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Preparation and characterization of a novel starch-based interpolyelectrolyte complex as matrix for controlled drug release

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ABSTRACT

A novel cationized starch-based interpolyelectrolyte complex (IPEC) was formed using kappa-carrageenan as the counter polyion. Characterization of the product by turbidity measurements and elemental analyses indicated a 1:1 interaction of the repeating units. FT-IR spectra for the IPEC showed some differences in comparison with either IPEC constituents or physical mixture. The swelling of tablets obtained by direct compression was independent of pH, and a maximum value of 742% was attained after 24 h. The performance of the IPEC as matrix for controlled release of ibuprofen indicates that drug delivery takes place in a zero-order manner. Experimental dissolution data in the buffer stage were properly represented by a model accounting for contributions of Fickian diffusion and relaxation phenomena; this model suggests that the former predominates over the latter, for the modeled range.

1. Introduction

Starch is known to produce low toxicity products that are biodegradable and quite stable in biological environments. Due to the cost-effective attraction of starch-based products, they can be important materials for use in drug delivery applications. However, in oral administration, native starch is almost completely broken down after its ingestion.[1] In addition, the use of native starch as an excipient is limited due to its low compactibility leading to the formation of weak tablets subject to capping.[2]

To improve the properties of starch as a controlled release matrix, chemical modifications of its functional groups have been proposed. A common modification is chemical cross-linking with epichlorohydrin (a bifunctional agent).[1,3,4] Other researchers introduced, after the crosslinking step, cationic (aminoethyl), anionic (carboxymethyl), or acetate groups to further modify the matrix behavior.[5]

In recent years, there has been an increasing interest in physically cross-linked hydrogels. The main reason is to avoid the use of toxic chemical cross-linking agents to prepare such hydrogels. These agents have to be subsequently removed from the gels before application.[6,7] Thus, the preparation and evaluation of starch-based interpolymer complexes by hydrogen bonding with polyacids have also been reported.[8]

Starches conveniently modified by the introduction of cationic groups could be easily crosslinked to form hydrogels by the interaction with an anionic polymer; this kind of complex is known as an interpolyelectrolyte complex (or IPEC). IPECs form readily between most polyanions and polycations and are constituted by ionic association of repeating units on the polymer chains.[9]

On the other hand, different types of carrageenans have been employed for controlled release applications. Gupta et al.[10] used lambda- and iota-carrageenan in its pure form as matrix, while other researchers used carrageenans as part of IPECs. In this sense, Tapia et al.[11] employed predominantly kappa with a lower amount of lambda carrageenan and chitosan, whereas we previously explored the use of kappa-carrageenan and Eudragit E PO for IPEC formation.[12]

IPEC systems involving a variety of anionic and cationic macromolecules have been formed and characterized. Nevertheless, studies devoted to IPECs for controlled release applications are still rather scarce.[11–16] Furthermore, to the best of our knowledge, cationized starch for IPECs formation has not been previously investigated.

Herein, we report a novel IPEC between a commercial cationic corn starch (MS), cationized by the introduction of a 2-hydroxy-3-(*N*,*N*,*N*-trimethylammonium)propyl group, with a degree of

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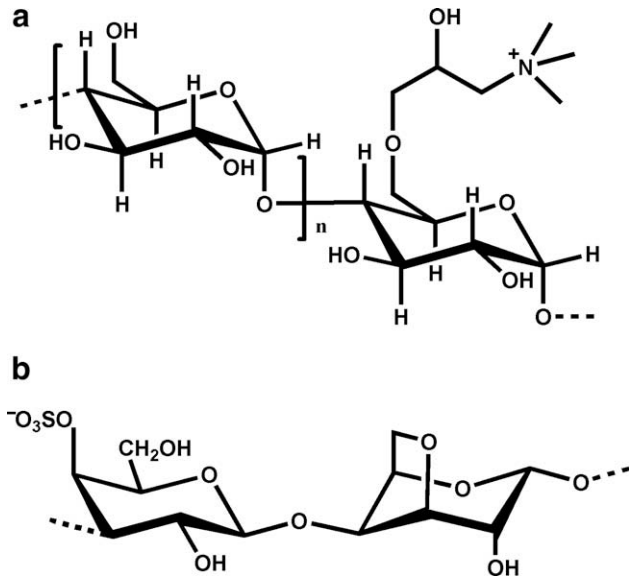

Figure 1. One possible repeating unit of modified (cationized) starch (MS) (a) and repeating unit of kappa-carrageenan (KC) (b).

substitution of 0.04 (amylose–amylopectin ratio = 27:73) (Fig. 1a), and kappa-carrageenan (KC) (Fig. 1b) as the counter-polyion. We also characterized the complex formed, and tested its performance as a matrix for controlled release of drugs, using ibuprofen (IBF) as a model.

2. Results and discussion

Turbidity measurements were initially employed to study the formation of the IPEC. Figure 2 shows the turbidimetric titration curve of a solution of MS with a solution of KC, and of a solution of KC with a solution of MS, where the relative turbidity is plotted as a function of the MS:KC molar ratio for a fixed final volume. The maximum turbidity was found for MS:KC molar ratio of 1:1, indicating that in this point equivalent quantities of both polymers reacted. The similarity of both curves and the same point of maximum turbidity are in agreement with the fact that IPEC composition is independent of the order of mixing.

The interaction or binding ratio of each component in the solid IPEC was confirmed by elemental analysis. The experimental values and those theoretically calculated by considering a 1:1 interaction of the repeating units (Fig. 1) are reported in Table 1. As seen, experimental and calculated results were alike.

The FT-IR spectra of MS–KC physical mixture and of IPEC were very similar to those corresponding to MS (not shown). This result is consistent with the composition of the physical mixture and IPEC that are constituted by 91% w/w of MS. The IPEC spectrum, however, presented small differences when compared with the spectrum of the physical mixture (Fig. 3): the band at 850 cm^{-1} assigned to the sulfate group of KC[17] shifted to 835 cm^{-1}, while the band at 1491 cm^{-1} assigned to the C–N bond of MS[18] shifted to 1480 cm^{-1}. These displacements could be due to ionic interactions between the sulfate groups and the quaternary ammonium groups in the IPEC.

The thermograms of MS and KC exhibited glass transition temperatures (T_g) of 90.2 °C and 82.4 °C, respectively. These values are in agreement with published data.[19,20] The IPEC presented a T_g of, 119.1 °C. A higher glass transition temperature is expected for a system with decreased mobility, due to interpolymer interaction.[14]

Typical SEM micrographs of MS, KC and of the IPEC are shown in Figure 4; the irregular shape of the IPEC particles, preliminary seen by optical microscopy, was also observed.

The Brunauer, Emmet, and Teller (BET) area determined for the IPEC was 0.58 $m^2\ g^{-1}$. This value agrees with a non-porous structure presenting a mean volume surface diameter (d_{vs}) of 91 μm, as calculated by optical microscopy[21] and observed by SEM. The static angle of repose measured was 38°, indicating a fair flowing

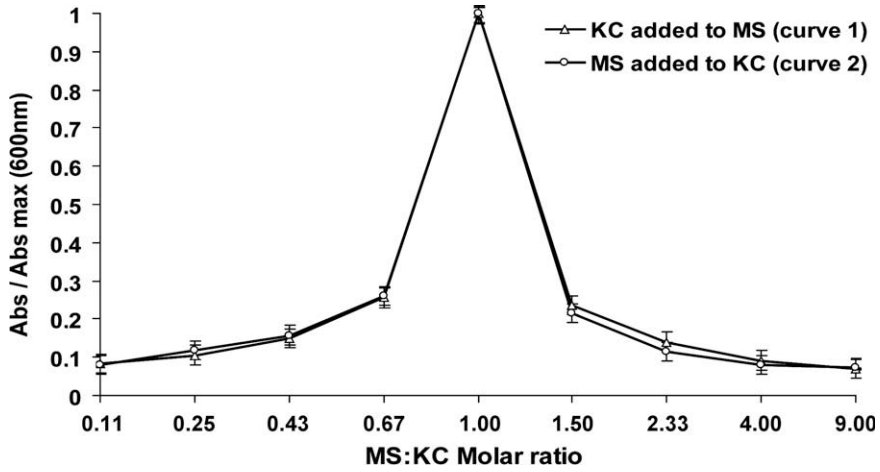

Figure 2. Turbidity of the MS–KC system as a function of the composition of the mixture and the mixing order.

Table 1
Elemental analyses of the IPEC

n	Experimental value, %				Calculated value, %				Molar ratio MS:KC
	C	H	N	S	C	H	N	S	
1	42.61	6.30	0.31	0.69					
2	44.87	6.17	0.33	0.74					
Mean	43.74	6.24	0.32	0.72	44.30	6.17	0.31	0.70	1:1