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European Journal of Pharmaceutics and Biopharmaceutics 66 (2007) 398–404
European Journal of Pharmaceutics and Biopharmaceutics
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Research paper

Chitosan/starch fibers and their properties for drug controlled release

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Received 14 July 2006; accepted in revised form 20 November 2006
Available online 26 November 2006

Abstract

Fibers of chitosan and starch, with salicylic acid (SA) as model drug incorporated in different concentrations, were obtained by spinning their solution through a viscose-type spinneret into a coagulating bath containing aqueous tripolyphosphate (TPP) and ethanol. Chemical, morphological and mechanical properties characterization was carried out, as well as the studies of the factors that influence the drug releasing from chitosan/starch fibers. These factors included the component ratio of chitosan and starch, the loaded amount of SA, the pH and the ionic strength of the release solution and others. The diameter of the fibers is around 15 ± 3 μm. The best values of the tensile strength at 12.21 cN/tex and breaking elongation at 25.13% of blend fibers were obtained when the starch content was 30 wt%; the water-retention value (WRV) of blend fibers increased as the composition of starch was raised. The results of controlled release tests showed that the amount of SA released increased with an increase in the proportion of starch present in the fiber. Moreover, the release rate of drug decreased as the amount of drug loaded in the fiber increased, but the cumulative release amount is increasing. The chitosan/starch fibers were also sensitive to pH and ionic strength. The release rate was being accelerated by a lower pH and a higher ionic strength, respectively. All the results indicated that the chitosan/starch fiber was potentially useful in drug delivery systems.

Keywords: Chitosan; Starch; Salicylic acid; Blend fibers; Drug delivery systems

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1. Introduction

Chitosan, the deacetylated derivative of chitin, is one of the most abundant naturally occurring polysaccharides. Recently, it has attracted much interest in the biomedical industry because of its excellent biodegradability, biocompatibility, and antimicrobial activity and accelerated wound-healing properties [1–4]. Chitosan has good film and fiber forming properties. When chitosan is resolved in dilute acetic acid solutions, the amino groups become protonated and associated with acetate counter-ions, making the charged polymer soluble. Therefore, net negatively charged compounds such as DNA, glycosaminoglycans, and most proteins can be incorporated into chitosan without the use of harsh and denaturing organic solvents, such as methylene chloride, which are needed for the processing of many biodegradable polymers. Therefore, chitosan has been extensively examined in the pharmaceutics industry for its potential use in the development of controlled release implant system [5–8].

Starch is a biodegradable polymer with excellent biocompatibility and non-toxicity [9]. It is often compounded with other polymers or used alone in the fields of drug controlled release [10–12].

With regard to the excellent fiber forming properties of chitosan, many new and original fiber materials have been achieved [13]. Drug loaded fiber is one of the applications by those fibers in pharmaceutical technology. In addition, numerous controlled or sustained-delivery systems have been described in the literature, whereby the active ingredient has been dissolved or dispersed within these matrixes [14–17]. For the development of fiber devices to be used in controlled release, tests carried out with them are very

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doi:10.1016/j.ejpb.2006.11.011

important and need to be performed [3]. And it is well known that blending is an effective and convenient method to improve the performance of polymer materials. In the present study, we prepared chitosan/starch blend fibers. To use these fibers in several controlled release applications, it was necessary to have an overall understanding of their properties. Using salicylic acid (SA), as a model drug, we studied some factors that may have influence on the drug release from chitosan/starch fibers as the ratio of chitosan and starch used, the loaded amount of SA, the pH and ionic strength of the release solution, etc. We wish this fiber can lead to a successful application for localized drug delivery in in vivo or in vitro environment.

2. Materials and methods

2.1. Materials

Chitosan from a shrimp shell was purchased from Yuhuan Ocean Biochemical Co. Ltd (Zhejiang, China), degree of deacetylation (DD) was 87%, and M_v was 8.0×10^5. The DD was measured by pH titration method [18] and the M_v was measured by viscometer method [19]. Starch and SA were all purchased from Shanghai Chemical Reagent Co. Ltd (Shanghai, China). Other reagents were all of analytical grade and all commercially available and used as received.

2.2. Preparation of drug loaded fibers

Chitosan/starch drug loaded fibers were obtained by spinning their solution through a viscose-type spinneret into a coagulating bath. Solutions of chitosan and starch, 5 wt.%, were prepared with 2 wt.% acetic acid solution and distilled water, respectively; and the latter one was dissolved in higher temperature. These solutions were mixed in different proportions to obtain final starch weight ratio (dry state) of 10, 30, 50 and 70 wt.%. The four solutions were made completely homogeneous under stirring, and then filtered through a 200 mesh filter cloth under pressure. After that, the filtrate was sonicated in sonication bath (FS-20, Jingrong Sonic Electronics Co. Ltd., Beijing, China), left to stand until trapped air bubbles were removed. Finally the clear solution as a spinning solution was poured into the spinning tank, and extruded at 25 °C from a 30-hole (0.08 mm diameter) viscose-type spinneret into a coagulating bath containing 10 wt.% tripolyphosphate (TPP) aqueous solutions with ethanol to form fibers. The volume ratio of TPP aqueous solution to ethanol was 50/50. The as-spun fibers were washed and stretched (stretching ratio is 20%) in distilled water, then were dried in an oven (GDW-250, Saiou Test Machine Co. Ltd., Shanghai, China) at 37 °C for 48 h, and finally dried under vacuum at room temperature until constant weight. The several chitosan/starch fibers, without drug, were designated as CS-1, CS-2, CS-3 and CS-4 (C, chitosan; S, starch; weight ratio of chitosan:starch is 90:10, 70:30, 50:50 and 30:70, respectively).

To make drug loaded fibers, 2.0 g SA was dissolved, under stirring, in 500 ml of each one of those four above solutions to make them completely homogeneous. And applying the same method to make fibers, we can get the drug loaded ones and designate them as CSS-1, CSS-2, CSS-3 and CSS-4 (C, chitosan; S, starch; S-SA, weight ratio of chitosan:starch is 90:10, 70:30, 50:50 and 30:70, respectively). Then 1.0 or 3.0 g of SA was dissolved in a solution of chitosan and starch (starch was 30 wt.%, dry state), producing drug loaded fibers designated as CSS-2(−) and CSS-2(+), respectively.

2.3. FT-IR analysis

The FT-IR spectra of pure chitosan, starch, CS-1 and CS-3 fibers were recorded with KBr pellets on a Nicolet FT-IR spectrometer, Model 170SX (USA).

2.4. X-ray diffraction studies

The X-ray diffraction patterns of pure chitosan, starch, CS-1 and CS-3 fibers were studied on a Shimadzu Lab-XRD-6000X diffractometer (Japan), using Nickel-filtered CuKα radiation at 40 kV and 50 mA in the 2θ range of 8°–40°.

2.5. Morphology observations

The morphologies of the CS-1 and CS-3 fibers were examined using scanning electron microscopy (SEM) Hitachi S-570 (Japan). Cross-sectional samples were prepared by fracturing fibers in liquid nitrogen. Prior to observation, samples were arranged on metal grids, using double-sided adhesive tape, and coated with gold under vacuum before observation.

2.6. Mechanical properties

The tensile strength (σ_b) and the elongation at break (ε_b) for fibers were determined on an electronic tester machine (CMT8502, Shenzhen SANS Test Machine Co. Ltd., China). The gauge length was 90 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. The sample size of each experiment is five.

2.7. Water-retention properties

The water-retention values (WRV) of fibers were calculated as follows:

$$\mathrm{WRV} = (W_1 - W_0)/W_0 \times 100\%$$

where W_0 denotes the weight (g) of fiber which was dried at 80 °C until a constant weight was achieved; W_1 is the weight of fully swollen fiber that was centrifuged at

4000 rev/min for 10 min. The sample size of each experiment is three.

2.8. Release studies

Drug loaded fibers (0.3 g) was suspended in glass vessels containing 50 ml of medium, and incubated on a shaking bed (HS-150, Saiou Test Machine Co., Ltd., Shanghai, China) at 37 °C, 130 rpm. At appropriate time intervals the solutions were withdrawn and the amount of SA released from the drug loaded fibers was evaluated by UV spectrophotometer (UV-721, Shanghai Analytical Instrument Co., China) at 300 nm. Then an equal volume of the same dissolution medium was added back to maintain a constant volume. The medium conditions for the controlled release studies were four typical solutions: pH 1.0 (0.1 N HCl solution, acts as simulated gastric fluid), pH 3.6 and pH 5.0 (10 mM HAc–NaAc buffered solution), and pH 7.4 (10 mM NaH_2PO_4–Na_2HPO_4 buffered solution, acts as simulated intestinal fluid). The ionic strength of the above-buffered solutions can be carefully adjusted to a relative level by adding an appropriate amount of NaCl. The sample size of each experiment is three.

3. Results and discussion

3.1. Structure and morphology characterization

3.1.1. FT-IR analysis

Fig. 1 shows the FT-IR spectra of chitosan, starch, blend fibers CS-1 and CS-3. About pure chitosan, two characteristic absorption bands at 1637 cm^{-1} and 1564 cm^{-1} were detected and attributed to Amide I(C=O) and Amide II(N–H), respectively; 1383 cm^{-1} was attributed to the distorting vibration of C–CH_3 [20]. The characteristic absorption bands at 1210 cm^{-1} and 1720 cm^{-1} of starch were attributed to the bending vibration and stretching vibration of C–O, respectively. Finally, the wide absorption band around 3423 cm^{-1} was due to the stretching vibration of O–H.

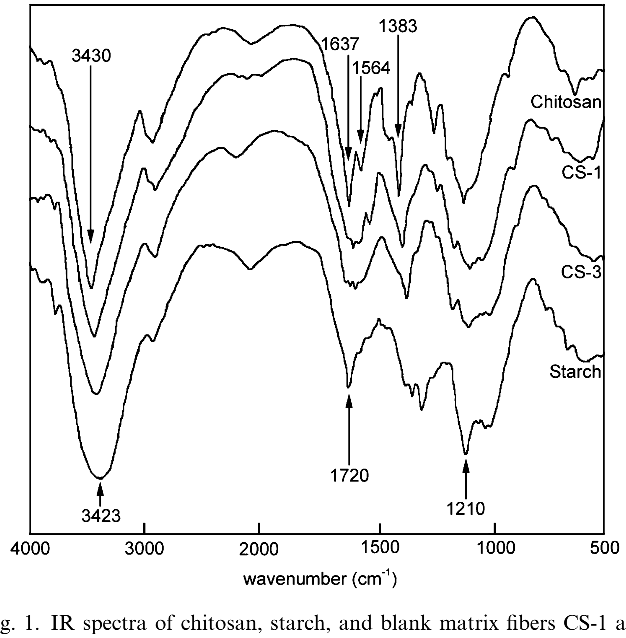


Fig. 1. IR spectra of chitosan, starch, and blank matrix fibers CS-1 and CS-3.

From the FT-IR spectra of blend fibers CS-1 and CS-3, we can see that the characteristic absorption bands at 1564 and 1637 cm^{-1} of chitosan shifted to lower wave number at 1556 and 1628 cm^{-1}. At the same time, the absorption band around 3430 cm^{-1} concerning the stretching vibration of N–H group bonded to O–H group shifted to a lower wave number at 3419 cm^{-1} and became wider, suggesting an increase in the hydrogen bonding [13]. All those changes show a strong evidence of the intermolecular interactions and good molecular compatibility between chitosan and starch.

3.1.2. X-ray diffraction studies

It may be seen, in Fig. 2, the X-ray diffraction patterns of chitosan, starch, blend fibers CS-1 and CS-3. The diffractogram of chitosan consisted of three typical crystalline peaks at $2\theta = 11.8°$, 15.7° and 20.9°. Starch had typical crystalline peaks at $2\theta = 17.1°$ and 22.0° because of its close molecular packing and regular crystallization. From the X-ray diffraction patterns of blend fibers CS-1 and CS-3, Fig. 2, it may be seen that the diffraction peaks of chitosan at 11.8° and 20.9° rapidly weakened and the diffraction peak at 15.7° disappeared with the increasing of starch content. This can be explained by the strong interaction between chitosan and starch which has destroyed the close packing of the chitosan molecules for the formation of regular crystallites. In other words, the results of X-ray diffraction could reinforce the existence of good compatibility between chitosan and starch due to both kinds of strong interactions like hydrogen bonds and ionic interactions.

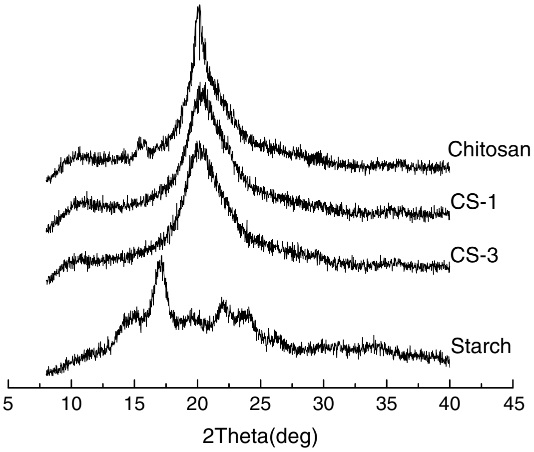


Fig. 2. XRD patterns of chitosan, starch, and blank matrix fibers CS-1 and CS-3.

3.1.3. Morphology observations

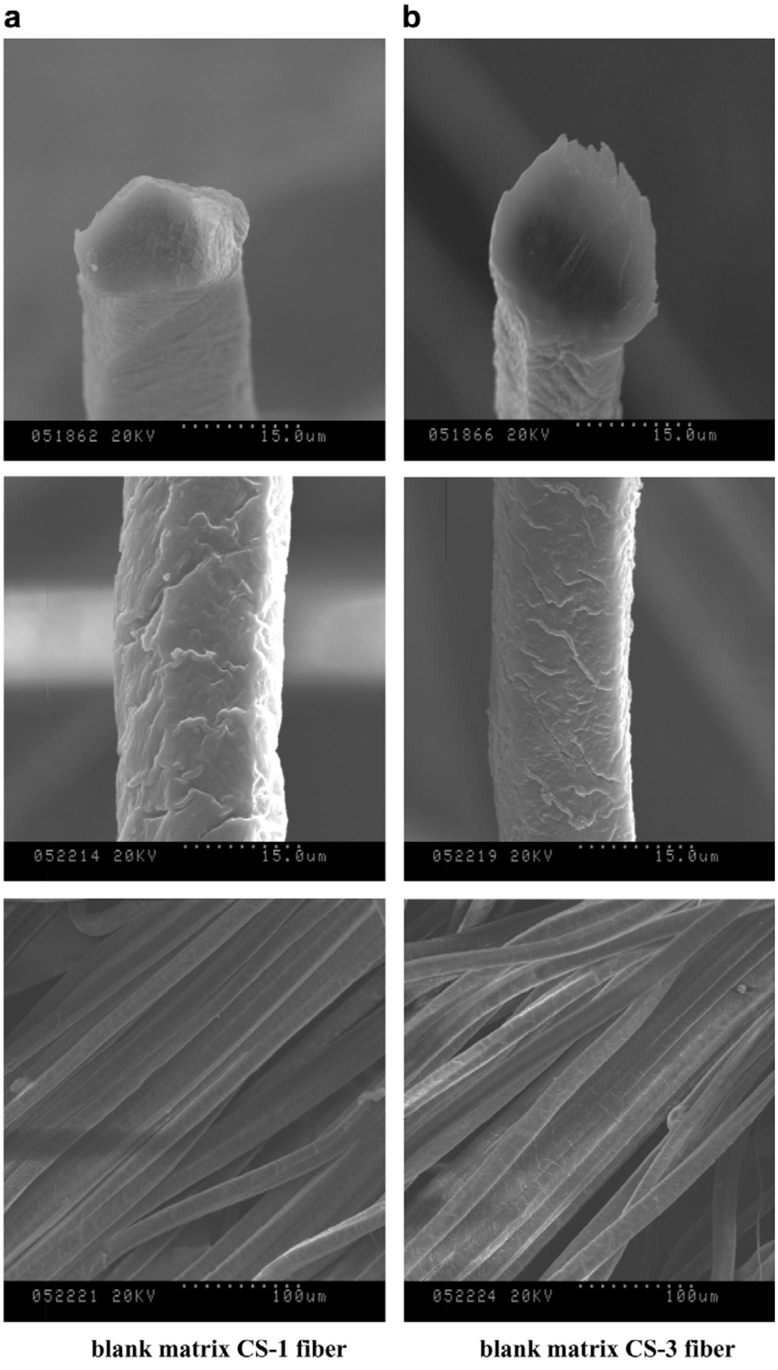
Analysis of the morphologies of CS-1 and CS-3 fibers obtained by Scanning Electron Microscopy (SEM), in Fig. 3, shows that the cross-section of both is smooth and homogeneous, with absence of micro phase separation. Again, the result obtained here also indicated good compatibility between chitosan and starch.

3.2. Mechanical properties

Fig. 4. shows the mechanical properties of the blend fibers. Tenacity (yarn count tenacity) is calculated from the breaking strength and yarn count and is expressed in centinewton per tex (cN/tex):

$$\text{Tenacity (cN/tex)} = \frac{\text{Breaking strength (N)}}{\text{Yarn count (dtex)} \times 0.001}$$

From the figure, it may be seen that the maximum values of tensile strength and elongation at breaking were observed when the content of starch was 30 wt%. The results indicated that blending is effective in improving the mechanical properties of the drug loaded fibers.



blank matrix CS-1 fiber **blank matrix CS-3 fiber**

Fig. 3. SEM photographs of chitosan, starch, and blank matrix fibers CS-1 and CS-3.

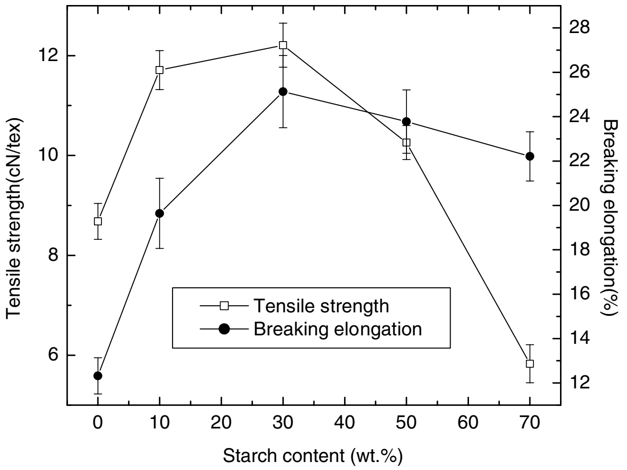


Fig. 4. Mechanical properties of blank chitosan/starch fibers with different composition.

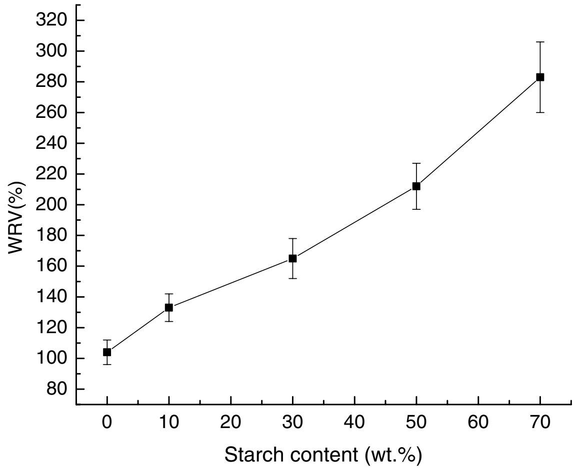


Fig. 5. Water-retention properties of blank chitosan/starch fibers with different composition.

3.3. Water retention properties

The WRV of the blank blend fibers are plotted in Fig. 5 as a function of starch content. It showed that the WRV of chitosan/starch fibers increased as the amount of starch was raised. The improvement in water-retention is due to starch being more hydrophilic than chitosan.

3.4. Release studies

3.4.1. Effect of the composition ratio of drug loaded fiber

The influence of the different composition ratios of chitosan and starch in the drug loaded fibers CSS-1, CSS-2, CSS-3 and CSS-4 (10, 30, 50 and 70 wt.% of starch, respectively) was investigated in this experiment. The release medium conditions, as mentioned before, were 10 mM NaH_2PO_4–Na_2HPO_4 buffered solution with pH 7.4 and ionic strength of 0.145 M. As Fig. 6 shows, the amount of the drug released increased as the content of starch increased. In other words, as starch is a kind of soluble macromolecule, it dissolves and leaves pores that accelerate the release of the drug from the matrix fiber.

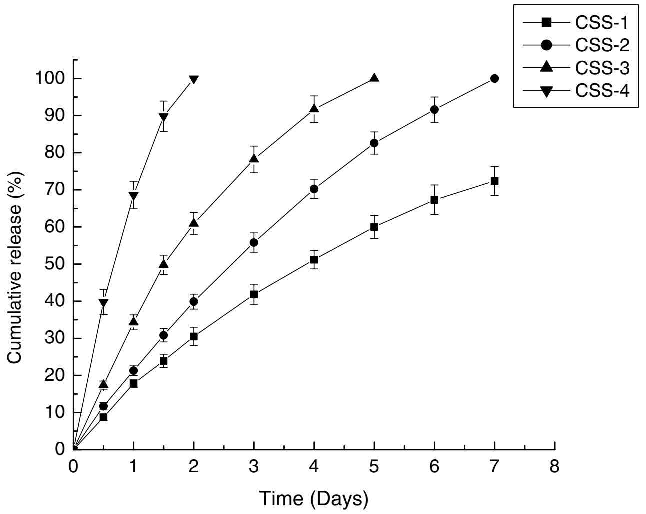


Fig. 6. Influence of the composition of the drug loaded in chitosan/starch fibers on the drug controlled release process.

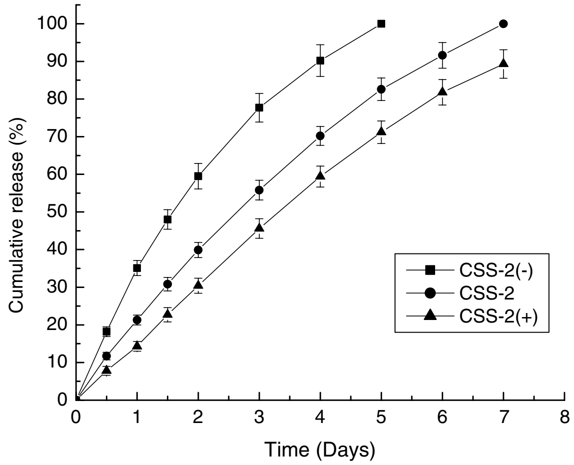


Fig. 7. Influence of the amount of drug loaded in chitosan/starch fibers on the drug controlled release process.

3.4.2. Effect of the drug loaded amount

Fibers CSS-2(−), CSS-2 and CSS-2(+), with different drug loaded amount (1.0, 2.0 and 3.0 g, respectively), were studied in the same release solution cited in item 3.3.1. From Fig. 7, it may be concluded that the more drugs loaded, the lower the drug release rate was; but according to the fact that more drugs were loaded, the cumulative release amount is increasing. So we can get a more persistent release by increasing the drug loaded amount.

3.4.3. Effect of pH

The drug release from loaded fiber CSS-2, in four different buffered solutions with pH 1.0, 3.6, 5.0 and 7.4, was studied. The ionic strength of those solutions was all adjusted to 0.145 M, by adding an appropriate amount of NaCl. Fig. 8. shows that the drug release from loaded fibers was very sensitive to the pH of the medium. The release was accelerated with the decrease of pH, because the electrostatic interaction between anions and chitosan was greatly influenced by solutions' pH [16]. The decrease of pH weakened salt bonds and therefore, facilitated fiber swelling. So, the drug release was accelerated. The pH also has a slight effect on the solubility of SA. A higher pH leads to a better solubility of SA, which results in higher drug release rate. But compared to the strong influence of pH on the fiber matrix, pH effects on SA could be neglected.

3.4.4. *Effect of ionic strength*

Drug loaded fiber CSS-2 was used in this experiment as release matrix. Adding an appropriate amount of NaCl to the 10 mM NaH_2PO_4–Na_2HPO_4 buffered solution with pH 7.4 produced the four different release mediums. Fig. 9 shows that with the increase of ionic strength the drug release rate also increased. The result was possibly related to the decrease of osmotic pressure inside the fiber with the increase of the salt concentration and the weakened salt bond between SA and fiber matrix by salt ion [21].

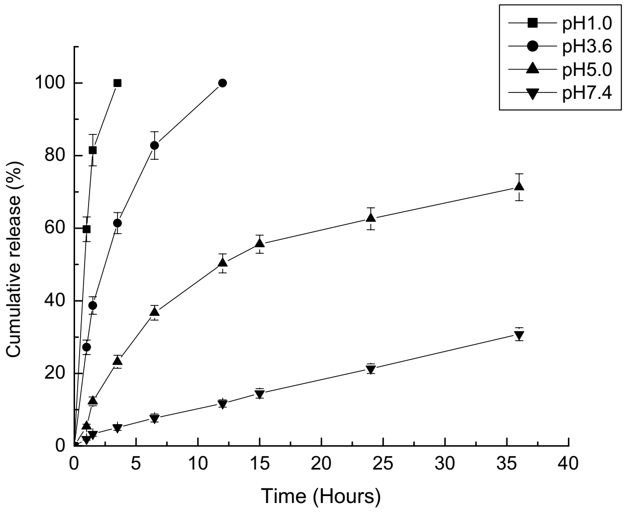


Fig. 8. pH influence of the release medium on the drug controlled release process from CSS-2 fiber.

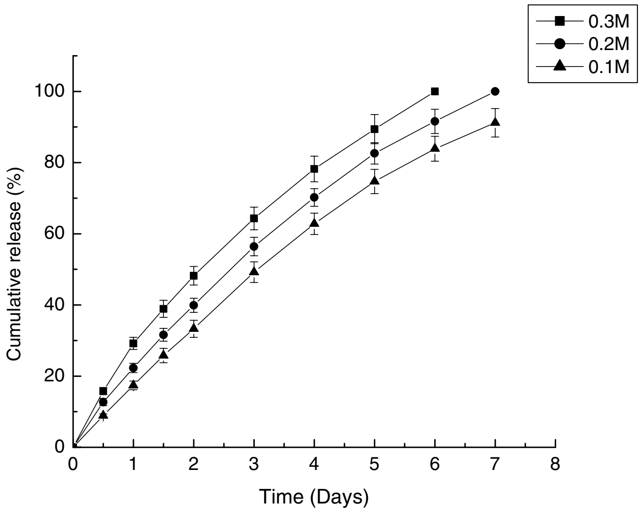


Fig. 9. Influence of the ionic strength of the release medium on drug controlled release from CSS-2 fiber.

4. Conclusions

Drug loaded fiber based on chitosan and starch was obtained by spinning their solution through a viscose-type spinneret into a coagulating bath containing aqueous TPP and ethanol. With SA as a model drug, we studied the fiber's structures and characterizations, especially its potential capacity in drug delivery system. The results indicated that the blended fiber was sensitive to pH and ionic strength of the release medium. However, the effect of pH is stronger. Furthermore, the fiber's composition and drug loaded amount both had relevant influence on the release properties of the fiber. Thus, we can control the drug release rate through changing some influential factors of the drug loaded fiber. The fiber can lead to a successful application for localized drug delivery in in vivo or in vitro environment.

Acknowledgement

We gratefully acknowledge financial support from the National Natural Science Foundation of China with Grant No. 29977014.

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