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RESEARCH ARTICLE

Effect of Pregelatinization on Suweg Tuber Starch (Amorphophallus Paeonifolius) as Tablet Crusher

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Abstract

Background: Disintegrant tablet from starch is more often used to crush the tablet that has been swallowed. However, the material of this starch is tablet crusher which very weak. In contrast to the suweg starch (Amorphophallus paeonifolius) which has undergone pregelatinization where the content of amylose and amylopectin and the water absorption capacity that is high enough so that it can crush the tablet quickly. The aim of this study was to determine the influence of pregelatinization towards elephant foot yam (*Amorpophallus paeonifolius)* starch as disintegrant against tablet physical quality profile of the Paracetamol tablet. Method: The research was carried out by making suweg natural starch which then it made a suspension in the water with a concentration of 20% and heated to the temperature of 60 ± 5 0C and 70 ± 5 0C within 15 minutes. After the suweg pregelatin starch has been made, then a paracetamol tablet and a qualitative examination also made which includes the determination of the paracetamol infrared spectrum, the examination of moisture content, the testing with iodine, the testing with optical microscopy, X-ray diffraction analysis, the starch thermal analysis with DTA, and the examination of swelling power which then compared to each tablet formula made by the wet granulation method. after that, it was continued with the examination of the granule quality, including the examination of moisture content, the examination of granule particle size and number of fines, the examination of flow velocity and rest angle of the granule. Moreover, it was carried out an evaluation of the paracetamol tablet physical quality in the form of hardness test, friability test, and disintegration time test. The data obtained was further analyzed by One Way ANOVA. Result: Tablet formula with pregelatinization of suweg natural starch can reduce the hardness, increased the tablet disintegration time, and made no difference in friability compared to the formulas containing natural suweg tuber starch and SSG. The result of increased disintegration time was then compared with the result of the swelling power test, but did not indicate a correlation both of them. The different of disintegration was not showed a correlation with values of swelling power.

Keywords: *Suweg Tuber Starch, Starch Pregelatinization, Pregelatinized Starch Tablet.*

Introduction

One of the most common forms of essential drug preparation today is tablet [1]. Tablet is available in various forms and is used orally [2]. The composition of additional material for the tablet serves as a crusher (disintegran). This material helps the crushing of the tablet has been swallowed which is expected as soon as possible the tablet can be dispersed so that the active material immediately give the pharmacological effects [3].

The most common used disintegrant tablet is starch (Kementrian Kesehatan Republik Indonesia, 2014). Starch is used as a crusher because of the swelling characteristic of starch granule in the water [5]. Starch in the natural form is produced by the tubers and has not undergone the changes in physical and chemical trait. Natural starch in the pharmaceutical industry is often used as filler and binder in the production of tablets, pills and capsules [6, 7]. However, as disintegrant, natural starch has the disadvantage of not being able to swelling and dispersing in the water at room temperature to cool temperature so that the effectiveness of using it as a crusher is very weak [3]. So it needs for modification of starch that will be used as disintegran. One of them is starch modification with gelatinization process. The main

characteristic obtained by starch after the gelatinization process are increased development capacity, solubility and disperse in the cold water [8]. Pregelatin starch has been available on the market, but so far only made from the starch of corn, potatoes and rice. In this research, the starch which will be used as a tablet disintegran is suweg (Amorphophallus paeonifolius). Suweg tuber is widely developed and consumed in Southeast Asian countries such as India, the Philippines, Malaysia and Indonesia [9]. Suweg tuber starch such as starch in other types of tubers, also contain of amylose and amylopectin. The amylose content in suweg tuber is 45.75% (w / w) with amylose and amylopectin content of 18.3% and 81.7% compared to the weight of other starches [10].

In addition, suweg tuber starch has a high water absorption capacity of 2.69 g / g. With the high absorption ability, it is expected that suweg tuber starch can become a new innovation as tablet crusher material and is modified to increase other characteristic that can support it. Based on this, the aim of this research was to determine the potential of pregelatin suweg tuber starch as a disintegrant and its effect on the physical quality of paracetamol tablet.

Methodology

In this research a laboratory experimental research was carried out on the potential of pregelatin suweg tuber starch as crusher on the physical quality of paracetamol tablet. The materials used in this research were Suweg Tuber Starch, Aquadest, Paracetamol, Avicel PH 101, Lactose, PVP K-30, Sodium Starch Glycolate, Mg Stearate, and Talk. While the instruments used in this research were the instrument of thermal analysis test such as Different Thermal Analysis, Diffractometer XRPD Phillips Xpert Netherland, drum dryer, optical microscope, Perkin Elmer Instrument FT-IR spectrophotometer, Retsch Vibrator 3D vibrator, Natoli NPRD10A tablet printer, tablet hardness test instrument (Erweka TBH 220 Hardness Tester, tablet friability test instrument (Erweka TAP 31914 Friability Tester), and tablet disintegration test instrument (Erweka Disintegrator Type ZT 501). The independent variable used in this research was the pregel critical point, namely the heating temperature.

The temperature used was 60 ± 5 0C and 70 ± 5 0C, with a heating time of 15 minutes. This was carried out to find out the best temperature for pregelatinization of suweg tuber starch related to its effect on physical quality, especially paracetamol tablet time.

Table 1: The Differences of Temperature and Time Pregelatinization.

Pregelatinzation	Temperature	Time
PPS 1	60±5 0C	15 minute
PPS 2	70±5 0C	15 minute

Note: PPS = Pregelatin Suweg Starch

The paracetamol tablet formula which was planned contained of 500 mg of paracetamol with the different material types of crusher used. It was made as many as 60 tablets. The formula can be seen in Table 2.

Table 2: Design of Paracetamol Tablet Formula

Material Name	Material Function	F1 (mg/tab)	F2 (mg/tab)	F3 (mg/tab)	F4 (mg/tab)
Paracetamol	Active Material (76, 92%)	500	500	500	500
Avicel PH101	Filler (15, 33%)	59,775	59,775	59,775	59,775
Lactose	0,6 : 0,4	39,85	39,85	39,85	39,85
PVP K-30	Binder Material (2%)	13	13	13	13
PAS	Disintegrant (4%)	26			
PPS 1			26		
PPS 2				26	
SSG					26
Talk	Glidan (1%)	6,5			
Mg Stearat	Lubrikan (0.75%)	4,875			
Aquadest	Wetting Agent	qs	qs	qs	qs
Tablet Weight		650	650	650	650

Explanation:

PAS is a Natural Starch of Suweg Tuber,

PPS 1 is Suweg Tuber Pregelatin Starch with heating temperature of 60 ± 2 0C,

PPS 2 is Suweg Tuber Pregelatin Starch with heating temperature of 70 ± 2 0C.

The research was conducted by making suweg natural starch. Then suweg tuber starch was made a suspension in water with a concentration of 20% (as a result of optimization). The starch suspension was heated according to the design of the research with a temperature of 60 ± 5 0C and 70 ± 5 0C within 15 minutes on the water heater.

After the suweg pregelatin starch has been made, then it was carried out the production of paracetamol tablet and qualitative examination of research material, namely: determination of the paracetamol infrared spectrum, examination of moisture content, testing with iodine, testing with optical microscopy, X-ray diffraction analysis, starch thermal analysis with DTA, and examination of swelling power.

Determination of the paracetamol infrared spectrum was made by the KBr disk method. Examination of moisture content was performed on the PAS, PPS 1 and PPS 2 with the Moisture Analyzer by replicating 3 (three) times. Testing with iodine was carried out by dripping the starch with a little iodine.

Testing with an optical microscope was performed to determine the amylose form of suweg tuber starch at 40x and 100x magnification. X-ray diffraction analysis was performed on the PAS, PPS 1, and PPS 2 by observing samples between 2 θ from 4^o to 30^o using the Diffractoeter XRPD Phillips Xpert Netherland tool. Starch thermal analysis with DTA was used to determine the starch melting distance which can be compared later with the starch after modification. Swelling power examination (developmental strength) using the swelling power formula [11].

After conducting a qualitative examination of the material, continued with the examination of the granule quality. The examination of the granule quality carried out with the examination of moisture content; the examination of granule particle size and number of fines; the examination of the flow velocity and rest angle of the granule.

Moisture content examination was carried out on the suweg tuber pregelatin starch using the Moisture Content Analyzer.

Examination of granule particle size and number of fines was carried out with a vibrator along with a standard sieving set. Examination of the flow velocity and rest angle of the granule was carried out directly using a funnel by placing the funnel on the stative with the distance of the bottom end of the pipe to a flat plane of 10.0 ± 0.2 cm.

Besides the examination of research material quality and granule quality, an evaluation of the paracetamol tablet physical quality was also carried out. This examination was carried out with a hardness test, friability test, and a disintegration time test. Tablet hardness examination was carried out with the Erweka TBH 220 Hardness Tester by turning on the instrument and testing 10 tablets and noted the hardness of the tablet that was read. Examination of the tablet's friability was carried out with the Erweka TAP 31914 Friability Tester.

Examination of the disintegration time of the tablet was carried out using the Erweka Disintegrator type ZT 501. Each data from the research were carried out an evaluation of the tablet physical quality (hardness test, friability, and disintegration time of the tablet) and were analyzed statistically by the One Way ANOVA method.

This design was used to find out whether there were significant differences between the F1, F2, F3, and F4 formulas by looking at significant prices (sig.). If the price was sig. <0.05 it meant there was a significant difference between formulas and if the price was sig. > 0.05 can be interpreted that there was no significant difference between formulas.

If the result showed a significant difference, the test was continued with a one-way ANOVA tiered test with the Tukey-HSD test method because the number of treatment groups was more than 3 (three) so that it was obtained how many the formula data which showed a significant difference.

If the price was sig. <0.05 it meant that there was significant difference among formulas with one another and if the price of sig. > 0.05 can be interpreted that there was no significant difference between formulas.

Result

Material Qualitative Examination

Paracetamol Infrared Spectrum Examination Result Infrared spectrum examination aimed to analyze the accuracy of the material content according to the standard or literature. The result of the paracetamol spectrum examination showed as follows:

Table 3: The Results of Paracetamol Spectrum Examination

Examination	Observation	Literature
Cluster Infrared Spectrum Identification:	Paracetamol Material	Standard Paracetamol (BPFI)
C=O	1650	1656
N-H	3291	3162
O-H	3489	3326

Besides the infrared spectrum examination, another test that can determine the accuracy of the material was the thermal analysis of the melting point determination.

Moisture Content Examination Result

The examination of moisture content was carried out on the suweg natural starch (PAS), starch pregelatin 1 (PPS 1), starch pregelatin 2 (PPS 2), because of the involvement of water and the existence of drying process in making this material. Moisture content examination result showed the consecutive numbers for the material was 4.30%; 7.41%; 7.13%.

Test Result with Iodine

PAS test result with iodine showed a change in color to purple after the material added 2 drops of iodine. Test images can be seen in Figure 1.

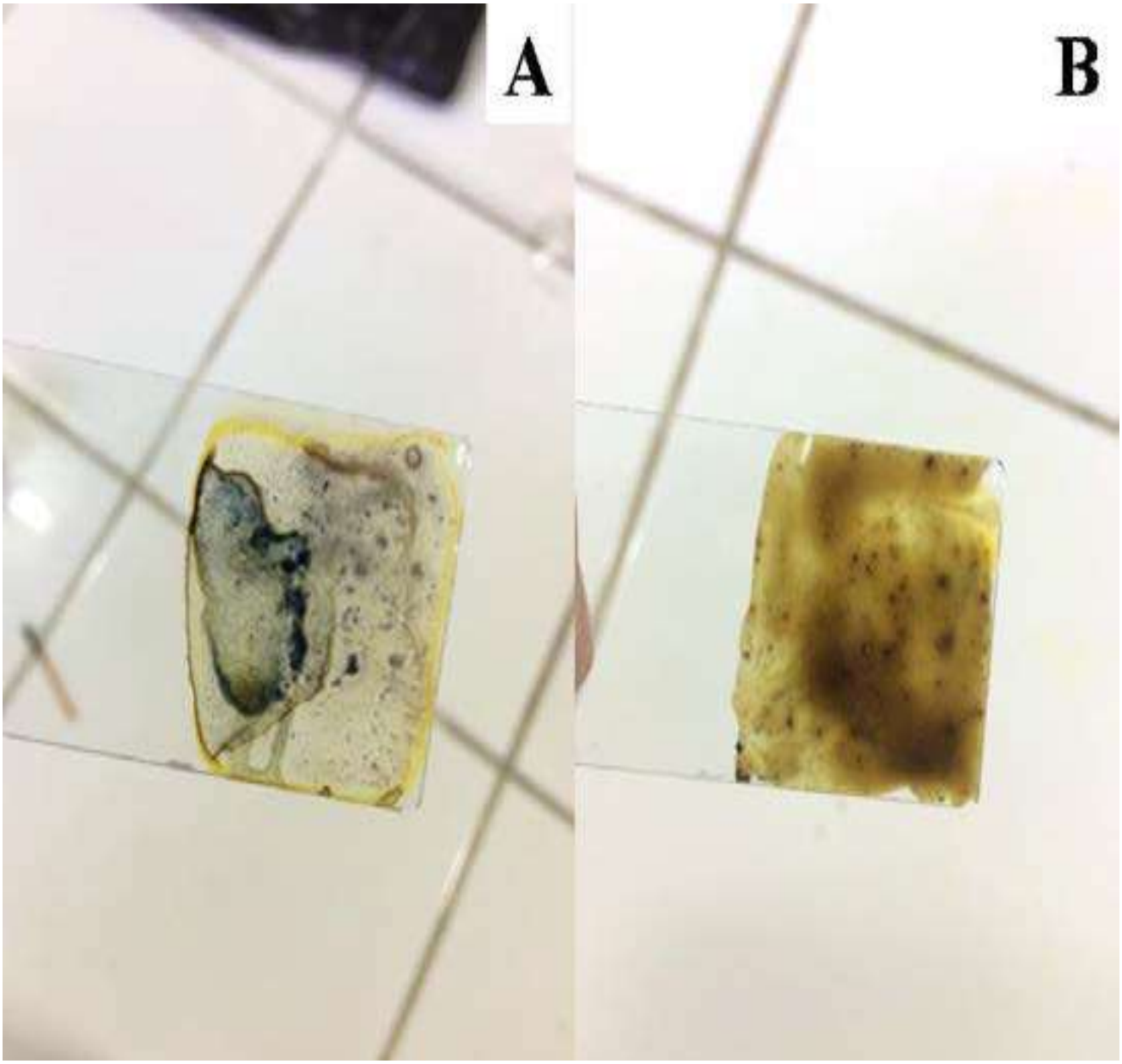

Figure 1: PAS test result with iodine (A) PAS + iodine, (B) PAS + iodine after heating

Microscopy Observation Result

Microscopy observation result of PAS, PPS 1, and PPS 2 showed the presence of hilum. The result can be seen in Figure 2.

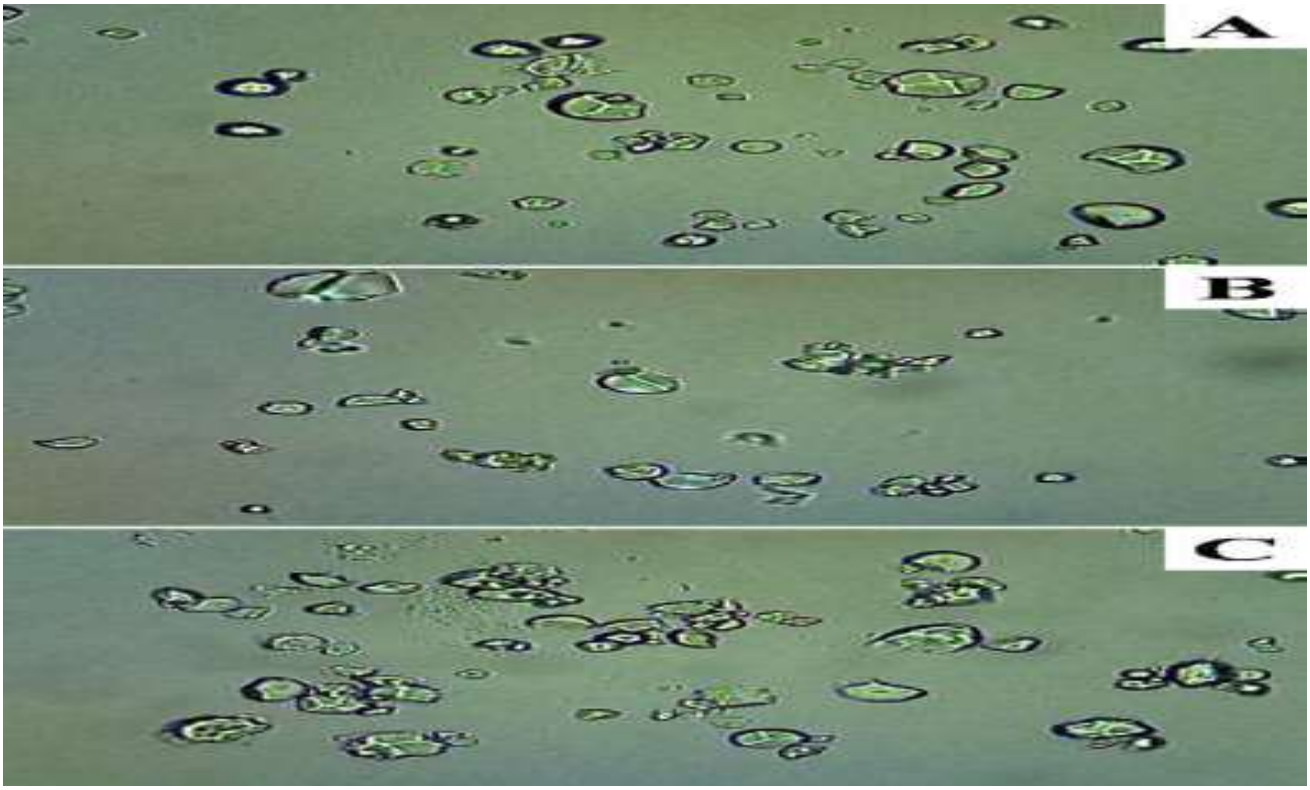

Figure 2: Microscopy observation result (A) PAS, (B) PPS 1, and (C) PPS. 400x magnification

X-ray Diffraction Analysis Result

X-ray diffraction analysis conducted on PAS, PPS 1, and PPS 2 materials showed several peaks in the following position:

Table 4: Results of X-ray Diffraction Analysis

Material	Position 2θ (o)	Intensity
PAS	15.0490	150.24
	17.0879	197.04
	17.9837	189.81
	22.9879	158.93
	38.3764*)	30.21
PPS 1	11.3740*)	13.99
	15.1825	149.89
	17.2579	195.15
	18.2658	163.60
	23.1606	169.64
PPS 2	15.1975	196.28
	16.9958	245.66
	18.2893	216.10
	23.1151	180.96
	26.5370*)	30.78

*) peak difference in diffractogram result

Thermal Analysis Result

Thermal analysis used the Differential Thermal Analysis instrument showed the melting points consecutively of PAS, PPS 1, PPS 2 and paracetamol were 149.0 0C; 145,0 0C; 134,5 0C and 170,9 0C.

The result of paracetamol material melting point in accordance with the literature was USP 30, which stated that the melting distance of paracetamol was 168-172 0C.

Swelling Power Test Result

Swelling power test result from PAS, PPS 1, PPS 2 and Sodium Starch Glycolate consecutively were 13.45 ± 0.05 (%), 13.89 ± 1.46 (%), 11.65 ± 1.34 (%), 34.51 ± 0.24 (%).

IPC Check (In Process Control)

In making paracetamol tablet using the wet granulation method, the powder mass was added with the binding solution to produce granules.

IPC in tablet making was a granule evaluation which was carried out to obtain mass of granule that have good characteristic and meet the requirement in accordance with the literature. Granule evaluation included distribution of granule size/ number of fines, moisture content/ MC, flow characteristic, and rest angle.

Table 5: IPC Granule Examination Result

Examination	Formula 1	Formula 2	Formula 3	Formula 4
Moisture Content (%)	1,39 ±0,19	1,73 ± 0,03	1,71 ± 0,08	1,22 ± 0,11
Particle Size Diameter (µm)	326,85	398,48	382,80	246,65
% fines	4,32	2,32	2,32	8,17
Flow Velocity (gram/second)	17,60	14,79	14,50	19,48
Rest Angle (o)	24,99	27,75	28,92	13,76

The result showed that all four formulas met the requirement of granule with a moisture content <2%. The moisture content must not be too high or too low. Moisture content that was too high will cause the material to adhere to the die and punch surface. Whereas moisture content that was too low will cause friability (Lachman et al., 1987).

The measurement test for granule particle size distribution needed to be carried out to make sure the number of fines in the granule mass. A granule mass was stated as good if the number of fines was <20% of the total weight of the granule (Remmington, 1975). The data obtained showed that all four formulas have met the requirement. These results can be observed that all four formulas have good granule flow characteristic. Judging from the price of the rest angle, according to the United State Pharmacopeia (USP), if the rest angle was <300, the flow characteristic was very good. The flow velocity of 14-20 g/sec was interpreted to have good flow characteristic of more than 10g/sec (Siregar and Wikarsa, 2010).

Physical Quality Examination of Paracetamol Tablet

Physical quality examination which carried out included hardness, friability and tablet disintegration time. Examination result and physical quality profiles can be seen in Table 6.

Table 6: The Result of Physical Quality Examination of Paracetamol Tablet

Examination	Formula 1	Formula 2	Formula 3	Formula 4
Hardness (kP)	6,29 ± 0,58	4,98 ± 0,28	4,53 ± 0,23	5,17 ± 0,52
Friability (%)	0,19 ± 0,18	0,37 ± 0,04	0,36 ± 0,12	0,17 ± 0,02
Disintegration Time (second)	45,89 ± 7,21	37,16 ± 4,37	25,74 ± 2,73	48,56 ± 4,20

Explanation:

F1 uses crusher (4%) that is PAS

F2 uses crusher (4%) that is PPS 1

F3 uses crusher (4%) that is PPS 2

F4 uses a destructive agent (4%) that is Sodium Starch Glycolate.

Data from the examination of the paracetamol tablet physical quality test was analyzed statistically by the analysis of variant (ANOVA) method. Analyzes were performed at a confidence level of 0.95 (α = 0.05). The test continued with the Tukey HSD test which formula was different. The following was the result of statistical analysis of hardness, friability, and disintegration time of the tablet with the HSBC TDE test (sig. Price) can be seen in Table 7.

Table 7: The Result of Statistical Analysis of Hardness, Friability, and Disintegration Time of the Tablet by the HSE Tukey Test (sig. Price)

Test	Formula	Formula 1	Formula 2	Formula 3	Formula 4

Hardness	Formula 1		+	+	+
	Formula 2	+		-	-
	Formula 3	+	-		+
	Formula 4	+	-	+	
Friability	Formula 1		-	-	-
	Formula 2	-	-	-	-
	Formula 3	-	-	-	-
	Formula 4	-	-	-	-
Disintegration Time	Formula 1		+	+	-
	Formula 2	+		+	+
	Formula 3	+	+		+
	Formula 4	-	+	+	

Note: (+) there is a significant difference between formulas
(-) There is no significant difference between formulas.

In the data analysis of the tablet hardness test result, a significant difference was showed by the price of sig. <0.05. The analysis result data of the tablet hardness value showed the price of sig. 5,521 x 10-10 <0.05. This indicated that there was a significant difference in the tablet hardness between formulas. For the analysis result of the tablet friability test, the price of sig. obtained 0.282> 0.05 which showed no significant difference between formulas. While the statistical analysis result of the disintegration time data the four formulas obtained sig price of 3,711x10-7 <0.05 which meant that there was a significant difference in the disintegration time tablet between formulas.

Discussion

PAS test result with iodine showed a change in color to purple after the material added 2 drops of iodine. This was in accordance with the theory that starch was not dissolved in the water and in the starch analysis, gave a blue color with iodine [12]. This study was aimed to determine the effect of pregelatinization of suweg tuber natural starch on the physical quality of tablet, namely hardness, friability, and disintegration time which were then compared with a formula containing commercial destructive material namely Sodium Starch Glycolate.

This was carried out by making the formula of paracetamol tablet as active material with the same additive and concentration material except the type of crusher, namely suweg natural starch, suweg tuber pregelatin starch (two types), and sodium starch glycolate (which called SSG). Tablet was made by the wet granulation method.

The thing which was done before the making of paracetamol tablet was making suweg natural starch (Amorphophallus paeniifolius) and making suweg pregelatin starch.

This was carried out by precipitating the starch from grated suweg tuber which then was washed until white and dried at a temperature of 70 0C to dry. Pregelatin starch was made as many as two types namely pregelatinization at 60 ± 5 0C (which was then called PPS 1) and 70 ± 5 0C (which was then called PPS 2) with a heating time of 15 minutes. Pregelatin starch was dried using a 65 ± 5 0C drum dryer with a speed of 10 rpm to dry.

Natural starch (which was then called PAS) and pregelatin starch that has been made, then it was carried out qualitative analysis and formulated as a crusher material in several different formulas. Qualitative analysis of iodine on the natural starch showed the change in color to blue which proved that the material was the starch and contained of amylose [12].

The result of microscopy analysis showed that the starch contained of hilum from starch. Besides the two tests above, PAS also analyzed x-ray diffraction in the angular range of 2θ 4-300, thermal analysis with the Different Thermal Analysis (DTA) and the swelling power test whose result will be

compared with similar analysis on pregelatin starch.

The diffractogram display between PAS with PPS 1 and PPS was quite similar but it appeared that some peaks which have different intensities 2. The difference was seen in PAS diffractogram which appeared

small peak at an angle of 38.37o with an intensity value of 15.33% which did not appear on the other diffractograms. While the PPS 1 diffractogram appeared new small peak at an angle of 11.370 and 26.730 with intensities of 7.17% and 12.07%, and on the PPS 2 diffractogram appeared new small peak at an angle of 26.530 and 30.280 with intensities of 12.53 and 9.22.

Other result that appeared was strong peak that have an intensity of up to 100% was seen to shift slightly between PAS, PPS 1, and PPS 2 i.e. consecutively at an angle of 17,080; 17,250; 16,990. It illustrated that there was a change in the crystalline structure and amorphism in starch with the process of pregelatinization [13].

Another analysis conducted on the material was the thermal analysis. The result of thermal analysis with DTA gave the melting point price of PAS, PPS 1, and PPS 2 consecutively was 149,0 0C; 145,0 0C; and 134,5 0C which showed a decrease of melting point.

Heating with the excess water during the pregelatinization process, the amorphous (amylose) portion of the starch absorbed the water and swelled which result in breaking of the crystalline bond so that it was decreasing the melting point [14]. Decreased melting point between PPS 1 and PPS 2 can be caused by the changes in the loss of intermolecular interaction and the starch granular structure as a whole with the higher heating temperature in the water.

This can also be seen from the PPS 2 thermogram which looked more sloping than other material thermo grams. Swelling power test result showed that PAS has a lower swelling power than PPS 1 but was higher than PPS 2 with consecutively result of 13.85; 13.89; and 11.65. The tablet physical quality test was carried out on each formula, namely the test of hardness, friability, and disintegration time.

In the hardness test result, the average hardness data obtained from formula 1 to formula 4 tablets was 6.29 ± 0.58 kP; 4.98 ± 0.28 kP; 4.53 ± 0.23 kP; and 5.17 ± 0.52 kP. The data obtained met the requirement of tablet hardness (4-8 kP). The average hardness of the formula containing pregelatin starch-crusher material, its hardness price has decreased, but the decrease was not too significant.

This was probably due to the differences in the value of its swelling power where the pregelatin starch has a greater swelling power so that it can hydrate the water which added with the binder and provided an influence on the bond strength that formed between the granules of the tablet. The data obtained was statistically analyzed using the SPSS One Way ANOVA method between the hardness value of tablet for each formula and the sig price was obtained of 5,521 x 10-10 <0.05 which meant that there was a significant difference in the formula.

Statistical testing was continued with multiple comparison Tukey method to find out which formulas had significant difference between them. The formula that showed the difference was formula 1 to the formula 2, 3, and 4. Formula 3 showed the difference with formula 4 but the comparison of other formulas did not show any significant difference in the price of its tablet hardness. The friability test result of the four formulas consecutively was 0.19 ± 0.18%; 0.37 ± 0.04%; 0.36 ± 0.12%; and 0.17 ± 0.02 that met the requirement in the United States Pharmacopeia (USP), i.e. friability was not more than 1%.

The average friability of the formula containing pregelatin starch crusher material, the percent price of its friability was decreases/ was less friable as the pregelatin temperature rises, but the decrease of the hardness was not too significant. The data obtained was statistically analyzed using the SPSS program One Way ANOVA method between the friability values of tablet for each formula, the sig price was obtained of 0.282> 0.05 which meant there was no significant difference in the formula. The disintegration time test result of the four formulas consecutively was 45.89 ± 7.21 second; 37.16 ± 4.37 second; 25.74 ± 2.73 second; and 48.56 ± 4.20 second. The data met the USP criteria which was no more than 15 minutes.

If you look at the average, the formula containing pregelatin starch crusher material, the price of its disintegration time was decreases by the pregelatin process and the increases of its pregelatin temperature. This was in accordance with the hypothesis, namely the pregelatinization of starch used as a crusher material which has the effect of accelerating the disintegration process.

Tablet disintegration time with pregelatin starch was lower than the natural starch between sorghum tuber, corn, and plantain [5]. The data obtained was analyzed statistically using the SPSS program One Way ANOVA method between the value of the disintegration time of tablet for each formula and obtained the sig prices of 3,711x10-7 <0.05 which meant that there was a significant difference in the formula.

Statistical testing was continued with multiple comparison Tukey method to find out which formulas had significant difference between them. The test showed a significant difference except between the formula 1 and formula 4. The physical quality result of the tablet showed that the tablet with pregelatin starch had low hardness and a high percent friability compared to the formulas containing natural starch and sodium starch glycolate.

This can happen because the pregelatin starch has a change in crystallinity as seen from qualitative analysis of X-ray diffraction and pregelatin starch thermogram. As a crusher material, the physical quality which was the most concerned was the tablet ability to disintegrate quickly.

The formula that has the fastest disintegration time was the formula 3 which contained PPS 2. The other mechanism that may occur in this disintegration process was porosity and capillary action (wicking). The porosity of the tablet provided a way for the liquid to enter the tablet. Liquid that entered through the pathway broke the bond between granule particles to break the tablet. Generally the crusher with this mechanism has poor compressibility [15]. This can be seen from the average value of the hardness and friability of formula 3 with the PPS 2 crusher material, which has the fastest disintegration time, smaller compared to the other formulas.

Conclusion

From the result, the formula containing pre-gelatinized starch decreases hardness, increases the disintegration time of tablet, and made no difference in friability compared to the formula containing suweg tuber natural starch and SSG. As for the price of swelling power did not correlate with the decreasing of disintegration time so that further research was needed regarding the disintegration mechanism of pregelatin starch.

Based on this, further research was needed regarding the disintegration mechanism of pregelatin starch, the influence of the pregelatinization process duration, and the effect of pregelatin starch concentration in the tablet to determine its effect on physical quality (hardness, friability, and disintegration time) on the tablet.

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