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Preparation of a novel chitosan-microcapsules/starch blend film and the study of its drug-release mechanism

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ABSTRACT

A novel drug delivery system, chitosan-microcapsules/starch blend film for antofloxacin controlled release, was prepared, and characterized by Fourier transform infrared spectroscopy (FT-IR), X-ray diffraction (X-RD), thermogravimetry and derivative thermogravimetry (TG/DTG), and scanning electron microscopy (SEM). Following incorporation of the chitosan-microcapsules in the film matrix, the synergistic interactions between these drug-carriers were significant. The thermostability and mechanical properties of the blend film were greatly improved by the incorporation of the microcapsules. The water resistance of the blend film was enhanced by increasing the content of microcapsules, indicating that the microcapsules acted as moisture barriers. After being incorporated, chitosan-microcapsules/starch blend film shows a sustained drug release. The extent of the film degradation and microcapsules swelling in the release system indicated that the drug released of the blend film was pH-sensitive. The blend film exhibited pharmacodynamic efficacy because of the efficient drug releasing.

1. Introduction

Starch, a renewable polymer with great biocompatibility, has been widely used as a base material in pharmaceutical applications [1]. Starch films processed with biodegradable plasticizers have been shown to have a promising potential in drug delivery especially for colon treatment, facial plastic surgery, and wound healing [2]. Nevertheless, the development of starch films is seriously impeded by its poor mechanical and strong hydrophilic properties, which causes an inevitable decline in its drug delivery efficiency. An efficient method of overcoming these disadvantages is to modify the structure of starch by blending with other polymers, such as xanthan gum and PVA, which are helpful in improving the mechanical property and water resistance [3,4].

Chitosan (CS)-microcapsules (MCs), which are biodegradable and non-toxic, provide an efficient and sustained delivery system for controlled drug release. These properties have drawn increasing attention to its potential applications in the fields of food processing, biomedical engineering, pharmaceutical preparation, etc. [5]. In the present study, we investigated the effects of combining two drug-carriers, microcapsules and films, on the preparation of a novel drug delivery system for pharmaceutical application. Therefore, the aim of this paper was to demonstrate the feasibility of preparing a CS-MCs and starch blend film, in which hydrogen bonds are expected to form between the hydroxyl (or amine) groups on the surface of MCs. We also determined the need to investigate if the characteristics of the novel delivery system would be either a simple combination of both carriers or constitute a potential synergistic interaction that would enhance drug delivery.

Antofloxacin, a novel drug, has excellent antibacterial activity against gram-positive and gram-negative bacteria as well as a relatively low cardio toxicity and phototoxicityas compared to other fluoroquinolones [6]. Therefore, in the recent years, antofloxacin has been used clinically for the treatment of urinary and respiratory tract infections caused by sensitive bacteria [7]. Here, antofloxacin was used as a model standard to study the drug release mechanism. The characterization of the blend film was performed by Fourier transform infrared spectroscopy (FT-IR), X-ray diffraction (X-RD), thermogravimetry (TG) and derivative thermogravimetry (DTG), and scanning electron microscopy (SEM). The mechanical properties (tensile strength and elongation at break), water vapor permeability (WVP), moisture sorption, and drug release mechanism were also tested. Finally, we elucidated the drug-

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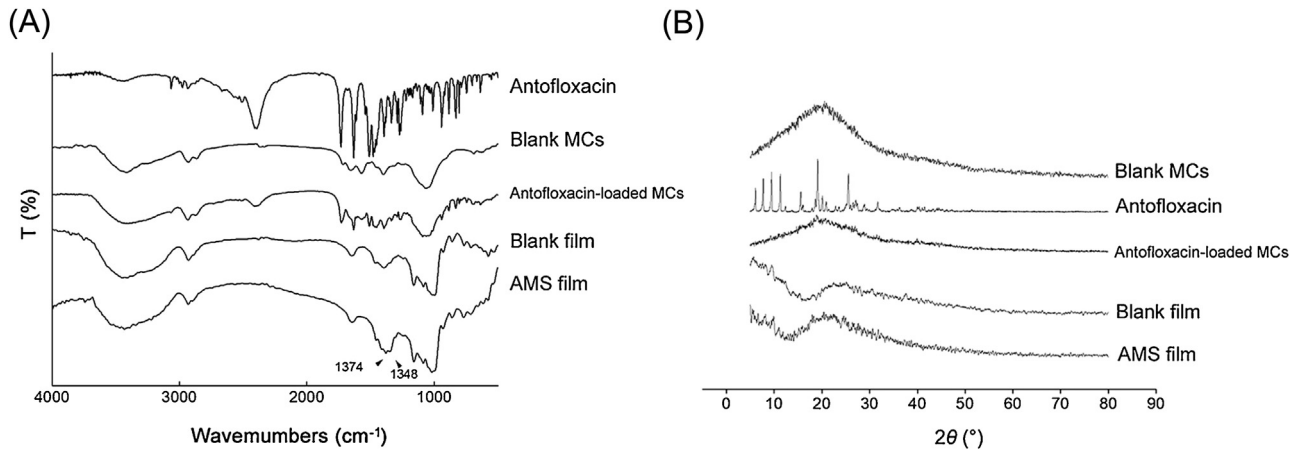

Fig. 1. The FT-IR spectra (A) of antofloxacin, blank MCs, antofloxacin-loaded MCs, blank film, AMS film and X-RD patterns; (B) of blank MCs, antofloxacin, antofloxacin-loaded MCs, blank film and AMS film.

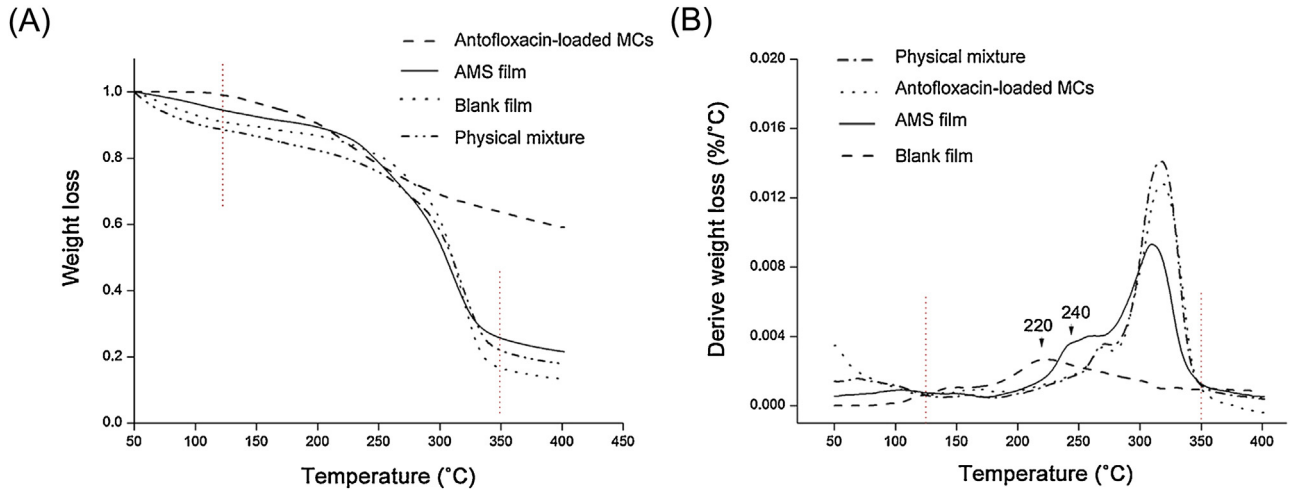

Fig. 2. TG (A) and DTG (B) curves of antofloxacin-loaded MCs, AMS film, blank film and physical mixture.

release mechanisms and evaluated the pharmacodynamic efficacy of the films.

2. Materials and methods

2.1. Materials

Antofloxacin (98.57% purity), was obtained from the Institute of Biomaterial, South China Agricultural University. Cornstarch (16% amylose content) and agar powder were obtained from the Aladdin Industrial Inc. Chitosan (CS), which had a degree of deacetylation (DD) of 89.2% and molecular weight (M_w) of 2.8×10^5, was purchased from Shandong Aokang Biotech Ltd. Mueller-Hinton Broth, paraffin liquid, glutaraldehyde (GA, 25% water solution), and glycerol were obtained from Guoling Instrument Inc. All the chemicals and reagents were of analytical grade.

2.2. Preparation of antofloxacin-loaded CS-MCs and starch (AMS) film

Antofloxacin-loaded CS-MCs were prepared according to previously reported methods [8]. The encapsulation efficiency (EE,%), which was determined by high-performance liquid chromatography (HPLC, Agilent 1260, USA) following previously reported methods [5], was found to be $61.69 \pm 1.52\%$. Antofloxacin-loaded CS-MCs and starch (AMS) film was prepared by using the casting method [9].

First, 1.00 g of the dry basis (0.80 g cornstarch; 0.20 g agar) and 0.25 g of glycerol were dispersed in 20.0 g of distilled water and stirred for 30 min. Second, the mixture was heated to 95 °C for 30 min. Third, 0.0–70.0 mg antofloxacin-loaded CS-MCs were dispersed in 1.0 mL of distilled water and added drop wise to the mixture. The mixture was stirred until a homogenous blend was obtained. After degassing with ultrasonic treatment, the solution was cast into glass molds and dried at 60 °C for 3 h to obtain a series of composite films with varying antofloxacin-loaded MCs content (0–7% dry basis).

2.3. Fourier-transform infrared spectra (FT-IR) and X-ray diffraction (X-RD) study

FT-IR spectra were obtained with an Avatar 360 spectrometer (Nicolet, America). MCs and the drug were tested by the potassium bromide (KBr) pellet method, and the film samples were investigated by the transmission method. X-RD spectra were determined with an X-ray diffractometer (XD-2X/M4600, China) to study the crystal structure of the MCs and films over a 2θ angular range from 5° to 80°.