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Research article

Preparation and characterization of alginate-chitosan capsule shells using tripoliphosphate crosslink method

Cut Intan Annisa Puteri*[1], Sumaiyah[1], Rosidah[2]

[1]Department of Pharmaceutical Technology, Faculty of Pharmacy, Universitas Sumatera Utara, Medan, Indonesia.
[2]Department of Pharmacology, Faculty of Pharmacy, Universitas Sumatera Utara, Medan, Indonesia.

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***Corresponding Author: Cut Intan Annisa Puteri,** Department of Pharmaceutical Technology, Faculty of Pharmacy, Universitas Sumatera Utara, Medan, Indonesia.

Abstract

Objective: This study aims to determined the effect of crosslinked tripolyphosphate (TPP) concentration variation on the nature of capsule shells formation and to determined the characteristics of capsule preparations that the best with alginate-chitosan and tripolyphosphate. **Method:** This research includes the preparation of alginate solution, chitosan and TPP, preparation of capsule shells, capsule shells characterization, disintegration time analysis, the swelling degree test, functional group analysis (FTIR) and morphology (SEM). **Result:** The results showed that the best capsule shells formulations produced from alginate-chitosan and TPP crosslinking compounds were Formula F7 and F8. However, from the characteristics of the swelling degree test, the capsule shells formula F8 had a better degree of swelling compared to the formula F7. The mechanical strength produced from the F8 capsule shells was also better than the formula F7. **Conclusions:** Based on the description above, it can be concluded that the concentration of chitosan and crosslinking compounds significantly influence the formation of capsule shells and the characteristics of capsule shells preparations with alginate-chitosan and TPP crosslinks produce good physical properties so that it can be used as a drug delivery system.

Introduction

One form of preparation with a conventional drug delivery system that is still commonly use is capsules. Capsules are solid preparations consisting of hard capsule shells or soft capsule shells which can dissolve. The capsule shells is generally made of gelatin, but can also be made from starch or other suitable parts [1].
Today the use of polymers in the preparation of capsule shells continues to increase and expand in various fields, especially in the pharmaceutical industry. This is due to the superiority of polymers that offer compatibility, mechanical strength and high selectivity. Capsule shells material is one variable that greatly determines capsule performance. Natural polymers are now getting very serious attention from researchers to be use as an ingredient in preparation of capsules because they are nontoxic, biodegradable, biocompatible, cheaper and easier to get it [2].
Alginate is a linear polysaccharide composed from residues of ß-D-manuronic acid and α-L-guluronic which are connected through 1.4 bond. Alginate comes from brown algae which are marine plants. Alginic acid is not soluble in water, so what is commonly use in industry is sodium alginate [3].
Chitosan is a polysaccharide which is present in abundant quantities in nature which is also a chitin deacetylation product. This material has been widely use in the field of biomedicine and pharmaceuticals because of its biodegradable, biocompatible and non-toxic properties. Alginates and chitosan are natural polymers that have the potential as a basic ingredient in preparation capsule shells. However, to further improve the mechanical resistance of a capsule, it is necessary to modify the capsule shells in the form of adding crosslinking substances (crosslinker) [4].
The crosslink compound use in this study is sodium tripolyphosphate / TPP which is considered as a good crosslinking agent,that the use of TPP for the formation of chitosan beads can increase the mechanical strength of the beads formed [4]. The results of Garud and Garud (2010) stated that the use of TPP as a crosslink in the manufacture of microcapsules with alginate-chitosan produced optimal microcapsules at all alginate-chitosan and TPP concentrations respectively (2; 1; 2), (2; 2 ; 2), (2; 3; 2), (2; 4; 2), (2; 4; 4), (2; 4; 4) %w/v [5].
A lot of research has been done on preparation alginate-based capsules, but studies used alginate and chitosan with tripolyphosphate crosslinking methods have not been done. Therefore, researchers need to develop capsule preparations from alginate-chitosan with crosslink tripolyphosphate.

Materials and methods

Materials

The materials used in this study include: sodium alginate 500-600 cp (Wako Pure Chemical Industries, Ltd. Japan), chitosan, sodium tripolyphosphate (Merck), Demineralized water, acetic acid, calcium chloride and silicone oil. The instrument used in this study: pH meter (Hanna), Scanning Electron Microscopy (SEM) TM3000 (Hitachi). FTIR (Fourier Transform Infra Red) (Shimadzu). Spectrophotometer Uv-Visible (Shimadzu).

Methods

Preparation of sodium tripolyphosphate solution 2; 3; and 4%

Sodium tripolyphosphate as much as 2; 3; and 4 grams each dissolved in 100 ml of demineralized water using magnetic stirrer on 500 rpm [6].

Preparation of alginate solution 2% and 4%

Sodium alginate as much as 2 grams and 4 grams each dissolved in 100 ml of demineralized water and added with 4 drops of glycerin then stirred using a magnetic stirrer on 500 rpm.

Preparation of chitosan solution 1; 2; 3; and 4%

Each chitosan of 1 to 4 grams was dissolved in 100 ml of solvent 0.1 M acetic acid using a magnetic stirrer on 500 rpm.

Preparation of alginate-chitosan capsule shells crosslinked tripolyphosphate

Capsule printing device were dipped in alginate solution for 1 minute, and then dipped back into 0.15 M calcium chloride solution for 5 minutes. After that the hardened capsule shells was washed with demineralized water. Then the capsule shells was dipped back into a variation of chitosan solution concentration for 1 minute, then dipped again in sodium tripolyphosphate solution and soaked for 10-20 minutes then dried in a drying cabinet [5]. The concentration of alginate, chitosan and tripolyphosphate used can be seen in Table 1.

Table 1. Comparison composition of alginate, chitosan and tripolyphosphate.

Formula	Alginate (%w/v)	Chitosan (%w/v)	Tripolyphosphate (%w/v)
F1	2	1	2
F2	2	2	2
F3	2	3	2
F4	2	4	2
F5	2	4	3
F6	2	4	4
F7	2	2	4
F8	4	2	4

Characterization of alginate-chitosan capsule shells crosslink TPP

Measurement of the capsule shells length and diameter

Measurement of the length and diameter of the capsule shells was made to the capsule shells body and lid capsule shells using a caliper [7].

Measurement of the capsule shells thickness and weight

Measurement of thickness and weight of the capsule was carried out on the capsule as a whole were measured using a micrometer. The weight of the capsule shells was weighed using an analytical balance.

Measurement of the capsule shells volume

Measurement of the capsule shells volume was only carried out on the body of the capsule shell. Measurement of the capsule shells volume was carried out using a burette by means of the capsule shells filled with water until the meniscus over the water touches the tip of the capsule.

Analysis of disintegration/ disintegration time

Analysis of disintegration of the capsule was carried out using a disintegration tester. As much as one capsule was inserted in each tube from the basket, then one disc was inserted in each tube, then all the tubes were closed, then the appliance was run. Media temperature was set to 37°C. Media used was 0.1N HCl for 2 hours then continued in phosphate buffer media pH 4.5 and 7.4 for 1 hour each. Basket lifted and all capsules were observed at the end of the time limit [7].

The swelling degree test

A total of 900 mL of each medium solution was put into a dissolved flask and the temperature was adjusted to 37 ± 0.5°C with a mixing speed of dissolution device was 100 rpm. Into the flask was put 1 dry capsule preparation which was weighed (W dry). At certain time intervals the capsules were lifted and weighed (W wet). This test was carried out for 9.5 hours [8].

The equation used to determine the degree of swelling is:

The swelling degree

$$= \frac{(\text{W wet} - \text{W dry})}{\text{W dry}} \text{x } 100\%$$

W was the mass of membrane material when wet (W wet) and dry (W dry) in grams.

Functional group analysis

Functional group analysis was performed using a Fourier Transform Infra Red spectrophotometer. The samples to be characterized are measured at a wave number of 4000-500 cm^{-1} at a resolution of 4 cm^{1} [9].

Scanning electron microscopy (SEM) test

The morphology of the shape and surface of alginate-chitosan capsules with tripolyphosphate crosslinks viewed using scanning electron microscopy (SEM) [6].

Results and discussion

Preparation of alginate-chitosan capsule shells crosslink tripolyphosphate

From formula F1; F2; F3; F4; F5; F6; F7; and F8 made in this study, formula F7 and F8 produces a good capsule shells. This was because the concentration of the solution at F7 and F8 was able to attach to the capsule printing device in the printing process so that it can form a capsule shells well compared to other formulas. The formula that did not get the results as expected was caused by the concentration of each solution used was not suitable to form a capsule shells. This can be seen during the capsule printing process, where the solution of each formula cannot be attached to the capsule printing device. The characteristic alginate-chitosan capsule shells can be seen in figure 1.

(a) (b)

Figure 1. Alginate-chitosan capsule shells crosslinked tripolyphosphate (a) formula F7; (b) formula F8

Characterization of alginate-chitosan capsule shells crosslink tripolyphosphate

The capsule shells were made in the study was a capsule shells with a size No. 0. This can be seen in table 2, 3 and 4.

Table 2. Characterization of alginate-chitosan capsule shells crosslink TPP on F7 size No. 0.

No.	Characterization	Shell body	Cover the shell	Overall capsule shells
1	Long (mm)	18.35±0.58	10.77±0.59	20.32±0.19
2	Diameter (mm)	7.10±0.44	7.47±0.16	-
3	Thick (mm)	0.19±0.005	0.20±0.01	-
4	Weight (mg)	57.6±17.31	29.5±7.42	87.1±22.93
5	Volume (ml)	0.64±0.02	-	-

Table 3. Characterization of alginate-chitosan capsule shells crosslink TPP on F8 size No. 0.

No.	Characterization	Shell body	Cover the shell	Overall capsule shells
1	Long (mm)	18.35±0.32	10.85±0.37	20.36±0.24
2	Diameter (mm)	7.32±0.42	7.54±0.25	-
3	Thick (mm)	0.28±0.01	0.30±0.007	-
4	Weight (mg)	95.35±29.35	55.7±10.71	151.05±35.17
5	Volume (ml)	0.64±0.02	-	-

Table 4. Characterization of capsule shells size 0 according to Capsuline ©.

Capsule	Shell body		Cover the shell		Overall capsule shells
	Long (mm)	Diameter (mm)	Long (mm)	Diameter (mm)	
0	18.35	7.35	10.85	7.64	21.6
Tolerance	±0.35	±0.35	±0.35	±0.35	±0.3

Analysis of disintegration / disintegration time

Test results using 0.1 N HCl solution for 2 hours can be seen that the capsule shell was not broken out but there was an increase in the diameter of the capsule shells. After 2 hours in 0.1 N HCl medium, disintegration was continued in a medium of phosphate buffer pH 4.5 and pH 7.4. With increasing pH on phosphate buffer pH 4.5 and pH 7.4, the capsule shell expands and eventually broken out in phosphate buffer solution. The time needed of the capsule shells to broken out in this study was 18:60 minutes for formula 7 (F7) and 42:11 minutes for formula 8 (F8).

The swelling degree test

Based on the results obtained (Figure 2) it can be seen that capsule preparation F8 experienced a lower degree of swelling compared to capsule F7. This was due to the factor of increasing concentration of alginate at F8. The increase in concentration causes the higher the viscosity of the solution, so that the ability of the capsule to absorb the liquid will decrease [2]. In addition to alginate, the reaction of tripolyphosphate with chitosan through the formation of crosslinking makes the capsule shells more dense so that water molecules were difficult to diffuse into the chitosan-tripolyphosphate structure. These results indicate that crosslinking can reduce solubility and improve the mechanical properties of chitosan. The swelling degree of the capsule shells was reduced by crosslinking. This indicates that crosslinking by TPP can reduce the hydrophility of the capsule shells because the reactive amino group has reacted with tripolyphosphate ions [10]. The swelling characteristic can be seen in figure 2.

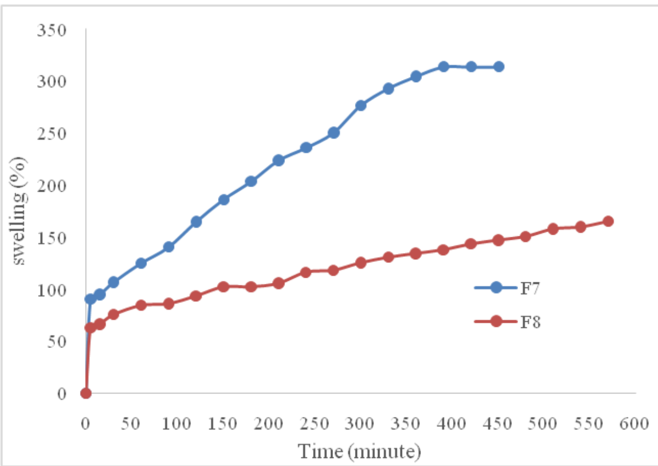
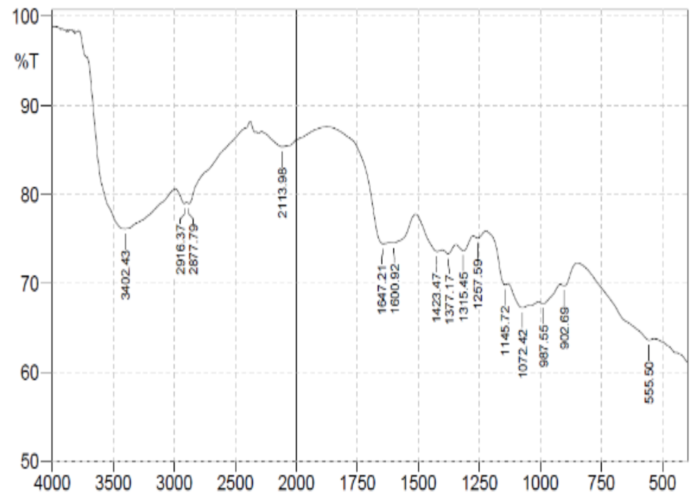


Figure 2. The swelling degree graph of the capsule preparations in the pH medium changes on each formula.

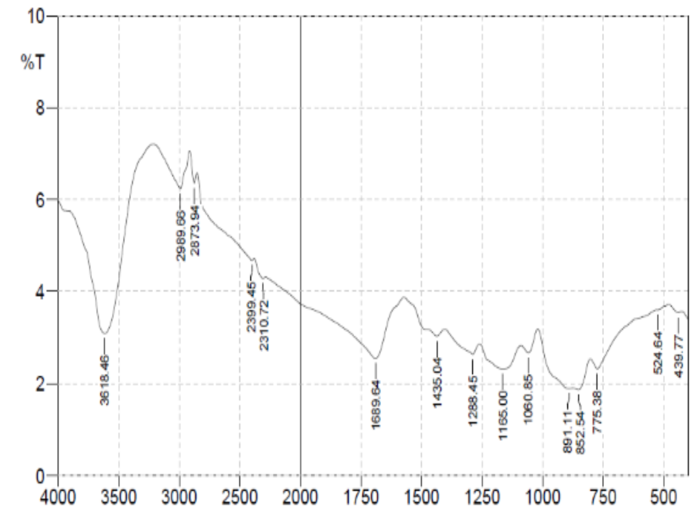
Functional group analysis

The FT-IR spectrum of chitosan in figure 3 showed the absorption band at wave number 3402.43 cm^{-1} which shows the overlap of vibration absorption in the range of –OH and –NH (NH_2) groups. Absorption band at wave number 2877.79 cm^{-1} indicates the presence of C-H group at -Ch-aliphatic. Absorption bands at wave numbers 1647.21 cm^{-1} and 1600.92 cm^{-1} indicate the absorption of C = O and CN from the amide group, while wave numbers 1423.47 cm^{-1} show the overlapping absorption of NH groups (secondary amines) .

In the FT-IR spectrum of chitosan appeared the peak C = O and CN at wave numbers 1647.21 cm^{-1} and 1600.92 cm^{-1} which showed the presence of amide group uptake. Whereas in capsules in figure 3 the peak of wave numbers 1647.21 cm^{-1} and 1600.92 cm^{-1} disappeared and appeared a new peak at wave number 1689.64 cm^{-1}. This showed that there was an interaction called crosslink between chitosan and TPP. Chitosan which experiences cross linking also showed the peak for group P = O at wave number 1165.00 cm^{-1}.



(a)

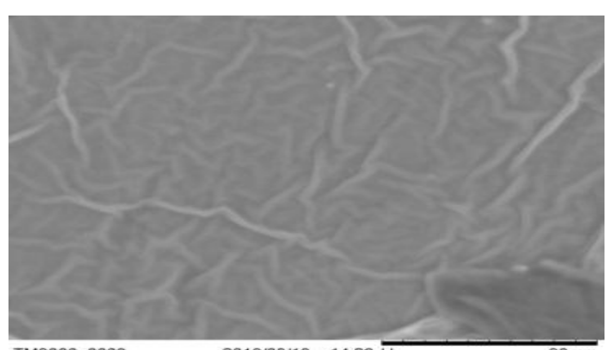


(b)

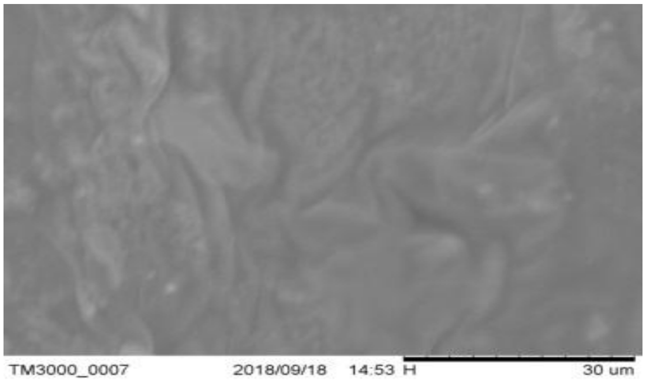
Figure 3. (a) FT-IR spectrum of chitosan; (b) FT-IR spectrum of alginate-chitosan-TPP capsules.

Scanning electron microscopy (SEM) test

Photographs from SEM showed that the surface of the two capsule formulas had a tight texture and appeared evenly distributed. But for the F8 capsule formula has a more homogeneous and smooth texture than the F7 formula. Photo of capsule surface morphology can be seen in Figure 4.



(a)



(b)

Figure 4. SEM photos of capsule shells morphology; (a) formula 7 (b) formula 8.

Conclusion

The results showed that variations in the concentration of alginate, chitosan and tripolyphosphate which can form capsule shells were in the formula F7 and F8. The best concentration of chitosan-tripolyphosphate used for preparation capsule shells was 2% chitosan concentration and 4% tripolyphosphate. The capsule shells made using the crossslink tripolyphosphate method produces good physical and mechanical properties.

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