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Formulation and In Vitro Evaluation of Gastroretentive Drug Delivery System of Antacids Using Alginate-Chitosan Films

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Abstract: The conventional antacids dosage forms have a short duration of action which is about 2-3 hours due to gastric emptying process. A gastroretentive dosage form of antacid is needed since the healing of gastric ulcers occurs when gastric pH is kept above 3-4 during 24 hours. The aim of this study was to formulate a gastroretentive films of antacids using Alginate-Chitosan (Alg-Ch) based which was able to neutralize gastric acid for longer time. Drugs model used were $Al(OH)_3$ and $Mg(OH)_2$. The gastroretentive films of antacid were prepared using Alg, Ch and glycerin in various ratio. The homogenous mixture of Alg mucillage, Ch mucillage, and glycerin and antacids was flattened on an object glass (2 cm x 5 cm) and allowed to dry at room temperature. Unfolding and integrity behaviors of the films were evaluated using the USP dissolution tester. Neutralization profile was determined by simulating gastric acid secretion. The simulation was carried out by dropping 10 ml/h of 0.1 N HCl solution to 30 ml of 0.1 N HCl solution containing Alg-Ch with antacid. Mucoadhesive property was tested using rats stomach by DuNoy tensiometer, and swelling properties in 0.1 N HCl solution was determined based on the increase of films size. The results showed that film containing 1.5 g of 4% Alg mucillage, 2 g of 4% Ch mucillage, 4 drops of glycerin, and 300 mg $Al(OH)_3$ had good characteristics as a gastroretentive drug delivery system. The unfolding time of the film was 8 minutes, the film was intact for about 7 hours. On simulating gastric acid secretion, the maintenance pH was found around 3.0-3.5 for about 6 hours. The mucoadhesive strength of the film was 107.47 ± 7.38 dyne/cm^2 and the swelling was 111.30%. However, Alg-Ch films containing $Mg(OH)_2$ could not form good films except using high amount of Alg but these films could not meet the requirement as gastroretentive films. The results indicate that Alg-Ch film containing $Al(OH)_3$ is potential to use as a gastroretentive drug delivery system.
Keywords: Alg-Ch films; antacids; gastroretentive; mucoadhesive; swelling.

Introduction

The major disease of the stomach and duodenum are gastritis, gastric ulcer, duodenitis, and duodenal ulcer, all of which are in some way related to gastritis with injury that is mediated by acid.[1] The normal pH of the stomach is 1.2 to 1.8. During most of the day, the food stimulates the acid secretion also neutralizes it, keeping the pH between 3 and 5. However, when the stomach is empty, approximately 2 to 3 hr after eating, then the pH again drop, and ulcer patients tend to suffer pain that is relieved by consuming antacids. In general, pain only occurs when the pH is below 2.[1-3]

Antacids are used widely for the relief of heartburn and dyspepsia, as well as a large variety of nonspecific gastrointestinal symptoms. The primary role of antacids in the management of peptic acid disorders

is to relief pain. Another action of antacids is to prevent the conversion of gastric pepsinogen to pepsin, the active form. This is a proteolytic enzyme thought to mediate tissue injury in ulcer disease.[3] Conventional dosage form of antacids have a short duration due to the short residence time. Conventional dosage form of antacids are cleared from the empty stomach in 30 minutes due to the regulary gastric emptying. If administered while food is in the stomach, the buffering action will last for 2 hours. An additional dose 3 hours after meals will extend the buffering time by 1 hour.[3-4] The ideal antacid should be rapid in onset and provide a continuous buffering action. The duration of buffering action is determined largely by when the antacid is administered. Healing of the peptic acid diseases occurs when the mean 24-h pH is kept above 3 to 4. The pH can be increased by either neutralizing acid (antacids) or inhibiting gastric secretion (H2-reseptor antagonists or proton pump inhibitors).[3]

Gastroretentive drug delivery is an approach to prolong gastric residence time, there by targeting site-specific drug release in the upper gastrointestinal tract for local or systemic effects. Gastroretentive dosage forms can remain in the gastric region for long periods and hence significantly prolong the gastric retention time of drugs. Prolonged gastric retention improves bioavailability, increases the duration of drug release, reduces drug waste, and could be advantageous for local action in the upper part of the small intestine e.g. treatment of peptic ulcer.[5]

Several previous studies on gastroretentive systems including: Mucoadhesive and floating Ch-coated Alg beads for the controlled gastric release of amoxicillin, showed the prolonging the release of drug for over 6 hours in stomach.[6] Antacid compositions of nonphospholipid lipid vesicles, with a particulate base with prolonged gastric residence time has been invented and patented.[7] Extended duration of antacid product also has been patented.[8] This invention includes two-phase solid oral pharmaceutical compositions: e.g. in the form of powder, tablets (effervescent, chewable), coated tablets or capsules, with prolonged antacid activity. Preparation and Evaluation of novel expandable drug delivery system using hydroxyl propyl methylcellulose and Eudragit as polymers and dibutyl phthalate as a plasticizer showed that the gastroretentive dosage form is retained in the stomach up to 6± 0.5 h in fasting condition and 8 h in fed state.[9]

Ch is a weak cationic polysaccharide, a biodegradable, non-toxic, mucoadhesive and film former. Alg is an anionic linear copolymer of (1,4) D-mannuronic acid and 1-guloronic acid residues arranged in a non-regular blockwise pattern. These two oppositely charged polysaccharides will form polyelectrolyte complexes that have interesting characteristics for controlled release applications.[10]

Recently, it was reported the preparation and evaluation of gastroretentive dug delivery system of ranitidine HCl using sperical Alg-Ch matrices.[11-12] The purpose of this research was to formulate and evaluate Alg-Ch films containing antacids as gastroretentive drug delivery system. Drugs model were used $Al(OH)_3$ and $Mg(OH)_2$. In this paper will be discussed about the preparation, unfolding and integrity properties, neutralization profile of simulating gastric acid secretion, mucoadhesive, and swelling properties of Alg-Ch films containing antacids.

Methods

Materials

Ch and sodium Alg 500~600 cP were the products of Wako Pure Chemical Industries, Ltd Japan. $Mg(OH)_2$ and $Al(OH)_2$ and glycerin were obtained from PT. Mutifa, Indonesia. Hydrochloric acid, sodium hydroxide, and acetic acid were the products of Merck.

Preparation of Alg-Ch films containing antacids

The films were prepared using the combination of sodium Alg and Ch as a matrix and glycerin as a plasticizer. The homogenous mixture of mucillage of 4% sodium Alg in water, mucillage of 4% Ch in 1% acetic acid, glycerin, and antacids (Table 1) was flattened on a object glass (2 cm x 5 cm) and then allowed to dry at room temperature for 48 hours. The films formed were removed carefully, placed in desiccator. Then, the films were rolled and filled into gelatin capsules.

Evaluation

Films thickness and weight

Weight was measured using a digital balance and the thickness was determined using a micrometer.

Table 1. Formula of various Alg-Ch films containing antacids

No	Formula	Polymers		Drugs		Glycerin
		Mucillage of 4% Alg	Mucillage of 4% Ch	$Al(OH)_3$	$Mg(OH)_2$	
1	F1	2.5 g	-	300 mg	-	2 drops
2	F2	2.5 g	-		300 mg	2 drops
3	F3	-	2.5 g	300 mg	-	2 drops
4	F4	-	2.5 g	-	300 mg	2 drops
5	F5	1.0 g	2.0 g	300 mg	-	4 drops
6	F6	1.5 g	2.0 g	300 mg	-	4 drops
7	F7	2.0 g	2.0 g	200 mg	200 mg	4 drops
8	F8	3.0 g	1.0 g	200 mg	200 mg	4 drops
9	F9	3.5 g	0.5 g	200 mg	200 mg	4 drops

Unfolding properties of Alg-Ch films containing antacids

The unfolding properties of films containing antacid were determined in order to look the ability of the films to stretch back (unfolded) when the gelatin capsule disintegrated in the stomach. Unfolding property was determined by using a USP dissolution apparatus II paddle) at 100 rpm in 900 ml 0.1 N HCl solution at 37ºC ± 0.5ºC. The films were examined for their unfolding behaviour at certain interval of time.

Integrity properties of Alg-Ch films containing antacids

Integrity properties were evaluated by using the USP XXIII Apparatus 1 (basket) at 100 rpm in 0.1 N HCl solution at 37ºC ± 0.5ºC. Basket was removed after 60, 120, 240, 480 and 720 minutes and the film was examined for their integrity behaviour. The films were examined for their unfolding behaviour at certain interval of time.

Neutralization of simulated gastric acid by antacids powder

The solution of 0.1 N HCl of pH 1.2 was used as a simulated gastric acid. Antacid was added to 30 ml of 0.1 N HCl solution. At the certain interval of time the pH solution was measured using a pH meter. The antacids were used 200 mg $Mg(OH)_2$, 200 mg $Al(OH)_2$, and combination of 200 mg $Mg(OH)_2$ and 200 mg $Al(OH)_2$.

Neutralization of simulated gastric acid secretion by antacids powder

The secretion of hydrochloric acid from human stomach in normal condition is 1 mEq/h; and the volume of gastric acid in fasting state is 20-30 ml. [2-13] Based on this condition, the secretion of gastric acid was simulated by dropping 10 ml/h of 0.1 N HCl solution that conducted by continously dropping 10 drops/minute (using micro drip infusion; 60 drops/ml) to 30 ml of 0.1 N HCl solution at 37±0.5°C containing antacid (Fig.1). During the experiment the solution was stirred with a magnetic stirrer. At the certain interval of time the pH solution was measured using a pH meter. The antacids powder were tested 200 mg $Al(OH)_3$, 200 mg $Mg(OH)_2$, combination of 200 mg $Al(OH)_3$ and 200 mg $Mg(OH)_2$, 400 mg $Al(OH)_3$, and 600 mg $Al(OH)_3$.

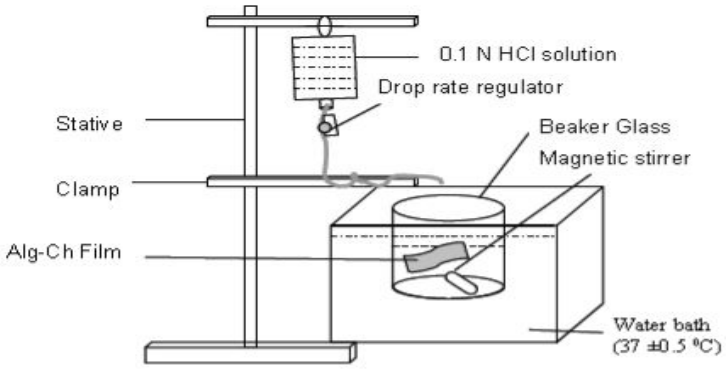


Figure 1. Schematic of neutralization test of simulated gastric acid secretion by Alg-Ch film containing acid

Neutralization of simulated gastric acid by films Alg-Ch containing antacids

The procedure of testing as described above in neutralization of simulated gastric acid by antacids powder. The Alg-Ch films were tested the films containing 300 mg $Al(OH)_3$ (F1, F5, F6, and F9). Some films (F1, F5, and F6) were used two films. Before the experiment the film was rolled and filled into gelatin capsule. The pH of solution was determined at certain interval of time.

Mucoadhesive properties of Alg-Ch films

The mucoadhesive properties of Alg-Ch films containing antacid were tested by using DuNoy tensiometer in rats stomach as reported previously with slight modification.[11-12] The platinum-iridium ring of the tensiometer was replaced by a piece of rat gastric mucosa (1 cm x 1 cm) which adhered to an acrylic plate (1 cm x 1 cm). The acrylic plate containing gastric mucosa was hanged using a spun cotton to the arm of tensiometer, where in the gastric mucosa faced down. The gastric mucosa was equilibrated at 37^0C for 10 minutes in 0.1 N HCl solution of pH 1.2 before the bioadhesion test. The Alg-Ch film containing antacid (2 cm x 5 cm) that had been immersed in 0.1 N HCl solution for 10 minutes was placed in the sample pot of tensiometer. Then, the arm of tensiometer was lowered until the gastric mucosa came in proper contact with Alg-Ch film containing antacid and it was kept contact for 15 minutes. Then, the knop of tensiometer was moved upward slowly until the gastric mucosa was completely detached from the film. During the experiment the gastric mucosa was wetted by dropping 0.1 N HCl solution.

Swelling properties of Alg-Ch films

Swelling properties of Alg-Ch films containing antacid in 0.1 N HCl solution were determined based on the increase of film size. The initial size (D1) of the film was measured and the film was immersed in 30 ml of stirred 0.1 N HCl solution at 37ºC ± 0.5ºC at 10, 15, 30, 60, 120, 180, 240 and 360 minutes. The size of the film was measured after swelling (D2). Thus, the degree of swelling (Sw) could be calculated as follows:

$$Sw = \frac{D2 - D1}{D1} x100\%$$

***In vitro* aluminium ions release from Alg-Ch films**

The release of aluminium ions from Alg-Ch films containing antacid was determined using USP Dissolution Testing Apparatus II (Paddle type). The study conditions were set at a stirring speed of 100 rpm and dissolution medium was 900 ml of 0.1 N HCl solution at 37ºC ± 0.5ºC. At certain interval of time 1 ml aliquot of dissolution medium was withdrawn and the sample was replaced with fresh dissolution medium. The samples were filtered through Whatman filter paper no. 41. Absorbance of these solutions was measured using Atomic Absorption Spectrophotometer (Hitachi Z-2000). Cumulative percentage metal ions released was calculated using an equation obtained from a standard curve.

Scanning electron microscopy (SEM)

The morphology of the Alg-Ch films was studied by using SEM (Dekstop SEM Phenom Pro X).

Results & Discussion

Preparation of Alg-Ch films containing antacids

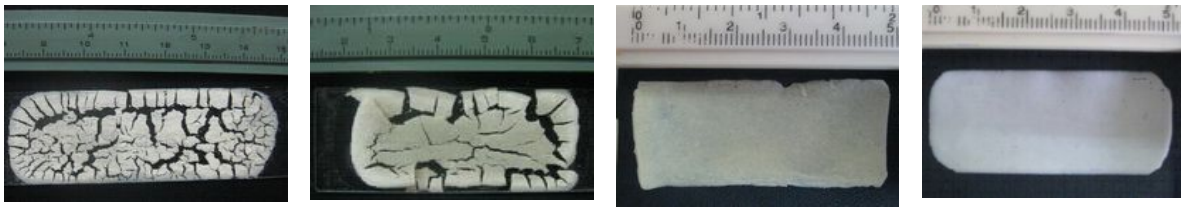
It was found that Alg-Ch could not form good film with $Mg(OH)_2$ and the mixture of $Al(OH)_3$ and $Mg(OH)_2$. When the formula containing $Mg(OH)_2$ and Ch (F4) or $Mg(OH)_2$ and Ch with Alg (F7 and F8) the good film could not be formed. The obtained film were cracked as shown in Figure 2 (a,b,c,d). The cracking phenomena of films is thought due to the interaction of $Mg(OH)_2$ with Ch and hence prevented the film formation. Ch is a widely used as a sorbent for metals and organic species because both amino (-NH2) and hydroxy (-OH) groups on Ch chains can serve as coordination and reaction sites.[14] To prevent the cracking in the film containing $Mg(OH)_2$ then the high amount of Alg should be used (F9). However, $Al(OH)_3$ formed good film Alg, Ch and Alg-Ch as shown in Figure 2 (b,c). The specifications of films obtained is listed in Table 2.

Table 2. Specification of Alg-Ch films containing antacids (n=3)

No	Formulation	Length (cm)	Width (cm)	Thickness (mm)	Weight (mg)
1	F1	5	2	0.37 ± 0.001	459± 0.008
2	F2	5	2	0.32 ± 0.014	445 ± 0.004
3	F3	5	2	0.44 ± 0.005	495 ± 0.034
4	F4	Could not formed films			
5	F5	5	2	0.53 ± 0.012	796 ± 0.023
6	F6	5	2	0.58 ± 0.011	852 ± 0.010
7	F7	Could not formed films			
8	F8	Could not formed films			
9	F9	5	2	0.63 ± 0.008	0.889 ± 0.016

Unfolding properties of Alg-Ch films

When the rolled film was immersed in the medium of 0.1N HCl solution, the film that containing only Alg and antacid like F1 (Alg and $Al(OH)_3$) and F2 (Alg and $Mg(OH)_2$ did not stretch back in the medium 0.1 N HCl solution. But, when the films containing Ch like F3 (Ch and $Al(OH)_3$) or the combination of Alg and Ch like F5 and F6 (Alg-Ch and $Al(OH)_3$) and F9 (Alg-Ch and $Al(OH)_3$ and $Mg(OH)_2$) stretched back (unfolded) after about 7 minutes in the medium of 0.1 N HCl solution, as shown in Figure 3. The Unfolding time of various formula of Alg-Ch films is listed in Table 3. Alg has property to shrink and stiff at a low pH and dissolve at a higher pH, whereas Ch dissolves and swells at a low pH and is insoluble in higher pH ranges.[15-16] Therefore, when the gelatine capsule disintegrated in the medium of 0.1N HCl solution, the film that containing Ch led to swell and the swollen film pushed the film to stretch back.



a **b** **c** **d**

Figure 2. (a) Ch and $Mg(OH)_2$ (F4) formed films were cracked.(b) Alg-Ch and $Mg(OH)_2$+$Al(OH)_3$ (F7) formed films were cracked. (c) Ch and $Al(OH)_3$ (F3) formed good films. (d) Alg-Ch and $Al(OH)_3$ formed good films

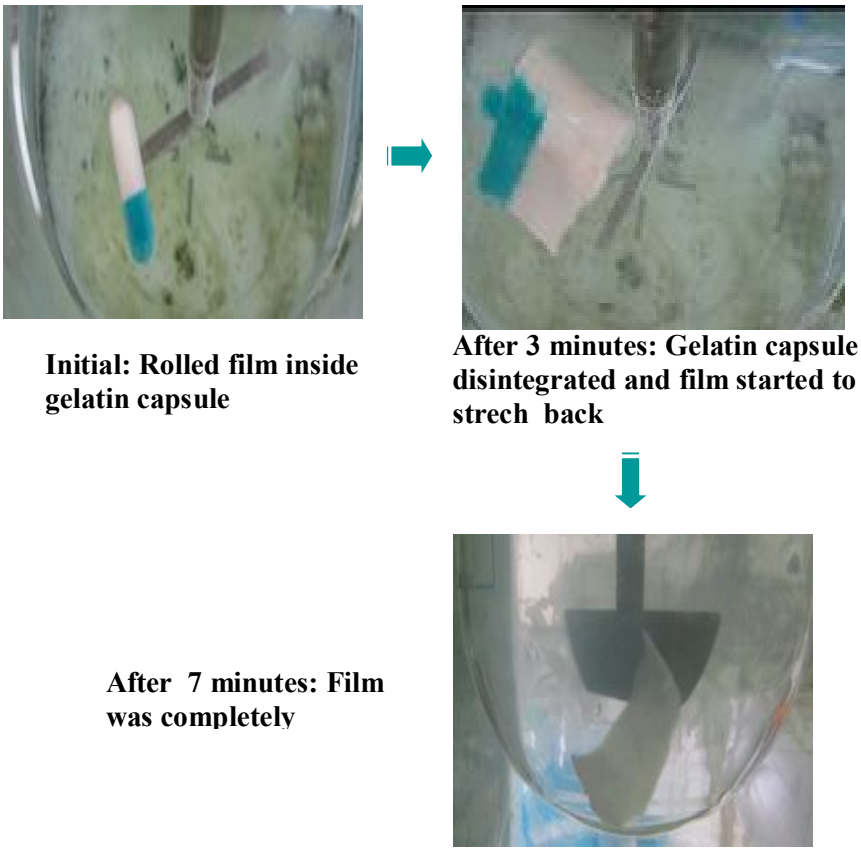


Figure 3. Unfolding process of Alg-Ch film containing $Al(OH)_3$ (F6) in the medium 0.1 N HCl solution.

Integrity properties of Alg-Ch films

The films prepared using Alg polymer only (F1, F2) and the films Alg-Ch with high content of Alg (F9) did not disintegrate for 12 hours. But, the films prepared using Ch polymer only (F3) disintegrated after 1 ± 0.5 h in the medium of 0.1 N HCl solution as well as films made by Alg-Ch; the disintegration time of films was longer with the higher Alg amount in the film (Table 4). The photograph of the integrity property of Alg-Ch film containing $Al(OH)_3$ is shown in Figure 4.

In this research, based on the results of unfolding and integrity properties of the films were evaluated, then only the films of formula F5, F6 and F9 were qualified to be continued to the next investigation.

Table 3. Unfolding properties of Alg-Ch films

No	Formula	Unfolding time	Unfolding properties
1	F1	-	did not stretch
2	F2	-	did not stretch
3	F3	7 minutes	Stretched back
4	F5	7 minutes	Stretched back
5	F6	8 minutes	stretched back
6	F9	6 minutes	stretched back

Table 4. Integrity properties of Alg-Ch films

No	For-mula	Properties
1	F1	Did not disintegrate for 12 h
2	F2	Did not disintegrate for 12 h
3	F3	Disintegrated after 1 ± 0.5 h
4	F5	Disintegrated after 4 ± 0.5 h
5	F6	Disintegrated after 7 ± 0.5 h
6	F9	Did not disintegrate for 12 h

Neutralization profile of simulated gastric acid

In this research the neutralization profiles of simulated gastric acid were divided in to three types: 1) Neutralization profile of simulated gastric acid by antacids powder, 2) neutralization profile of simulated gastric acid secretion by antacids powder, and 3) neutralization profile of simulated gastric acid secretion by Alg-Ch films containing antacids.

Neutralization profile of simulated gastric acid by antacid powder

The neutralization of simulated gastric acid by antacids is shown in Figure 5. After the addition of $Mg(OH)_2$ to 30 ml of 0.1 N HCl solution, the pH solution was rapidly increased until pH 9.1 and then the pH was constant. While, the addition of $Al(OH)_3$ the increase of pH was slower than the addition of $Mg(OH)_2$ and the maximum pH was also lower, 3.5. This results were due to $Mg(OH)_2$ is a strong base and has a rapid action of acid neutralization, while $Al(OH)_3$ has a slower action of acid neutralization.[4-17] The combination of $Mg(OH)_2$ and $Al(OH)_3$ gave the maximum pH 8.2 and this pH was slightly lower than that only $Mg(OH)_2$.

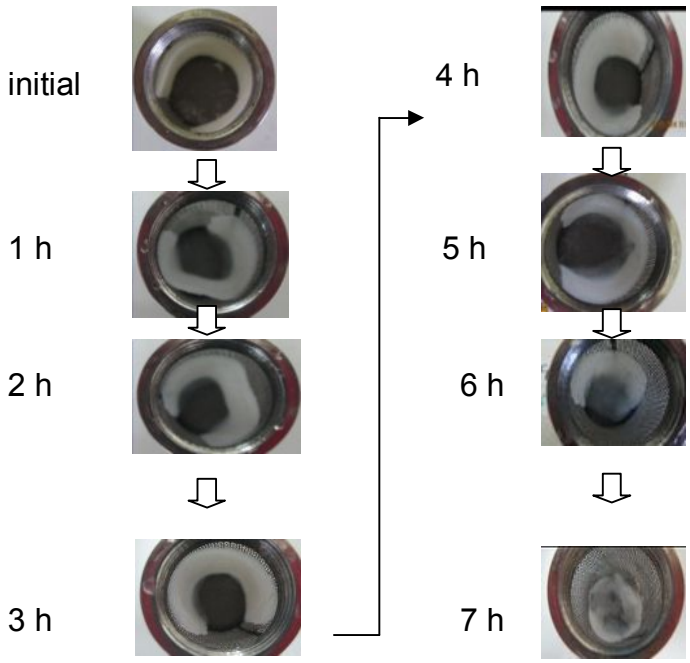


Figure 4. Integrity properties of Alg-Ch film containing $Al(OH)_3$ (F6) in the 0.1 N HCl solution.

Neutralization profile of simulated gastric acid secretion by antacids powder

The addition of antacid powder to the 30 ml of 0.1 HCL solution caused the pH of solution rapidly increased and then the pH decreased with the addition dropwise of 0.1 N HCl solution (Figure 6). The decrease of pH was due to the neutralization of antacid by HCl solution added. The neutralization profile graphs is different with Figure 5 as shown above. The neutralization degree of $Mg(OH)_2$ was stronger than that of

$Al(OH)_3$, and the combination of $Mg(OH)_2$ and $Al(OH)_3$ gave lower pH than only $Mg(OH)_2$. The higher dose of $Al(OH)_3$ gave the higher pH of solution.

In *in vitro* evaluation, $Al(OH)_3$ at dose of 400 mg maintained the pH 3.0-3.5 for 8 hours and at dose 600 mg for 8.5 hours. Even though, $Al(OH)_3$ powder is not a gastroretentive preparation. Therefore, in *in vivo* condition $Al(OH)_3$ powder only retained in the stomach about 30 minutes, so that it could not maintain the stomach pH for long time.

Neutralization profile of simulated gastric acid secretion by Alg-Ch films containing antacid

Figure 7 shows the neutralization profile of simulated gastric acid by Alg-Ch film containing antacid. The film based on only Alg (F1) containing 300 mg $Al(OH)_3$ was used two films; film based on only Ch (F5) containing 300 mg $Al(OH)_3$ was used two films; film based on Alg-Ch (F6) containing 300 mg $Al(OH)_3$ was used one and two films; and film based on Alg-Ch with high content of Alg (F9) containing 200 mg $Al(OH)_3$ and 200 mg $Mg(OH)_2$ was used one film.

The films of F1 that the polymer only Alg and the films that containing high amount of Alg (F9) gave the low neutralization degree against acid solution was indicated from the lower pH of solution. The higher amount of Alg the lower ability to neutralize acid solution and to maintain the pH of solution. Alg was insoluble and shrank at low pH, so that reduced the medium penetration into the film, resulting the lower of acid neutalization. But, the films with high content of Ch gave the higher pH and maintain the higher pH for longer time. The film with Alg Ch ratio was 3:4 (F6) containing 300 mg $Al(OH)_3$ and by using two films were able to maintain the pH solution at 3.0 - 3.43 for about 6 hours. This type of films showed the ability to neutralize and maintain the pH better than the other type of films tested. The films of F5, Alg Ch ratio was 1:2 gave higher pH, 3.1-3.5, but these films disintegrated after 4 hours in the medium. Therefore, the film of F6 was the the best candidate for gastroretentive drug delivery system of $Al(OH)_3$ among other films tested.

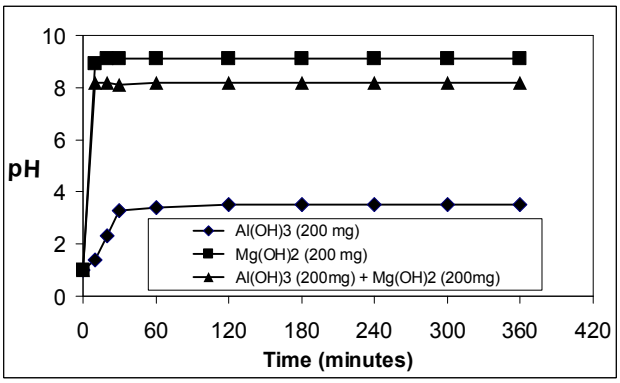


Figure 5. Neutralization profile of 0.1 N HCl solution by antacids powder.

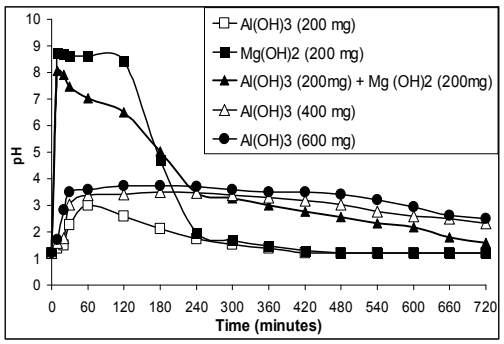


Figure 6. Neutralization of simulated gastric acid secretion by antacids powder.

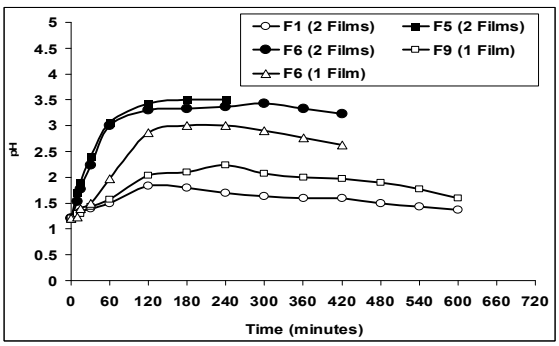


Figure 7. Neutralization of simulated gastric acid by Alg-Ch films containing $Al(OH)_3$.

Swelling properties

The results of in vitro swelling tests are shown in Figure 8 and the photograph of initial and swollen film is shown in Figure 9. The higher amount or the higher ratio of Ch to Alg in the films caused the higher swelling degree of the films. On the other hand, the films with high amount of Alg resulted in the lower swelling degree. Polymers containing carboxyl groups and amino groups respond to the pH changes by changing their size in the swollen state. At low pH values, the carboxyl residues of Alg display the minimum of ionization and hence reduce of hydration. On the contrary, the amino groups of Ch are protonated in low pH and caused the repulsion among positive charges and the osmosis occurs because the high osmotic pressure of the matrix as a result of protonation of amine groups. As a result, the swelling of films in the medium of 0.1 N HCl solution.[12-18]

The ability of the Alg-Ch films to swell at low pH is useful for the application of Alg-Ch films as a gastroretentive drug delivery system of $Al(OH)_3$. The increase of films size after stretching in the stomach will prevent the film to pass through the pylorus so that the film will remain in the stomach for a longer period of time.

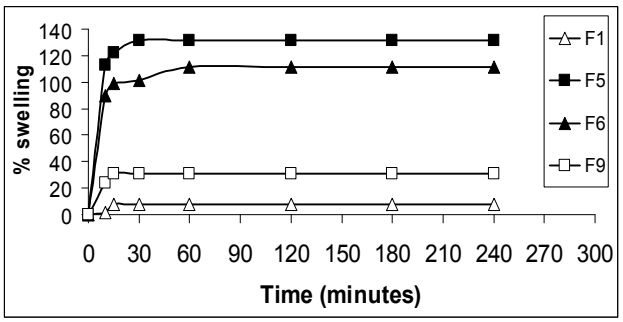
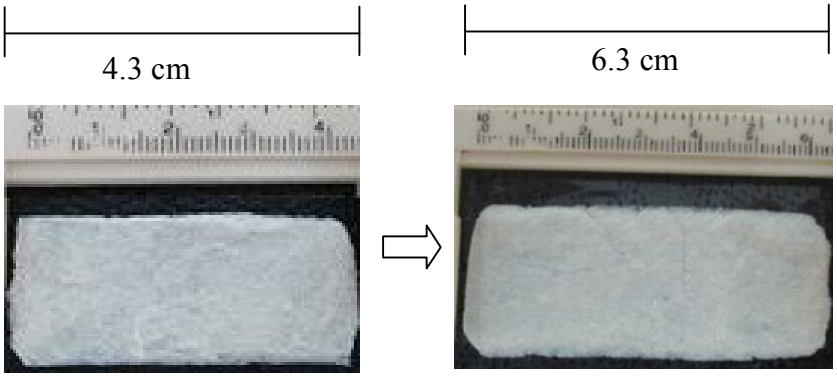


Figure 8. Swelling properties of Alg-Ch films in 0.1 N HCl solution.



Initial After 30 minutes in 0.1 N HCl sol.

Figure 9. Initial and swollen Alg-Ch film containing Al $(OH)_3$ (F6) in 0.1 N HCl solution.

Mucoadhesive properties of Alg-Ch films

The complex of Alg-Ch has a mucoadhesive properties as reported previously in spherical of Alg-Ch matrices.[11-12] The mucoadhesive strength of some Alg-Ch films containing $Al(OH)_3$ is listed in Table 5. Among the films tested the highest mucoadhesive strength was obtained in F5. The swelling of the film caused the contact area of the film to gastric mucosa became larger and as a result, the film is more sticky on the gastric mucosa. During the experiment, the Alg-Ch films hydrated, swelled and got in contact on the surface of gastric mucus. The formation of hydrogen-bonds between functional groups of Alg-Ch polymers and mucosa layers may be responsible for the mucoadhesive properties of the films.[12]

Table 5. Mucoadhesive properties of Alg-Ch films.

No	Formula	Bioadhesion strength (dyne/cm^2)
1	F1	44.73 ± 12.10
2	F5	181.20 ± 9.07
3	F6	107.47 ± 7.38
4	F9	57.60 ± 10.04

Aluminum ions release from Alg-Ch films

The neutralization reaction between $Al(OH)_3$ and HCl took place inside the Alg-Ch film. The neutralization was preceded by the penetration of HCl solution into the film then the neutralization reaction occured between $Al(OH)_3$ and HCl. The neutralization reaction followed by the release of aluminum ions to the medium as shown in Figure 10. The aluminum ions released from the film was a sustained release which released as much as 96% from the initial concentration after 6 hours. The neutralization reaction occurs in side the film is illustrated in Figure 11.

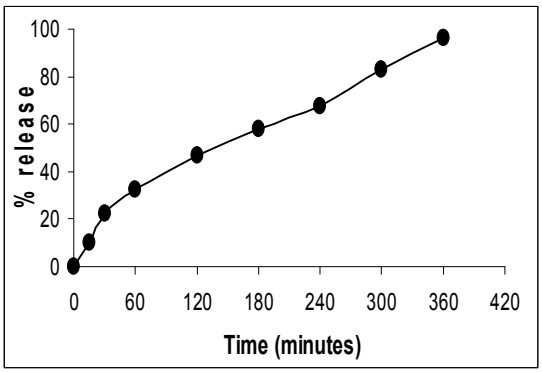


Figure 10. $AlCl_3$ release from film containing Al $(OH)_3$ to the medium of 0.1 N HCl solution.

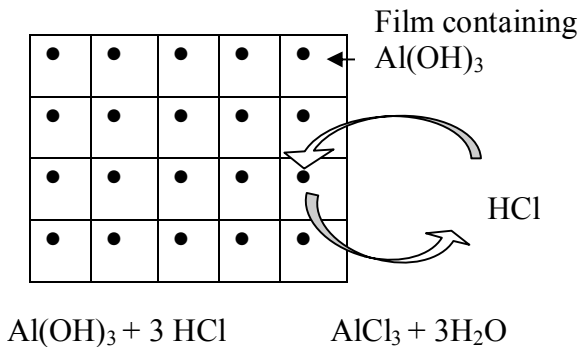
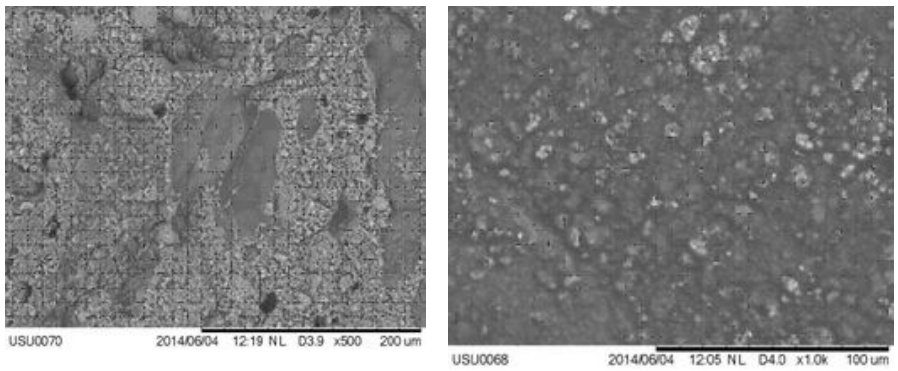


Fig 11. Illustration of the neutralization reaction in Alg-Ch film.

Scanning electron microscopy (SEM)

The SEM analysis revealed that the surfaces of the initial Alg-Ch film containing $Al(OH)_3$ was different with the Alg-Ch film after the release experiment. The less amount of $Al(OH)_3$ particles was showed after the release experiment (Figure 12).



a **b**

Fig 12. Scanning electron microscopy (SEM) image of Alg-Ch film. (a) Initial Alg-Ch film containing $Al(OH)_3$ (b) Alg-Ch film after the release experiment.

Conclusions

Alg-Ch films which contain $Al(OH)_3$ can be prepared using sodium Alg and Ch. These films have good properties as a gastroretentive drug delivery system, such as unfolding, integrity, swelling, and mucoadhesive properties. For the application in the treatment of stomach ulcer, it is still necessary to continue the research by testing in experimental animal.

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