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In vitro drug controlled-release behavior of electrospun modified Poly(lactic acid)/ Bacitracin drug delivery system

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Abstract: Poly(lactic acid-*co*-lysine) (PLL) was applied as a modified material to improve the hydrophilicity, reactivity, and degradation rate Poly(L-lactic acid) (PLLA) as well as its degradation rate. In the drug delivery system, PLLA and PLLA/PLL were selected as carrier materials of drug-loaded fibers, and Bacitracin (BAC) as the sustained release drug. Uniaxial drug-loaded fibers (PLLA/BAC, PLLA/PLL/BAC) and coaxial drug-loaded fibers ((PLLA/PLL/BAC)-PLLA, (PLLA/BAC)-(PLLA/PLL)) were prepared by electrospinning. The chemical structures and thermal properties of electrospun drug-loaded fibers were analyzed by Infrared Spectroscopy (IR) and Differential Scanning Colorimetry (DSC) separately and Ultraviolet Spectrophotometer (UV) was used to characterize the extracorporeal drug releasing behavior. The results indicated that the main combination between BAC and carrier materials such as PLLA and PLLA/PLL was physical force; the uniaxial drug-loaded fibers with uniform diameters showed higher release rate compared with coaxial drug-loaded fibers owing to the protection of shell materials in coaxial fibers. The drug release rate of drug-loaded fibers increased due to the addition of hydrophilic PLL; the drug release mechanism in both uniaxial and coaxial drug delivery system could be interpreted by Biexponential- biphase kinetics function. Two kinds of fibers of different drug release patterns could be fabricated by uniaxial and coaxial electrospinning. Drug in uniaxial fibers could be quickly released and was suitable for antibiotic treatment while the release of drug in coaxial fibers was a kind of controlled release which could be applied for the drug delivery system of long-term and small doses.

Key words: Poly(lactic acid) ; Poly(lactic acid-*co*-lysine); Bacitracin; Electrospinning; Drug delivery system

Introduction

Poly(L-lactic acid) (PLLA) is a kind of biomedical polymer material and has become the most attractive medical biological material on account of its excellent biocompatibility, appropriate biodegradability and metabolism of degradation product.[1-3] Poly(lactic acid-*co*-lysine) (PLL) copolymerized by L-lactic acid and L- lysine possesses excellent biocompatibility, certain reactive activity, good hydrophilicity and short degradation of cycle. The blends of PLLA/PLL have different degradation periods, functional groups, good hydrophilicity, favourable medical and processing properties, so they can be utilized in tissue engineering and drug delivery system.[4] The drug-loaded nano-fiber obtained by electrospinning with large surface area and high porosity has been applied in the fields of local release of drugs and wound cure widely, especially as postoperative gauze to protect the skin tissue from being infected by bacteria.[5-10] Therefore, PLLA and its composite materials present broad prospects in drug release.[11] The fibers with core-shell structure where medicine can be introduced into core layers and shell materials can be prepared by coaxial electrospinning technology, and the shell materials play a role of barrier forming a drug delivery system just like a repository.[12, 13] Drug in the delivery system is released sustainedly with the continuous degradation of shell materials so as to maintain a effective concentration of medicine in blood constantly and minimize the side-effect.[14]

Bacitracin (BAC) is a kind of peptide antibody as strong fungicide, whose antibacterial spectrum is similar to penicillin. BAC can strongly inhibit gram-positive bacteria and be used for staphylococcus infections and topical skin infections mainly.[15] In this study, BAC was employed as a sustained release drug, and the uniaxial drug-loaded fibers (PLLA/BAC, PLLA/PLL/BAC) and coaxial drug-loaded fibers ((PLLA/PLL/BAC)-PLLA, (PLLA/BAC)-(PLLA/PLL)) were fabricated by electrospinning. Infrared Spectroscope (IR) and Differential Scanning Colorimetry (DSC) were applied to characterize the chemical structures and thermal properties of electrospun drug-loaded fibers. The mass loss of the drug-loaded fibers was evaluated and UV Spectrophotometer was used to investigate the drug of different drug-loaded fibers in vitro releasing behavior.

Experimental

Materials

PLA, Molecular weight (M_w) of 3.05×105 g mol^{-1}, purchased; PLL, M_w of 1.98×10^4 g mol^{-1}, lab-made; N, N-dimethyl formamide (DMF) and dichloroethane (DCE), analytical reagent, purchased;

Phosphate buffered saline (PBS), purchased; BAC, purchased, Aladdin (Shanghai) Industrial Corporation.

Preparation of electrospun fibers

9 wt% of PLLA, PLLA/BAC, PLLA/BAC and PLLA/PLL/BAC were prepared by dissolving PLLA, PLLA/PLL, PLLA/BAC and PLLA/BAC/BAC in DCE and DMF (DCE:DMF=9:1, wt%). The content of BAC in solute was 9 wt% in uniaxial drug-loaded fibers and the content of BAC in core layer was 15 wt%. Then stirring in sealed for 24 h and dispersing 0.5 h with ultrasonic. Subsequently, uniaxial drug-loaded fibers (PLLA/BAC, PLLA/PLL/BAC) and coaxial drug-loaded fibers ((PLLA/PLL/BAC)-PLLA, (PLLA/BAC)-(PLLA/PLL)) were fabricated by SS-2554 Electrospinning Set (UCALERY BEIJING CO., Ltd). (A)- (B) fibers stand for (core)-(shell) coaxial fibers.

Characterization

Scanning Electron Microscope (SEM) of TESCAN. Ltd., Czech Republic (VEGA 3 LMH) was used to investigate the surface and cross-section morphology of the drug-loaded fibers, and the average fiber diameter and the standard deviation was determined by taking at least 50 measurements for each image using Image J software.

In order to evaluate the thermal properties such as T_g, T_c, T_m and Cr_{PLLA} of the electrospun fibers, it was necessary to use the Differential Scanning Colorimetry (DSC) from METTLER TOLEDO. Ltd. (Switzerland) with a heating rate of 10 °C min^{-1} from 0 °C to 200 °C under nitrogen. The crystallinity of the spinning fibers was calculated according to the melting heat of the heating DSC curve by Eq. 1, and the PLLA crystallinity of the fibers was calculated according to Eq. 2. Wherein *Cr* is the crystallinity of the spinning fiber, Cr_{PLLA} is the crystallinity of PLLA, ΔH^0_f is the heat of melting of the complete crystallization of PLLA and its value is -93.7 J g^{-1}. ΔH_f is the melting heat of spinning fibers and w_{PLLA} is the PLLA content (wt%) in drug-loaded fibers.

$$Cr = \left(\Delta H_f / \Delta H_f^0\right) \times 100\% \quad (1)$$

$$Cr_{PLLA} = \left(\Delta H_f / \Delta H_f^0\right) / w_{PLLA} \times 100\% \quad (2)$$

The chemical character of drug-loaded fibers was analyzed by Fourier Transform Infrared Spectroscopy (FT-IR) from Thermo Scientific. Ltd., US (Nicolet iS10). Dissolve the superfine fibers in DCE, then coat the solutions on the surface of potassium chloride tablet. After solvents were volatilized thoroughly, scan in the wave numbers of 4000 cm^{-1} to 400 cm^{-1}.

The extracorporeal drug releasing behavior was performed by the UV Spectrophotometer (UV-2550) of SHIMADZU. Ltd., Japan. The different concentrations of BAC were dissolved in the PBS (pH7.4). The characteristic absorption peak of 254 nm could be defined in the UV absorbance curve. Then the fitting equation (Eq. 3) could be obtained by the linear regression of different BAC concentrations and absorbance values. The concentration of BAC could be calculated by measuring the absorbance value (A) of drug-loaded fiber near 254 nm with UV Spectrophotometer, and the cumulative release rate could be calculated from Eq. 3.

$$C(\mathrm{mg/L}) = -10.68 + 597Abs \quad (3)$$

Among the equation, *C* is the concentration of BAC, and *Abs* is the absorbance value.

The equation of cumulative drug release rate and drug release time was fitted by Biexponential-biphase kinetics function Eq. 4[16-18], wherein M_t and M_∞ are the drug release doses after drug releasing t h and the total drug-loaded amount, respectively. α and β are drug release rate constants, Q_0 is the initial drug concentration in the buffer solvent. The equation is consist of fast and slow phases, namely the impact and slow-release phase, and impact phase indicates the sudden release effect at the outset, while slow-release phase express the controlled release subsequently.

$$Q_0 - \frac{M_t}{M_\infty} = Ae^{\alpha t} + Be^{\beta t} \quad (4)$$

The degradation property of the drug-loaded fibers was analyzed by water bath at 37.2 °C temperature. The mass loss rate of the fibers could be calculated by Eq. 5 in which W_0 and W_1 are the mass of fibers before and after degradation, respectively.

$$\text{Mass loss rate} = \left(W_0 - W_1\right) / W_0 \times 100\% \quad (5)$$

Results and discussion

Surface morphology of the drug-loaded fibers

The PLLA/ BAC fibers, PLLA/PLL/BAC fibers, (PLLA/PLL/BAC)-PLLA fibers and (PLLA/BAC)-(PLLA/PLL) fibers were obtained with the parameters as shown in Tab. 1.

Table 1 The parameters of electrospun fibers

Drug-loaded Fibers	PLLA/BAC	PLLA/PLL /BAC	(PLLA/BAC) -(PLLA/PLL)	(PLLA/PLL/ BAC)-PLLA
Concentration of solutions / wt%	9	9	9[×], 9*	9[×], 9*
Voltage/ kV	18	18	24	24
Collecting Distance/ cm	13	13	15	15
Feed Rate /mL min^{-1}	0.02	0.02	0.01[×], 0.02*	0.01[×], 0.02*
Drug-loaded Amount / wt%	9	9	5	5

Notes: [×], * are for the concentration and feed rate of shell solutions and shell solutions respectively.

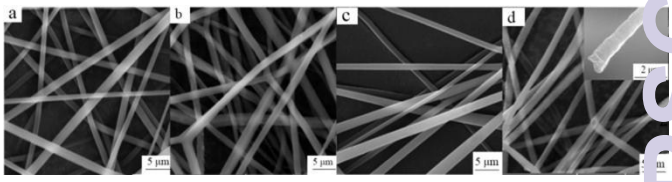

Fig. 1 SEM micrographs of the drug-loaded fibers and average diameters
(a) PLLA/BAC (Φ1634±192.6 nm); (b) PLLA/PLL/BAC (Φ1465±216.3 nm); (c) (PLLA/PLL/BAC)-PLLA (Φ1852±201.4 nm); (d) (PLLA/BAC)-(PLLA/PLL) (Φ1826±208.5 nm)

The following conclusions could be drawn from the SEM micrographs of the drug-loaded fibers in Fig. 1. The fibers' surface was smooth and the morphologies were neat. There were no BAC particles on the fibers' surface which demonstrated with carrier materials well. Due to the core-shell structure of the coaxial fibers and larger diameter of the coaxial spinning needle than that of uniaxial spinning needle, the average diameter of uniaxial drug-loaded fibers was smaller than those of the coaxial drug-loaded fibers. Since the addition of PLL with low relative molecular weight reduced the electrospinning solution viscosity and the reactive groups of PLL improved the conductivity of the spinning solution, the average diameter and standard deviation of PLLA/PLL/BAC fibers was much smaller than PLLA/BAC fibers, making the spinning solution to be drawn and stretched easily. The average diameter of (PLLA/BAC)-(PLLA/PLL) fibers were smaller than that of (PLLA/PLL/BAC)-PLLA fibers, which could be attributed to the faster feed rate of shell materials than that of core materials in spinning process. Therefore, there was a higher content of PLL in (PLLA/BAC)-(PLLA/PLL) fibers, making the fibers have finer diameters and wider diameter distribution.

Chemical structure analysis of the drug-loaded fibers

The FT-IR spectra of BAC, PLLA/BAC, PLLA/PLL/BAC, (PLLA/BAC)-(PLLA/PLL), (PLLA/PLL/BAC)-PLLA fibers are observed in Fig. 2.

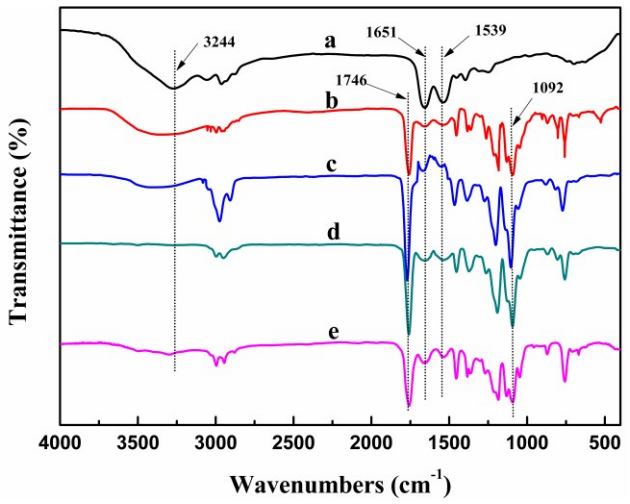

Fig. 2 FT-IR spectra of BAC and BAC-loaded fibers
(a) BAC; (b) PLLA/BAC; (c) PLLA/PLL/BAC; (d) (PLLA/PLL/BAC)-PLLA. (e) (PLLA/BAC)-(PLLA/PLL)

The common characteristic absorption peaks of PLLA fibers and PLLA/PLL fibers in infrared spectrum were 1900-1650 cm^{-1}(stretching vibration of C=O), 1300-1000 cm^{-1}(stretching vibration of C-O and framework vibration of C-C). There were two acute peaks at 3540-3180 cm^{-1} on account of NH_2 and NH in PLL.

In the FT-IR spectra, the specific absorption peaks (1746 cm^{-1}, 1092 cm^{-1}) of PLLA and PLLA/PLL didn't disappear with no obvious deviation. The main chemical groups of BAC were C=O, C=N, NH_2, NH, -OH and C-S. The peak superposition of the partial functional groups of PLLA, PLL and BAC occurred because of their same groups. The strength of characteristic absorption peaks (3244 cm^{-1}, 1651 cm^{-1}, 1539 cm^{-1}) of BAC decreased significantly, which indicated the combination of BAC with carrier materials was physical and the addition of BAC into PLLA and PLLA/PLL did not change their chemical structures.

Thermal and crystallization properties of electrospun fibers

Fig. 3 shows the DSC curves of PLLA/BAC fibers, PLLA/PLL/BAC fibers, (PLLA/PLL/BAC)-PLLA fibers and (PLLA/BAC)-(PLLA/PLL) fibers, and the analysis of the crystallization and thermal properties are summarized in Table 2.

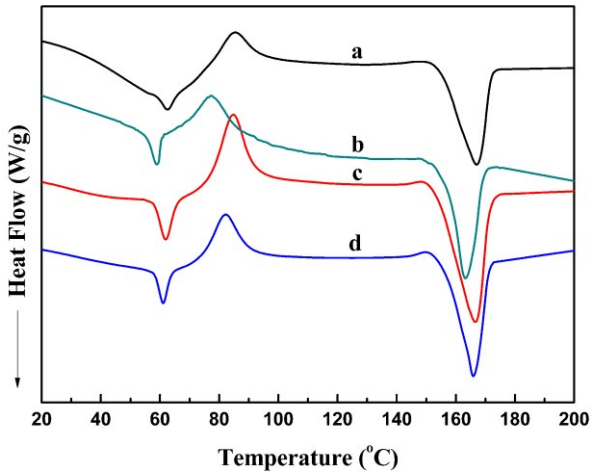

Fig. 3 DSC curves of BAC-loaded fibers
(a) PLLA/BAC; (b) PLLA/PLL/BAC; (c) (PLLA/PLL/BAC)-PLLA; (d) (PLLA/BAC)-(PLLA/PLL)

Table 2 Crystallization and thermal properties of BAC-loaded fibers

Crystallization and Thermal properties	T_g/°C	T_c/°C	T_m/°C	Cr_{PLLA}/%
PLLA/BAC	62.5	85.1	167.2	43.5
PLLA/PLL/BAC	58.8	77.2	163.1	44.0
(PLLA/PLL/BAC)-PLLA	61.8	84.6	166.7	42.9
(PLLA/BAC)-(PLLA/PLL)	61.0	82.3	166.1	42.4
PLLA/PLL	56.5	75.8	162.9	44.2
PLLA	63.3	87.3	169.6	42.1

T_g is the glass transition temperature; T_c is the cold crystallization temperature; T_m is the melting temperature.

The addition of PLL and BAC could affect the thermal and crystallization properties of the PLLA fibers. PLL played the role of diluent. On the one hand, it provided active environment for the chain segments of PLLA, lowered the internal rotation resistance between PLLA chains, promoted the regularity of PLLA molecular chains. Consequently, the T_g of modified PLLA fibers declined and the crystallinity increased. On the other hand, the dilution effect could increase the adjacent distance of PLLA intermolecular chains, weaken the entanglement of PLLA molecules, decrease the intermolecular force and make it difficult to grow into wafer and crystal. Thus, the T_g and crystallinity of PLLA in the modified PLLA fibers declined.

BAC was not soluble in the spinning solution. BAC could improve the crystallinity of PLLA owning to its role of nucleating agent. Nevertheless, it could impede the movement of PLLA molecular chains. The addition of BAC improved the crystallinity of PLLA because the nucleation of BAC was a stronger effect in the electrospinning process than impediment at room temperature. In addition, high density amines and imines in PLL and BAC could form hydrogen bonds with the carbonyl group of PLLA, which reduced the interaction between the PLLA molecular chains and resulted in the T_g increase and the crystallinity decline of PLLA.

The T_gs of PLLA/BAC fibers, PLLA/PLL/BAC fibers, (PLLA/PLL/BAC)-PLLA fibers and (PLLA/BAC)-(PLLA/PLL) fibers were lower than those of PLLA fibers and PLLA/PLL fibers under the mutual effect of above factors, among which the dilution effect of PLL affected obviously. The crystallinity increased due to the mutual influence of dilution and nucleation of BAC.

There appeared obvious cold crystallization peaks in the DSC heating curve of modified PLLA electrospun fibers, and T_c had a sharp decline compared with the neat PLLA fibers. The cold crystallization peak temperature of PLLA resin of M_w 359×10^3 is 122.4 ^oC.[19] However, T_c of PLLA fibers and modified PLLA fibers reduced to 72-88 ^oC because the effect of electrospinning charge led to the stretch of PLLA chains and the formation of α' crystal structure with weak stability. The α' crystal structure converted into more stable α crystal structure along with the temperature increase in DSC test. The reason why T_c of PLLA/PLL fibers was lower than that of PLLA fibers was that the dilution effect of PLL was conducive to the formation of crystals in the electrospinning process for PLLA molecular chains. The hydrogen bond formed between amines and imines of PLL and BAC with carbonyl of PLLA in modified fibers decreased the molecular chain flexibility, so the stability of crystal declined due to the difficult molecular chain movement, which made T_c depressed. In contrast, BAC had little effect on the cold crystallization temperature of PLLA in the modified fibers.

The drug releasing behavior in vitro

The drug release curves of PLLA/BAC, PLLA/PLL/BAC, (PLLA/BAC)- (PLLA/PLL) and (PLLA/PLL/BAC)-PLLA are shown in Fig. 4.

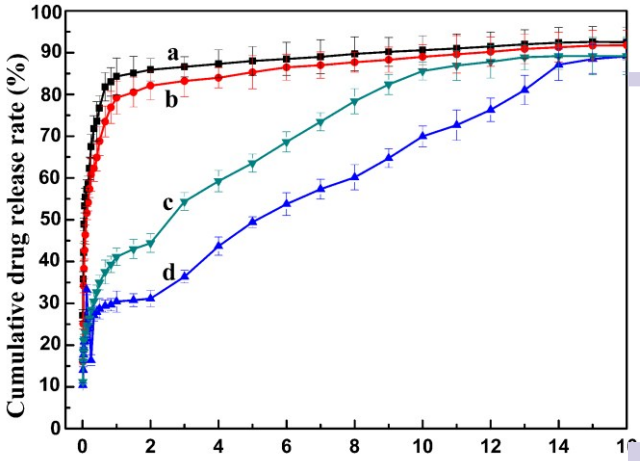

Fig. 4 Drug release curves of drug-loaded fibers
(a) PLLA/PLL/BAC; (b) PLLA/BAC; (c) (PLLA/ BAC)-(PLLA/PLL); (d) (PLLA/PLL/BAC)-PLLA

The drug release curves of PLLA/BAC fibers, PLLA/PLL/BAC fibers, (PLLA/BAC)-(PLLA/PLL) fibers and (PLLA/PLL/BAC)-PLLA fibers are shown in Fig. 4. The uniaxial drug-loaded fibers had a faster drug release rates than coaxial drug-loaded fibers did because of the homogeneous mixing drug delivery system of the uniaxial drug-loaded fibers. The uniaxial drug-loaded fibers had higher drug contents and exhibited concentration gradients in PBS, so the drug release behaviors conformed to the drug diffusion mechanism. However, the coaxial fibers belonged to the storage reservoir drug delivery system, and their main release rates depended on the shell corrosion and degradation of PLLA and PLLA/PLL because of the protection from shell materials.

The PLLA/PLL/BAC fibers showed a faster drug release rate than PLLA/BAC fibers due to the containing of hydrophilic PLL which was more easily infiltrated by PBS and broke away from the fibers quickly. The drug release rate of (PLLA/BAC)-(PLLA/PLL) fibers was faster than that of (PLLA/PLL/BAC)-PLLA fibers. PLLA/PLL of shell material was more easily corroded than PLLA, so the (PLLA/BAC)-(PLLA/PLL) fibers showed a faster drug release rate. The encapsulation of the dense PLLA protected BAC from totally diffusing from the fibers, leading to incomplete drug release with the cumulative release amount less than 95 % in 16 days.

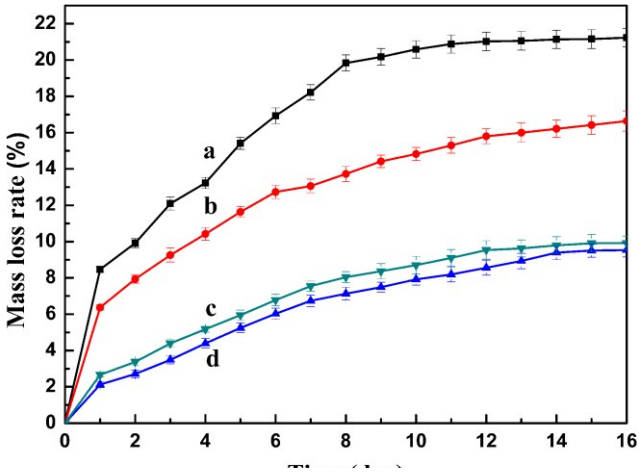

Fig. 5 The mass loss of BAC-loaded fibers in a 16 day period (a) PLLA/PLL/BAC; (b) PLLA/BAC; (c) (PLLA/BAC)-(PLLA/PLL); (d) (PLLA/PLL/BAC)-PLLA

The mass loss of BAC-loaded fibers within a degradation period of 16 days could be seen in Fig. 5. The reason of the mass loss of fibers included the drug release and the degradation of carrier material. The uniaxial fibers with the larger specific surface areas degraded faster than coaxial fibers and the drug in uniaxial fiber was inclined to release. Thus, the mass-loss rates of the uniaxial drug-loaded fibers were faster than those of the coaxial drug-loaded fibers. The addition of hydrophilic PLL in the carrier promoted the erosion and degradation which could increase the drug release and the degradation of carrier material. The mass loss was based on the drug release at the beginning of five days, and the subsequent mass loss mainly attributed to the degradation of the carrier material.

The sketch of coaxial electrospinning fibers are shown in Fig. 6. Taylor cone is stretched and fibers are formed with the function of electric field at coaxial needle. Splitting theory[20] have indicated that Taylor cone can be further split to be finer fibers during the movement towards the receiver under the high electric field force. The fibers could form four different types in coaxial electrospinning process with the splitting of Tylor cone, and the profile and cross-sectional sketches of the coaxial spun fibers are also shown in Fig. 6.

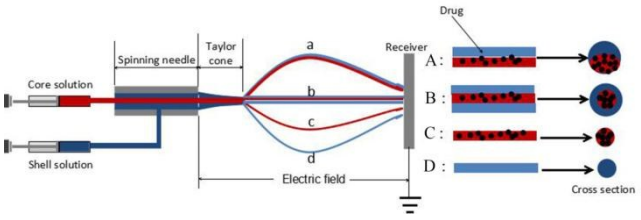

Fig. 6 Sketches of electrospinning process of coaxial fibers. A, B, C and D are four different types of fibers

In Fig. 6, A displays that part of the core-shell coaxial fibers is split under the high voltage, and there appear bistratal drug-loaded materials where the core drug is exposed outside. The drug release rate of the fibers is faster than that of the coaxial fiber but slower than that of the uniaxial fibers. B demonstrates that drug is completely encapsulated into the core material and the drug release is controlled by the shell materials. C indicates that there only exist the core materials with drug in the fiber because of the split. D represents the fibers which merely have the shell materials.

According to research by now[21], the release of the drug in hydrophobic carrier material is influenced by both diffusion mechanism and corrosion degradation mechanism. The BAC release in the uniaxial PLLA/BAC fibers was followed the three stages mainly. First, as the BAC dropped from the superficies of PLLA by the interaction with PBS, there appeared some micropores serving as the channels of the fiber surfaces for the BAC further release. Secondly, the BAC was released in the PLLA amorphous region, and the diffusion and release rates were slower than those in PBS because the BAC diffusion in PLLA mainly was depended on the formed micropores. In the other words, the BAC in the micropore surfaces were infiltrated by PBS, dissolved and diffused by the force of the concentration gradient. Third, the BAC was released with the degradation and erosion of the PLLA of crystalline region. These three stages were carried out successively and the diffusion was the dominant dynamic force.

The BAC in the hydrophilic carrier PLL was released along with the PLL hydration expansion, surface erosion, and the diffusion of the BAC in the PLL. The release of the BAC in the PLLA/PLL fiber was the result of interaction between the diffusion and corrosion of PLLA and PLL.

Uniaxial fibers belonged to the homogeneous mixing type drug delivery system in which the drug was uniformly dispersed into the carrier material and the drug release rate was dependent on the diffusion in the expanded polymer carrier. Coaxial drug-loaded fibers belonged to storage reservoir system and the drug was physically encapsulated in the polymer and the release of drug mainly relied on the degradation and corrosion of polymer carriers.

It could be illustrated by Fig. 4 and Fig. 6 that the drug release within 16 days in coaxial fibers, such as (PLLA/BAC)-(PLLA/PLL) fibers and (PLLA/PLL/BAC)-PLLA fibers, could be mainly divided into the following three periods (as Fig. 4). In the first stage (the early 24 hours), the BAC in the generated fibers like A and C in Fig. 5 due to the split was exposed and peeled off from the external surface, then dissolved into the PBS, which caused faster release rates at the outset. The initial slight burst release emerged in both the (PLLA/BAC)-(PLLA/PLL) fibers and the (PLLA/PLL/BAC)-PLLA fibers, and the cumulative BAC release rate of (PLLA/BAC)-(PLLA/PLL) was 40%-45% while that of (PLLA/PLL/BAC)-PLLA was 30%-35%. The second stage was a transient stationary period from 24 h to 48 h when the drug in the fiber surface was almost completely released. In the situation, the drug release rates were slower down because the core drug needed to diffuse in the shell materials and reached the surface of fibers and were released with the degradation and erosion of shell materials. The last stage from 48 h to 16 days showed a slow acceleration drug release rate,

which could be attributed to the generated channels by the diffusion of drugs on the second phase.

Biexponential- biphase kinetics function is the most popular diffusion kinetics equation at present, and can be used to explain the release mechanism of the drug-loaded fiber in this experiment. Fitting process was conducted on the cumulative drug release rate along with the drug release period. The fitting curves are shown in Fig. 7 and the fitting results are shown in Tab. 3.

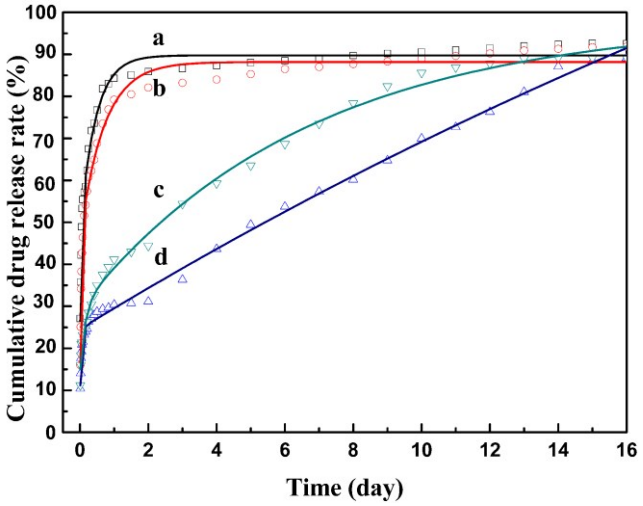

Fig. 7 Fitting curves of different drug-loaded fibers
(a) PLLA/PLL/BAC; (b) PLLA/BAC; (c) (PLLA/ BAC)-(PLLA/PLL); (d) (PLLA/PLL/BAC)-PLLA

Table 3 The fitting results of different drug-loaded fibers

Drug-loaded fibers	Fitting results	R^2
PLLA/BAC	$\frac{M_t}{M_\infty} = 0.898 - (0.389e^{-51.3t} + 0.414e^{-2.22t})$	0.998
PLLA/PLL/BAC	$\frac{M_t}{M_\infty} = 0.882 - (0.442e^{-30.9t} + 0.416e^{-1.43t})$	0.998
(PLLA/BAC)-(PLLA/PLL)	$\frac{M_t}{M_\infty} = 2.45 - (2.21e^{-0.022t} + 0.172e^{-23.5t})$	0.997
(PLLA/PLL/BAC)- PLLA	$\frac{M_t}{M_\infty} = 0.981 - (0.159e^{-7.04t} + 0.685e^{-0.15t})$	0.995

From the fitting curves, the initial burst releases of uniaxial fibers were more obvious than those of the coaxial fibers because the shell materials of the coaxial fibers hindered the diffusion of the drug at the beginning. The controlled release of the coaxial fibers was more effective than that of the uniaxial fibers because the impediment of the shell materials of the coaxial fibers. The drug release were going on with the degradation of the carriers. The major release of the drug in the uniaxial fibers resulted from the diffusion of the drug in the carrier, while the release of the drug in the coaxial fibers was the result of the diffusion and corrosion at the same time.

The studies above have verified that the fibers of different drug release patterns can be fabricated by uniaxial or coaxial electrospinning. Drug in uniaxial fibers could be quickly released and the drug release pattern might reduce the effectiveness of drugs and cause the side effect due to its burst release. However, this release is not inadvisable, for example, this pattern of drug release is preferred in the case that the large doses of drugs within a short time are needed in order to eliminate viruses and bacteria in antibiotic treatment. The drug release in coaxial fibers is a kind of controlled release which is more suitable for the drug release system of long-term and small-dose drugs, such as hormonal drugs and long-acting anticancer drugs. Additionally, the coaxial drug controlled release could reduce the harm on human body in the process of taking drugs with toxic effects. For the drug producers, different drug-loaded patterns can be chosen according to the different therapeutic purposes.

Conclusions

In this study, BAC was encapsulated into PLLA and PLLA/PLL as a kind of controlled-release drug. The combination between the drug and the carriers was mainly physical and most of BAC was embedded in the electrospun fibers by the analysis of FT-IR, DSC and SEM. The uniaxial drug-loaded fibers showed a higher release rate than coaxial drug-loaded fibers did, and the drug release rate of uniaxial PLLA/PLL/BAC fiber was the fastest among the fibers. The drug release rates of these fibers with PLL were higher than those of the fibers without PLL due to the hydrophilicity of PLL. The fibers with different drug release patterns were achieved by the way of uniaxial and coaxial electrospinning process. The drug in uniaxial fibers could be quickly released while the drug in coaxial fibers showed a kind of slow and controlled release. The drug releases of these drug-loaded fibers conformed to the Biexponential- biphase kinetics equation. The drug release mechanism of uniaxial fibers mainly was the diffusion while that of coaxial fibers was the conjunct effect of drug diffusion and carrier corrosion.

Acknowledgements

This work was supported by the Northwestern Polytechnical University Fundamental Research Fund under Grant (JCY20130148).

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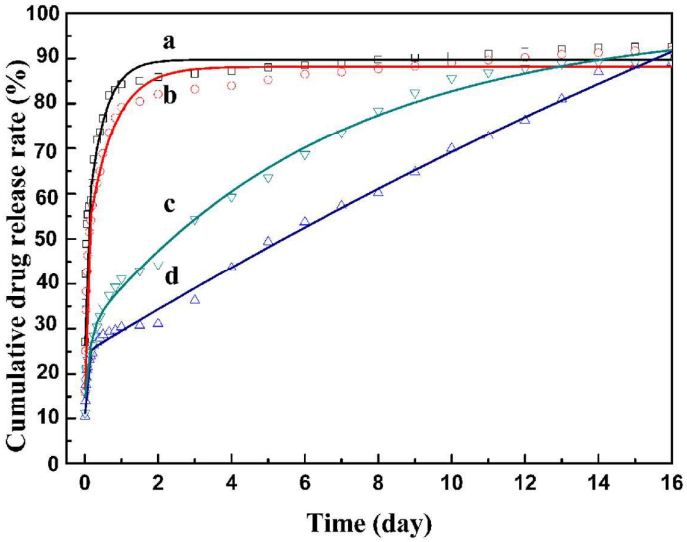

BAC-loaded electrospun uniaxial and coaxial fibers were achieved with different drug release patterns whose carrier materials were PLLA and PLLA/PLL.