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FORMULATION OF CAPSULE SHELL FROM CORNCOB HEMICELLULOSE COMBINED WITH ISOLATED SODIUM ALGINATE

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ABSTRACT

Corn cob contains the highest hemicellulose compared to other agricultural wastes such as bagasse, oats hulls. The aimed of this research was to formulate capsule shell from hemicellulose in corncob's waste combined with sodium alginate isolated with various compositions, namely Formula F1 (1: 1), F2 (2: 1) and F3 (3: 1). The characterization test of corncob hemicellulose consists of the organoleptic test, solubility test, FTIR test, while characterization of sodium alginate consists of the organoleptic test, pH determination, viscosity test, determination of sodium hypochlorite level in sodium alginate and FTIR. Capsule shell specifications were captured by measuring the length and diameter of the capsule shell, weighing the capsule, observing the capsule shell's color, measuring capsule shell's volume, conducting brittleness test, disintegration time test, and weight uniformity test. The yield of hemicellulose obtained from 500 g of corncob powder was 61 g (12.2%). The yield of sodium alginate from 50 g of isolated seaweed *Sargassum plagyophyllum* was 10.57 g (21.14%). The characterization result of sodium alginate was pH 8.1, viscosity 63.1cps, sodium hypochlorite 3.36%, FTIR result showed OH, C-O, and C = O group. The specification of the combined hemicellulose capsule shell was determined. The test result showed that the best Formula F (3) has a length of 18.33 (mm), diameter 6.5 (mm), weight 54.13 (mg), brown color and with 0.678 ml in volume. Based on the fragility test, there is no fragile capsule. The disintegration time test result was 29.66 minutes (with disc method), the weighted uniformity test result was the average of capsule shell weight 3.8542 g.

Keywords: Isolation, Hemicellulose, Sodium Alginate, Capsule Shell

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INTRODUCTION

Corn is a staple food and industrial material which has been increasing. As the production increase, the waste in the form of corn cob has increased as well. It comprises around 30% of corn's production. The production of corn in 2014 is 19,008,426 tons; it increased by 496.57 thousand tons compared to corn's production in 2013. It happened due to increasing productivity at around 1.1 quintal / hectare¹. Therefore, it requires specific attention in handling and utilizing corncobs, whereby corncobs will not pollute the environment and will be valuable. Chemical composition of corncobs consists of 35.5% crude fiber, 2.5% protein, 0.12% calcium, 0.04% phosphorus, 40% cellulose, 36% hemicellulose, 16% lignin and other substances 6%. Corn cob contains the highest hemicellulose compared to other agricultural waste such as bagasse, oats hulls, husk, peanut shell, and cottonseed leather².

Sargassum plagyophyllum (Mertens) J.G. Agardh or brown algae is one of the raw materials in alginate production that is widely used and found in Indonesian ocean, especially in North Sumatra, Indonesia³. Brown algae contain santophil pigment which gave a brown color and can produce algin or alginate. The presence of alginate in brown algae depends on the season, the location it grows, the age of harvest, and the type of algae.⁴

Sodium alginate is the end product of alginate extraction process. Na-alginate is formed through alginic acid and calcium alginate method. In the first method, alginic acid will form a gel and then directly converted to Na-alginate through the dehydration process. The second method, fibers, are formed from alginic acid before the addition of sodium carbonate in Na-alginate formation. Alginic acid is insoluble in water⁷ but sodium alginate is soluble in water. Due to the solubility, alginic acid must be converted first into hydrophilic sodium alginate before it was used. Alginate is a substance that is non-toxic, non-allergic, and biodegradable. Sodium alginate is widely used in the pharmaceutical field as a suspending agent, thickening agent, an oil-in-water emulsion stabilizer, binder and as a tablet crusher⁵.

In general, capsule shells are made from gelatin. Gelatin is a heterogeneous mixture of polypeptides obtained by collagen hydrolysis of animal connective tissue⁶. However, the gelatin capsule shell has some disadvantages, such as it dissolved in gastric juices, which caused the capsule shell inability to alleviate the side effects of drugs (irritation of gastric mucosa). The gelatin capsule shell becomes brittle if it was stored in low humidity conditions⁷. This brittleness also occurs when capsule shells were filled with hygroscopic materials⁸. Therefore, multiple research has been conducted to make a better and safer capsule shell.

The capsule shells made from the combination between hemicellulose and sodium alginate can prolong the disintegration time and the transit time of the drug. One of the characters of hemicellulose is insoluble in the gastric fluids and small intestine fluids. The aim is to increase the efficacy in the treatment, to reduce and even eliminate the side effects. However, hemicellulose is degradable by the bacteria in the intestine, which caused a drug compound to be released in the abdominal area if they were formulated with hemicellulose⁹.

The capsules are usually used for highly soluble materials such as potassium bromide, potassium chloride, or ammonium chloride because the sudden solubility of these compounds in the stomach might irritate. Capsules should not be used for highly soluble and volatile ingredients. The highly soluble ingredient could cause the capsule to soften while volatile ingredients could cause the capsule to dry and become brittle¹⁰.

EXPERIMENTAL

Tools and Materials

The tools used in this study were Fourier Transform Infra-Red (FTIR), Himac Compact Centrifuges (Hitachi RXII series), Dissolution Tester (Erweka DT), sonicator (Branson), centrifuge, stirrer, cellulose nitrate filter paper 0.45 μm (Whatman) membrane, 0.45 μm nylon filter paper membrane (Whatman), 0.2 μm (Whatman) PTFE filter, micrometer (Delta), stopwatch, analytic balance (Dickson).

The materials used in this study were hemicellulose corn cobs (isolated), sodium alginate (isolated) from *Sargassum plagyophyllum* (Mertens) J.G. Agardh, Sodium Tripolipospat (Merck), propylene glycol / PG (Brand), metronidazole (Merck), NaOH 0.1 N, (Merck), CaCl₂ (Brand), KH₂PO₄ (Merk), HCl (Merck), 5% NaOCl (E Brand), Talc (Yuanfen), glacial acetic acid (Merck), 20% TCA, Alcohol 96%, heparin, Distilled water (Ikapharmando Putramas), Metronidazole (E Merck) and generic metronidazole tablets (Indofarma) and all quality ingredients Pro Analysis (PA).

Sample Preparation

Corn cob (*Zea mays L.*) waste was collected and cleaned. The waste was cut into small pieces and washed in running water to remove the soil and other foreign objects and then let it dry. The dried corncob was weighed and dried in an oven at 105°C for 12 hours. The dried corncob was weighed again. Afterward, it was turned into powder using a grinder and a blender (National). The powder was then sieved, weighed, and stored in a clean and tightly closed container.

Isolation of Alginate

50 g of *Sargassum plagyophyllum* powder (Mertens) J.G. Agardh was added with 500 ml 1% CaCl₂ solution, heated at 40 - 500 C for 2 hours, then filtered. Afterward, it was washed with distilled water until it reached a neutral pH. 500 ml of 5% HCl solutions were added then immersed for 2 hours. Finally, the solution was filtered, and the result was washed with distilled water until it reached a neutral pH.

Finally, the result of alginate were weighed¹¹. Alginate's sample was further tested by organoleptic test and Transform Infrared (FTIR) to determine the constituent of sodium alginate.

Isolation of Hemicellulose from Waste of Corn Cobs

50 g of dried sample was diluted with 0.1M sodium hydroxide in 70% ethanol, continued heated at 60°C at 6 one hours (h) of de-lignification to eliminate lignin process by dissolving a lignin. The result of precipitated was diluted with 0.1 M sodium hydroxide in 70% ethanol and continued with three to dissolve hemicellulose. The filtrate was heated at a temperature of 65°C, and added 137 cm³ of 3% H₂O₂ in stages to eliminate lignin leftovers. The resulting sample was dried, and then it was crushed and weighed. The purpose of adding 70% ethanol was to precipitate and separate the hemicellulose from lignin because lignin could dissolve into 70% ethanol and hemicellulose settles with 70% ethanol. Hence, the purpose of using distilled water in washing the sample to dissolve cellulose¹². Hemicellulose's sample was further tested by Transform Infrared (FTIR) to confirm their structure.

Capsule's Production of Hemicellulose from Corn Cobs Combine with Alginate

2 g of glycerin was dissolved with 50 ml of distilled water (Mass I). 3 g (Formula 2), 4 g (Formula 3) and 3 g (Formula 4) of hemicellulose are dissolved separately with 20 ml of distilled water (mass II). 5 g (F1), 3 g (F2), 2 g (F3) and 1 g (F4) of sodium alginate was dissolved with 40 ml of mass I until homogeneous. The remaining solution of mass I was added with 0.2 g of TiO₂ 0.2 g (mass III). Subsequently, mass III and mass II were added into sodium alginate's solution and stirred until homogeneous. Except for F1 (+ control), mass III was directly added to sodium alginate's solution. The viscosity of each formula was determined by viscometer MyrVr 3000¹³.

The capsule shell's molding device was made from stainless steel with 10 cm of length and 5.5 mm (capsule's body); 6 mm (capsule cap) of diameters. Molding devices were dipped into a sodium alginate solution with hemicellulose as deep as 3 cm and then continued by soaking it into CaCl₂ solution for 30 minutes. Hardened capsule shells were soaked into distilled water for 12 hours to remove calcium that is attached in the capsule shell. The capsule shell was dried in the open air for 12 hours afterward, and the dried capsules were pulled from the printer and stored in plastic bottles.

Determination of Capsule Shell Specification

The length and diameter of the capsule shell were measured using a sliding range. The weight of the capsule shell was tested by using the analytic balance. The color of the capsule shell was observed visually. Capsule's volume was determined by using a burette whereby the capsule was filled with water until full.

Disintegration's Time Test

Several iron balls with 2.94 mm in diameter were inserted into 6 pieces of capsule's body. Each capsule's body was closed by pushing it into their capsule cap. An adhesive (sodium alginate solution containing TiO₂) were applied to each filled capsule. The filled capsules were inserted into each tube and placed into a basket whereby this basket could float and sink in the solution¹⁴. In order to observe the disintegration time, the basket was inserted in 0.1 N HCl medium at 37 ± 2 ° C for 2 hours then inserted in phosphate buffer medium pH 6.8 at 37 ± 2 ° C.

Brittleness Test

Capsule shells that have been filled with medicinal substances were placed in the box and pressed with 2 kg of weighing stone. Brittleness of the capsule was observed. 6 capsules were used for this test¹⁴.

Uniformity Test of Metronidazole's Capsule

The uniformity test was conducted by weighing 20 capsules at once and weighing the contents of each capsule one by one. Afterward, the empty shells of the 20 capsules were weighed. Then, the weight of the capsule contents and the average weight of each capsule's content were calculated¹⁴. The difference in the weight of the contents of each capsule to the average weight of each capsules contents shall not exceed

the limit specified in column A and for every two capsules, it should not exceed the specified weight in the column that showed in Table 1.

Table-1: Standardization of Capsule's Weight

Average weight	The difference in the capsule's physical weight (%)	
	A	B
120 mg	10	20
120 mg or more	7.5	15

RESULTS AND DISCUSSION

Isolation of Sodium Alginate from *Sargassum plagyophyllum* (Mertens) J.G. Agardh

Result of three different treatments showed that the average yield of sodium alginate from isolation fulfilled the standard of sodium alginate, which is > 18%. Characterization of sodium alginate was conducted by organoleptic test, pH determination, viscosity, moisture content, ash content, sodium hypochlorite level determination in the sodium alginate and infrared spectrum examination. The characterization result can be seen in table 2. Result of water content in sodium alginate is 11.45% (Table 2), this value was still within the allowed range of <15%; hence the water content of sodium alginate still meets the quality standard. A constituent of sodium hypochlorite in sodium alginate was 3.36% (Table 2) while the requirement of sodium hypochlorite which can be used is 3-6%¹⁵.

Table-2: Result of Characterization of Sodium Alginate

Quality Parameters	Na-alginate isolation results	Standard quality of Na-alginate
Organoleptic:		
Smell	No smell	No smell
Flavor	No taste	No taste
Color	Ivory	White- ivory
pH	8.1	3.5 – 10
Viscosity	63.1 cps	10 - 5000 cps
Water content	11.45 %	< 15 %
Ash content	21.61 %	18-27 %
Sodium hypochlorite level	3.36 %	3-6 %

Sodium alginate's isomer in the functional group of the isolated product compared to the manufactured sodium alginate can be seen in Fig.-1 and Table-3. It showed that sodium alginate from the isolation process has a similar pattern of peaks and wavenumbers with factory-made sodium alginate. Therefore, the result of the isolation can be expected to be an alginate compound.

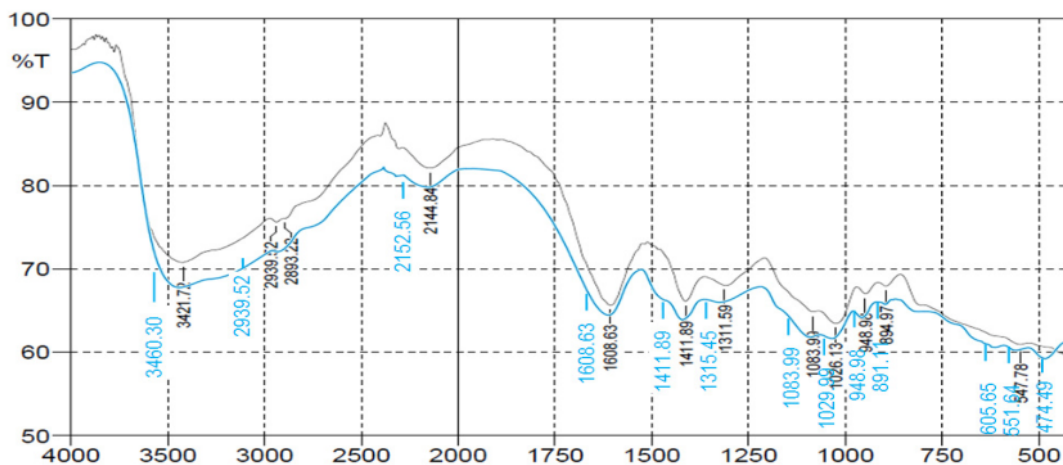


Fig.-1: Infrared Spectra of isolated Na-alginate (patent), Blue Color: Na-alginate isolation of Insulation Results, Black Color: Na-alginate Factory (patent)

Table-3: Infrared Spectrum Data of Sodium Alginate as a Result of Insulation and Sodium Alginate (patent)

Wave Numbers (cm ⁻¹)		Interpretation of Functional Groups	Reference Range of Wave Numbers (cm-1)
Results of isolation	Patent		
3460.30	3421.72	Hydroxyl (O-H)	3500 – 3200
1608.63	1608.63	Carbonyl (C=O)	1600 – 1680
1083.99	1083.99	Carboxyl (C-O)	1000 – 1300
1029.99	1026.13		
1411.89	1411.89	Na in alginate isomers	1400 – 1650

Isolation of Hemicellulose from Corn Cobs' Waste

The yield of isolated hemicellulose from 50 g corncob powder was 21%, the amount of hemicellulose obtained in this study, which was quite high.

Absorption Results of infrared spectrophotometer showed that the functional groups present in hemicellulose cobs of isolated products (Fig.-2 and Table-4) were similar to the functional groups found in corncob's hemicellulose.

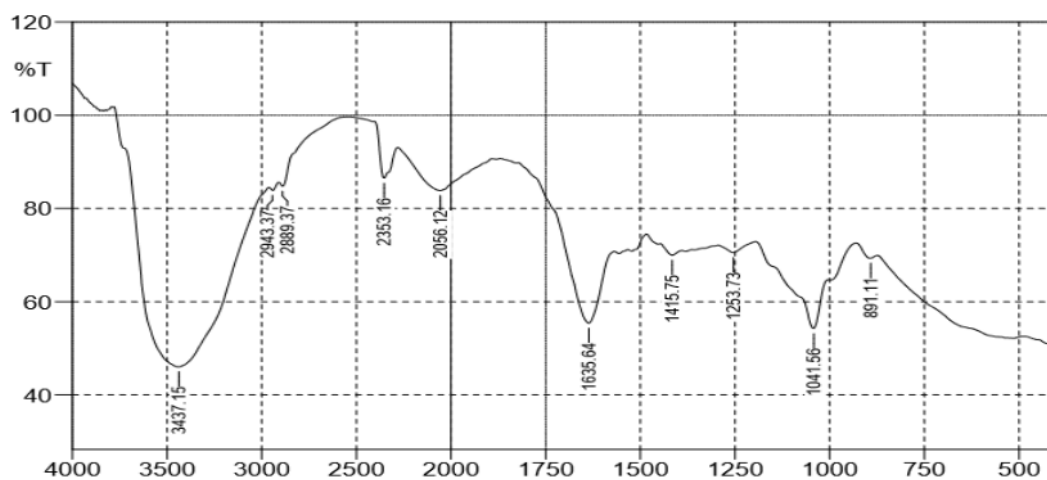


Fig.-2: Infrared Spectra of Corn cobs' Hemicellulose

Table-4: Data Interpretation of Hemicellulose FTIR Corn Cob

No.	Graph FTIR in this Research	
	Wavelength	Functional Groups
1	3437.15 cm ⁻¹	OH
2	2943.37 cm ⁻¹	CH
3	1635.64 cm ⁻¹	C=O
4	1041.56 cm ⁻¹	C-OH
5	891.11 cm ⁻¹	C-C

Capsule's Production of Hemicellulose from Corn Cobs Combine with Alginate

The viscosity result of formula 1, 2, 3, and 4 solutions were 520, 567, 579, and 598 cps, respectively (Table-5). It showed that different formulation resulted in different viscosity because hemicellulose's concentration in each formula is different; where the highest viscosity was found in the solution with the highest concentration of hemicellulose. Viscosity differences in the solution will affect the thickness of the capsule shell.

Table-5: Result of Viscosity Measurement

No.	Sample	Viscosity (cps)
1	Formula 1	520
2	Formula 2	567
3	Formula 3	579
4	Formula 4	598

Determination of Capsule's Shell Specification

Determination of the capsule's shell specification includes measurement of length, diameter, thickness, and color of the capsule shell. The result of each formula could be seen in the following table:

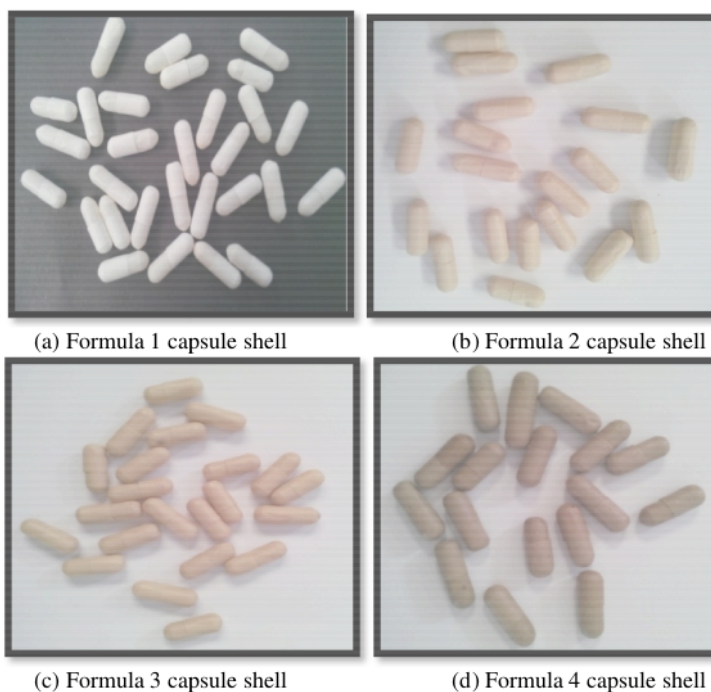


Fig.-3: Picture of Capsule's Shell for each formula

Disintegration Time Test

Result of the average disintegration time for each formula were 17,66 minutes (F1), 24,33 minutes (F2), 27,33 minutes (F3) and 29,66 minutes (F4). It showed that the best formulation for pharmaceutical's drug release was a formula which contains hemicellulose corn cob combination of sodium alginate with ratio 3: 1. This formula increased the disintegration time of capsule when compared with the positive control group (F1). It showed that the combination of sodium alginate with hemicellulose could decrease the solubility of the capsule's shell in gastric juice.

Brittleness Test

Result of brittleness test from 6 capsule shells showed that all of them were not brittle. It indicated that the moisture content of the capsule shell was still within the standard's range of moisture content (Table-7).

Table-6: Result of Capsule's Shell Specification

No	Specification	F(1)	F(2)	F(3)	F(4)
1	long(mm)	18.41	18.5	18.33	18.33
2	Diameter (mm)	6.5	6.5	6.5	6.5
3	violent (mm)	0.18	0.25	0.27	0.29
4	Color	White	Cream	Light brown	brown

Table-7: Result of Brittleness Test for each Formula.

No	Sample	Amount of Tested Capsule	Amount of Brittle Capsule	Percentage of Moisture Content
1	Alginate	6	0	22.48
2	Hemicellulose - alginate 1: 1	6	0	23.07
3	Hemicellulose - alginate 2: 1	6	0	24.02
4	Hemicellulose - alginate 3: 1	6	0	23.01

Uniformity of Capsule Shell Weight

The uniformity test was performed on the capsule's shell from Formula 1, 2, 3 and 4. Based on the weigh of 20 capsule shells of each formula, the percentage of capsule shell weight is shown in Table 8.

Table-8: Result of Uniformity Test

No.	Sample	Average Weight (mg)	% Difference in Weight of the Capsule		Standard Difference in Capsule Weight (%)	
			A	B	A	B
1	Formula 1	55.1	4.6	4.4	10	20
2	Formula 2	55.8	5.1	5.3	10	20
3	Formula 3	57.4	3.3	3.4	10	20
4	Formula 4	58.8	2.8	2.4	10	20

It showed that the capsule shells of formulations 1, 2, 3 and 4 meet the requirements of weight uniformity tests because the weight difference of each capsule's shell does not exceed the specified weight in column A and every two capsule shells also do not exceed the specified weight in column B.

CONCLUSION

The yield of hemicellulose obtained from 50 g of corncob powder (*Zea mays L.*) was 10.55g (20%). The yield of sodium alginate from 50 g of brown algae isolation (*Sargassum plagyophyllum*) was 10.57g (21.14%). Based on FTIR test, the structure of hemicellulose from corncob has the same structure with the control group's structure. The characterization of sodium alginate showed 8.1 pH; viscosity is 63.1cps, sodium hypochlorite 3.36%, and FTIR's result displayed the same structure between isolated sodium alginate and standard. Result of capsule shells specification showed that the best combination of hemicellulose with alginate was 3: 1 (F4), which is 18.33 mm in length, 6.5 mm in diameters, the weight of capsule's shell is 54.13 mg, brown color and has volume 0.678 ml. Based on the brittleness test, there was no fragile capsule in F4. The disintegration time test of F4 was 29.66 minutes, and the average weight of the capsule shell was 3.8542 g.

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