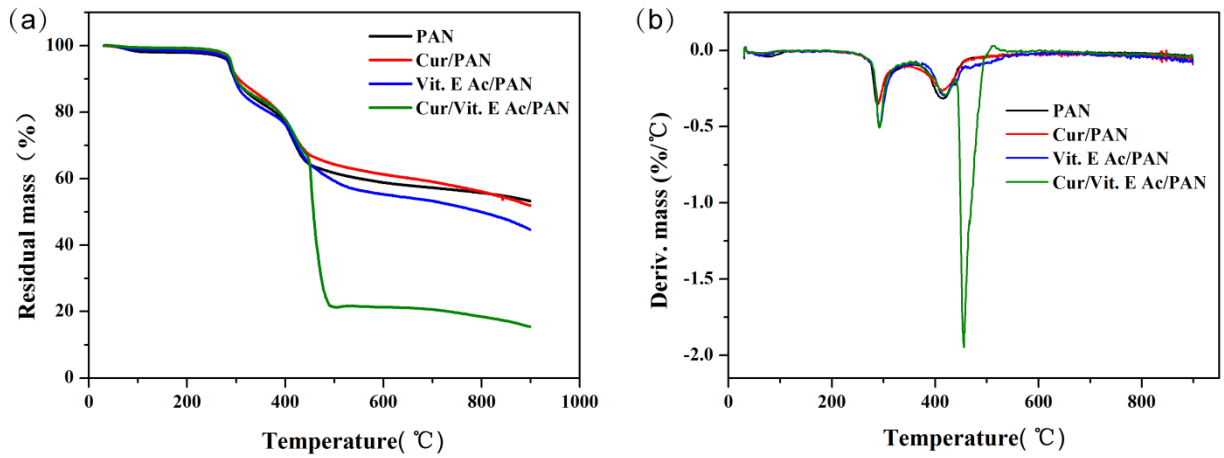


Figure 7. (a) TG and (b) DTG traces of the blank PAN, curcumin / PAN; Vit. E Ac / PAN; and curcumin / Vit. E Ac / PAN microfibers.

3.7. *In vitro* release of drugs

The drug release properties of the curcumin / PAN and Vit. E Ac / PAN fibers at 37 °C in a mixed buffer are shown in Fig. 8. Since the absorption spectrum of Vit. E Ac can be affected by the interference of curcumin, the Cur / Vit. E Ac / PAN fibers were not tested. It can be seen that a sustained release of the drugs from the two kinds of microfiber was observed with a cumulative release of about 14% for curcumin and 10% for Vit. E Ac over 15 days and the amount of curcumin and Vit. E Ac released into the buffer remained constant after 25 days of immersion. However, the amount released is relatively low probably due to two factors: firstly, PAN, curcumin and Vit. E Ac are all hydrophobic and when they are blended together there is a strong affinity between them and consequently the drugs are difficult to dissolve out of the fibers particularly in aqueous conditions and, secondly, PAN cannot swell in the buffer due to its hydrophobic nature, consequently, the drugs do not easily diffuse out of the fiber channel.

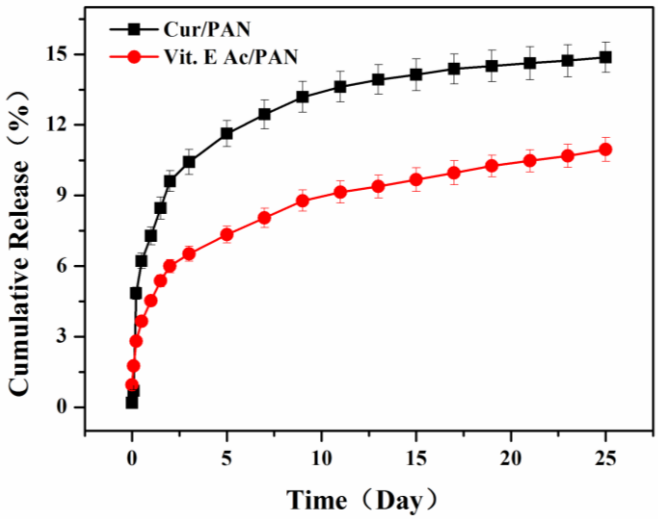


Figure 8. *In vitro* drug-release curves of the curcumin / PAN and Vit. E Ac / PAN fibers (n=3).

3.8. Evaluation of the *In Vitro* Cytocompatibility

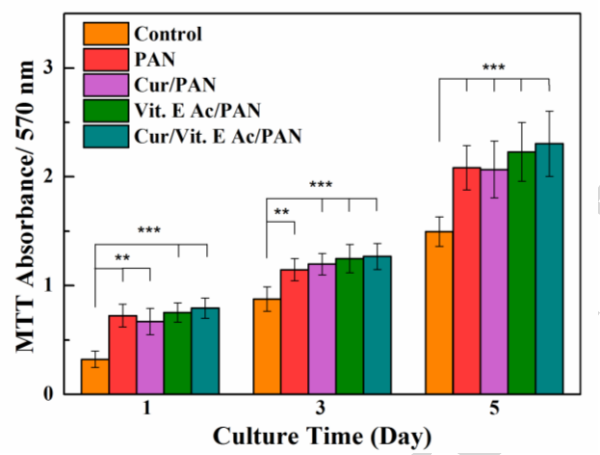


Figure 9. Cell proliferation of the L929 cells on different fabrics woven from PAN and its blended fibers. Data are reported as mean ± S.D. from six independent experiments. Data are annotated with * for $p < 0.05$, ** for $p < 0.01$, and *** for $p < 0.001$ which were used to evaluate the significance of the experimental data.

An ideal biomaterial should not cause any negative effects or release toxic products so in order to evaluate the cytotoxicity of the fibers, *in vitro* cytotoxicity tests were performed and the results are shown in Fig. 9. Fabrics made from fibers have a porous structure and hence have a large specific surface area which offers a structure suitable for cell adhesion and proliferation. The cells grow mainly on the surface of the fabric, though inevitably some cells will grow into the woven fabrics and also on the bottom of the plates but according to the test procedure, only the cells that grew on the surface of the fabric pieces were used. It is clearly evident (Fig. 9) that after incubation for 1, 3 and 5 days, all of the fabric samples showed good cytocompatibility, although the L929 cells proliferated at different rates on the substrates with the Vit. E Ac / PAN and curcumin / Vit. E Ac / PAN fabric showing the highest rate, indicating that these fabrics had better cytocompatibility. Whereas the MTT absorbance of the curcumin-loaded fabrics was similar to that of PAN alone, indicating that the addition of 5% (w/w) curcumin, at least does not inhibit the proliferation of the L929 cells. Thus, the results of *in-vitro* cytocompatibility testing showed that no cytotoxicty on the L929 cells was found up to 5% (w/w) and 10% (w/w) respectively of the theoretical drug loading content (TDLC) of curcumin and vitamin E acetate.

4. Conclusions

In this study, an improved wet-spinning technique using co-dissolving solutions has been developed to successfully incorporate two kinds of drugs, curcumin and Vitamin E acetate, into PAN fibers. A comprehensive study of the drug-loaded microfibers was carried out and all the wet-spun drug-loaded filaments showed good mechanical properties which could be woven into fabrics (with those loaded with curcumin being bright yellow). TG and DTG data indicated that incorporation of the drugs into the PAN matrix did not significantly change the thermal stability and the Cur / Vit. E Ac / PAN filaments had a microvoid structure which can increase the specific surface area, improve the air permeability and help the release of drugs. *In-vitro* release experiments indicated that the drug in the DDS had excellent drug release characteristics over more than 25 days and furthermore, all the fabrics woven from the spun filaments exhibited good cytocompatibility. Overall, the drug-loaded microfibers showed excellent properties and could be developed further as multifunctional textile or biomedical materials.

Acknowledgments

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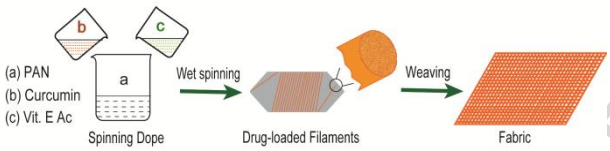
Graphical Abstract



Highlights

- 1 Based on a wet spinning technique, a series of filaments which have potential applications in the field of biological materials, have been successfully prepared.
- 2 The drug loading filaments showed good mechanical properties and could be woven into fabrics.
- 3 The Cur / Vit. E Ac / PAN filaments exhibited a unique microvoid cross-sectional morphology.
- 4 No cytotoxicty was found up to 5% and 10% respectively of the theoretical drug loading content (TDLC) of curcumin and vitamin E acetate.