Characterization of alginate/carboxymethyl scleroglucan hydrogels as a delivery system for protein drug

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Abstract

The aim of this study was to prepare a hydrogels composed of alginate blended with a carboxymethyl scleroglucan (CMSC) and evaluate the feasibility of the hydrogels as a drug delivery system for a protein. The main advantage of the alginate/CMSC hydrogels is to improve a restricted drug release from alginate hydrogels. The CMSC was chemically synthesized with chloroacetic acid and confirmed using a FT-IR. The alginate/CMSC hydrogels were prepared at distinct compositions by crosslinking with calcium ions. The swelling ratios of these hydrogels increased significantly with increasing the content of CMSC. At pH 7.4, the swelling ratios of the hydrogels increased remarkably as compared to those at pH 1.2. In ovalbumin (OVA) release test, the amount of OVA released from the hydrogels showed higher as compared to those released at pH 1.2. In addition, the release of OVA was improved with increasing the content of CMSC. Thus, the alginate/CMSC hydrogels may be used as a potential system for oral delivery of protein drugs.

Introduction

Oral delivery of protein and peptide drugs is not easy to achieve possibly because they are readily degraded by the low pH in stomach and gastro- intestinal enzymes.[1)]

Therefore, these drugs need to be protected from the harsh environment in stomach. These problems can be eliminated by encapsulating protein drugs into natural polymers such as alginate, chitosan, carboxymethyl cellulose, pectin etc.[2] Alginate is gelled when divalent cations (usually Ca^{2+}) interact ionically with blocks of guluronic acid residues. The specific properties of alginate enable several senstivie drugs to encapsulate successfully under mild conditions. However, alginate beads crosslinked with calcium ions show minimal drug release profiles due to the relatively strong ionic interaction between the carboxylic groups on alginate and calcium ions.[1] In order to this problem, a complex composed of alginate blended with a caboxymethylated scleroglucan (CMSC) was prepared to form hydrogels by dropping alginate/CMSC into a calcium solution. The negatively charged scleroglucan forms a hydrogel and is used for drug delivery systems. In this study, preparation of alginate/CMSC hydrogels was reported. Swelling characteristics of these hydrogels were investigated at pH 1.2 and 7.4. Additionally, release profiles of a model protein drug (ovalbumin, OVA) from the hydrogels were studied.

Materials and Methods

Materials

Alginate of low viscosity (250 cps for a 2% solution at 25℃), calcium chloride, ovalbumin (OVA) and Bradford reagent were purchased from Sigma Chemical Co. (St. Louis, MO). Scleroglucan was presented from Deggusa (Trostberg, Germany). All other chemicals used were of analytical grade.

Synthesis of carboxymethyl scleroglucan(CMSC)

CMSC was synthesized according to a procedure described in the paper with some modifications.[1] Detailed procedures were previously reported by Crescenzi et al. The synthesized CMSC was analyzed by the FT-IR.

Preparation of alginate-CMSC hydrogels

The alginate-CMSC hydrogels were prepared by dropping aqueous alginate- CMSC into a calcium chloride solution. Alginate-CMSC soltuions at distinct compositions (alginate:CMSC=2%:0%, 1.5%:0.5%, 1%:1%, 0.5%:1.5% and 0%:2% by w/v) were prepared.

The prepared alginate-CMSC solutions were dropped into a stirred 0.1 M of calcium chloride solution through a syringe needle. The hydrogels were rinsed with distilled water to remove unreacted calcium chloride and then dried at 37℃.

Swelling characteristics of alginate-CMSC hydrogels

The dried hydrogels were immersed to swell in 1 ml of HCl buffer (0.1 M pH1.2) or PBS buffer (0.1 M, pH 7.4) at 37℃. At the specific intervals, the samples were removed from the swelling medium and placed to whatman filter paper in order to absorb excess water on surface. The swelling ratios (Qs) were calcualted from the following expression:

$$Qs = (W_s - W_d)/W_d \times 100$$

where W_s is the weight of the swollen hydrogels and W_d is the weight of the dried hydrogels.

Release profiles of alginate-CMSC hydrogels

In order to study the release profiles for the hydrogels, the dried hydrogels were immersed in HCl buffer or PBS buffer at 37℃. At predetermined time points, 100 μl of the solution was taken out and analyzed by Bradford method at 595 nm using a spectrophotometer. The percentage of cumulative amount of released OVA was calculated from standard calibration curves.

Results and Discussion

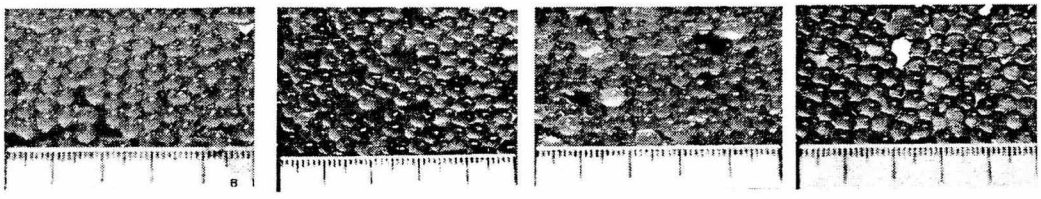
Formation of alginate-CMSC hydrogels

In all the cases, alginate-CMSC hydrogels were successfully formed with the exception of a composition without alginate. The formed hydrogels were spherical beads(Fig. 1). With increasing a composition of alginate, the hydrogels were rigid relatively. This is because CMSC forms a weak hydrogel in crosslinking with calcium chloride.

Swelling characteristics and release profiles of alginate-CMSC hydrogels

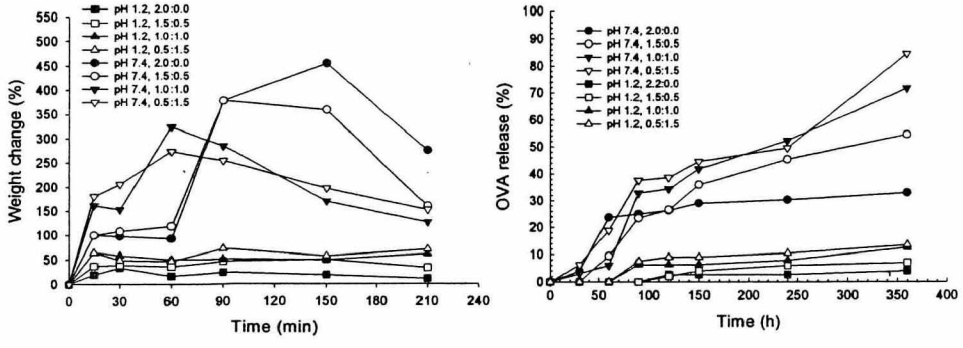
The swelling ratios of alginate-CMSC hydrogels increased significantly with increasing the content of CMSC. At pH 7.4, the swelling ratios of the hydrogels increased remarkably as compared to those at pH 1.2 (Fig. 2 (a)). In ovalbumin (OVA) release test, the amount of OVA released from the hydrogels showed higher as compared to those released at pH 1.2. In addition, the release of OVA was improved with increasing

the content of CMSC (Fig. 2 (b)). Thus, the alginate/CMSC hydrogels may be used as a potential system for oral delivery of protein drugs.



(a) (b) (c) (d)

Fig. 1. Photographs of alginate/CMSC hydrogels prepared at a distinct compositions, alginate: CMSC=(a) 2%:0%, (b)1.5%:0.5%, (c)1%:1%, (d)0.5%:1.5%.



(a) (b)

Fig. 2. Swelling ratios of alginate/CMSC hydrogels (a) and release profiles of OVA from alginate/CMSC hydrogels (b) at pH 1.2 and 7.4.

Acknowledgements

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