International Journal of Pharmaceutics 373 (2009) 4–9

Contents lists available at ScienceDirect

International Journal of Pharmaceutics

journal homepage: www.elsevier.com/locate/ijpharm

Rapid communication

Polyacrylonitrile fibers efficiently loaded with tamoxifen citrate using wet-spinning from co-dissolving solution

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ARTICLE INFO

Article history:
Received 5 December 2008
Received in revised form 10 March 2009
Accepted 16 March 2009
Available online 27 March 2009

Keywords:
Wet-spinning
Co-dissolving solution
TAM
PAN
Drug release

ABSTRACT

Tamoxifen citrate (TAM)-loaded polyacrylonitrile (PAN) fibers were prepared using an improved wet-spinning technique. TAM was used as a model drug to evaluate the potential application of the loaded fiber system for drug delivery. PAN was first homogeneously dissolved in the N,N-dimethylacetamide (DMAc) solution containing TAM and then the co-dissolving solution was solidified to prepare the fibers using a wet-spinning method. Chemical, morphological and mechanical property characterizations were carried out, as well as the studies of the drug release properties. TAM was successfully encapsulated into a monofilament fiber, and this system was stable in terms of high loading capacity and effectiveness in release. The diameter of drug-loaded fiber was in the range of 40–60 μm. The best values of the tensile strength at 2.968 cN/dtex and breaking elongation at 14.9% of drug-loaded fibers were obtained when the drug loading content was 23.1 wt.%. These characteristics were suitable for the weaving process. The *in vitro* release experiment indicated that constant drug release from the fiber was observed for a long duration of time. Kinetic studies demonstrated that the system followed the Higuchi kinetics. These findings demonstrate that controlled release of drugs from PAN fibers could be potentially useful in drug delivery systems.

1. Introduction

Drug-loaded fiber technology is one of many techniques that have been investigated for pharmaceutical application (Q. Wang et al., 2007). Polymer-based drug delivery systems are often used to optimize the therapeutic properties of drugs and to render them safer, effective and reliable (Kenawy et al., 2007). Tamoxifen citrate (TAM) has been a clinical choice for the treatment of advanced breast cancer and is often an adjuvant therapy after surgical resection. The drug has also been used in treating menopause. However, one of the side effects of TAM is the proliferative effect on the endometrium (Memisoglu-Bilensoy et al., 2005). Thus, a controlled delivery device is desired for successful local chemotherapy.

Polyacrylonitrile (PAN) is a polymer with good stability and mechanical properties. It has been widely studied in terms of adsorption properties (Z.G. Wang et al., 2007; Li et al., 2007), morphology and preparation (S.J. Zhang et al., 2008). Due to its good solvent resistance PAN is one of a group of versatile polymers that are used widely for synthesizing membranes (G.J. Zhang et al., 2008; Zhang; Tsai et al., 2008). Another advantage of a PAN polymer over other polymer structures is that it can be converted into activated carbon fiber (Chen et al., 2008; Wang et al., 2008). PAN is generally more difficult for fiber spinning purposes compared to its analogous polymers as it is less soluble in solvents (Ismail et al., 2007). Thus the PAN fibers are rarely used as a drug carrier source. Only (Tian et al., 2006) reported the drug adsorption properties on PAN haemofilters. There has been no report about the fabrication of drug-loaded PAN fibers. Therefore, the purpose of the present study is to consider the preparation of drug-loaded fibers and to examine these in terms of structure and drug release properties.

Among all the methods of fabricating blank fibers, wet-spinning method has been most widely used in the textile industry (Foroughi et al., 2008; Lee et al., 2007; Liu et al., 2008). In conventional blending process based on wet-spinning (Wang et al., 2004; Ding et al., 2004, 2005), drugs are first ground into fine powder and blended into the spinning dope of the polymers that are used as drug carriers. In this method, it is difficult to evenly disperse the drug powder in the spinning dope due to the high viscosity of the dope. Agents that can help to disperse the drug powder are needed to obtain spinning dope where the drugs are evenly distributed in the matrix. However, the "large size" of the drug powder restricts the reduction of the diameter and length of the fiber or filament.

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doi:10.1016/j.ijpharm.2009.03.022

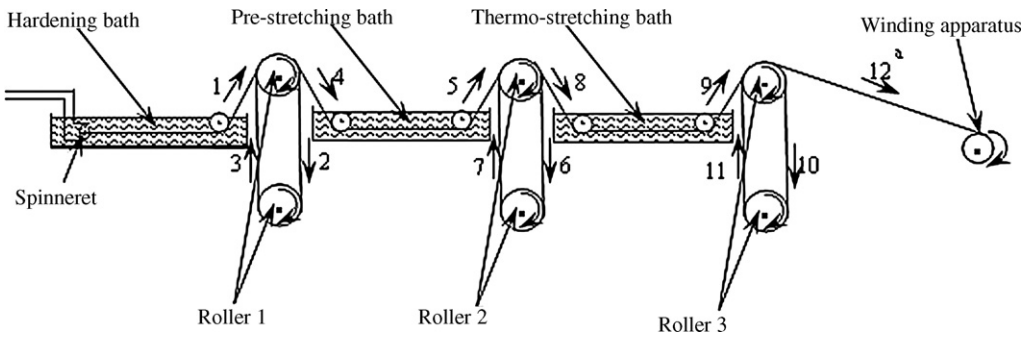

Fig. 1. Laboratory improved wet-spinning line. [a]1–12 showed the moving direction of the fiber.

Therefore, it is difficult to get fine and continuous filament that can be used for textile processing using this blending method. Studies on another popular technique, electro-spinning (Taepaiboon et al., 2007; Suwantong et al., 2007) showed to be unsatisfactory for drug loading and the tensile strength of the fibers was unsuitable for textile processing. Recently, Crow et al. (2005), Crow and Nelson (2006) and Gao et al. (2007) separately developed wet-spinning techniques that included the introduction of an emulsification stage and this increased the efficiency of drug loading by more than 10%. Unfortunately, the drug-loaded fiber had a wide range of diameters (50–250 μm), but no data relating to tensile strength was provided. If the tensile strength is low, then this may contribute to difficulties in processing the fibers further. The synthesis of fibers with high drug loading capacity, high tensile strength and long-term release characteristics will contribute to local chemotherapy and functional properties of the textiles to the development of medicated textile patches applied. To date, wet-spinning in a co-dissolving system has not been used for the incorporation of drug into fibers.

This is the first reported use of wet-spinning in a co-dissolving system for the incorporation of drug into fibers, producing an effective drug delivery system. TAM, an anticancer drug, was chosen as the model drug. The structure, morphology, tensile strength, drug content and *in vitro* release properties of the fiber were studied in this research. These studies could provide a reference to develop functional textiles and to explore the fibers in biomedical textile field.

2. Materials and methods

2.1. Materials

PAN (Mw ~ 80,000) was provided by Jinshan Petrochemistry Co., Ltd. (Shanghai, China). TAM was provided by Suzhou Sunary Pharmaceutical Co., Ltd. (Suzhou, China). All chemicals were of analytical quality from Sinopharm Chemical Reagent Co., Ltd. (Shanghai, China). Water used in the experiments was deionized and filtered (Milli-Q Academic, Millipore, France).

2.2. Preparation of spinning dope

In order to facilitate evenly dissolution of PAN and drug powders different methods of adding TAM and PAN into DMAc were selected: (i) PAN powder was added into DMAc and dissolved by stirring. TAM was then added into the PAN/DMAc solution, and all solutions were maintained at 70 °C; (ii) TAM was added into DMAc and dissolved by stirring at 70 °C as above. PAN was then added to the DMAc/TAM solution (70 °C); (iii) PAN and TAM were both added simultaneously by stirring to DMAc and kept at 70 °C. The spinning dope was transferred into a solution bottle and then degassed by sonication. Solution viscosities were measured with JDN-79 viscometer at 25 °C.

2.3. Preparation of TAM-loaded PAN fibers

An improved wet-spinning method was used to fabricate TAM-loaded PAN fibers. The schematic diagram of the spinning machine as shown in Fig. 1 consists of a hardening bath, spinneret, pre-stretching bath, thermo-stretching bath, and winding apparatus. The spinning equipment was a laboratory-scale mini-wet-spinning equipment designed by our group. The parameters adopted for the wet-spinning process were shown in Table 1. Fibers were further treated at 110 °C to ensure that PAN molecules are aligned tightly to improve the mechanical properties of the fiber. TAM was loaded into the PAN fibers during the fiber formation. Different amounts of TAM were dissolved with DMAc solutions before loading the drug into the PAN fibers.

2.4. Characterization of TAM-loaded fibers

The morphology of the fibers was studied using a JEOL, Model JSM-5600 scanning electron microscopy (Tokyo, Japan) at 30 kV accelerating voltage. X-ray diffraction (XRD) patterns of the sample were measured with a Shimadu Labx-XRD-6000 diffractometer (Kyoto, Japan) and the diffraction angle ranged from 4° to 50°. The diameter of the fiber was measured by an optical microscope (XP-700, Shanghai, China). The tensile strength and breaking elongation for fibers were determined on a fiber electron tensile tester machine (XQ-1, Shanghai, China). The gauge length was 20 mm and crosshead speed was 50 mm/min. All samples were preconditioned at 20 °C and 65% relative humidity, for 24 h prior to mechanical testing. A ^{1}H NMR spectrometer (Bruker DRX 400 MHz NMR spectrometer, Germany) was used to investigate the chemical stability of the loaded drug during fabrication process, using deuterated dimethylsulfoxide (DMSO-d_6) as solvent.

Table 1
The wet-spinning process specifications.

Spinning bath	Hardening bath	Pre-stretching bath	Thermo-stretching bath
Composition	50% DMAc	Water	Water
Temperature (°C)	30 °C	70 °C	100 °C
Rollers	Roller 1	Roller 2	Roller 3
Diameter of rollers (cm)	14	14	14
Speed of rollers (rpm)	1.1	1.5	10
Stretching ratio		9	
Winding speed (m/min)		70	

Table 2
Composition of spinning solution and properties of the TAM-loaded PAN fibers (n = 3).

Samples	Spinning solution[a]		Properties of fibers				
	TDLC (%)	Viscosity (Pa s)	Average diameter (μm)	Tensile strength (cN/dtex)	Breaking elongation (%)	DLC (%)	DLE (%)
S_0	0	98	59.45	2.312	19.2	0	n/a
S_1	5%	102	58.51	2.574	18.7	4.062	81.24%
S_2	10%	104	54.73	2.690	17.9	7.055	70.55%
S_3	20%	107	42.67	2.808	16.4	14.285	71.43%
S_4	30%	113	46.94	2.968	14.9	23.174	77.24%

[a] The weight ratio of PAN and DMAc is 1:4.

2.5. Drug loading content determination

The actual content of TAM in the TAM-loaded fiber was quantified by dissolving each sample in DMAc and was measured by a Unico UV-2102PC spectrometer method (Shanghai, China) at 293 nm. The actual amount of TAM in the fibers was back-calculated from the obtained data against a predetermined calibration curve for TAM. Drug loading content (DLC) was defined as follows:

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

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

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

The drug loading efficacy (DLE) could be determined:

$$\text{DLE}(\%) = \frac{\text{DLC}}{\text{TDLC}} \times 100\% \quad (3)$$

2.6. Release of TAM from TAM-loaded PAN fiber

To determine the *in vitro* drug release property of the drug-loaded fiber a drug release instrument (Tianjin RCZ-8A dissolution apparatus, Tianjin, China) was used. Due to the solubility limitation of TAM in aqueous solutions, the releasing medium contained 30% ethanol was used. Drug-loaded fibers were weighed and placed in releasing medium (1 l) at 37 °C and the instrument was set at 100 rpm. At appropriate time intervals, a 5 ml of the release medium was withdrawn and an equal amount of the fresh medium was returned to the system. The amount of TAM in the sample solutions was determined using UV spectrophotometer at the wavelength of 298 nm. The obtained data were calculated to determine the cumulative amount of TAM released from the specimens at each time point. The experiments were carried out in triplicate and the results were reported as average values.

3. Results and discussion

3.1. Fabrication technique by using an improved wet-spinning method

The wet-spinning technique is a standard method to produce blank PAN fibers. In this study we have considered the relationship between the blank fiber and TAM as the drug was dissolved in DMAc and this may influence the characteristics of fiber formation. We have considered a number of parameters (see Section 2.2.2) to prepare the drug-loaded fiber where TAM is homogenously dispersed and encapsulated at high drug loading concentrations. In order to obtain the homogenous solutions, three methods of preparing spinning solution were investigated. For the first method where TAM was added to PAN, PAN was found to be completely dissolved whereas TAM was only partly soluble. For the second method, both PAN and TAM were easily dissolved, so enabling the drug to be evenly dispersed in the spinning medium. For the last method, TAM and PAN were not easily dissolved. Therefore the second method was chosen for further studies. Table 2 outlines the composition and viscosity of the four spinning solutions used. It was observed that with increasing the TAM content, the viscosity of the spinning dope also increased. Thus we have been able to identify the ideal conditions and viscosity for the spinning dope process.

3.2. Characterization of TAM-loaded fibers

The drug-loaded fibers were successfully fabricated by wet-spinning from the co-dissolving solutions. The morphology and properties of the TAM-loaded PAN fibers were shown in Table 2. The average diameter of drug-loaded fibers was 40–60 μm. This was similar to the estimated diameter of neat PAN fiber. The effect of TAM content on the tensile strength of fibers was also given in Table 2. The tensile strengths of TAM-loaded fibers were higher than that of pure PAN, and the maximum value observed at 30 wt.% TAM content was 2.968 cN/dtex. The increase in ten-

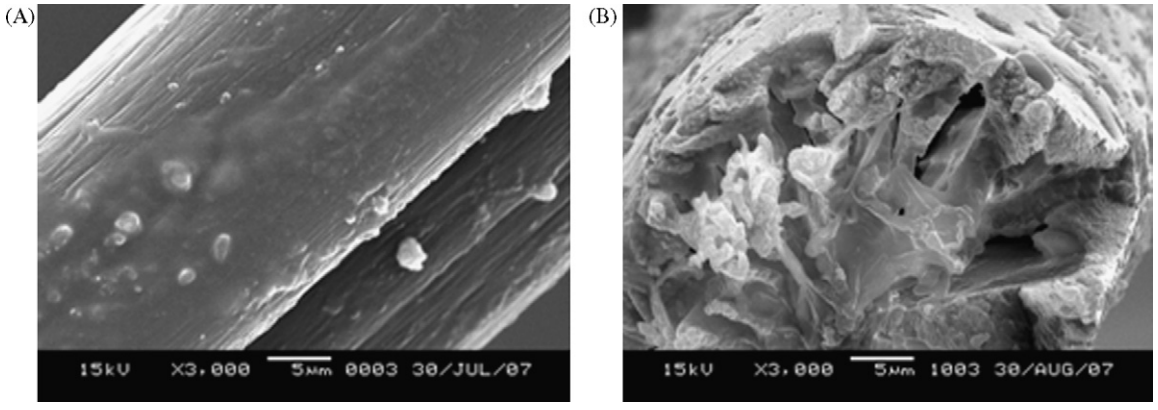

Fig. 2. SEM surface image (A) and SEM cross-sectional image (B) of S4.

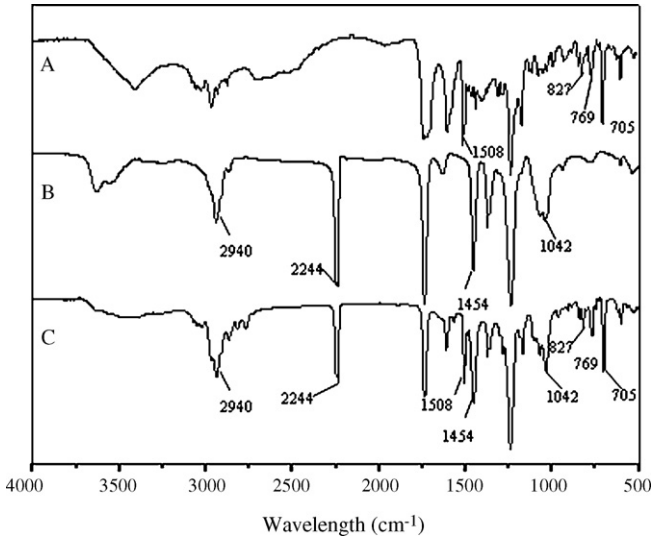

Fig. 3. FT-IR spectrums of TAM (A), pure PAN fiber (B) and drug-loaded fiber (C).

sile strength of fibers may be due to the presence of beneficial interactions between TAM and PAN molecules in the blend. The most common interactions in the blends are hydrogen bond, ionic and dipole and charge-transfer complexes. Also it can be seen that the tensile strengths of TAM-loaded fibers were all above the minimal value 2.0 cN/dtex for the weaving process. These results indicated that the fibers could be used for textile processing as the breaking elongation decreased with an increase of TAM content. So through controlling the spinning conditions, the designing of fibers that have stronger mechanical properties than PAN can be achieved.

Fig. 2A and B showed the SEM profiles and forms of the surface and the cross-section of the fiber respectively. Particles of TAM with size ranging from several hundred nanometers to several micrometers can be seen both on the surface and cross-section of the fiber (Fig. 2A). This indicated that phase separation between TAM citrate and PAN occurred in the fiber with the removal of the solvent DMAc during the wet-spinning process.

The blank and drug-loaded fibers were characterized by FT-IR spectra and XRD. The FT-IR spectra of the drug-loaded fiber showed both characteristic peaks of PAN (e.g. the stretching vibration of methylene (–CH_2–), the stretching vibration of nitrile groups (–C≡N–) and bending vibration of methylene of PAN fibers at 2940, 2244, and 1454 cm^{-1}, respectively (Ji and Zhang, 2007) and TAM (e.g. the aromatic rings of TAM at 1508, 827, 769, and 705 cm^{-1} (Gamberini et al., 2007)), and no new peak or migration was observed (Fig. 3). Fig. 4 showed the wide-angle XRD analysis. Pure TAM showed two typical peak 1 and peak 2. The diffraction intensities of the TAM-loaded fiber at peak 1 and peak 2 decreased drastically with increasing content of TAM, suggesting the formation of TAM crystal in the fiber.

To further confirm the stability of TAM in the fiber and during the wet-spinning process, the TAM-loaded fibers were dissolved in DMSO-d_6 and the resulting solutions were investigated by ^{1}H NMR. Solutions of both the neat PAN fibers and TAM in DMSO-d_6 were used as references. Fig. 5 shows ^{1}H NMR spectra of the drug TAM, the pure PAN and the drug-loaded fibers that were obtained from the solution containing 30 wt.% TAM. Evidently, the chemical integrity of the as-loaded TAM was sustained after wet-spinning process, as the peaks corresponding to both PAN and TAM were observed in the ^{1}H NMR spectrum of the TAM-drug-loaded fibers that were obtained from the solution containing 30 wt.% TAM.

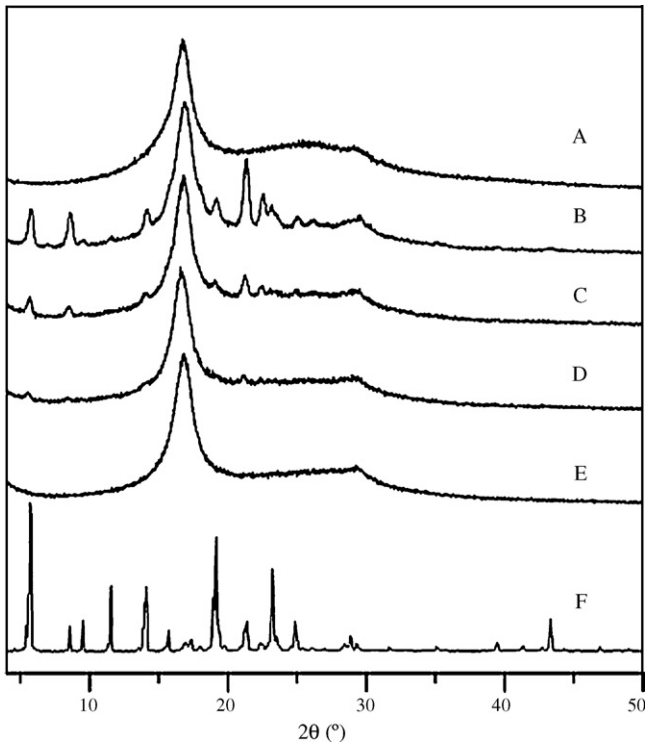

Fig. 4. XRD patterns of PAN (A), S_4 (B), S_3 (C), S_2 (D), S_1 (E) and TAM (F).

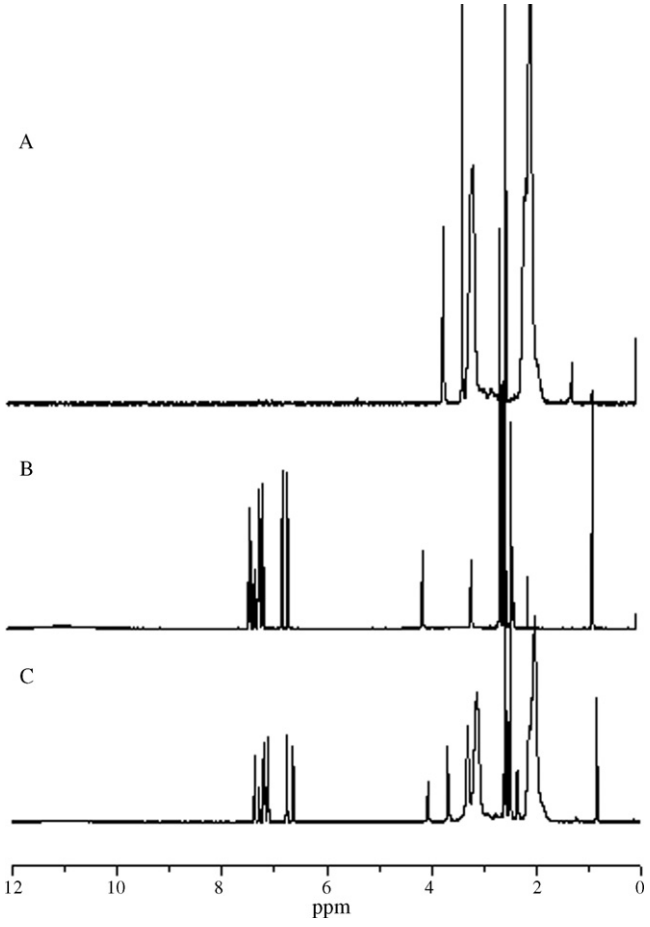

Fig. 5. ^{1}H NMR spectrums of PAN (A), TAM (B) and TAM-loaded PAN fibers S_4 from the solution containing 30 wt.% TAM after being dissolved in DMSO-d_6 (C).

3.3. TAM loading content and efficacy

In order to control the amount of drug loading within the fibers, the initial drug concentrations were changed during spinning process. Table 2 showed the high drug loading content was successfully achieved. There was a clear relationship between initial drug concentration and the amount of TAM loaded onto the fibers. The TAM drug loading content of the PAN fibers fabricated by the wet-spinning technique from co-dissolving solution was more than 20% and was much higher than that of fibers fabricated by other reported techniques. For example, the electrospinning method only gave 0.5% vitamin A acid and 5% vitamin E into cellulose acetate fibers (Taepaiboon et al., 2007). Furthermore, for wet-spinning system, higher yields are possible as reported by Gao et al. (2007) who were able to develop fibers from a suspension that contained 10% 5-fluorouracil in poly(L-lactic acid), whereas Crow et al. (2005) used an emulsion to create a 2.3% BSA in poly(L-lactic acid) fibers. The high yields of TAM loaded onto the fibers in this study may be explained by fast solidification of the fibers in the course of precipitation and also due to the high solubility of the drug in DMAc. In addition, the high drug loading efficacy was also obtained. As shown in Table 2, drug loading efficacy of all the fibers was more than 70%. This study clearly demonstrated the benefit of the ternary system of PAN–TAM–DMAc for wet-spinning system, it is possible to develop a medical textile that is loaded with an effective anti-cancer reagent.

3.4. Release of TAM from drug-loaded PAN fibers

TAM-loaded PAN fibers were prepared under the optimal conditions, with the different initial drug concentrations (Table 2). *In vitro* release behavior was examined using a dynamic dialysis method. Based on the variation of the slope of the release curve, the release curve can be divided into 3 segments (O–A, A–B and B–C) as shown in Fig. 6. The slope of section O–A was the largest, the section including A–B was smaller, whereas the B–C region was the smallest. This trend indicates that the release process of TAM from the fibers with different drug loadings is similar. It can be seen that at the beginning of the experiment larger amount of TAM is freed from the surface of the fibers. This is possibly due to surface location and the physical binding of TAM to the fibers as it can easily remove into the media. Therefore, this phenomenon possibly accounts for the section O–A (Fig. 6). It could be postulated that as the time of incubation proceeds TAM gradually moves from within fibers to the surface and this relates to the section B–C.

The data given in Fig. 6 also suggested that the higher drug loading would reduce the drug release rate. This could be explained in terms that when more drugs were loaded to the fibers, the particles became more compact induced by hydrophobic forces. Since PAN was mildly hydrophobic, the drug molecules self-aggregated within the fibers, resulting in a reduction in the release rate. Such phenomenon was also reported in the literature (Q. Wang et al., 2007; Tan et al., 2008).

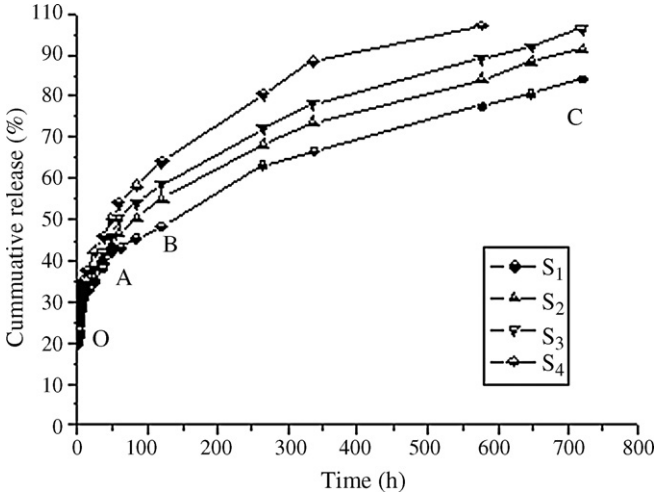

Fig. 6. Drug release profiles from the TAM fibers with different drug loading content (the experiments were carried out in triplicate and the results were reported as average values).

3.5. Release mechanism

Kinetics studies of drug release from PAN fibers were determined using four sets of different data relating to Higuchi, Korsmeyer–Peppas, zero-order and first-order kinetics. The correlation coefficients calculated from four models (Table 3) indicated that TAM release from PAN fibers was best described using the Higuchi model where the R^2 was greater than 0.98 under all conditions.

The Korsmeyer–Peppas equation (see below) is often used to describe the drug release behavior from polymeric systems when the mechanism is not well-known or when more than one type of release phenomena are involved (Limmatvapirat et al., 2008). We used this equation to determine the release mechanism of TAM from our drug-loaded fibers.

$$\frac{M_t}{M_\infty} = kt^n, \quad \text{for } \frac{M_t}{M_\infty} < 0.6, \tag{4}$$

or the logarithmic form of this equation:

$$\log\frac{M_t}{M_\infty} = \log(k) + n\log(t) \tag{5}$$

where M_t/M_∞ is the fractional drug release and t is the release time, k is a constant incorporating the structural and geometric characteristics of fibers and n is the release exponent indicative of the drug release mechanism. The kinetic parameters (n and k) were calculated from the plot of $\log(M_t/M_\infty)$ versus $\log(t)$ where $(M_t/M_\infty) < 0.6$.

The n values given in Table 3, S_1, S_2, S_3, and S_4 were 0.1350, 0.1247, 0.1234, and 0.1154, respectively. These results suggest that the TAM has similar diffusion properties regardless of the drug loading capacity. Previous work on non-swelling polymeric cylinder fibers showed the threshold of n value between Fickian and non-Fickian mechanism was 0.45 (Gao et al., 2007). All the release

Table 3
Mathematic modeling and drug release kinetics from TAM-loaded PAN fibers.

Samples	Correlation coefficient (R^2)				Parameters obtained from Korsmeyer–Peppas model	
	Zero order	First order	Higuchi	Korsmeyer–Peppas	Diffusional exponent (n)	Kinetic constant (k)
S_0	n/a	n/a	n/a	n/a	n/a	n/a
S_1	0.8449	0.6992	0.9876	0.9027	0.1350	27.741
S_2	0.8916	0.7626	0.9920	0.9176	0.1247	27.175
S_3	0.8976	0.7675	0.9937	0.9299	0.1234	25.868
S_4	0.9053	0.7760	0.9935	0.9604	0.1154	25.272

profiles tested in this paper were calculated by the equation and no value above 0.45 was found. The *n* values based on four profiles are shown in Fig. 6. The characteristic exponent confirms that the release mechanism of the fibers is a typical Fickian diffusion and consistent with those result of experiments.

4. Conclusion

In this investigation we have demonstrated and developed an improved wet-spinning technique using co-dissolving solutions to successfully incorporate an anticancer drug TAM, into the PAN fibers. This new method involved the co-dissolving system, which included developing spinning solution that contained TAM and PAN, and this enhanced the compatibility of the drug and PAN in DMAc. Most of TAM was entirely encapsulated in the PAN fibers. The drug loading content was higher than other reported techniques using the similar wet-spinning systems. The drug release was fast at the initial period, however, after a given time a constant release profile was observed and this lasted for 24 days. Thus this system is highly suitable for developing drug delivery systems where the active compounds are selectively bound to an inert, nonreactive insoluble support. It therefore has potential for the long-term treatment of areas that require drugs and in this case TAM was used. The wet-spinning technique as modified here provides constant fibers that are easy to weave process further. They have high tensile strengths and the system could be developed for large-scale purposes. The fibers prepared by our system could be developed further as a functional textile that has the potential to provide a transdermal drug delivery system.

References

Chen, J.J., Wu, R.B., Yang, G.Y., Pan, Y., Lin, J., Wu, L.L., Zhai, R., 2008. Synthesis and photoluminescence of needle-shaped 3C–SiC nanowires on the substrate of PAN carbon fiber. J. Alloys Compd. 456, 320–323.

Crow, B.B., Borneman, A.F., Hawkins, D.L., Smith, G.M., Nelson, K.D., 2005. Evaluation of in vitro drug release, pH change, and molecular weight degradation of poly(L-lactic acid) and poly(D,L-lactide-co-glycolide) fibers. Tissue Eng. 11, 1077–1084.

Crow, B.B., Nelson, K.D., 2006. Release of bovine serum albumin from a hydrogel-cored biodegradable polymer fiber. Biopolymers 81, 419–427.

Ding, H.G., Li, L., Shen, X., Shen, Q., 2004. Studies of preparation, structure and properties of fibers containing Chinese herbs: II. Preparation, structure and properties of cellulose/poly(ethylene glycol)/ginger blend fiber. Xianweisu Kexue Yu Jishu 12, 31–35.

Ding, H.G., Wang, Z.X., Liu, D.S., Gu, Q.F., 2005. Study on preparation, structure and properties of fibers containing Chinese herbs: III. Dynamical model for drug release of cellulose/poly(ethylene glycol)/ginger blend fiber. Xianweisu Kexue Yu Jishu 13, 25–28.

Foroughi, J., Spinks, G.M., Wallace, G.G., Whitten, P.G., 2008. Production of polypyrrole fibres by wet spinning. Synth. Met. 158, 104–107.

Gamberini, M.C., Baraldi, C., Tinti, A., Palazzoli, F., Ferioli, V., 2007. Vibrational study of tamoxifen citrate polymorphism. J. Mol. Struct. 840, 29–37.

Gao, H., Gu, Y., Ping, Q, 2007. The implantable 5-fluorouracil-loaded poly(L-lactic acid) fibers prepared by wet-spinning from suspension. J. Control. Release 118, 325–332.

Ismail, A.F., Rahman, M.A., Mustafa, A., Matsuura, T., 2007. The effect of processing conditions on a polyacrylonitrile fiber produced using a solvent-free free coagulation process. Mater. Sci. Eng. A 485, 251–257.

Ji, L., Zhang, X., 2007. Ultrafine polyacrylonitrile/silica composite fibers via electrospinning. Mater. Lett. 62, 2161–2164.

Kenawy, E.R., Abedl-Hay, F.I., El-Newehy, M.H., Wnek, G.E., 2007. Controlled release of ketoprofen from electrospun poly(vinyl alcohol) nanofibers. Mater. Sci. Eng. A: Mater. 459, 390–396.

Lee, K.H., Baek, D.H., Ki, C.S., Park, Y.H., 2007. Preparation and characterization of wet spun silk fibroin/poly(vinyl alcohol) blend filaments. Int. J. Biol. Macromol. 41, 168–172.

Limmatvapirat, S., Limmatvapirat, C., Puttipipatkhachorn, S., Nunthanid, J., Luangtana-anan, M., Sriamornsak, P., 2008. Modulation of drug release kinetics of shellac-based matrix tablets by in-situ polymerization through annealing process. Eur. J. Pharm. Biopharm. 69, 1004–1013.

Liu, H., Xu, W., Zou, H., Ke, G., Li, W., Ouyang, C., 2008. Feasibility of wet spinning of silk-inspired polyurethane elastic biofiber. Mater. Lett. 62, 1949–1952.

Li, S.F., Chen, J.P., Wu, W.T., 2007. Electrospun polyacrylonitrile nanofibrous membranes for lipase immobilization. J. Mol. Catal. B: Enzyme 47, 117–124.

Memisoglu-Bilensoy, E., Vural, I., Bochot, A., Renoir, J.M., Duchene, D., Hıncal, A.A., 2005. Tamoxifen citrate loaded amphiphilic ß-cyclodextrin nanoparticles: In vitro characterization and cytotoxicity. J. Control. Release 104, 489–496.

Suwantong, O., Opanasopit, P., Ruktanonchai, U., Supaphol, P., 2007. Electrospun cellulose acetate fiber mats containing curcumin and release characteristic of the herbal substance. Polymer 48, 7546–7557.

Taepaiboon, P., Rungsardthong, U., Supaphol, P., 2007. Vitamin-loaded electrospun cellulose acetate nanofiber mats as transdermal and dermal therapeutic agents of vitamin A acid and vitamin E. Eur. J. Pharm. Biopharm. 67, 387–397.

Tan, J.P.K., Zeng, A.Q.F., Chang, C.C., Tam, K.C., 2008. Release kinetics of procaine hydrochloride (PrHy) from pH-responsive nanogels: theory and experiments. Int. J. Pharm. 357, 305–313.

Tian, Q., Gomersall, C.D., Wong, A., Leung, P., Choi, G., Joynt, G.M., Tan, P., Lipman, J., 2006. Effect of drug concentration on adsorption of levofloxacin by polyacrylonitrile haemofilters. Int. J. Antimicrob. Agents 28, 147–150.

Tsai, H.A., Chen, W.H., Kuo, C.Y., Lee, K.R., Lai, J.Y., 2008. Study on the pervaporation performance and long-term stability of aqueous iso-propanol solution through chitosan/polyacrylonitrile hollow fiber membrane. J. Membr. Sci. 309, 146–155.

Wang, Q., Zhang, N., Hu, X., Yang, J., Du, Y., 2007. Chitosan/starch fibers and their properties for drug controlled release. Eur. J. Pharm. Biopharm. 66, 398–404.

Wang, W., Murthy, N.S., Chae, H.G., Kumar, S., 2008. Structural changes during deformation in carbon nanotube-reinforced polyacrylonitrile fibers. Polymer 49, 2133–2145.

Wang, Z.G., Wan, L.S., Xu, Z.K., 2007. Surface engineerings of polyacrylonitrile-based asymmetric membranes towards biomedical applications: an overview. J. Membr. Sci. 304, 8–23.

Wang, Z.X., Shen, Q., Gu, Q.F., 2004. Study on preparation and properties of fibers containing Chinese herbs: I. Preparation and mechanical properties of persimmon leaves/cellulose blend fiber. Hecheng Xianwei Gongye 27, 7–9.

Zhang, G.J., Ji, S.L., Gao, X., Liu, Z.Z., 2008. Adsorptive fouling of extracellular polymeric substances with polymeric ultrafiltration membranes. J. Membr. Sci. 309, 28–35.

Zhang, S.J., Chen, S.X., Zhang, Q.K., Li, P.Y., Yuan, C., 2008. Preparation and characterization of an ion exchanger based on semi-carbonized polyacrylonitrile. React. Funct. Polym. 68, 891–898.