Pectin-chitosan complex: Preparation and application in colon-specific capsule

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Abstract: Pectin-chitosan complex was prepared as a candidate material for colon-specific capsule. First, the effects of beating on the properties of complex films were explored. Fourier transform infrared (FT-IR) spectroscopy was used to analyze the reaction mechanics, and an in vitro simulation experiment was performed to determine the degradation performance. Second, the capsule was prepared using pectin-chitosan complex as the main raw material; its targeting effect was evaluated and analyzed. Results indicated that the film became smooth and compact by beating. FT-IR data indicated that cross-linking occurred between the hydroxyl group of pectin and the amino group of chitosan to form a network structure. In vitro experiment showed that the pectin-chitosan complex film could not be degraded in the simulated gastric and intestinal fluids. However, pectin-chitosan complex could be degraded in the simulated colonic fluid, so it could be a potential candidate for colon-specific capsule. Because the complex has no ability for forming hard capsule, the carrageenan and starch were added to increase the flexibility, gelation, transparency and mechanical properties of the film. The preferred composition suitable for preparing the capsule was a mass ratio (2:1:1) of pectin-chitosan/carrageenan/starch mixture. The capsule showed excellent features in terms of shape, water content, and brittleness. The drug release rate reached 93.33% in colonic fluid for 1 h when bovine serum albumin was the model drug. Therefore, pectin-chitosan may be considered as a new material for colon- targeted capsule.

Keywords: pectin-chitosan complex, polyelectrolyte, carrageenan, starch, capsule, colon-specific drug delivery system
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1 Introduction

Pectin widely presents in the cell wall of green plants, particularly fruits, such as apples, lemons, citrus[1]. At present, pectin mostly acts as the thickening agent for food, which is with a low value added. Chitosan is a component derived from the waste of marine organisms, which enriching functional ingredients. However, the value added of pectin and chitosan can be improved significantly if using them as drug carriers.

Colon-specific drug delivery system presently attracts considerable attention[2-5] because of its advantages of increasing the bioavailability of drugs. The main application methods for colon-specific drugs are characterized as time-dependent, pressure-controlling,

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pH-sensitive and bacterially triggered[6-9]. However, time-dependent, pressure-controlling and pH-sensitive release systems are sometimes unreliable for individual differences[10-12]. With further investigation of the study area, bacterially triggered drugs have become a popular research topic in colon-specific drug delivery systems. The colon contains more than 400 species of microorganisms with a population of 10^{11} - 10^{12} CFU/mL. Microorganisms can produce a wide range of enzymes that degrade undigested carbohydrates and proteins in the gastrointestinal tract[13]. This significant variety and quantity of colonic microorganisms make bacterially triggered delivery systems more reliable than other methods. Thus, drugs are almost unaffected by differences in personality[14].

The development of novel materials for controlling drug release is the basis for developing colon-targeted drug. Azoic compounds and polysaccharides are the main materials used in a bacterially triggered delivery system[15-16]. Polysaccharides possess excellent properties, such as non-toxicity, biodegradability and biocompatibility, and have been employed in various biomedical systems. However, few problems still exist in the preparation of targeting capsules, such as the coating method, which is the main technology. Several methods use three-coatings, which is complex and costly. Therefore, a bacterially triggered colon-specific capsule with simple process is necessary.

Pectin is a polysaccharide, that is selectively degraded by the pectinolytic enzymes of the colonic microflora[17-19]. However, pectin cannot independently fabricate colon-specific carriers because of its water-solubility, hence, divalent cations, such as Ca^{2+}, have been added to cross-link pectin and increase its hydrophobicity[20]. Although drug release from pectin-Ca^{2+} is delayed, it is unable to perform colon-specific drug release. The drug is released in the intestinal fluid after being exposed in gastric fluid[14].

Ploymers have the characteristics of wide range of applications[21]. The performance and applicability depend on their physical and chemical properties. Under normal circumstances, pectin and chitosan react readily to produce polymer. The reaction between the polycations of chitosan and the polyanions of pectin leads to the formation of a polyelectrolyte complex[22], which can protect the drug from being released in the intestinal fluid and from being degraded in the colon. Various forms of drug carriers made from the pectin-chitosan polyelectrolyte complex are used for the controlled and colonic drug deliveries. These drug carriers include hydrogel, films, tablets, pellets and beads. Researchers approved the good performance of the aforementioned drug carriers[23-26]. However, the application of the pectin-chitosan polyelectrolyte complex to hard capsules involves a few discussions. Capsule formatin, degradation, and drug release at the right time are the most important elements to prepare hard capsule for colonic drug delivery.

This study aimed to prepare a pectin-chitosan complex with better surface and structure performance and to evaluate the degradation characteristics of the pectin-chitosan complex by in vitro test. This study also aimed to investigate the possibility of this complex as a new material for colon-specific capsules and to obtain optimal formulations of capsule production through a comparative study of degradation behavior and drug release.

2 Materials and methods

2.1 Materials

Pectin (extracted from citrus fruits with an esterification degree of approximately 24%) was purchased from Quzhou Pectin Co., Ltd. (Quzhou, China). Chitosan (with an average deacetylation degree of approximately 90%) was obtained from Shenbotai Biological Technology Co., Ltd. (Shenzhen, China). Carrageenan (with a 6:4 combination of K- and I-carrageenan) was supplied by Gangyang Flavour Chemistry Group. Starch (made from green banana) was provided by Foshan Jiaoye Bio-technology Co., Ltd. (Foshan, China). Gelatin (with an adfreezing force of 228) was provided by Baotou Dongbao Bio-technology Co., Ltd. (Baotou, China). Pepsin and pancreatin was supplied from Guangzhou Qiyun Bio-technology Co., Ltd (Guangzhou, China). Sprague-Dawley (SD) rats were obtained from South Medical University (Guangzhou, China). Bovine serum albumin (BSA) was purchased from Sigma-Aldrich Co. Ltd. (Shanghai, China). All

other reagents were of analytical grade. Deionized water was used in all the experiments.

2.2 Preparation of pectin-chitosan complex

Pectin powder was dissolved in deionized water to prepare pectin solution (5%, w/v). Chitosan powder was dissolved in deionized water containing 0.3% (v/v) acetic acid to prepare the chitosan solution (1%, w/v). Subsequently, 100 mL of chitosan solutions were added to 20, 40, 60, 80 and 100 mL of pectin solutions, beaten at 20 000 r/min by a beater (JYL-C010, Joyoung Co., Ltd, Zhejiang, China) or not beaten, and placed at room temperature for 48 h. Thus, different mass ratios (1:1, 1:2, 1:3, 1:4, and 1:5) of pectin-chitosan solution were obtained. Each complex was then centrifuged to remove the supernatant and washed with deionized water once.

2.3 Preparation of pectin-chitosan film

Glycerol (2%) was placed in the obtained pectin-chitosan complex, and mixed. The mixture was applied on a acrylic glass plate and dried at 50ºC in a vacuum drying chamber (DZF-6020, Shanghai Yiheng Scientific Instrument Co., Ltd, Shanghai, China) for 12 h. Then a light yellow film formed on the glass plate.

2.4 Fourier transform infrared (FT-IR) spectrometer analysis

FT-IR spectra of pectin, chitosan and pectin-chitosan films were obtained with a spectrometer (VERTEX 70, Bruker Corporation, Germany). The spectra were scanned over the wavenumber range of 4 000-400 cm^{-1} at ambient temperature.

2.5 Preparation of pectin-chitosan/carrageenan/starch mixture film

Proper proportion of starch was initially dissolved in deionized water with stirring and heated between 70ºC and 80ºC for 5-8 min to reach gelatinization. Carrageenan powder was then added to the solution with strong stirring. After the powder was totally dissolved, the pectin-chitosan complex produced was slowly added to the solution and stirred continuously to ensure uniform distribution. Deionized water was then replenished in moderation to reach the total concentration of 6%-8% (w/v). A total of 2% (v/v) glycerol and 1% (w/v) poly alcohol were added as the plasticizer and hydrophobing agent, respectively. Then the solution was stirred for 1 h at (80 ± 5)ºC and deaerated with a vacuum force. Table 1 lists the composition of the pectin-chitosan/ carrageenan/starch mixed solution. (The weight of pectin-chitosan was the dry weight after washing and drying)

Table 1 The composition of the pectin-chitosan/carrageenan/ starch mixed solution

Sample number	Pectin-chitosan: carrageenan:starch	Pectin-chitosan/g	Carra-geenan/g	Starch /g	Glycerol /g	Poly alcohol/g
1	1:1:1	2.00	2.00	2.00	2.00	1.00
2	2:1:1	4.00	2.00	2.00	2.67	1.33
3	3:1:1	6.00	2.00	2.00	3.33	1.67

The solution was mixed homogeneously, cast on an acrylic glass plate and dried at 50ºC in a vacuum drying chamber for 12 h. A white and transparent film formed on the glass plate.

The gelatin film, which was contrasted with pectin-chitosan/carrageenan/starch mixed film, was prepared using the aforementioned method**.**

2.6 Thickness measurement

Thickness was measured using a micrometer (PS811, Paster Corp., Zhejiang, China) at the four corners and the middle positions of each specimen. The measurement results were accurate to 0.01 mm.

2.7 Tensile strength (TS) and elongation (E)

Tensile strength (TS) is the maximum stress that the material can withstand while being stretched or pulled before failing or breaking. The elongation (E) at the breaking point is the change percentage of the original length of a material. Both of the films were analyzed on a texture analyzer (EZ Test, Shimadzu Corp., Japan) based on the ASTM Standard Method D882-12 (ASTM, 2012). Prior to measurement, each sample was cut into 10 cm×2.5 cm and conditioned for 45 h at 25ºC and 50% relative humidity in a constant temperature and humidity chamber (Model QA-HPZ-30, Dongguan Jiecheng Equipment Co., Ltd., Guangdong, China). The initial grip separation and cross-head speed were set at 4 cm and 3 mm/s, respectively. Five replications of the measurements were performed.

2.8 In vitro degradation behavior

The degradation test aimed to determine whether the chitosan-pectin complex is a potential material for the colon-specific drug delivery system. This test was conducted based on the Chinese Pharmacopoeia (2010) method.

Simulated gastric fluid (SGF): Pepsin (1 g) was dispersed in 100 mL of 0.01 mol HCl solution (pH 1.5).

Simulated intestinal fluid (SIF): Pancreatin (1 g) was dispersed in 100 mL of 0.05 mol phosphate buffered solution (pH 6.8).

Simulated colonic fluid (SCF): The cecum of the rats was exteriorized, and the cecum contents (30 g) were dispersed in 100 mL of 0.05 mol phosphate buffered solution (pH 7.8). This step was conducted under nitrogen conditions to maintain an anaerobic environment[27].

The film samples were cut into 20 mm×20 mm, weighed (W_0), and then were degraded by simulated fluid. First, the samples were immersed in SGF for 2 h (0 h to 2 h), removed, and washed with distilled water. Second, the samples were immersed in SIF for 3 h (2 h to 5 h), removed, and washed with distilled water. Finally, the samples were immersed in the simulated colonic fluid for 7 h (5 h to 12 h). In the entire process, the chitosan-pectin complex film samples were maintained at 37ºC and stirred at 100 r/min in a shaker (XMTD-204, Changzhou Putian Apparatus Manufacture Co., Ltd., Jiangsu, China). For every half hour, the samples were removed, cleaned with distilled water, and dried at 50ºC in a vacuum drying chamber for 12 h. The mass of each sample was accurately weighed (W_t) at the t^{th} hour. The degradation rate, D_{ts} at t (h) was calculated using Equation (1):

$$D_{ts} = \frac{(W_0 - W_t)}{W_0} \times 100 \quad (1)$$

where, W_t is the weight of the sample at t hour and W_0 is the initial weight of the sample.

2.9 Preparation of hard capsule with pectin-chitosan/carrageenan/starch mixture

The capsules were prepared by dipping a stainless steel rod into the pectin-chitosan/carrageenan/starch mixed solution and drying at 50ºC in a vacuum drying chamber for 12 h. Finally, the formed capsules were carefully demolded (1# mould, Shaoxing Tuopu Machinery Co., Ltd, Zhejiang, China), cut, capped and sealed.

2.10 Water content measurement

The water content of the capsule was determined based on the Chinese Pharmacopoeia (2010) method. Capsule samples (1 g) were accurately weighted (W_0). The cap and body of the capsules were separated and dried at 105ºC in a drying chamber for 6 h. The capsules were then accurately reweighed (W_d), and the water content (C) was calculated based on Equation (2):

$$C(\%) = \frac{(W_0 - W_d)}{W_0} \times 100 \quad (2)$$

where, W_d is the weight of capsule after drying and W_0 is the initial weight of the capsule.

2.11 Brittleness measurement

The brittleness of the capsule was determined based on the Chinese Pharmacopoeia (2010) method. Fifty capsules were placed in a desiccator filled with magnesium nitrate-saturated solution for 24 h at (25±1)ºC , and then placed in an upright glass tube on a wooden board. A weight of 20 g with a diameter of 22 mm was dropped from the mouth of the glass tube. The breaking of the capsule was observed.

2.12 In vitro release profile

To determine the release behavior of the capsule, 25 mg BSA was used as the model drug. After filling with BSA, the capsules were sealed and placed in a vessel containing SGF for 2 h, and then removed to SIF for 3 h. Subsequently, the capsules were removed and immersed in SCF for 9 h. In the entire process, the simulated fluid was placed in a water bath at 37ºC and shaken at 100 r/min. The release content of BSA was determined every half an hour. At a predetermined time, 5 mL of simulated fluid was collected as sample for measurement and a fresh simulated fluid with equal volume was added.

An ultraviolet spectrophotometer (UV-5100, Shimadzu Corp., Japan) was used to measure the release content of BSA. BSA solution (1 mg/mL) was prepared and diluted gradually to 0.1 mg/mL as the standard solution. The absorbance was determined by ultraviolet spectrophotometer at 280 mm, and the standard curve was drawn. The BAS content of the sample at time t obtained based on the corresponding absorbance. SCF was selected as a blank solution in the test. The BSA release rate (R) was calculated based on Equation (3):

$$R(\%) = \frac{R_t}{M_i} \times 100 \quad (3)$$

where, R_t is the cumulative amount of BSA released at t hour and M_i is the initial amount of BSA (25 mg).

2.13 Scanning electron microscope (SEM) analysis

After being degraded by SGF, SIF, and SCF, the capsule was dried using the vacuum freeze-drying method (FD-1PF, Beijing Detianyou Science and Technology Development Co., Ltd. China) and observed under an SEM. The surface morphology of the film was determined by environmental SEM (XL-30 SESM, Royal Dutch Philips Electronics Ltd., Dutch). The films were fixed on the specimen stage by using a double sided adhesive tape and then sprayed with a layer of platinum, which allowed surface visualization. The accelerating voltage used in this process was 20 kV. The micrographs were magnified 10 000 times.

2.14 Statistical analysis

Results are expressed as the mean±standard deviation (SD) and treated by one-way analysis of variance (ANOVA) to assess the significance of the differences between the data. p-values <0.05 were considered statistically significant.

3 Results and discussion

3.1 Preparation of pectin-chitosan complex

When the chitosan and pectin were mixed, cross-linking reaction occurred and polyelectrolytes were produced. The rationale for the formation of the polyanion-polycation (polyelectrolyte) complexes was previously described[28]. The cause is the formation of electrostatic attraction between the cationic amino groups of chitosan and the anionic carboxyl groups of the pectin[29-31].

The characteristics of the complex are different with the change of the reaction conditions based on the documents[32-34]. The concentration of acetic acid solution, the proportion of pectin and chitosan, and stirring are the main parameters in the preparation of the pectin-chitosan complex.

In the aforementioned process, 0.3% was selected as the concentration of acetic acid solution because of two important reasons. First, acid with low concentration can reduce the wash times in the following steps. Neutral complex can be achieved and only needs to be washed once. Second, if the acid concentration is lower than 0.3%, then the particles of the produced complex are large, and the complex could not exhibit fine consistency and moderate viscosity.

The production percentage of the complex was the indicator to measure the proportion of added chitosan and pectin in the reaction. The production percentage (P) was calculated using Equation (4):

$$P(\%) = \frac{W_{PC}}{W_P + W_C} \times 100 \quad (4)$$

where, W_{PC} is the weight of complex after washing and drying to constant weight; W_P is the dry weight of pectin before dissolving; and W_C is the dry weight of chitosan before dissolving.

Table 2 lists the composition of the pectin-chitosan complex sample to investigate their addition.

Table 2 The composition of pectin-chitosan complex sample

Chitosan		Pectin		Pectin-chitosan complex	Productivity /%
Volume of solution/mL	Dry weight/g	Volume of solution/mL	Dry weight/g	Dry weight /g	
100	1	20	1	1.34±0.17	67.00
100	1	40	2	2.29±0.33	76.33
100	1	60	3	3.37±0.28	84.25
100	1	80	4	3.53±0.44	70.60
100	1	100	5	3.69±0.58	61.50

Table 2 shows a clear phenomenon: the best mass ratio of chitosan to pectin was 1:3. In this case, the production percentage was the highest. We also observed that the weight of the complex was almost unchanged with increasing pectin weight. This result is attributed to excess pectin, which was unpolymerized and removed by centrifugation and washing. If the amount of pectin is insufficient, then the chitosan cannot react completely and will be removed.

Beating is the highly important step in the preparation of the chitosan-pectin complex. The smooth and delicate emulsion can be obtained by beating and can be mixed evenly with other components being added in the preparation of the capsule. Furthermore, the film obtained after casting and drying was dense and free from bubbles. Because the complex exists in the form of irregular particles, the film shrinks when dried and the film surface becomes uneven and splits in the long chain of polymer overlays[27]. Through homogenization treatment, high-speed shearing action makes the long chain polymers become shorter chains, reduces accumulation, and reduces the gap between them.

Moreover, the contraction splitting of the film is reduced; thus, the film becomes smooth and compact. The product obtained in this way is more suitable for the fabrication of capsules. Figure 1 presents the morphology of the complex samples. Figure 2 shows the morphology of film samples.

a. Preparation without beating b. Preparation with beating

Figure 1 Morphology of pectin-chitosan complex

a. Preparation without beating b. Preparation with beating

Figure 2 Morphology of pectin-chitosan film

3.2 FTIR Analysis

In the FT-IR spectra of chitosan (Figure 3), the stretching vibration peak of C-H bond in chitosan was at 2 879 cm^{-1}; the stretching vibration peak of acylated 2-amino-glucamine N-H in chitosan was at 1 657 cm^{-1}; and the bending vibration peak of N-H was at 1 599 cm^{-1}. In the FT-IR spectra, the stretching vibration peak of carboxylic acid -OH was at 3 415 cm^{-1}, and the stretching vibration peak of carboxylic acid C=O was at 1 744 cm^{-1}. However, in the FT-IR spectra of the pectin-chitosan complex film, the stretching vibration peak of acylated 2-amino-glucamine N-H in chitosan at 1 657 cm^{-1} disappeared; the bending vibration peak of N- H at 1 599 cm^{-1} gradually decreased and moved to 1 591 cm^{-1}; and the -OH peak at 3 415 cm^{-1} and C=O peak at 1 744 cm^{-1} gradually decreased. The $-NH^{+3}$ symmetric bending vibration absorption peak appeared at 1 326 cm^{-1}, and the $-COO^{-}$ symmetric stretching vibration absorption peak appeared at 1 410 cm^{-1}, indicating that pectin and chitosan have polymerization reaction. This result is consistent with literature and reports[29-31].

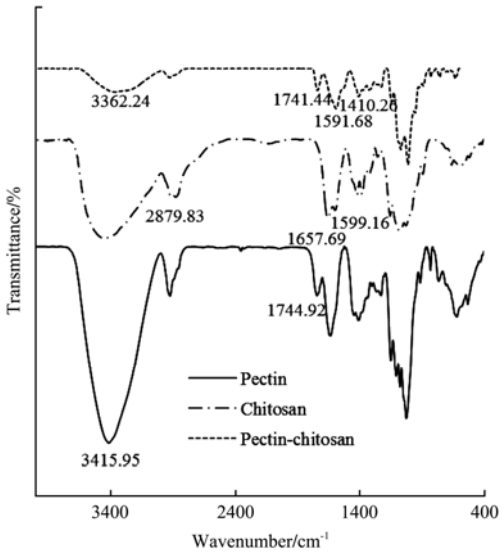


Figure 3 FT-IR spectra of pectin, chitosan and pectin-chitosan complex film

3.3 Mechanical properties of films

(0.110±0.05) mm of the pectin-chitosan complex, pectin-chitosan/carrageenan/starch mixture, and gelatin films were obtained based on the aforementioned method. TS and E are the parameters representing the mechanical properties of the film materials. Table 3 presents the mechanical properties of the pectin-chitosan complex, pectin-chitosan/carrageenan/starch mixture and gelatin films.

Table 3 Mechanical properties of films

Material type	TS/MPa	Elongation/%
Pectin-chitosan	10.32±0.6[b]	32.86±4.8[c]
Pectin-chitosan/carrageenan/starch	18.41±2.3[a]	58.75±12.4[b]
Gelatin	19.24±1.5[a]	107.99±8.2[a]

Note: [A] a, b indicate significant differences (p<0.05) within columns TS (MPa). [B] a-c indicate significant differences (p<0.05) within columns elongation (%).

The results indicated that the TS and E of the pectin-chitosan film were significantly different from gelatin. When the appropriate amount of carrageenan and starch were added, the TS of the mixture were higher and not significantly different from that of the gelatin. Thus, the composite material of pectin-chitosan/ carrageenan/starch may likely be used to prepare hard capsules.

3.4 Degradation behavior of films in vitro

The degradation behavior of the pectin-chitosan complex film and pectin-chitosan/carrageenan/starch mixture film (Samples 1 to 3 were prepared based on the formulation in Table 1) was carried out by immersing them in SGF, SIF and SCF. Figure 4 shows the plotted

degradation percentage of both the pectin-chitosan complex film and pectin-chitosan/carrageenan/starch mixture film. In addition, it shows that the pectin-chitosan complex film did not degrade in SGF and SIF within the first 5 h; however, it was degraded in the SCF from the seventh hour. Pectin–chitosan ploymer film degradation was not observed from the sixth to seventh hour because the enzymes and microorganisms in SCF took some time to take effect. This characteristic indicates that this film can be used as a new material for the colon-specific drug delivery system. However, it cannot be used exclusively because of the nondegradation in the first hour when dipped in the SCF, which delays the release time of the drug. Carrageenan and starch were added to enhance the degradation. Moreover, carrageenan can increase the flexibility and gelation, and starch can increase the flexibility and transparency.

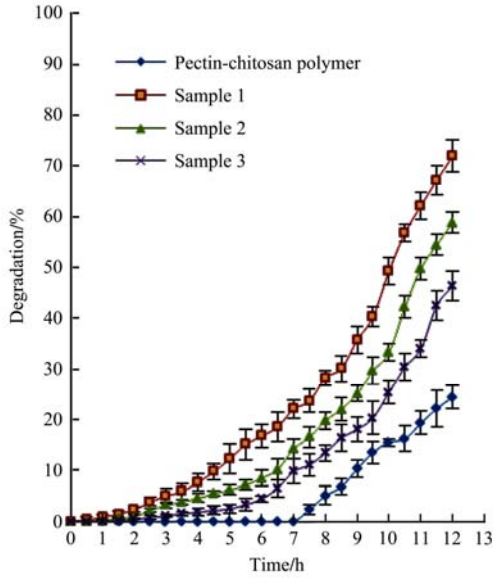


Figure 4 Degradation behavior of films in vitro

In the aforementioned process, the mass ratios of pectin-chitosan, carrageenan and starch (1:1:1, 2:1:1, 3:1:1) were different. This reveals that the degradation of the pectin-chitosan/carrageenan/starch mixture film depends on the pectin-chitosan complex; the former reduced with the increase of the latter. Carrageenan and starch could be degraded by pepsin and pancreatin. The degradation rate of carrageenan and starch reduced with the increasing of the pectin-chitosan complex because the latter can tie the former to prevent rapid dissolution.

The pectin-chitosan complex film and pectin-chitosan/ carrageenan/starch mixture film (sample 1, 2 and 3) were immersed in SGF, SIF and SCF in sequence. The mass ratios of pectin-chitosan, carrageenan and starch were 1:1:1 (sample 1), 2:1:1 (sample 2), and 3:1:1 (sample 3), respectively.

3.5 Hard capsules and the characteristics

Figure 5 presents the hard capsules (capsule 1, 2 and 3 were prepared based on the formulation in Table 1). The three samples were all highly similar to one another based on their external characteristics. The body length, cap length, thickness of the external diameter of the body and the external diameter of the cap were (16.60±0.5) mm, (9.80±0.5) mm, (6.63 ± 0.5) mm and (6.91 ± 0.5) mm, respectively. The water content was (8.8±0.8)%, and the brittleness was 0.

Figure 5 Hard capsules: capsule 1, 2 and 3

3.6 In vitro drug release from the capsule

BSA was utilized as the model drug to examine the release profile. Figure 6 shows that in SGF, BSA was not released from the three sample capsules. Although the external layer of the capsule was degraded, the result was only a minimal mass loss. Thus, BSA could not penetrate the capsule and be released. In SIF, BSA was released from the capsules at a low rate. Among the capsule samples, capsule 1 exhibited the highest release rate at 53.12%. The release rate of capsule 2 and 3 were 7.82% and 2.47% respectively, which were attributed to the degradation of the carrageenan and starch by SIF. Several tiny holes, through which the water permeated into the capsules, were formed. Thus, BSA was dissolved by water and released. In SCF, BSA was released from the capsules and increased significantly. The release rate at 95.08% of capsule 1 at 5.5 h was the highest. Capsule 2 had a release rate of 93.33% at 6 h, and capsule 3 had a release rate of 90.93% at 7 h. These release rates are due the mixed materials of the capsule, which were degraded by the enzymes and microbials in the colonic fluid; several small cracks formed beside the

holes[35]. Thereafter, the release rate decreased because the released BSA was also degraded by the enzyme and microorganisms. The results indicated that the release of BSA depended on the content of the pectin-chitosan complex. Extremely excessive content resulted in the low release rate and long release time, whereas too little content resulted in the high release rate in the intestinal fluid, which was not suitable for colon targeting. Therefore, capsule 2 exhibited a good behavior at the colon-specific aspect and could be considered as a new material for colon- targeted capsule. Figures 7 and 8 present the morphology of capsule 2, as seen through the naked eye and SEM, respectively, which was dipped in SGF, SIF, and SCF.

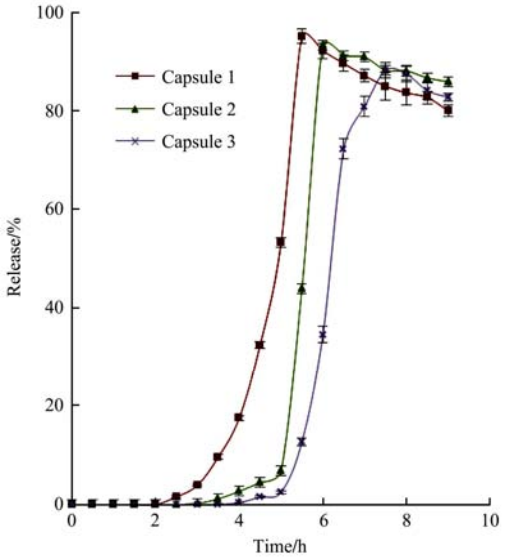
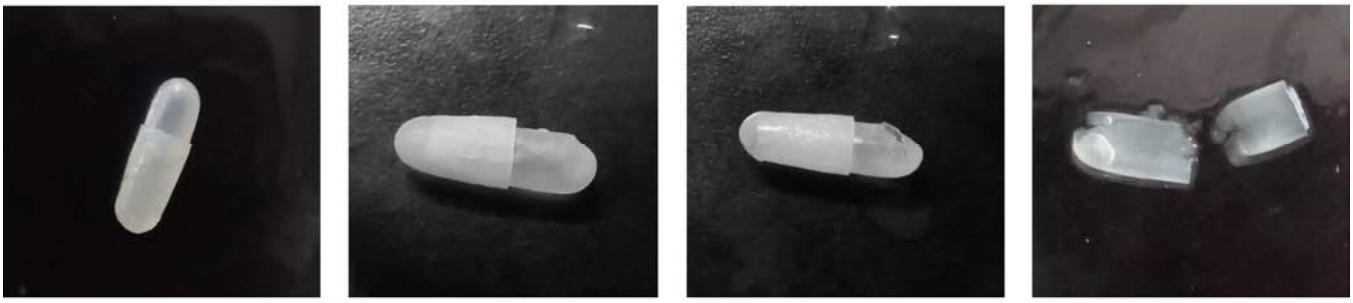


Figure 6 Release of BAS from the capsule in vitro



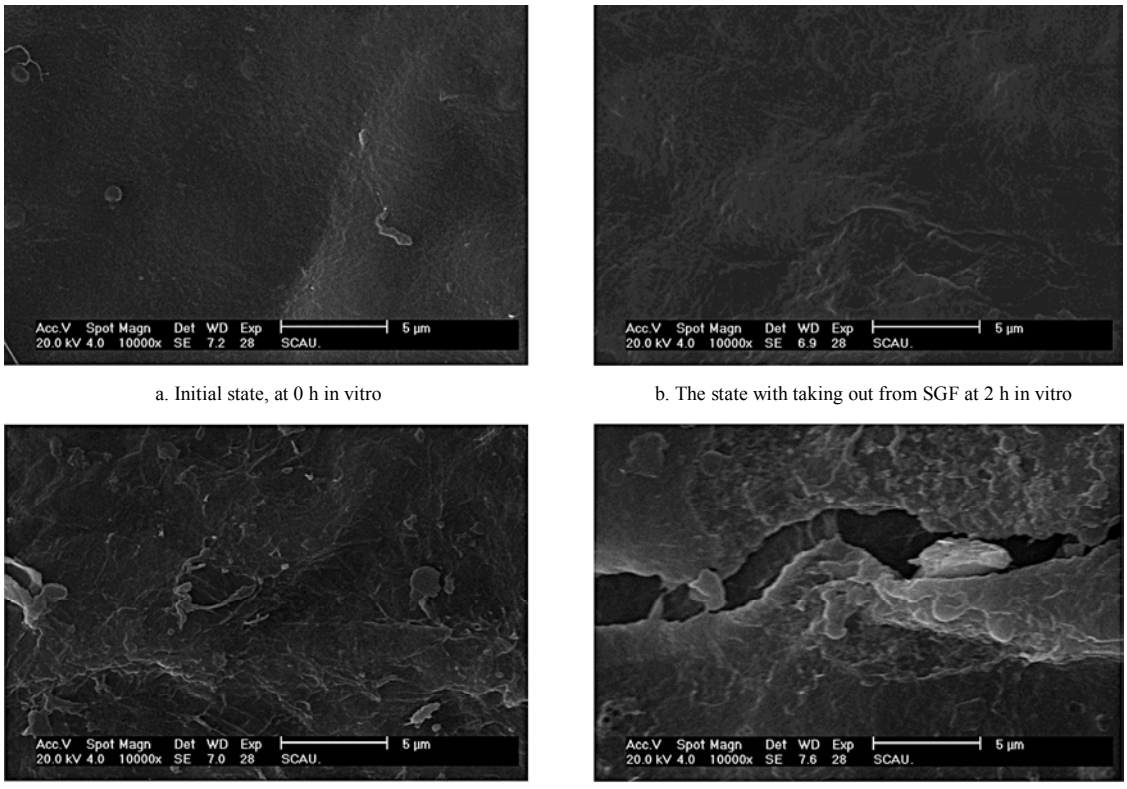
a. The state with taking out from SGF at 2 h in vitro

b. The state with taking out from SIF at 5 h in vitro

c. The state with taking out from SCF) at 6 h in vitro

d. The state with taking out from SCF at 7 h in vitro

Figure 7 Degradation morphology of capsule 2 with the naked eye



a. Initial state, at 0 h in vitro

b. The state with taking out from SGF at 2 h in vitro

c. The state with taking out from SIF at 5 h in vitro

d. The state with taking out from SCF at 6 h in vitro

Figure 8 Degradation morphology of capsule 2 in vitro with SME (×10000)

The capsules were immersed in SGF for 1 h, removed and immersed in SIF for 3 h, and then removed and immersed in SCF for 5 h. The mass ratios of pectin-chitosan, carrageenan, and starch were 1:1:1 (capsule 1), 2:1:1 (capsule 2), and 3:1:1 (capsule 3), respectively.

4 Conclusions

A pectin-chitosan complex was prepared and degraded. The important factors in the preparation process are as follows: 0.3% (v/v) acetic acid, 3:1 mass ratio of pectin and chitosan, and beating at 20 000 r/min. These factors yielded a homogeneous pectin–chitosan film. The pectin–chitosan film did not degrade in SGF and SIF but degraded in SCF as observed in in vitro experiment. Thus, the pectin-chitosan complex could be a potential candidate for colon-specific capsule. However, this polymer gradually degraded in the colonic fluid which was unfavourable for the timely drug release from the capsule. Adding carrageenan and starch increased the flexibility, gelation, transparency and mechanical properties of the films. The mass ratio (2:1:1) of the pectin-chitosan/carrageenan/starch mixture was suitable for the drug release, which exhibited a BSA release rate of 93.33% at 6 h. The capsule produced from the mixture possessed excellent properties, and the water content (8.8% ± 0.8%) was lower than that of gelatin capsule (13%-17%). Therefore, pectin-chitosan may be considered as a new material for colon-targeted capsule.

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