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RESEARCH ARTICLE

Colon-specific drug delivery using ethylcellulose and chitosan in the coat of compression-coated tablets

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Abstract

Background: This study investigates a new means to achieve colon-specific drug delivery. *Objective:* This study assesses the use of chitosan and ethylcellulose in the coat of a compression-coated tablet to achieve colon-specific drug delivery. The effects of chitosan type and its level as well as the coat thickness were evaluated.

Materials and methods: Caffeine-containing core tablets were prepared by direct compression. Three chitosan samples with different molecular weight and degree of deacetylation were used. Direct compression produced the finished coated tablet. The product was tested for its potential in colon-specific drug delivery by conducting release studies in simulated gastric and intestinal fluids. Enzymes harvested from rat cecal and colonic contents contributed to a medium to study drug release under colonic conditions.

Results: Essentially no drug was released until action on the tablet by either the acidic pH or the presence of enzymes in the release medium. Chitosan type had no effect on drug release as long as the coating level was the same. Lowering the chitosan level in the coat or increasing the coat thickness increased the lag time.

Discussion: The type of chitosan can be changed and yet the product is still susceptible to enzyme or pH effects. This indicates that chitosan present in the coat is still available for such action by the release medium. One can control the chitosan level or the thickness of the coat to achieve a desired delivery profile.

Conclusion: As colonic media can dramatically promote drug release, the potential for colon-specific drug delivery is confirmed.

Keywords: Direct compression, bacteria-dependent drug delivery, colon-specific drug delivery, controlled release, targeted drug delivery

Introduction

Colon-specific drug delivery is intended mainly to treat local conditions and diseases of the colon, such as Crohn's diseases, ulcerative colitis, colorectal cancer, and amebiasis[1–4]. In addition, peptides, proteins, and vaccines demonstrate candidature for colon-targeted drug delivery for systemic absorption with limited gastrointestinal degradation prior to absorption[5,6]. Drug delivery to the colon can be achieved by various delivery systems, such as, those involving pH-dependent, time-dependent, pressure-dependent, or bacteria-dependent delivery[5]. Bacteria-dependent drug delivery takes advantage of the fact that bacteria present in the colon secrete enzymes that can catalyze the degradation reactions that aid in drug release. Materials that are degraded by these enzymatic reactions in the colon are therefore used to accomplish bacteria-dependent drug delivery. Naturally occurring polysaccharides that constitute human dietary fiber can typically qualify for this role[1,7–9].

Compression-coated tablets have been prepared to target drug release to the colon environment. With pectin[10–12] or calcium pectinate[13] as the major component in the coat, the coated tablet relied on pectinolytic enzymes to cause drug delivery. Guar gum has also constituted the major component of a compression coat to achieve

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colon-specific drug delivery[14] after it was demonstrated that guar gum in the compression coat is susceptible to fermentation in pH 6.8 phosphate buffered saline containing 4% w/v rat cecal contents[15]. A fine particle version of ethylcellulose has been used as the sole component of a compression coat to cause time-delayed drug release, where the lag time was greatly influenced by the thickness of the coat[16]. Although microcrystalline cellulose (MCC) swells when hydrated, incorporation of MCC in the core tablet did not result in rapid rupture of the outer ethylcellulose coating[17]. The coated tablets in the present study were prepared with chitosan included in a fine particle ethylcellulose coat in anticipation that chitosan would encourage colon-specific drug delivery of the model drug, caffeine, contained in the core, as suggested in the literature[18].

Degradation of chitosan by enzymes found in rat cecal and colonic contents has been reported for chitosan alone[19] as well as when it is a component in a hydrogel[20] or in a film or a membrane[21]. Therefore, bacteria-dependent delivery best describes the mechanism expected to take place in the present study, although, a reduction in pH in the gastrointestinal tract upon arrival at the colon has been reported. In particular, radiotelemetry has been used to measure the gastrointestinal pH of healthy human subjects[22]. The highest pH levels of 7.5 ± 0.5 were found in the terminal ileum. On entry into the colon, the pH dropped to 6.4 ± 0.6. Short chain fatty acids (e.g. acetic, propionic, and butyric acid) that are products of microbial fermentation are believed to be responsible for this drop in pH[23]. The *in vitro* fermentation of pharmaceutical polysaccharides by fecal bacteria resulted in a reduction of pH due to the short chain fatty acid production[9]. Colonic pH has also been shown to be reduced in disease. The mean pH in a group of patients with untreated ulcerative colitis was 4.7 ± 0.7, whereas, in five patients receiving treatment it was 5.5 ± 0.4[24]. In the present case, this reduction in pH could encourage the dissolution of chitosan, a component of the coat, and result in delivery at the terminal ileum or proximal colon. Either the pH or enzymatic mechanism, or even a combination of the two, will result in desirable outcomes with the proposed drug delivery device.

It has been reported that there is an acid mammalian chitinase expressed in the human stomach[25] and present in gastric fluid[26] but not in the human small intestine or colon[27]. This chitinase is reported to degrade chitin-like substances as well as chitin found in crab shell[27]. It was noted that a patient from the Philippines had no detectable level of the chitinase and that other patients, such as those from Western cultures, might have an inactive polymorph of the wild gene[26]. The presence or absence of a chitinase in human gastric fluid is not an issue as an enteric coating applied to the device described herein is recommended because an aqueous medium with an acidic pH can dissolve the chitosan component of the coat and result in premature drug release.

Ethylcellulose has been used as the primary component of coatings to achieve sustained release over the course of the gastrointestinal tract. In those cases where the drug-release rate was too slow, a faster drug-release rate can be obtained by including in the coat a water-soluble material such as urea[28], or a water-soluble polymer such as hydroxypropylmethylcellulose[29], or a polymer that is degraded by the enzymatic reactions in the colon such as guar gum[8]. A polymer can hydrate and swell to provide a medium-filled, reduced tortuosity pathway through which dissolved drug can diffuse. By using polymers that are degraded by enzymatic reactions in the colon, hydration of the polymer should prove to be insufficient for drug release, but degradation of this polymer component of the coat when the device reaches the colon should allow ready release of the drug from the core.

Fine particle ethylcellulose and chitosan were used in the compression coat in an attempt to achieve colon-specific drug delivery. Ethylcellulose, being hydrophobic in nature, does not allow ready water penetration into the coat. After the tablet stays in the small intestine for a certain amount of time, the coat, and eventually, the core tablet swell. Some amount of drug might be released from the tablet due to swollen chitosan that provides a less tortuous pathway than does the initial coat. As the chitosan is still present in the coat, the drug release should not be appreciable until the device arrives at the colon. When the tablet reaches the colon, chitinase, chitosanase, or other enzyme(s) present in the colon can degrade the chitosan to allow disruption of the coat and the ready release of drug in the colon environment.

Materials and methods

Materials

Ethylcellulose (Ethocel FP Premium, 7 centipoise grade, 48–49.5% ethoxy content, from Dow Chemical Company, Midland, MI) was used as the diluent for the coat, whereas chitosan (DCV BioNutritionals, Wilmington, DE) of different grades and ~250 μm particle size provides the hydrophilic, enzyme-sensitive component of the coat. The core tablet consists of Avicel RC-591 (MCC with 11% sodium carboxymethylcellulose, FMC Corporation, Philadelphia, PA) as the diluent with a binder included, with caffeine (Pfizer, Groton, CT) as the model drug. Magnesium stearate was used as a lubricant both in the core tablet and in the coat.

Chitosan is a linear polysaccharide similar to cellulose, with a free or an acetylated amine group at C-2 of the repeating unit (Figure 1). The degree of deacetylation (DD) is the percentage of the amine groups that are not acetylated. The characteristics of the chitosan samples are presented in Table 1. Ethylcellulose is similar to cellulose with essentially only ethoxy groups instead of alcohol groups (Figure 1). Ethoxy groups impart hydrophobicity to the polymer, and, with a 48–49.5% ethoxy content, few alcohol groups remain.

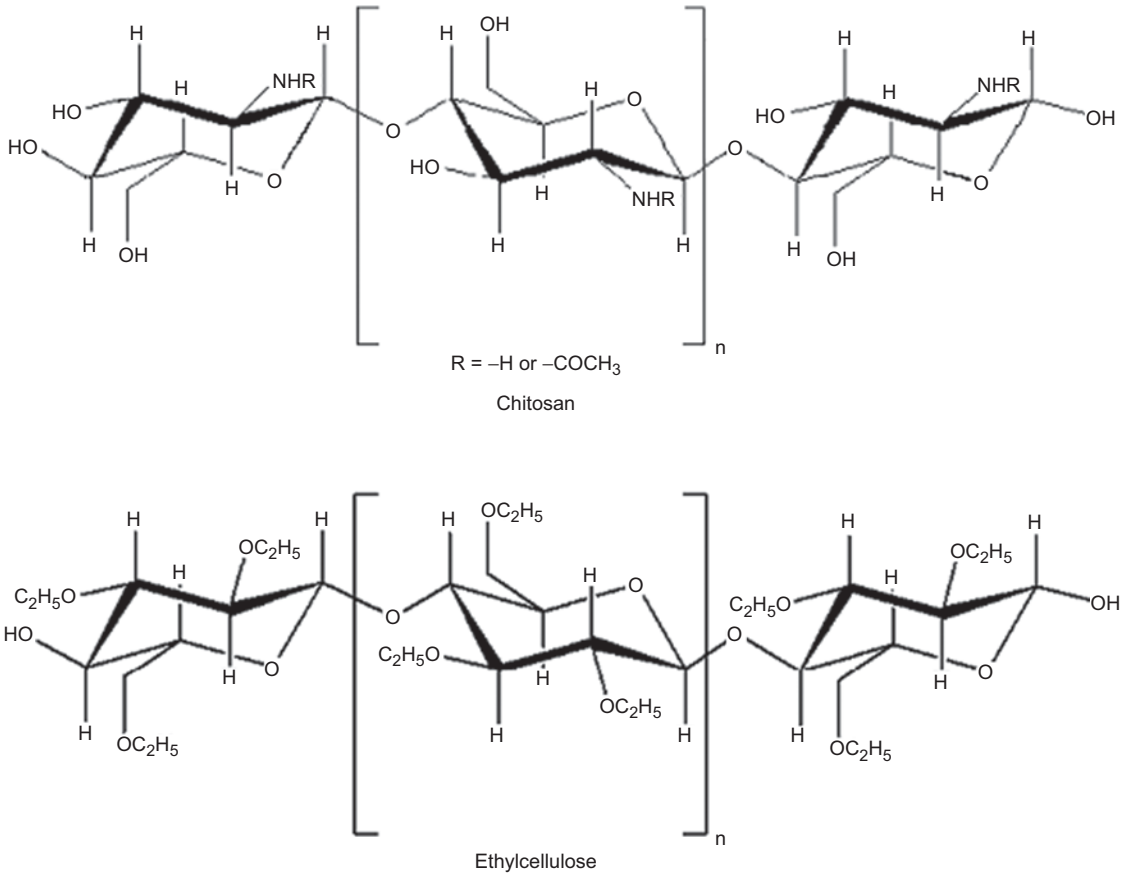

Figure 1. Chemical structures of chitosan and ethylcellulose.

Study design

Initially, four factors were to be varied to see their effect on release, namely, compression force, the type of chitosan, its particle size, and the percentage of chitosan in the coat. To study the type of chitosan, it was necessary to first characterize the different chitosan samples available for this study. The DD and molecular weight were determined using circular dichroism[30] and viscometric[31] literature methods, respectively. Three chitosan samples were identified for use in this study. Two have similar DDs but different molecular weights and the third has both a DD and a molecular weight different from those of the other two. The two with similar DDs will allow an examination of the molecular weight effect on different responses. The sample with the different DD will allow assessment of the DD effect after the molecular weight effect is accounted for. It was anticipated that the lower molecular weight and lower DD chitosan sample will provide the greater susceptibility to enzymatic degradation, as observed with chitosan solutions[19].

Tablet compression

Core tablets of 200 mg were prepared by 2000 psi compression of the powder blend consisting of 50% caffeine as the model drug, 48% Avicel as the diluent, and 2% magnesium stearate as the lubricant, using a 5/16" flat-faced circular punch and die set and a Korsch PH103 tablet press. The coating consisted of 20, 30, or 40% w/w chitosan, 2% w/w magnesium stearate, and fine particle ethylcellulose bringing it to 100% w/w. Core tablets were centered in a 7/16" flat-faced punch and die set on half of the powder that would become the coat. The remainder of the coat powder was placed on top, and the coat was compressed at 2000 psi using a Carver press to produce a coated tablet of 717 mg mass. The compression-coated tablets therefore have a lower mass ratio of the coated to uncoated tablets than those found in the literature[10] and were compressed at a lower pressure[16].

Tablet characterization

Hardness in kilograms was measured in triplicate using a Pfizer hardness tester, and friability using a Vanderkamp friabilator according to USP23 (1995)[32]. For the release studies, the release medium was initially simulated intestinal fluid (SIF) without enzymes at 37°C to seek evidence of sustained release. SIF is defined here as 0.05 M, pH 6.8 phosphate buffer. Release studies were conducted using six tablets from each batch in individual vessels of a USP Dissolution Apparatus 2 with 900 ml of release medium and a paddle stirring rate of 100 rpm. The amount of caffeine released in the simulated gastric fluid (SGF) without enzymes (0.01 N HCl) or SIF without enzymes was determined at 273 nm using a UV/Vis spectrophotometer.

Bacteria found in the rat cecum and colon have been shown to closely resemble those found in the

human colon in type and relative quantity[33]. Rat cecal and colonic contents were collected and the enzymes were isolated by a literature differential centrifugation technique[34]. At 0–4°C, the contents were weighed in a centrifuge tube, diluted with cold SIF at pH 6.8 to a final dilution of 33.3% w/v cecal and colonic material, and then centrifuged at 500*g* for 15 min to remove the debris. Supernatants were then centrifuged at 15,000*g* for 30 min in order to obtain a clear supernatant containing extracellular enzymes. The protein content of the isolated enzymes in that supernatant was quantified using the Bio-Rad assay. The protein content was adjusted to 1.2 mg/ml by further dilution with SIF before use in the enzyme catalysis study.

The tablet batches where tablets released less than 20% of the caffeine after 6 h in SIF without enzymes were identified. Tablets from these batches were tested for susceptibility of the coat to enzymatic degradation for as long as 24 h using a solution that included rat cecum and colon extracellular enzymes. Each of three tablets from a test batch was taken from the SIF after 6 h and placed in 60 ml of cecal and colonic enzyme solution in a 100 ml ground glass-stoppered Erlenmeyer flask. The flask was placed in a 37°C shaker bath at 100 rpm. The shaking speed was adjusted so that the tablet rocks but doesn't hit the inner wall of the flask. Samples of 500 µl were taken each hour and replaced with an equal volume of enzyme solution. Samples were analyzed for caffeine using an HPLC method.

Statistical analysis

Statistical analysis was conducted using Sigmaplot 10.0 (Systat Software, Inc., Chicago, IL). Analysis of Variance (ANOVA) was employed to determine significant differences between responses at the 95% confidence level.

Regression analysis was performed using the three parameter sigmoidal model (Equation 1, available with Sigmaplot software) that best fit the data for each release profile (R-Sq ≥ 0.999):

Table 1. Characteristics of the chitosan samples.

Chitosan type	Degree of deacetylation (%)	Molecular weight (x10^5)
CH1	73	8.2
CH2	75	13.4
CH3	92	4.7

$$\% = \frac{a}{1+e^{-\left(\frac{t-t_0}{b}\right)}} \quad (1)$$

where % is the percentage of drug released at time *t*, *t* is the time of release, and *a*, *b*, and t_0 are constants. The half-life for drug release ($t_{1/2}$) was calculated using Equation 2, which is obtained by rearranging Equation 1 and setting % = 50.

$$t_{1/2} = t_0 - b\ln(0.02a - 1) \quad (2)$$

Results

Compression force

When compression forces were applied, a decrease in the thickness of the tablets was not observed as the compression force was increased from 2000 to 3000 to 4000 psi, indicating that a further reduction in porosity was not possible beyond 2000 psi. As tablets prepared at 1500 psi were not strong enough to withstand the handling abuse experienced during further processing, such as the coating process, the compression force was fixed at 2000 psi. The first factor, compression force, was therefore eliminated from further consideration. The 2000 psi force was also applied during the coating of the tablets with each blend of ethylcellulose and chitosan. Representative tablets were sliced either horizontally or vertically to show that the core tablet could be centered in the coat (Figure 2).

Table 2 presents friability and hardness results for tablets prepared with different types and percentages of chitosan in the coat. ANOVA results (Table 3) revealed that use of different types and percentages of chitosan in the coat resulted in no statistically significant differences

Table 2. Friability (as percentage mass loss) and hardness (kg) results of tablets coated at the 40% level. Each cell contains friability and hardness values separated by a forward slash. Hardness data is presented as mean ± s.d.

	Chitosan level in the coat		
Chitosan type	20%	30%	40%
CH1	0.15/18.1 ± 0.3	0.14/18.2 ± 0.2	0.15/18.1 ± 0.1
CH2	0.13/18.2 ± 0.2	0.13/18.0 ± 0.2	0.13/17.8 ± 0.2
CH3	0.15/18.3 ± 0.3	0.17/17.9 ± 0.1	0.17/18.1 ± 0.1

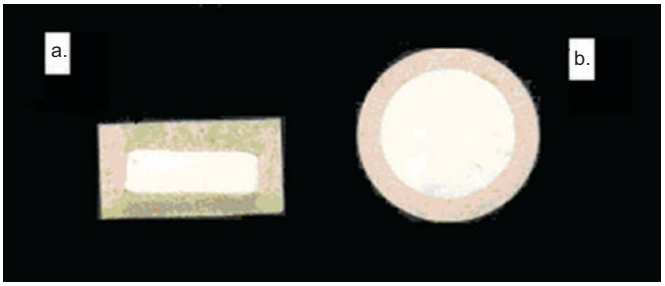

Figure 2. A digital photograph of two tablets cut vertically (A) and horizontally (B).

($P > 0.05$) among the hardness values. The friability values were so low and consistent that statistical analysis was unwarranted.

Release studies

Uncoated tablets released 100% of the drug in SIF in about 4 min. This rapid release is undesirable in colon-specific delivery and thus, the tablets were coated with a blend of ethylcellulose and chitosan to delay the release. The release profiles in SIF for tablets with 40% chitosan in the coat, but with different types of chitosan, are shown in Figure 3. The release profiles were essentially superimposed, showing that different types of chitosan in the coat did not influence the release of caffeine from the coated tablets. The release profiles are summarized by their half-lives for drug release, estimated as described in Methods, and these are presented in Table 4. In Table 3, ANOVA results reveal that chitosan type in the coat causes no statistical significant difference among $t_{1/2}$ values, as long as the chitosan level is kept the same. The effect of chitosan level in the coat on drug release was assessed, and the results for one type of chitosan (CH2) are shown in Figure 4. It is clear that lowering the chitosan level in the coat causes a statistically significant delay in drug release ($P = 0.0000$, see Table 2). This may be explained in part to an increase in the hydrophobic character of the coat as a result of an increased amount of ethylcellulose in the coat. Ethylcellulose drastically slows down entry of the release medium into the coat of the tablets, and this discourages hydration and swelling, which subsequently leads to a delay in drug release. Tablets coated with ethylcellulose alone released about 0.24% of the active after 60 h. The use of CH1 or CH3 in the coat gave results similar to those in Figure 4. Therefore, the presence, but not the type, of chitosan plays a profoundly important role in the modulation of drug release from the coated tablets.

Chitosan particle size effect on the drug release

To assess the effect of particle size on drug release, chitosan (CH2) with a particle size of 105–125 μm was isolated. Tablets with 40% chitosan (CH2 of 105–125 μm) included in the ethylcellulose coat were prepared. The release profiles revealed that the use of large particle size chitosan in the coat resulted in a more delayed drug release (Figure 5). This may be due to a more even distribution of the smaller chitosan particles in the coat, leading to relatively well hydrated tablets that ruptured at an earlier time. The half-lives for drug release are presented in Table 4. One-way ANOVA results for the effect of particle size indicated that a significant difference ($P = 0.0000$) existed for the effect of particle size on drug release (see Table 3). As the goal of this project was to achieve colon-specific delivery, the larger particle size chitosan was selected for further studies.

Drug release influenced by the release conditions

To assess the effect of gastric fluid on drug release, coated tablets containing 40% CH3 in the coat were first placed in SGF for 2 h, and then transferred to SIF. Caffeine release started at about 7 h, and essentially complete drug release was observed in about 13 h (Figure 6). However, the coated tablets containing the same type and level of chitosan in the coat and only exposed to SIF, started releasing at about 13.5 h and took until 19 h to release 100% of the drug (Figure 6). ANOVA results (Table 3) for $t_{1/2}$ values showed that a significant difference ($P = 0.0000$) exists between the half-lives associated with drug released

Table 3. Analysis of variance (ANOVA) results.

	Factor that led to $t_{1/2}$ value						
	Chitosan level in the coat (20, 30 or 40%)	Different chitosan types (CH1, CH2, and CH3) but same level in the Coat			Hardness	Chitosan particle size	SIF vs. SGF+SIF
ANOVA result		20%	30%	40%			
P value	0.0000	0.0990	0.2960	0.9930	0.1460	0.0000	0.0000
R-Sq	0.9977	0.5381	0.3333	0.0023	0.4423	0.9721	0.9957
R-Sq (adj)	0.9975	0.3841	0.1111	0.0000	0.1944	0.9652	0.9946

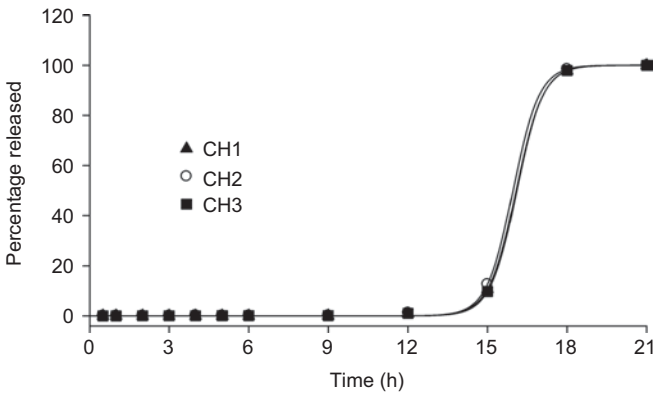

Figure 3. The negligible effect of different chitosan types in the coat on drug release.

under these two release conditions. At gastric pH, the chitosan contained in the coat will have its free amines protonated leading to subsequent dissolution of some chitosan from the coat. This may facilitate the hydration process, significantly reduce the tortuosity of the pathways in the coat, and thereby enhance the rate of drug release. As colon-specific delivery is the goal of the present study, an enteric coating will be necessary to ensure no drug release occurs in the stomach due to acidic pH or the presence of an endogenous gastric chitinase.

Table 4. $t_{1/2}$ for different chitosan types and levels in the coat, chitosan particle size, and release conditions (SIF and SGF + SIF) presented as mean ± standard deviation (n = 3).

		$t_{1/2}$ ± s.d. (h)
Chitosan Type and Levels in the Coat	CH1-40%	15.7 ± 0.6
	CH2-40%	15.7 ± 0.1
	CH3-40%	15.7 ± 0.3
	CH1-30%	23.6 ± 0.2
	CH2-30%	23.6 ± 0.1
	CH3-30%	23.8 ± 0.1
	CH1-20%	30.6 ± 0.3
	CH2-20%	31.1 ± 0.3
	CH3-20%	31.6 ± 0.3
Chitosan Particle Size (μm)	210-250	16.0 ± 0.1
	105-125	11.2 ± 0.1
Release Conditions	SIF	15.7 ± 0.3
	SGF+SIF	9.0 ± 0.2

Drug release studies in the presence of rat cecal and colonic enzymes

To assess the feasibility of these compression-coated tablets in colon-specific delivery, the tablets were placed in SIF for 6 h, and then transferred to the release medium containing rat cecal and colonic enzymes. Figure 7 gives some idea of the limited extent of swelling of a typical tablet following 6 h of exposure to SIF. It was anticipated that enzymes in the release medium would catalyze degradation of chitosan in the coat, causing a decrease in tortuosity and thereby reducing the delay in drug release. In these studies, chitosan sample CH2 was used because it is expected to be the least readily degraded by rat cecal and colonic enzymes[19]. In this way, if the enzymes could act on CH2, they would be expected to act more readily on coats involving the other two chitosan samples.

It can be seen from the results in Figure 8 that release of caffeine was facilitated by the presence of enzymes. At 15 h, the cumulative amount of caffeine released from

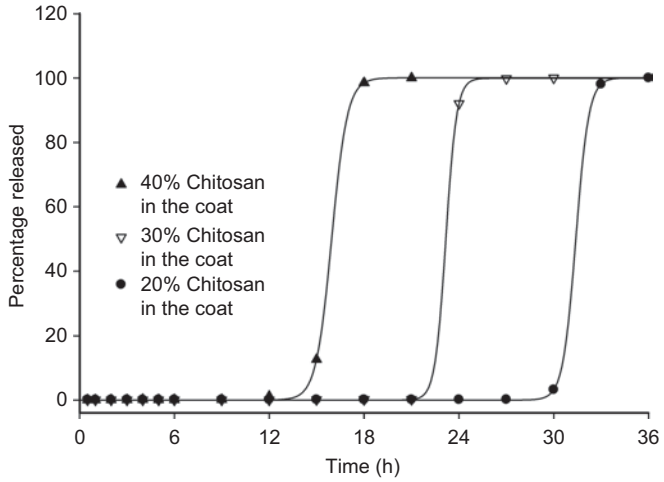

Figure 4. The effect of chitosan (CH2) level in the coat on the release profile.

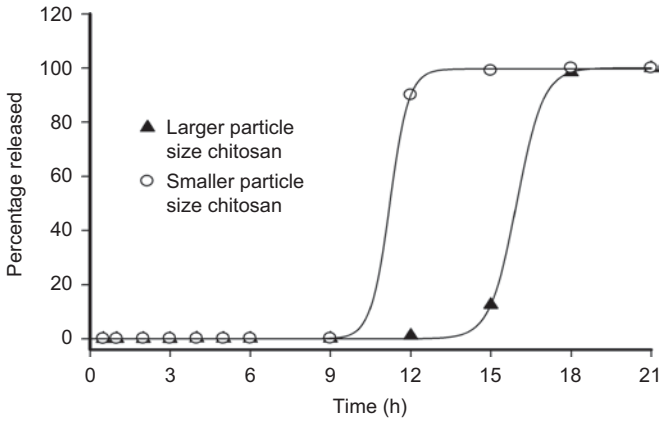

Figure 5. The effect of chitosan (CH2) particle size of chitosan in the coat on drug release.

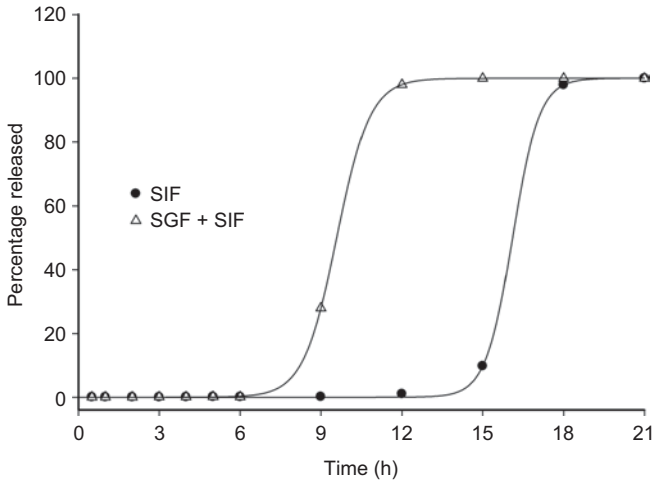

Figure 6. The influence of simulated gastric fluid (SGF) on drug release from coated tablets containing 40% chitosan (CH3) in the coat.

the coated tablets containing 40% chitosan level in the coat increased from 12.6% in the absence of enzymes to 70.7% in the presence of enzymes in the dissolution medium. Similarly, at 30 h, there was more drug released from coated tablets containing 20% chitosan level in the coat in the presence of enzymes, increasing from 3.2% to 19.0%. These results reveal that the role of enzymes in encouraging drug release diminishes as the chitosan level in the coat is decreased.

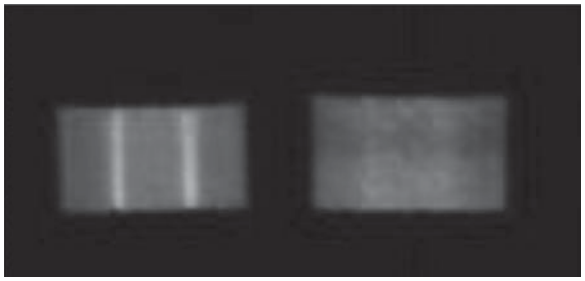

Figure 7. The compression-coated tablet before and after exposure for 6 h to SIF.

Discussion

Ethylcellulose, as the hydrophobic component in the compression coat of the tablets, should deter water entry into the coating. With discouragement of water entry, a lag time occurs and only after that will the whole coat and then the core tablet hydrate to finally allow drug dissolution and release. Due to the limited hydrophilic component in the coat, it was anticipated that less than 20% of the caffeine should be released under conditions simulating the small intestine environment in the 6 h allowed.

A higher molecular weight will deter the swelling of chitosan but a higher DD will encourage swelling. Chitosan with 75% DD and 13.4×10^5 MW would be the least susceptible to enzyme degradation based on its molecular weight and DD[19]. As ethylcellulose does not swell as much as chitosan does, chitosan particles can swell only to a limited extent, but could allow some dissolved drug to be released at a slow rate via a release medium–soaked pathway that has less tortuosity than the hydrated ethylcellulose offers. Upon reaching the large intestine, swollen chitosan particles can be degraded by reactions catalyzed by chitinases, chitosanases, or other enzyme(s) secreted by bacteria as their means to ferment dietary fiber found in the human diet. Degraded chitosan reduces the tortuosity even further and might even allow rapid drug release as there is no longer a tortuous pathway.

Contrary to what was anticipated, the MW and DD of the chitosan had no profound effect on the release profile. For this reason, a chitosan sample that provides better coat qualities or that facilitates manufacture of the product could be chosen. A lower chitosan content, however, can result in a profound further delay in the release of the drug. Exposure to gastric fluid can dramatically shorten the duration before drug release and an enteric coating might be necessary to insure colon-specific drug release. A finer chitosan particle size can result in a shorter duration before drug release, probably due to generating hydrated pathways for dissolved drug release that might be smaller but that are greater in number. A larger particle size would therefore be more appropriate for colon-specific drug delivery.

Enzymes obtained from the rat cecum and colon can shorten the duration before drug release occurs, but the magnitude of this effect depends on the chitosan content in the coat. The fit of a sigmoidal equation to the data confirms relatively rapid drug release upon exposure to the enzymes suggesting the feasibility of targeting drug to the ascending colon where such enzymes would be present in high number to accomplish fermentation. It is unlikely that sustained release across the colon could be accomplished with such a product.

The compression-coated tablets became hydrated with little swelling. Images in Figure 7 reveal only a slight increase in tablet height after hydration of the tablet for 6 h in SIF. Rupture of the coat (Figure 9), however, exposes the hydrated core to the release medium,

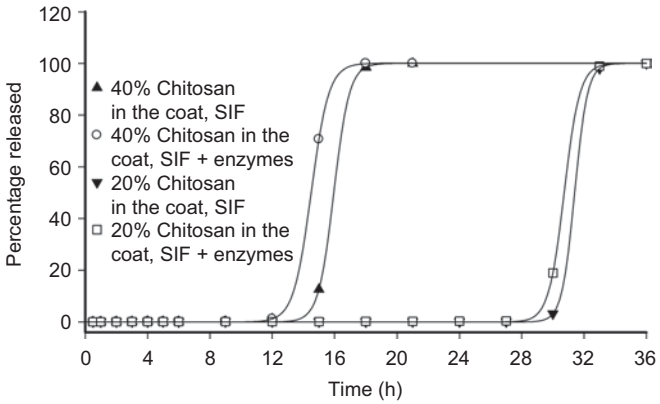

Figure 8. The influence of rat cecal and colonic enzymes on drug release from coated tablets containing 20% or 40% chitosan level in the coat.

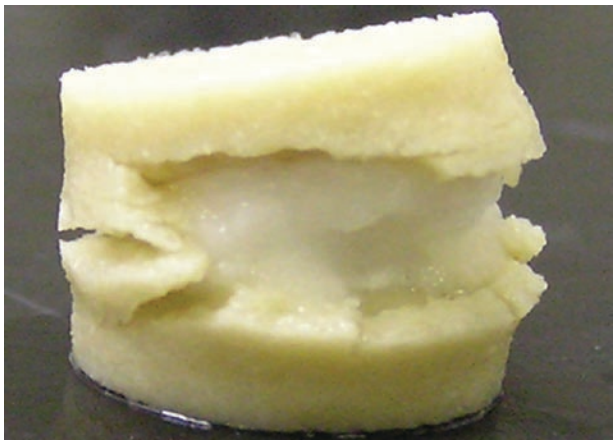

Figure 9. Ruptured coat of the type of tablet in Figure 7 with its core revealed to the release medium.

which results in rapid release of drug from the core. It has been reported that, after a lag time, the outer shell of compression-coated tablets with only fine particle (average 4.6 μm particle size) ethylcellulose in the coat broke into two halves and resulted in a rapid drug release[16]. In the present study, the rupture that occurred after a lag time, though dependent on the chitosan content in the coat and the release medium, could be due to the swelling of the core tablet. The coat has experienced the least compression forces at the equatorial region of the tablet (the dark area at the middle of the hydrated tablet in Figure 7) due to the presence of the core tablet. Hydrated and swollen chitosan would weaken the coat to the greatest extent in the equatorial region of the tablet because densification would be least at this region, leading to a faster influx of water and greater physical opportunities for chitosan to swell and degrade. The higher chitosan level in the coat would allow greater swelling and a weakened hydrated coat at the equatorial region that would result in facilitated rupture. The SGF would result in at least partial dissolution of chitosan found in this equatorial region and cecal and colonic enzymes would result in at least partial degradation of chitosan in this same region. Figure 9 provides evidence that rupture would then occur at the equatorial region of the tablet due to the swelling of the core material.

Conclusions

The chitosan in the coat of the ethylcellulose compression-coated tablet can provide a release profile appropriate for colon-specific drug delivery. The DD and the molecular weight of the chitosan do not substantially affect the release profile at a particular chitosan level in the coat. However, the chitosan level affects the time required for release of half the drug, estimated by a sigmoidal fit to the release data. A lower chitosan content can result in a profound further delay in the release of drug. As exposure to gastric fluid can dramatically shorten the duration before drug release begins, an enteric coat might be necessary to achieve colon-specific drug delivery.

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Declaration of interest

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