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Fabrication and property of chitosan film carrying ethyl cellulose microspheres

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Abstract

Chitosan (CS) film carrying ethyl cellulose (EC) microspheres (comatrix) is reported in this paper. The properties including interaction, shape change under different condition and its mechanical variety in different ratio of CS to EC microspheres were analyzed by using scanning electron microscope (SEM), X-ray diffraction (XRD), infrared spectra (IR), differential scanning calorimetry (DSC) and mechanical testing. The results indicated that the round EC microspheres dispersed in the CS film, and there was interaction between EC and CS matrix. The comatrix may offer an appropriate property for degradation and drug releasing.

Keywords: Chitosan; Film; Ethyl cellulose; Microsphere

1. Introduction

Drug delivery system is a field attracting much attention. Many polymers have been used as drug carriers, such as synthetic compounds (polyacrylates, -methacrylate and methacrylesters), semi-synthetic compound (methyl-, ethyl-, hydroxycellulose) and natural compounds (protein, chitosan and alginate). It is reported that ethyl cellulose microcapsules can slow drug releasing rate (Gunder, Lippold, & Lippold, 1995). The ethyl cellulose dispersion with different plasticizers as diffusion pellets coating can obviously give them different drug releasing rate (Frohoff-Hulsmann, Lippold, & McGinity, 1998). When dimenhydrinate is in ethyl cellulose matrix, releasing rate of dimenhydrinate fits to zero-order kinetics; the more ethyl cellulose was in the matrix, the slower the drug releasing rate became (Desai, Alexander, & Riga, 2006). Ethyl cellulose microspheres carrying diclofenac sodium are made by using stabilizers, such as PVA, alginate, pectin and gelatin, which have excellent drug releasing property (Jani & Gohel, 1997). When they are blended by using different plasticizers, CS and ethyl cellulose always have phase separation, however, the interaction between them has been detected (He, Du, & Fan, 2006). CS microspheres in PLG film shows unusual sustained releasing rate, compared with microspheres (Blanco, Gomez, Olmo, Muniz, & Teijon, 2000). The cytarabine releasing rate of albumin microspheres carried by film is slow in vivo and in vitro; when the comatrix is implanted in the rat, no repulsion reaction takes place (Gomez et al., 2004). In addition, a silica film containing polystyrene microspheres is made by dip coating method to form an inorganic–organic thin film. (Adachi, Suzuki, Kashiwagi, Isobe, & Senna, 1998).

EC is an infirmly polar and water-insoluble polymer. The main chain of EC is given by anhydroglucose units linked by 1,4-β-glucodidic bonds. Generally, the OH functional groups are available for ester and ether reactions (Fig. 1a). EC is widely used as coating film of pharmaceutical purpose (Hyppola, Husson, & Sundholm, 1996). On the other hand, chitosan is an N-deacetylation product of chitin and a cationic polysaccharide under acidic conditions. It consists of glucosamine and *N*-acetylglucosamine units linked through 1–4 glycosidic bonds (Fig. 1b). In

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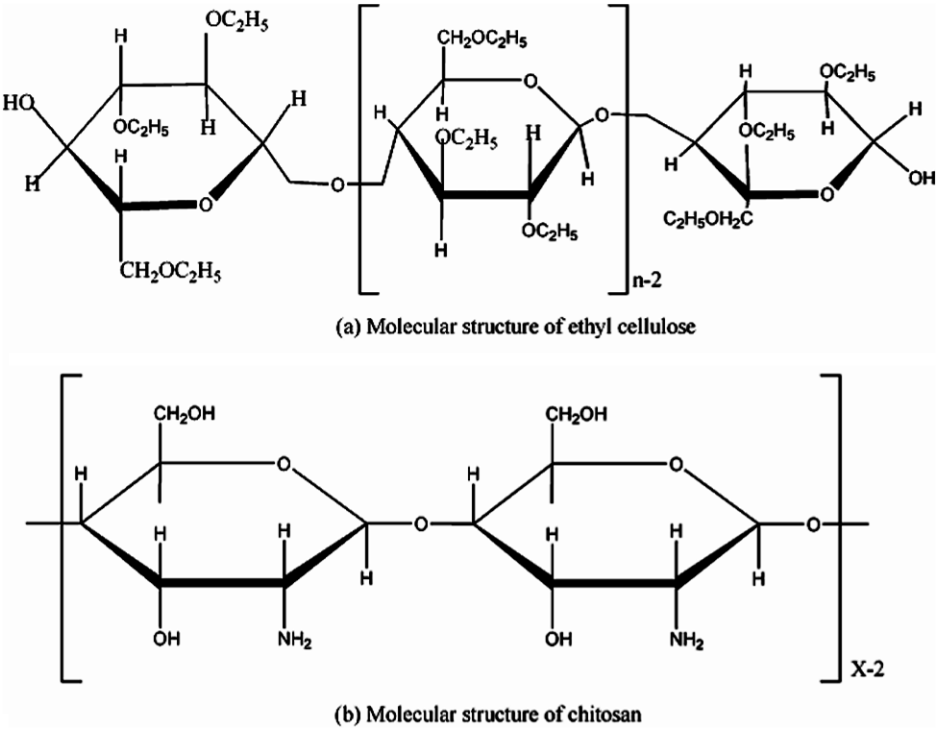

Fig. 1. Molecular structure of ethyl cellulose (a) and chitosan (b).

addition, chitosan is flexible and has a high resistance upon heating, because its intramolecular hydrogen bonds formed between its hydroxyl group and its amino group.

Although the number of articles focusing on microspheres of EC or CS, EC/CS blended film increases quickly, a few researches have been done on film carrying microspheres. In this study, EC is dissolved in acetone–methanol–CH_2Cl_2 ternary mixture. The EC microspheres, then, are made by solvent remove/solvent evaporation method in CS solution. The comatrix is poured on glass plate to form CS film carrying EC microspheres.

2. Materials and methods

2.1. Materials

Chitosan was supplied by Haidebei Technological Co. Ltd of Shandong Province, China. Ethyl cellulose was purchased from Niansha Chemical Reagent Company of Kunshan, Jiangshu, China. Methanol, acetone and glacial acetic acid were supplied by Changlian Chemical Reagent Co. Ltd of Chengdu, China. CH_2Cl_2 was from Chemical Reagent Factory of Tianjin, China. Other reagents used here were analytical grade.

2.2. Microspheres preparation

(a) Ethyl cellulose microspheres preparation in chitosan solution of various concentrations: EC (0.5 g) was dissolved in ternary mixture (40 ml) consisted of CH_2Cl_2, methanol and acetone. Different chitosan solution (2%, 4%, 6%, w/v) was prepared by dissolving 2, 4 and 6 g chitosan in 100 ml diluted acetic acid (3% v/v), respectively. The primary O/W emulsion was obtained by injecting 40 ml EC solution in 100 ml chitosan aqueous solution. Emulsification was performed at room temperature under continuous stirring at 1000 rpm for 30 min. The emulsion, then, was put in water incubator for 3 h at 40 °C. After the organic solvent being evaporated, the microspheres were separated by centrifugation, and then they were fully washed and freeze-dried by using distill water and desiccator.

(b) Heat treated ethyl cellulose microspheres prepared in chitosan solution: 40 ml above-mentioned ternary solution containing 0.5 g EC was injected in 100 ml 6% CS solution with stirring at 1000 rpm for 30 min. This step was repeated 3 times, respectively. After the three O/W emulsion being formed, they were encircled by water at 40, 70 and 100 °C respectively, until CH_2Cl_2, methanol and acetone evaporated completely. When they were solidified, EC microspheres were separated as above-mentioned methods.

2.3. Comatrix fabrication of CS film carrying EC microspheres

CS film carrying EC microspheres was prepared by dripping 40 ml ternary solution containing 0.5 g EC in 100 ml CS solution (6 wt%), then they were stirred at 1000 rpm. Half hour later, the emulsion was maintained at 40 °C.