Journal of Research in Pharmacy

Research Article

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Reworking potential of *Cassava starch* as a binder in the production of paracetamol tablets using wet granulation method

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Received: 7 September 2024 / Revised: 16 December 2024 / Accepted: 21 December 2024

ABSTRACT: Paracetamol is a drug that is commonly used as an analgesic and antipyretic. In the pharmaceutical industry, tablets are usually produced in large quantities, and it's possible to find tablets that don't fulfill the quality standards after testing their physical properties, including hardness, friability, and disintegration time. One of the excipients in tablets that may affect them is the binder, which in this study used cassava starch in two different concentrations. This study was pure experimental research using a two-way completely randomized research design to determine the effect of repeated compression on the potential of cassava starch as a binder with concentration levels, based on the mixture and paracetamol tablets characteristics, which is done by crushing tablets that had been compressed to test the physical properties of the mixture and tablets. The data obtained were analyzed statistically with SPSS to check normality, then continued with TwoWay Anova if the data obtained were normally distributed or the KruskalWallis test for abnormal distribution. The results showed that repeated compression affected the mixture characteristics and tablet hardness. By analyzing the AUC of the compactibility test data, it was found that the reworking potential value was greater, which showed that cassava starch could maintain its quality as a binder after being recompressed twice.

KEYWORDS: *Cassava* starch; paracetamol tablets; reworking potential; wet granulation

1. INTRODUCTION

Tablet is a solid dosage form that is commonly used and widely available on the market compared to other dosage forms, because its use is quite convenient and simple, has accurate dosage, bad taste and odor can be masked by coating, and is relatively cheap and stable in storage, modifiable release profile, and easy handling. In general, tablets consist of active ingredients and excipients that play an important role in the quality of the tablets. Excipients can serve to protect, assist, support, and improve the stability and bioavailability of the preparation. In addition, excipients play a role in helping to improve the safety and effectiveness of the product during distribution and use [1].

Based on the manufacturing method, tablets can be prepared by direct compress and granulation method, both wet granulation and dry granulation methods. The main difference between the various methods can be observed based on the granule formation in wet and dry granulation, while the direct compress method allows some excipients to be compressed directly without any granulation process involved. Therefore, the quality pearls of active substances and excipients are required to have good flow properties and compressibility.

Paracetamol as a model active ingredient has poor flow characteristics and compressibility [2]. Therefore, a strategy that can be carried out to improve the characteristics of the flow properties is through granule formation to produce particles larger than the original powder particles [3]. Based on its properties that are heat and moisture resistant, and a large enough dose, the wet granulation method will be more suitable for paracetamol tablet formulation [4]. It is because when the moist mass is sieved and obtained granules, it needs to be dried in a drying cabinet at a certain hot temperature and then molded into tablets.

One of the excipients that plays an important role in uniting powder particles to form tablets properly and compactly is a binder. Binders can provide adhesion to the powder mass during granulation and direct

How to cite this article: Lestari ABS, Eliana R. Reworking potential of *Cassava starch* as a binder in the production of paracetamol tablets using wet granulation method. J Res Pharm. 2025; 29(5): 1918-1929.

https://doi.org/10.12991/jrespharm.1763611
ISSN: 2630-6344

compression. The smaller particle size may generally provide a stronger bond due to the increased surface area [5]. The criteria for selecting binders also need to consider compatibility with other tablet components, especially in terms of physicochemical properties [6].

In practice, amylum as an additive in tablet formulations is often used in the pharmaceutical industry due to its inert and non-reactive properties. Amylum is a carbohydrate derived from plants that contains amylose and amylopectin. One of the plants that produce amylum/starch is cassava. Cassava starch has better binding ability over other amylums such as corn or potato. The higher amount of amylopectin in cassava starch, about 83%, is capable of producing a colloidal solution that forms a sticky mass when heated so that it can improve the flow properties of amylum. Therefore, cassava starch is suitable as a binder in the wet granulation method because it can improve its poor flow properties and compressibility [7].

When carrying out the production process to fulfill the demands of the market, the pharmaceutical industry usually produces a large batch of products at one time to produce tablets in large quantities and in a relatively short time. However, it is not possible that the industry also experiences an obstacle in the production process, causing the tablet products produced to not fulfill the requirements. One thing that becomes an obstacle is the production cost, which is certainly not small. Therefore, the industry needs to think about how to reuse the product so that it does not suffer losses.

Reworking is one way to reprocess a product or batch to overcome quality problems or specifications that are not in compliance with established requirements. The reworking form carried out is the repeated compression process of paracetamol tablets seen from cassava starch as a binder that plays a very important role in being able to produce good quality tablets. Since there have been no studies found so far related to the potential of cassava starch binder if it is compressed repeatedly, it encourages researchers to see the effect of the repeated compression process on the potential of cassava starch as a binder that is given based on concentration levels, seen through the characteristics of the mixture and the quality of 300 mg paracetamol tablets made by wet granulation.

2. RESULTS AND DISCUSSION

2.1. Mixture's Flow Properties Testing

Granules that have met the requirements of good moisture are ready to be continued checking the flow properties. It was found that 18.229% (day I), 2.059% (day II) moisture content in formula 1 granules and 18.05% (day I), 2.238% (day II) in formula 2 granules. The drying temperature was set at 50°C [31]. The dried granules were then sieved first with a 12/50 mesh and added the outer phase in the form of adding lubricants and extragranular disintegrant. Flow properties testing of granule mixtures is important to ensure the consistency of the flow during pressing so that it can obtain uniform weight variation as well. Good flow allows ease in filling the compression chamber of the hopper at a constant volume. Poor flow can cause weight variation so that the active substance content in individual tablets may not be uniform.

Table 1. Result of Mixtures' Flow Properties

Flow Properties	Formula 1			Formula 2		
	I	II	III	I	II	III
Flow Rate (g/s)	44.8 ± 1.1	58.8 ± 0	65.3 ± 2.4	42.3 ± 1	61.3 ± 2.1	68.3 ± 2.7
Compressibility (%)	4.6 ± 0.2	6.5 ± 0.1	7.4 ± 0.5	2.3 ± 0.03	9.1 ± 0.5	5.7 ± 0.5

Numeric data presented as mean±SD, standard deviation

Formula 1 : Formula with 1.8% binder concentration Formula 2 : Formula with 2.0% binder concentration

I: First compression tablet, II: Second compression tablet, III: Third compression tablet

Based on Table 1, the results of testing the flow rate of the initial mixture, the first and second of formula 1, were respectively 44.8 g/s, 58.8 g/s, 65.3 g/s, while in formula 2, 42.3 g/s, 61.3 g/s, 68.3 g/s. The results showed that at 100 g, the tested mixture took less than 10 seconds to flow, thus already fulfilling the requirements of a good flow time and rate. The compressibility index is conducted to determine the feasibility of the mixture and whether it can be forged into tablets by looking at the compressibility after going through the pressing process. The mixture is free-flowing with a low compressibility index value, which indicates that the interaction between particles tends to be less significant. For mixtures with poor flow properties, the difference between bulk density and tapped density is large so the interaction between particles is even greater [26]. This is related to the porosity or space formed. According to Kovačević et al. (2024), it is said that there is an inverse relationship between the binder concentration and percent

compressibility index. The higher concentration of binder can produce a smaller compressibility index. This statement already matched with the result of this study.

Based on the test results of the index of fixation in Table 1, the values obtained in each formula for each compression were 4.6%, 6.5%, 7.4% for formula 1, and 2.3%, 9.1%, 5.7% for formula 2, respectively. Along with the increasing number of compressions, the value of the compressibility index is getting higher, but as the binder concentration increases, the results of the compressibility index are getting smaller. It can be explained due to the higher granule binding process that enables the spherical shape with a low number of fines. Therefore, the granule will have a greater weight force and when tapping the granule is easier to organize itself so it can produce a smaller compressibility index value which describes better flow properties.

However, there were results of the impermanence test between formula 1 and formula 2 that were higher as the concentration increased, especially in the first crushing mixture. It is known that can affect the test were the size and shape of the granule [8]. While crushing tablets, the crushing technique is hardly controlled so that every formula in each pressing can produce variations in granule size differences which leads to increased percent compressibility results. Based on the statistical data analysis results, both types of flow properties testing didn't obtain normally distributed data, so the Kruskal-Wallis test was continued which resulted in p-values <0.05, at 0.007 and 0.005, which concluded that the data had significant differences.

2.2. Tablet Compactibility Testing

Compactibility is defined as the ability of a granule to form a compact mass (solid) when applied to pressure. Compactibility testing parameters could be seen based on the tablet hardness produced. Tablets were pressed with regularly set top punch depth and a fixed bottom punch of 10 mm. Most of the mixtures that were pressed at a decrease in punch scale of 1 - 4 mm could not form tablets properly because the hardness was very low, thus causing these tablets to easily crumble and were very fragile when handled. In the compactability test, all tablets could be pressed with punch depths of 5 mm, 6 mm, and 7 mm, and only the first pressed tablet that had not been crushed could be pressed with a scale of 8 mm.

Table 2. Result of Compactibility Testing

Top Punch Scale Drop (mm)	Hardness (kP)					
	Formula 1			Formula 2		
	I	II	III	I	II	III
1	*	*	*	*	*	*
2	*	*	*	*	*	*
3	*	*	*	*	*	*
4	*	*	*	*	*	*
5	0.023±0.01	0.32±0.04	0.67±0.02	0.043±0.01	0.45±0.02	0.81±0.02
6	0.08±0.01	1.1±0.23	3.147±0.18	0.083±0.01	1.7±0.23	3.687±0.2
7	0.38±0.08	4.463±0.4	5.903±0.89	0.537±0.01	6.177±0.18	7.447±0.09
8	3.6±0.34	#	#	3.757±0.33	#	#
9	#	#	#	#	#	#

Numeric data presented as mean±SD, standard deviation
* : the mixture couldn't be compressed
\# : the mixture could be compressed, but the machine couldn't run normally
Formula 1 : Formula with 1.8% binder concentration
Formula 2 : Formula with 2.0% binder concentration
I: First compression tablet, II : Second compression tablet, III: Third compression tablet

Based on the compactibility test data in Table 2, the first compression tablet had smaller hardness than the second and third compression tablets or the first and second crushing results. Tablet compactibility in each formula increased along the repeated compression. It indicates that when the mixture of the compression results is forged with the same pressure it can form tablets well compared to the initial mixture. The increasing tablet hardness is due to the cavity or space between granule particles filled by the numerous fines from repeated tablet crushing. The statement was supported by research conducted by Wünsch et al. (2021), which states that the higher number of fines may affect the increase of compactibility. In addition, it can also be observed in the results of the compactibility test of formula 2 with higher concentrations of cassava amylum producing greater hardness that represents better compactibility. These results are in line with research conducted by Angelina and Lestari. (2024), repeated tablet compression will affect the

compactibility produced. The more number of compression tablets, the better compactibility will be, therefore by giving a minimum pressure, the ability to form granules into tablets can already produce tablets with optimum hardness [30].

2.3. Reworking Potential

According to Sun and Kleinebudde (2016), reworking potential can be expressed as the ratio of the area under the curve of a reworked tablet to the first pressed tablet in percent (%). AUC of the compactibility test and reworking potential are shown in Table 3 below.

Table 3. Result of AUC of the Compactibility Test and Reworking Potential

Description	Tablet					
	Formula 1			Formula 2		
	I	II	III	I	II	III
AUC of the Compactibility Test	0.3	3.9	6.5	0.4	5.6	8
Reworking Potential	-	13	21.7	-	14	20

Formula 1 : Formula with 1.8% binder concentration Formula 2 : Formula with 2.0% binder concentration

I: First compression tablet, II: Second compression tablet, III: Third compression tablet

Based on Table 3, it can be observed that the results of AUC of the compactibility test and reworking potential are directly proportional as the number of compressions increased. The AUC of the compactibility test and reworking potential values were increased when the tablets were reworked. Based on these results, it can be argued that cassava starch as a binder can maintain its quality when experiencing the recompression process twice, considered by the results of the compactibility test which states hardness as a parameter. Then, AUC of the compactibility test for each formula can be seen in Figures 1 (Formula 1) and Figures 2 (Formula 2).

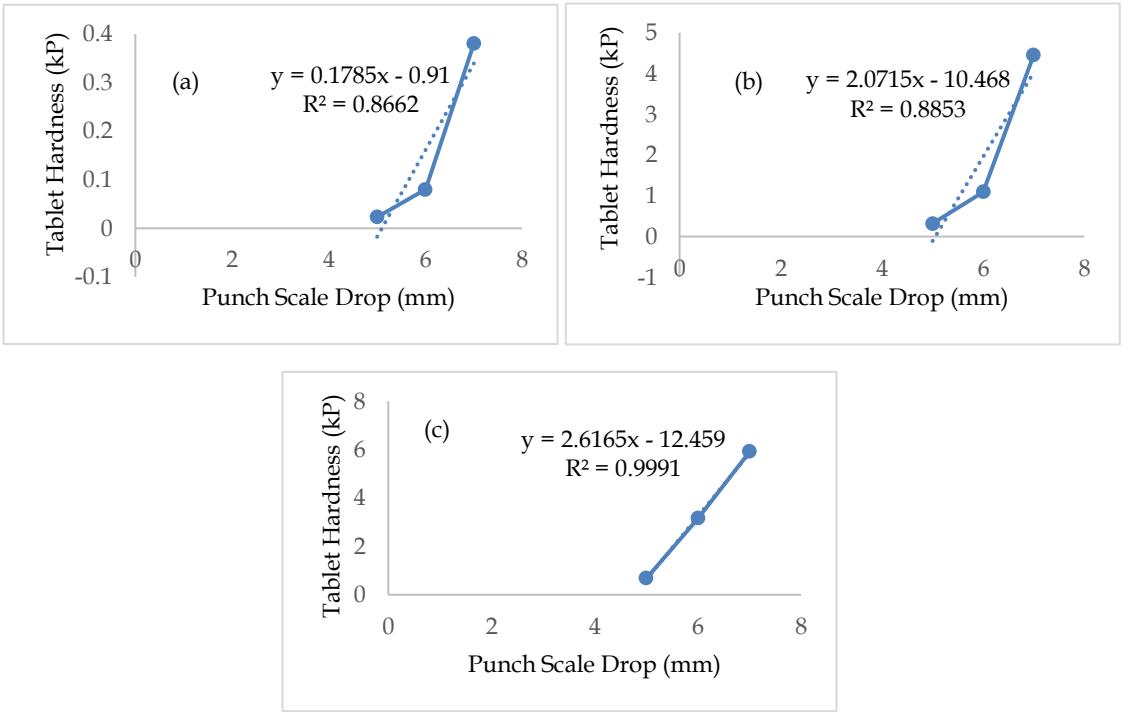

Figure 1. AUC of the compactibility test of Formula 1 at 1st compression (a), 2nd compression (b), 3rd compression (c).

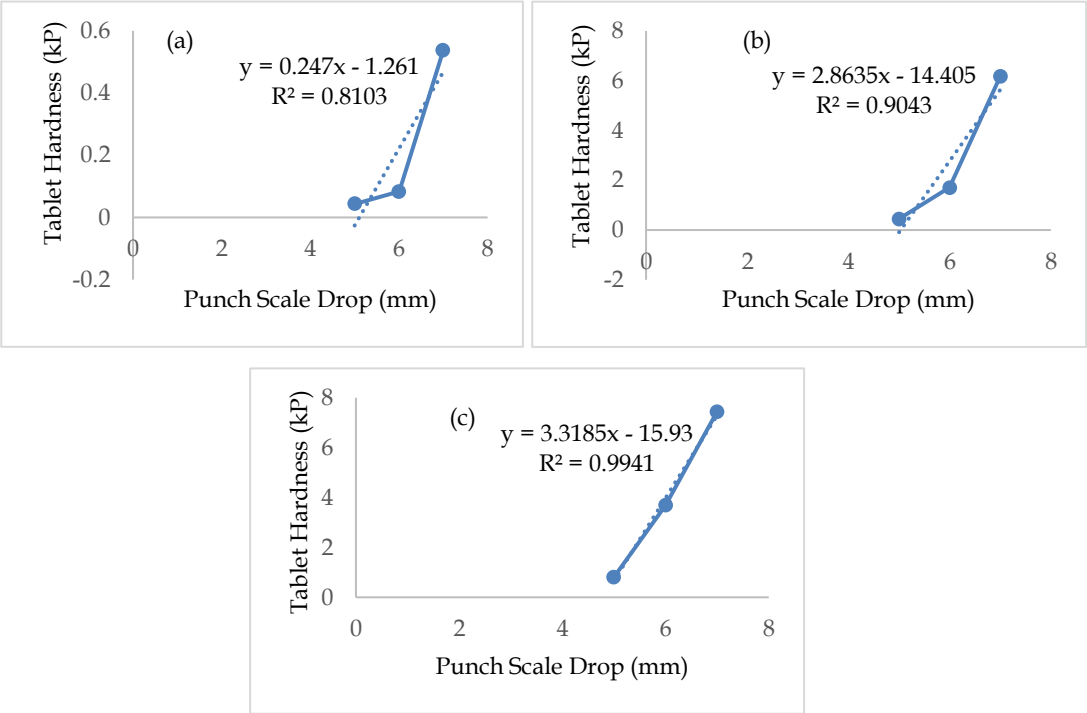

Figure 2. AUC of the compactibility test of Formula 2 at 1st compression (a), 2nd compression (b), 3rd compression (c)

2.4. Tablet Physical Properties Testing

2.4.1. Organoleptic Testing

Organoleptic testing of tablets is used to observe the appearance and physical properties of tablets produced after repeated compression. The organoleptical testing results are shown in Table 4 below.

Table 4. Result of Paracetamol Tablet Organoleptic

Component	Formula 1			Formula 2		
	I	II	III	I	II	III
Smell	No smell	No smell	No smell	No smell	No smell	No smell
Color	White	White	White	White	White	White
Shape	Flat round	Flat round	Flat round	Flat round	Flat round	Flat round
Diameter (mm)	13	13	13	13	13	13
Thickness (mm)	3.5	4	5	3.5	5	6
Physical Defects	-	Capping	Capping, chipping	-	Capping	Capping, chipping

Formula 1 : Formula with 1.8% binder concentration Formula 2 : Formula with 2.0% binder concentration

I: First compression tablet, II: Second compression tablet, III: Third compression tablet

Based on the results of organoleptical testing as shown in Table 4, all tablet formulas in each compression have the same color, smell, shape, and diameter. The tablets were white and had no smell, flat and round with a 13 mm diameter. This was due to the size of the punch and die used in each compression was always the same, so the factors that influenced were the thickness and physical properties of the tablets formed after the crushing treatment. In formula 1, the thickness of tablets in the first, second, and third pressing was 3.5 mm, 4 mm, and 5 mm, respectively. In formula 2, the tablet thickness at the first pressing was similar to formula 1 at 3.5 mm, but there were changes in the second and third pressing from 4 mm and 5 mm to 5 mm and 6 mm.

The same physical properties of tablets were obtained in formula 1 and formula 2. The first compression tablet had no physical defects, while the tablets in the next compression had capping and capping combined with chipping. These physical defects may be caused by the crushing of tablets which produces a lot of fines so that the capping occurs when the tablet is forged. The capping phenomenon is a condition of separation between the top layer of the tablet and the other parts, while the chipping

phenomenon on the third pressing was because of the binder conditions that were no longer sufficient to bind the particles together so there was damage to the tablet edges because of being too dry [11].

2.4.2. Tablet Weight Variation Testing

Weight variation is a form of dosage uniformity testing that aims to determine the consistency of dosage units by ensuring the individual contents are within the specified limits. Tablet weight diversity testing concerns the degree of uniformity of the amount of active substance contained in each dosage unit. Therefore, tablets that have uniform weights are expected to contain active substances in uniform amounts as well as those that have been formulated, so the dosage of each unit can be more guaranteed.

The formulated paracetamol tablets contain 300 mg of active substance, which holds the largest component of the formula. Since the active substance contained was 50% of the tablet weight at 600 mg, the weight variability test assumed that the concentration was homogeneous so that the active substance content could be determined in a representative batch. The batches in this study were formula 1 and formula 2 tablets from the first, second, and third compression.

Table 5. Result of Tablet Weight Variation Testing

Tablet	Tablet Weight (mg)	
	Formula 1	**Formula 2**
I	593.5 ± 6.47	599.5 ± 5.72
AV	6.493	4.363
II	776.8 ± 5.01	899.5 ± 6.93
AV	1.531	1.858
III	897.9 ± 5.02	1003.1 ± 11.16
AV	3.699	6.227

Numeric data presented as mean±SD, standard deviation

Formula 1 : Formula with 1.8% binder concentration Formula 2 : Formula with 2.0% binder concentration

I: First compression tablet, II: Second compression tablet, III: Third compression tablet

Based on Table 5, we could see that in formula 1, the first, second, and third compressions respectively weighed 593.5 mg, 776.8 mg, and 897.9 mg, and in formula 2 weighed 599.5 mg, 899.5 mg, and 1003.1 mg. The results obtained are directly proportional to the number of compressions and the weight produced. The more compression the more the tablet weight will increase. Weight variation can be affected by flow properties and particle size distribution [12]. The good flow properties describe the uniform flow of the granule mixture from the hopper to the die space as a molding place. It is consistent with the results obtained, whereas all tablet formulas meet the requirements of a good acceptance value. According to Table 5, L1 as a parameter of the acceptance value for each formula is less than 15.0. It was also known that each re-compressed tablet had increased weight. This is due to the large number of fines that arise after the crushing process. The particle size distribution was not uniform causing the space formed to be filled by fines, denser particles, and there is also the difference in punch depth in the first and second compression which causes the weight difference quite far. Therefore, these tablets also increase in thickness.

2.4.3. Tablet Hardness, Friability, and Disintegration Time Testing

To ensure the dosage of each unit preparation, tablets have to meet the quality standards of physical properties testing such as hardness, friability, and disintegration time. Tablets must be hard enough and not brittle so that they can withstand the impact, shock, or scraping that may occur during the production process until it's finally packaged and stored, as well as the transportation process when distributed to the customer. The hardness parameter plays a very important role in obtaining tablets in good condition because it begins with hardness which, if not controlled, will affect other physical properties. Generally, low tablet hardness can increase friability, conversely, if the tablet gets too hard, the disintegration time will be longer [13]. The test results of hardness, friability, and disintegration time of tablets can be found in Table 6.

Table 6. Result of Tablet Hardness, Friability, and Disintegration Time Testing

Physical Properties	Tablet					
	Formula 1			Formula 2		
	I	**II**	**III**	**I**	**II**	**III**
Hardness (kP)	1.11±0.02	3.51±0.03	5.53±0.1	3.37±0.13	4.44±0.14	5.13±0.06
Friability	2.95±0.4	5.87±0.6	8.86±0.2	1.99±0.23	5.34±0.09	9.6±0.16

(%)						
Disintegration time (minute)	0.74±0.02	0.7±0.01	0.44±0.05	0.79±0.03	0.72±0.02	0.7±0.02

Numeric data presented as mean±SD, standard deviation
Formula 1 : Formula with 1.8% binder concentration Formula 2 : Formula with 2.0% binder concentration

I: First compression tablet, II: Second compression tablet, III: Third compression tablet

Based on the results of statistical analysis, the hardness data were not normally distributed, so the Kruskal-Wallis test was continued with the p-value at 0.005 and it was stated that the results showed a significant difference. Unlike hardness, the results of friability testing data and disintegration time data were normally distributed so that the homogeneity and between-subjects tests were continued. The p-value > 0.05 was found thus in these two tests could be stated that there was no significant difference between the two groups of data.

Based on the tablet hardness test results presented in Table 6, it can be observed that only formula 1 on the third pressing and formula 2 on the second and third pressing meet the requirements for good tablet hardness. However, it can be observed from the results of the reworking phenomenon that with an increase in the compression number, there is also a corresponding hardness increase across the formulas. The hardness of the first compression tablet in Formula 1 was made minimum, with a weight of 600 mg to ensure that the punch depth applied in the first compression could be applied in the next compression.

During the crushing process, the first compression tablet had a minimum hardness, so when it was crushed there were a lot of small powders (fines). When pressed, the large number of fines can produce tablets with higher hardness [14]. This is because the smaller particle sizes that fill the compression space in the die, especially the mixture conditions of the compression results are denser, causing the porosity between the particles tighter. Thus, when compressed with the same pressure or as close as possible to the first compression, the hardness is increased. This corresponds to the results of the compactibility test which states hardness as a parameter. The hardness and compactibility test results carried out were appropriate, which along with increasing the number of compressions, also increased the tablet hardness. According to Wünsch et al. (2021), the high quantity of fines can have an impact on increasing compactibility. Therefore, the compactibility of tablets on the second and third compression is better than the first compression. Likewise, with formula 2, a higher binder concentration affected the tablet's hardness. The tablets that were compressed at the same pressure as formula 1 could have higher and appropriate hardness, thereby stating better compactibility.

The opposite result occurred in the friability test. Tablets with enough hardness generally have a good percentage of friability. The friability test determination was conducted by calculating the tablet weight that decreased after being rotated on the friability tester for a certain time and had been through the dust-freeing stage. Tablet friability correlates with the quantity of active substance contained in each preparation unit. The higher percentage of friability indicates the greater the weight lost, so the remaining active substance content is also reduced. Based on the results of the friability test in Table 6, it was found that all formulas in each tablet compression don't fulfill the requirements of a good friability test because it is over 1%. By increasing the number of pressings, tablet friability also became higher. The results of this friability test were contrary to the tablet hardness, but directly proportional to the disintegration time test results. In general, tablets with a good hardness have good friability as well. Meanwhile, the tablets that met the hardness requirements had greater friability. The higher percentage of friability affects the fast disintegration time of the tablets. All tablets in each formula could disintegrate within under one minute.

The factor that underlies this could be the addition technique of the crusher used. Croscarmellose sodium as the crusher agent was added by a combination, either intragranular or extragranular. According to research conducted by Ainurofiq and Azizah (2016), the formulated tablets using the addition of crushers as the inner and outer phases have a higher percentage of friability. It is due to the strength of binding material to unite the interparticles decreased. Meanwhile, the crushing process can cause the formation of new particle surfaces. Hence, it cannot be ascertained whether the binder contained in the crushed granule is still uniformly distributed like the initial granule. Therefore, its capability to bind interparticles to form tablets wasn't optimal compared to the initial granule to form the first pressed tablet.

The crushers added were also included as süper disintegrant, which affected the percent friability and tablet disintegration time that occurred. It is known that the second and third tablets which resulted from the previous crushing produced a lot of fines. These fines can reduce the surface bond of the tablet so that the

friability increases, and the molded tablet is capping [24]. The lower strength of binders and crusher types categorized as süper disintegrants have caused a very fast tablet disintegration during contact with the body medium. The mechanism of croscarmellose sodium as süper disintegrant with a small quantity of addition has been able to break the tablet quickly, it is through water wicking and rapid swelling up to 4-8 times the original volume [22, 23, 27]. Therefore, the crusher will be distributed more quickly on the surface of the tablet causing the time taken for the tablets to break into granules, then granules into powders occur faster, especially on the second and third tablets with higher friability. Furthermore, it can be seen that formula 2 with a higher binder concentration, had a longer disintegration time than formula 1, which illustrates that as the hardness increases, it has a longer disintegration time [25].

3. CONCLUSION

Based on the results of this study, it was concluded that the repeated compression process affects the characteristics of the mixture and the quality of 300 mg paracetamol tablets, especially for hardness tests. It was found that the reworking potential of cassava starch on paracetamol tablet formulation with different concentration levels was able to maintain its quality as a binder after being recompressed twice. The physical properties of the mixture and paracetamol tablets (hardness, disintegration time) generated fulfill the requirements of a good test. Meanwhile, the friability test didn't show optimal results because all tablets from the beginning to the last compression of each formula had values out of the required range. Tablets in the second and third compression were capping due to the large number of fines produced during crushing. In further research, it is recommended that after the granule crushing process be sieved at a closer mesh range and the mixture re-stirred using a cube mixer to ensure the particles are uniformly distributed. In addition, it is suggested to modify the formula with a higher binder concentration for formula 1 and the type of disintegrant, while considering the properties of the active substance and the formulated tablet type.

4. MATERIALS AND METHODS

4.1. Materials

The materials used in this research were paracetamol (batch 2150096), standard paracetamol (SIGMA-ALDRICH, Lot #MKCJ5427), cassava starch (Tapioca Starch, batch 00202040423), lactose monohydrate (batch 23208277 (J0172/23)), croscarmellose sodium (Primellose®, Lot 108N54T), magnesium stearate (batch MGSV1230092), talc (batch 20220322), distilled water, and ethanol p.a.

4.2. Study Design

This research was pure experimental using a two-way completely randomized research design to determine the effect of repeated compression on the potential of cassava starch as a binder with concentration levels, based on the physical properties of the mixture and 300 mg paracetamol tablets.

4.3. Variable

The main variables in this research were the number of repeated compressions of 300 mg paracetamol tablets (twice) and the concentration of cassava starch (1.8% w/w and 2.0% w/w). The physical properties of granules (flow rate and compressibility index) and tablets (compactibility, hardness, friability, and disintegration time) were the result values.

4.4. Instrumentations

The instruments used in this research were an analytical balance (OHAUS Pioneer PA213), all-purpose machine (Erweka AR-401), cube mixer, flowability tester (Erweka GmbH AR 401), tap density volumeter (HY-100B), single punch tablet machine (Korsch Maschinenfabrik Berlin 9979-76), friability tester (Lorderan CS-2), hardness tester (Pharma Test PTB 302), disintegration tester (Develop BJ-2), hotplate magnetic stirrer (Cenco 34532), vacuum (Boombastic BM19VC), UV-Vis spectrophotometer (UVmini-1240 Shimadzu®), cuvette, drying cabinet, mortar, stamper, 12/50 mesh sieve, caliper, stopwatch, and glassware.

4.5. Making Mucilago Amili 10%

Mucilage starch 10% w/v was made by adding 10 g of cassava starch to a beaker and dissolving it with a certain amount of water while heating until a total volume of mucilage is 100 mL, with a thick texture like gel mucus, then mucilage that has been formed is cooled.

4.6. Making Powder Mixtures

Paracetamol, lactose monohydrate, and 1/3 of croscarmellose sodium as active ingredients, filler, and intragranular disintegrant which have been weighed according to the formula in Table 7 were put into the cube mixer then mixed for 15 minutes, at 135 rpm. The intragranular mixture was transferred to a plastic tray and added the cooled mucilago slowly until a good moist mass was formed. Sifted the mass and dried at 50°C [31].

Table 7. The Formula of Paracetamol Tablet @300 mg

Ingredients	Amount of each ingredient (mg/tablet)	
	Formula 1	**Formula 2**
Paracetamol	300	300
Lactose monohydrate	241.4	240.2
Cassava starch	10.6	11.8
Croscarmellose sodium	18	18
Magnesium stearate	3	3
Talc	27	27
Total	600	600

Formula 1: Formula with 1.8% binder concentration Formula 2: Formula with 2.0% binder concentration

4.7. Moisture Content Testing

Granule moisture was tested using the gravimetric method. A total of 25 g of sieved wet granule was placed on a petri dish and observed for weight changes until it was constant and reached the moisture content requirement, at less than 5% [16]. The drying temperature was set at 50°C [31]. The calculation of moisture content can be done using the following formula:

$$\text{MC} = \frac{\text{water weight in sample}}{\text{dry sample weight}} \times 100\%$$

4.8. Lubrication

Dry granules were sieved and mixed with talc and 2/3 of croscarmellose sodium as a glidant and extragranular disintegrant into the cube mixer for 5 minutes. Then proceed by adding magnesium stearate at the end for 5 minutes.

4.9. Testing Flow Properties of the Mixture

4.9.1 Flow Rate Measurement

100 g of granules were put into the funnel of the flowability tester through the edge. The measurement is started by pressing the F1 button indicating start so that the granule comes out and the speed results are recorded. A good flow rate value is more than 10 g/s, which indicates the flow time of 100 grams of granules is less than 10 seconds [17].

4.9.2 Bulk Density, Tapped Density, Hausner Ratio, and Compressibility Index

Bulk density and tapped density measurements can be done simultaneously by putting as much as 40 g of the mixture that has been weighed into a 100 mL measuring cup through the edge of the glass that has been attached to the tap density volumeter. The surface of the mixture is slowly flattened without compression and the initial volume of the mixture is recorded, then the bulk density can be calculated using the following formula:

$$\text{Bulk density} = \frac{\text{M}}{\text{Vo}}$$

In the tapped density measurement, the mixture that has been flattened without prior compression is tapped 500 times and the final volume is recorded. The tapped density measurement is done using the following formula:

$$\text{Tapped density} = \frac{\text{M}}{\text{Vf}}$$

The calculation of the Hausner ratio and compressibility index of the mixture is done using the following formula:

$$\text{Hausner ratio} = \frac{\text{Vo}}{\text{Vf}}$$

$$\text{Compressibility index} = \left(\frac{Vo - Vf}{Vo}\right) \times 100$$

M is the mixture's weight (g), Vo is the initial volume (mL), and Vf is the final volume (mL). The mixture is qualified if its Hausner ratio is 1.00 – 1.11 and the compressibility index is less than 10% which represents that the mixture has excellent flow properties [29].

4.10. Tablet Compactibility Testing

The compactibility test was conducted by putting the lubricated granule mixture into the hopper, then setting the scale of the upper punch at each decrease of 1 mm, 2 mm, 3 mm, 4 mm, 5 mm, 6 mm, 7 mm, and 8 mm, while the lower punch was set with a 10 mm depth. The tablet machine was turned on and the pressed tablets were tested for hardness using a hardness tester.

4.11. Tableting Process

The lubricated granule mixture was put into the hopper and forged using a single punch tablet machine, with the same punch strength in each formula, as well as the punch and die diameter of each formula was 13 mm, and the weight of 600 mg for each tablet.

4.12. Testing Physical Properties of the Tablet

4.12.1 Tablet Organoleptic Testing

The tablets produced were observed for their physical properties, including smell, color, shape (diameter and thickness), and physical defects of tablets [18].

4.12.2 Tablet Weight Variation Testing

The weight variability test was carried out by weighing them individually of ten paracetamol tablets from each pressing randomly taken. The results of the weighing were recorded, then the average weight value and the estimated content of each tablet were calculated as X value.

The concentration measurement on a representative batch of tablets was carried out using a spectrophotometer at 247 nm wavelength, initially by making a linearity standard curve at five concentration levels as the x-axis and absorbance as the y-axis. The assay determination was carried out by dissolving 20 mg of crushed powder of one paracetamol tablet taken randomly in each compression using ethanol in a beaker glass, then filtered and transferred to a 50 ml volumetric flask and diluted to the borderline mark.

The solution obtained was pipetted back 0.1 mL and diluted with the addition of ethanol to the borderline mark of the 10 mL flask. A concentration of 4 ppm was obtained, then the absorbance was measured at a wavelength of 247 nm. The absorbance value was plotted as the y value of the regression equation obtained previously to calculate the concentration, then the assay, content of each tablet, and acceptance value can be calculated according to the following formula:

$$\text{Assay} = \frac{C \times Df \times Vo}{W} \times 100\%$$

$$X_i = w_i \times \frac{A}{\bar{W}}$$

$$AV = |M - \bar{X}| + k\,s$$

C is the concentration (mg/mL), Df is the dilution factor, Vo is the initial volume (mL), W is the sample weight in mg, Xi (X1, X2, …, Xn) is the estimated contents of each unit tested, wi (w1, w2, …, wn) is the weight of each unit tested, A is the active substance content (% of label claim), $\bar{W}$ is the mean weight of each unit, AVis the acceptance value, M is the reference value, $\bar{X}$is the mean of the estimated content of the individual tablets tested, k is the acceptability constant (if n = 10, then k = 2.4; if n = 30, then k = 2.0), and s is the standard deviation. For the first 10 tablets, if the acceptability value is not greater nor equal to L1 = 15.0, it is declared qualified, whereas if the value obtained is more than L1 (L1 > 15.0), it must be done on 20 additional tablets [28].

4.12.3 Tablet Hardness Testing

A total of five tablets were placed one by one on the hardness tester [19]. The scale in kP units showing the hardness of the tablet that can be shattered read on the instrument is recorded. Tablet hardness is approved with a requirement of 4-8 kP [20].

4.12.4 Tablet Friability Testing

Twenty of the tablets compressed were dusted by vacuum, and then the initial weight was recorded. The friability tester was cleaned and the tablets were placed, to run at 25 rpm, 100 revolutions for 4 minutes. The tablets were re-vacuumed, and the final weight was recorded. A good friability percentage is less than 1%, which can be calculated using the following formula:

$$\text{Friability (\%)} = \left(\frac{W_0 - W_1}{W_0}\right) \times 100$$

W_0 is the initial weight and W_1 is the final weight in grams.

4.12.5 Tablet Disintegration Time Testing

One tablet was inserted in each six-cylinder basket of the disintegration tester which was conditioned with aqueous media at 37 ± 2°C. The stopwatch was stopped and the tablet disintegration time could be recorded when the last tablet disintegrated which was shown by no clear core mass. The time required for uncoated paracetamol tablets to disintegrate is no longer than 15 minutes [20, 26].

4.13. Tablet Crushing

Tablets that have already been tested for quality were crushed again using a mortar and stamper until granule size, then sieved with a 12/50 mesh number. Granule quality testing was carried out back and the tablets were recompressed to test their physical properties as in the previous stage.

4.14. Data Analysis

Research data including flow rate, compressibility index, compactibility, hardness, friability, and disintegration time were statistically analyzed using SPSS software in the Shapiro-Wilk normality test. Data that was normally distributed continued with Two-Way Anova testing with a confidence level of 95% and a significant value of 5%. However, if the data wasn't normally distributed, it was analyzed by the Kruskal-Wallis test and Mann-Whitney post-hoc test. The p-value of 0.05 indicates that there is no significant difference between the two groups of data.

Acknowledgements: The authors would like to thank LPPM Sanata Dharma University for providing the research fund and PT Konimex for providing the research material croscarmellose sodium used in this study.
Author contributions: Concept – A.B.S; Design – A.B.S, R.E.; Supervision – A.B.S.; Resources – A.B.S, R.E.; Materials – A.B.S, R.E.; Data Collection and/or Processing – A.B.S, R.E.; Analysis and/or Interpretation – A.B.S, R.E., Literature Search – R.E.; Writing – A.B.S, R.E; Critical Reviews – A.B.S, R.E.
Conflict of interest statement: The authors declared no conflict of interest.

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Outlook

Re: Journal of Research in Pharmacy : Correction Required

From A. Budi Susiana Lestari <a_budi@usd.ac.id>
Date Sun 2024-09-08 9:17 AM
To Journal of Research in Pharmacy <editor@jrespharm.com>

Dear Prof.Dr.Hatice Kübra
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I have sent the similarity index file.

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Dear PhD. Agatha Budi Susiana Lestari,

Some changes are needed on your article named Reworking potential of cassava starch as a binder in the production of paracetamol tablets using wet granulation method which you have sent to Journal of Research in Pharmacy . We need you to make these changes and send your article again, before the editor evaluation.

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Could you please check your paper\'s similarity index and attach iThenticate/ Turnitin report ? (Could you please note that; According to the law declared by Scientific and Technological Research Council of Turkey, we are not allowed to evaluate an article with the similarity index higher than 25%.)
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2 attachments (633 KB)
27_19469_20771-MPJ_Lestari and Eliana_rev_galleyproof.pdf; Orchid ID.docx;

Dear Sir,

I enclose the revised galley proof and the Orchid ID data from the authors.

Agatha Budi Susiana Lestari's orchid ID: https://orcid.org/0000-0003-3260-6093
Rika Eliana's orchid ID: https://orcid.org/0009-0001-4106-4129

Thank you for your attention.

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Agatha Budi Susiana Lestari

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Suggestions

1. Reviewer Comments

None

2. Reviewer Comments

Dear Authors,

I believe that addressing the following points will enhance the value of the publication:

It should be ensured that the terminology used throughout the text is applied correctly. Terms found through translation may fall short in matching the terminology used in the literature. Some terms were addressed below. Therefore, the entire text should be reviewed.

The AUC references should be revised to “AUC of the compactibility test.” When AUC is used alone, it tends to suggest the "area under the curve" used in plasma concentration calculations. Therefore, the term AUC should not be used on its own in the text.

The authors should ensure that the term "compactability" is used correctly. Typically, compactability, compressibility, and tabletability are used interchangeably, but they are calculated differently. The relevant source can be consulted.

Independent variables should be considered as variables. The values referred to as dependent variables are the result values to be used in comparison.

A confounding variable refers to a variable that influences both the dependent variable and the independent variable. However, the confounding variable mentioned in the text does not correspond to this term.

The moisture test should be detailed (e.g., at what temperature the drying will be done), and it should be indicated that it can be used for powders, with a reference provided.

The term “curve” should not be used after AUC because "curve" is already included in the abbreviation.

In Table 7, the notations given in the footnotes were not used in the table. Similarly, the notations used in Table 3 were not explained.

The number of compressions represented by I, II, and III should be explained in all tables.

In the conclusion section, despite the observation of capping in tablets, it was mentioned that it was deemed acceptable in the second press. This section should be re-evaluated. Additionally, while the optimization of multiple compression tablets is quite challenging, the role of the binder in this scenario should be discussed.

Manuscript Information

Manuscript ID:	**MPJ-19469**
Title in English:	Reworking potential of cassava starch as a binder in the production of paracetamol tablets using wet granulation method
Small Title in English:	No information entered
Authors:	Agatha Budi Susiana Lestari[1], Rika Eliana[2]
Institutions:	[1]Faculty of Pharmacy, Sanata Dharma University, Pharmaceutical, Daerah Istimewa Yogyakarta, Indonesia [2]Faculty of Pharmacy, Sanata Dharma University, Pharmacist Profession Education, Daerah Istimewa Yogyakarta, Indonesia
Keywords in English:	Cassava starch; paracetamol tablets; reworking potential; wet granulation
Manuscript Type:	Research article
Processing Status:	Major Revision

Abstract in English

Paracetamol is a drug that is commonly used as an analgesic and antipyretic. In the pharmaceutical industry, tablets are usually produced in large quantities, and it's possible to find tablets that don't fulfill the quality standards after testing their physical properties, including hardness, friability, and disintegration time. One of the excipients in tablets that may affect them is the binder, which in this study used cassava starch in two different concentrations. This study was pure experimental research using a two-way completely randomized research design to determine the effect of repeated compression on the potential of cassava starch as a binder with concentration levels, based on the mixture and paracetamol tablets characteristics, which is done by crushing tablets that had been compressed to test the physical properties of the mixture and tablets. The data obtained were analyzed statistically with SPSS to check normality, then continued with TwoWay Anova if the data obtained were normally distributed or the KruskalWallis test for abnormal distribution. The results showed that repeated compression affected the mixture characteristics and tablet hardness. By analyzing the AUC data, it was found that the reworking potential value was greater, which showed that cassava starch could maintain its quality as a binder after being recompressed twice.

Manuscript Files

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MPJ-19469-8-similarity-index-agatha-rika.pdf (../pdf-files/in/19469-MPJ-19469-8-similarity-index-agatha-rika.pdf)	2443 KB	Sep 08, 2024	Responses to technical check results	None

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MPJ-19469.REV-3	Reworking potential of cassava starch as a binder in the production of paracetamol tablets using wet granulation method (view-manuscript.php?id=20771&nocache=1da2c3b78a9449e671ae3207434ca41b)	Dec 16, 2024	Accepted	
MPJ-19469.REV-2	Reworking potential of cassava starch as a binder in the production of paracetamol tablets using wet granulation method (view-manuscript.php?id=20378&nocache=1da2c3b78a9449e671ae3207434ca41b)	Nov 06, 2024	Minor Revision	
MPJ-19469.REV-1	Reworking potential of cassava starch as a binder in the production of paracetamol tablets using wet granulation method (view-manuscript.php?id=19797&nocache=1da2c3b78a9449e671ae3207434ca41b)	Sep 28, 2024	Minor Revision	
MPJ-19469	Reworking potential of cassava starch as a binder in the production of paracetamol tablets using wet granulation method (view-manuscript.php?id=19469&nocache=1da2c3b78a9449e671ae3207434ca41b)	Sep 08, 2024	Major Revision	

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Suggestions

1. Reviewer Comments

The AUC references should be revised to "AUC of the compactibility test." When AUC is used alone, it tends to suggest the "area under the curve" used in plasma concentration calculations. Therefore, the term AUC should not be used on its own in the text.

The moisture test should be detailed (e.g., at what temperature the drying will be done), and it should be indicated that it can be used for powders, with a reference provided.

The term "curve" should not be used after AUC because "curve" is already included in the abbreviation.

Manuscript Information

Manuscript ID:	**MPJ-19469.REV-1**
Title in English:	Reworking potential of cassava starch as a binder in the production of paracetamol tablets using wet granulation method
Small Title in English:	No information entered
Authors:	Agatha Budi Susiana Lestari[1], Rika Eliana[2]
Institutions:	[1]Faculty of Pharmacy, Sanata Dharma University, Pharmaceutical, Daerah Istimewa Yogyakarta, Indonesia [2]Faculty of Pharmacy, Sanata Dharma University, Pharmacist Profession Education, Daerah Istimewa Yogyakarta, Indonesia
Keywords in English:	Cassava starch; paracetamol tablets; reworking potential; wet granulation
Manuscript Type:	Research article
Processing Status:	Minor Revision

Manuscript Files

File Name	File Size	Date Created	Category	Description
MPJ-19469-4-lestari-and-eliana-jrp.pdf (../pdf-files/out/19797-MPJ-19469-4-lestari-and-eliana-jrp.pdf)	152 KB	Sep 07, 2024	Main Document	None
MPJ-19469-1-figure-1.jpg (../pdf-files/in/19797-MPJ-19469-1-figure-1.jpg)	118 KB	Sep 07, 2024	Figure	None

MPJ-19469-3-figure-2.jpg (../pdf-files/in/19797-MPJ-19469-3-figure-2.jpg)	116 KB	Sep 07, 2024	Figure	None
MPJ-19469-3-copyrightform.pdf (../pdf-files/in/19797-MPJ-19469-3-copyrightform.pdf)	866 KB	Sep 07, 2024	Copyright Transfer Form	None
MPJ-19469-2-jrp-checklist.pdf (../pdf-files/in/19797-MPJ-19469-2-jrp-checklist.pdf)	428 KB	Sep 07, 2024	Author Checklist Form	None
MPJ-19469-1-covering-letter.pdf (../pdf-files/in/19797-MPJ-19469-1-covering-letter.pdf)	168 KB	Sep 07, 2024	Cover letter	None
MPJ-19469-8-similarity-index-agatha-rika.pdf (../pdf-files/in/19797-MPJ-19469-8-similarity-index-agatha-rika.pdf)	2443 KB	Sep 08, 2024	Responses to technical check results	None
MPJ-19797-5-lestari-and-eliana-jrp-revfinal.rev-1.pdf (../pdf-files/out/19797-MPJ-19797-5-lestari-and-eliana-jrp-revfinal.rev-1.pdf)	156 KB	Sep 28, 2024	Main Document	None
MPJ-19797-0-cover-letter-2.rev-1.pdf (../pdf-files/in/19797-MPJ-19797-0-cover-letter-2.rev-1.pdf)	93 KB	Sep 28, 2024	Cover letter	None
MPJ-19797-1-response-to-reviewers.rev-1.pdf (../pdf-files/in/19797-MPJ-19797-1-response-to-reviewers.rev-1.pdf)	0 KB	Sep 28, 2024	Response to Reviewers	None
MPJ-19797-4-response-to-reviewer.rev-1.pdf (../pdf-files/in/19797-MPJ-19797-4-response-to-reviewer.rev-1.pdf)	94 KB	Sep 28, 2024	Response to Reviewers	None

Score Sheet

1. Reviewer

Does the content and value of the work justify publication in Marmara Pharmaceutical Journal ?	Yes
Does the title of the manuscript reflect the contents of the study ?	Yes
Are the keywords sufficient and appropriate ?	Yes
Is the summary concise and informative?	Yes

Is the text divided appropriately according to the article type ?	Yes
Is the language adequate?	Yes
Are the nomenclature and scientific terminology correct?	Yes
Are the references complete and recent?	Yes
Are the figures tables and graphics necessary ?	Yes
Are the figures tables and graphics clear ?	Yes
Is the introduction part	sufficiently developed
Are the experimental procedures sound?	Yes
Is the results and discussion part	sufficiently developed
Is the information about the approval of ETHICAL COMMISSION presented ?	Not applicable

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Suggestions

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[2] Tatar E, Karakuş S, Küçükgüzel ŞG, Öktem Okullu S, Ünübol N, Kocagöz T, De Clercq E, Andrei G, Snoeck R, Pannecouque C, Kalaycı S, Şahin F, Sriram D, Yogeeswari P, Küçükgüzel İ. Design, synthesis, and molecular docking studies of a conjugated thiadiazole-thiourea scaffold as antituberculosis agents. Biol Pharm Bull. 2016; 39(4): 502-515. http://dx.doi.org/10.1248/bpb.b15-00698.
[3] Kulabaş N, Bingöl Özakpınar Ö, Özsavcı D, Leyssen P, Neyts J, Küçükgüzel İ. Synthesis, characterization and biological evaluation of thioureas, acylthioureas and 4-thiazolidinones as anticancer and antiviral agents. J Res Pharm. 2017; 21(2): 371-384. http://dx.doi.org/10.12991/marupj.300913.
Reference to a book:
[6] Silverman RB, The Organic Chemistry of Drug Design and Drug Action, fourth ed., Elsever, Burlington, MA, USA 2000.
Reference to a chapter in an edited book:
[7] Şener G, Sakarcan A, Yeğen B. Melatonin as a radioprotective agent. In: Montilla P, Túnez I. (Eds). Melatonin: Present and Future. Nova Science Publishers, Inc., New York, 2008, pp.127-142.
Theses:
[8] Tatar E. PhD Thesis. Synthesis and characterization of novel 1,3-thiazolidine-4-ones derived from 2-(aroylamino)-3-methyl butyric acid hydrazide. Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Marmara University, Haydarpaşa, İstanbul, Turkey, 2009.
Reference to a website:
[9] VCCLAB, Virtual Computational Chemistry Laboratory. http://www.vcclab.org (accessed March 18, 2017).
[10] PASS (Prediction of Activity Spectra for Substances) program. http://www.way2drug.com/passonline (accessed July 18, 2015).

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Thank you for the revision. We wish you success in your work.
Best regards,

Minor Revision

Manuscript Information

Manuscript ID:	**MPJ-19469.REV-2**
Title in English:	Reworking potential of cassava starch as a binder in the production of paracetamol tablets using wet granulation method
Small Title in English:	No information entered
Authors:	Agatha Budi Susiana Lestari[1], Rika Eliana[2]
Institutions:	[1]Faculty of Pharmacy, Sanata Dharma University, Pharmaceutical, Daerah Istimewa Yogyakarta, Indonesia [2]Faculty of Pharmacy, Sanata Dharma University, Pharmacist Profession Education, Daerah Istimewa Yogyakarta, Indonesia
Keywords in English:	Cassava starch; paracetamol tablets; reworking potential; wet granulation
Manuscript Type:	Research article
Processing Status:	Minor Revision

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MPJ-19469-4-lestari-and-eliana-jrp.pdf (../pdf-files/out/20378-MPJ-19469-4-lestari-and-eliana-jrp.pdf)	152 KB	Sep 07, 2024	Main Document	None
MPJ-19469-1-figure-1.jpg (../pdf-files/in/20378-MPJ-19469-1-figure-1.jpg)	118 KB	Sep 07, 2024	Figure	None
MPJ-19469-3-figure-2.jpg (../pdf-files/in/20378-MPJ-19469-3-figure-2.jpg)	116 KB	Sep 07, 2024	Figure	None
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MPJ-19469-1-covering-letter.pdf (../pdf-files/in/20378-MPJ-19469-1-covering-letter.pdf)	168 KB	Sep 07, 2024	Cover letter	None
MPJ-19469-8-similarity-index-agatha-rika.pdf (../pdf-files/in/20378-MPJ-19469-8-similarity-index-agatha-rika.pdf)	2443 KB	Sep 08, 2024	Responses to technical check results	None
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MPJ-19797-0-cover-letter-2.rev-1.pdf (../pdf-files/in/20378-MPJ-19797-0-cover-letter-2.rev-1.pdf)	93 KB	Sep 28, 2024	Cover letter	None
MPJ-19797-4-response-to-reviewer.rev-1.pdf (../pdf-files/in/20378-MPJ-19797-4-response-to-reviewer.rev-1.pdf)	94 KB	Sep 28, 2024	Response to Reviewers	None
MPJ-20378-4-lestari-and-eliana-jrp-rev-minor.rev-2.pdf (../pdf-files/out/20378-MPJ-20378-4-lestari-and-eliana-jrp-rev-minor.rev-2.pdf)	0 KB	Nov 06, 2024	Main Document	None
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MPJ-20378-1-response-to-reviewer-rev-minor.rev-2.pdf (../pdf-files/in/20378-MPJ-20378-1-response-to-reviewer-rev-minor.rev-2.pdf)	94 KB	Nov 06, 2024	Response to Reviewers	None
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Suggestions

Dear Author,
I am pleased to inform you that our reviewers and the section editor have recommended your manuscript for publication. Your manuscript has been scheduled for the FIRST issue of Journal of Research in Pharmacy in JANUARY 2026. The proof of your manuscript will be provided in DECEMBER, 2025. Thank you for choosing to publish in our journal.
Kindest regards
Prof.Hatice Kübra ELÇİOĞLU
Editor-in-Chief

Accepted

Manuscript Information

Manuscript ID: **MPJ-19469.REV-3**

Title in English: Reworking potential of cassava starch as a binder in the production of paracetamol tablets using wet granulation method

Small Title in English: No information entered

Authors: Agatha Budi Susiana Lestari[1], Rika Eliana[2]

Institutions: [1]Faculty of Pharmacy, Sanata Dharma University, Pharmaceutical, Daerah Istimewa Yogyakarta, Indonesia
[2]Faculty of Pharmacy, Sanata Dharma University, Pharmacist Profession Education, Daerah Istimewa Yogyakarta, Indonesia

Keywords in English: Cassava starch; paracetamol tablets; reworking potential; wet granulation

Manuscript Type: Research article

Processing Status: Accepted

Abstract in English

Paracetamol is a drug that is commonly used as an analgesic and antipyretic. In the pharmaceutical industry, tablets are usually produced in large quantities, and it's possible to find tablets that don't fulfill the quality standards after testing their physical properties, including hardness, friability, and disintegration time. One of the excipients in tablets that may affect them is the binder, which in this study used cassava starch in two different concentrations. This study was pure experimental research using a two-way completely randomized research design to determine the effect of repeated compression on the potential of cassava starch as a binder with concentration levels, based on the mixture and paracetamol tablets characteristics, which is done

by crushing tablets that had been compressed to test the physical properties of the mixture and tablets. The data obtained were analyzed statistically with SPSS to check normality, then continued with TwoWay Anova if the data obtained were normally distributed or the KruskalWallis test for abnormal distribution. The results showed that repeated compression affected the mixture characteristics and tablet hardness. By analyzing the AUC of the compactibility test data, it was found that the reworking potential value was greater, which showed that cassava starch could maintain its quality as a binder after being recompressed twice.

Manuscript Files

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MPJ-19469-4-lestari-and-eliana-jrp.pdf (../pdf-files/out/20771-MPJ-19469-4-lestari-and-eliana-jrp.pdf)	152 KB	Sep 07, 2024	Main Document	None
MPJ-19469-1-figure-1.jpg (../pdf-files/in/20771-MPJ-19469-1-figure-1.jpg)	118 KB	Sep 07, 2024	Figure	None
MPJ-19469-3-figure-2.jpg (../pdf-files/in/20771-MPJ-19469-3-figure-2.jpg)	116 KB	Sep 07, 2024	Figure	None
MPJ-19469-3-copyrightform.pdf (../pdf-files/in/20771-MPJ-19469-3-copyrightform.pdf)	866 KB	Sep 07, 2024	Copyright Transfer Form	None
MPJ-19469-2-jrp-checklist.pdf (../pdf-files/in/20771-MPJ-19469-2-jrp-checklist.pdf)	428 KB	Sep 07, 2024	Author Checklist Form	None
MPJ-19469-1-covering-letter.pdf (../pdf-files/in/20771-MPJ-19469-1-covering-letter.pdf)	168 KB	Sep 07, 2024	Cover letter	None
MPJ-19469-8-similarity-index-agatha-rika.pdf (../pdf-files/in/20771-MPJ-19469-8-similarity-index-agatha-rika.pdf)	2443 KB	Sep 08, 2024	Responses to technical check results	None
MPJ-19797-5-lestari-and-eliana-jrp-revfinal.rev-1.pdf (../pdf-files/out/20771-MPJ-19797-5-lestari-and-eliana-jrp-revfinal.rev-1.pdf)	156 KB	Sep 28, 2024	Main Document	None
MPJ-19797-0-cover-letter-2.rev-1.pdf (../pdf-files/in/20771-MPJ-19797-0-cover-letter-2.rev-1.pdf)	93 KB	Sep 28, 2024	Cover letter	None
MPJ-19797-4-response-to-reviewer.rev-1.pdf (../pdf-files/in/20771-MPJ-19797-4-response-to-reviewer.rev-1.pdf)	94 KB	Sep 28, 2024	Response to Reviewers	None
MPJ-20378-7-lestari-and-eliana-jrp-rev-minor.rev-2.pdf (../pdf-files/out/20771-MPJ-20378-7-lestari-and-eliana-jrp-rev-minor.rev-2.pdf)	155 KB	Nov 06, 2024	Main Document	None
MPJ-20378-1-response-to-reviewer-rev-minor.rev-2.pdf (../pdf-files/in/20771-MPJ-20378-1-response-to-reviewer-rev-minor.rev-2.pdf)	94 KB	Nov 06, 2024	Response to Reviewers	None
MPJ-20771-9-lestari-and-eliana-jrp-rev-minor12des.rev-3.pdf (../pdf-files/out/20771-MPJ-20771-9-lestari-and-eliana-jrp-rev-minor12des.rev-3.pdf)	128 KB	Dec 16, 2024	Main Document	None
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Research Article

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11. Reworking potential of Cassava starch as a binder in the production of paracetamol tablets using wet granulation method

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21. Glibenclamide co-crystals: Development and characterization using D-Mannitol and citric acid as a carrier to improve its dissolution profile

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24. Antimycobacterial activity of the secondary metabolite fraction derived from endophytic bacterium Bacillus velezensis strain DJ4 isolated from Archidendron pauciflorum

Genia Sotya Sinarawadi , Jepri Agung Priyanto *, Muhammad Eka Prastya , Zetryana Puteri Tachrim

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25. Immunohistochemical study of matrix metalloproteinases 2 and 9 in the placenta of spontaneous miscarriage

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26. Optimization of phenolic and flavonoid content from Graptophyllum pictum (L.) Griff. leaf under maceration extraction methods using response surface methodology and its antioxidant activity

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27. Antioxidant and antibacterial activity of extracts and compounds from endophytic fungi isolated from roots of Physalis angulata and their combination effects

Elfita Elfita *, Budi Eko Wahyudi , Hary Widjajanti , Salni Salni , Mardiyanto Mardiyanto , Rian Oktiansyah , Julinar Julinar

Reviews

Review

3. Genetic scissors: A new era in gene therapy

Dhanashree Sanap *

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17. Transferosomes: Advanced nanocarriers for enhanced drug delivery

Sreehari Nair , Dhanashree P. Sanap *, Kisan R. Jadhav

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Review

33. Comparative analysis of FDA-approved Alzheimer's therapies: symptomatic and disease-modifying approaches

Mohammed Abdo Qasem Radman Khaled , Ayşe Nur Hazar-yavuz *

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Journal of Research in Pharmacy

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Pharmacology, Toxicology and Pharmaceutics
Pharmacology, Toxicology and Pharmaceutics (miscellaneous)

PUBLISHER

Marmara University

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PUBLICATION TYPE

Journals

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COVERAGE

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INFORMATION

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SCOPE

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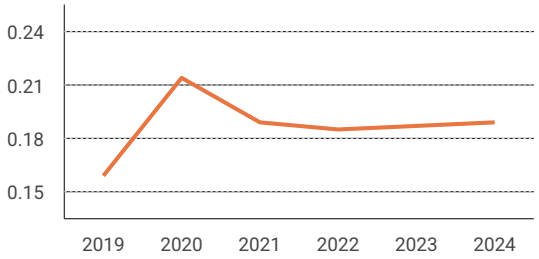

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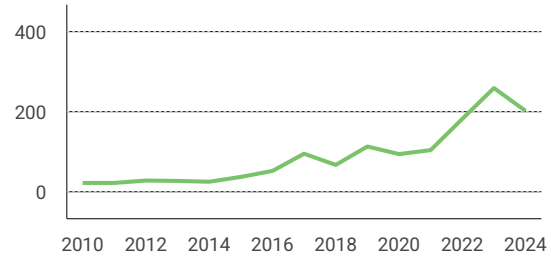

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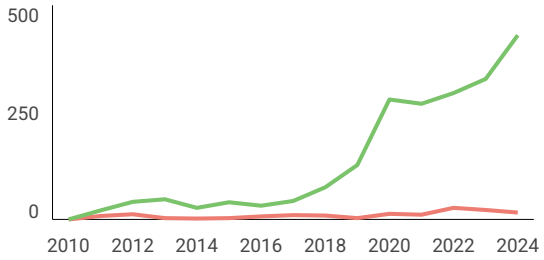

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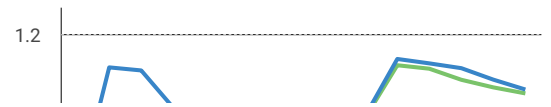

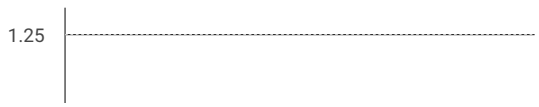

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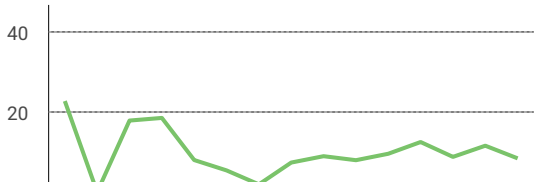

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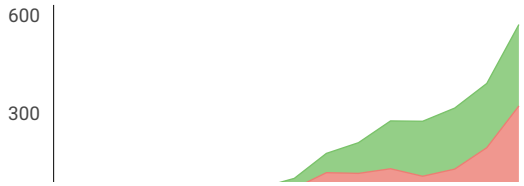

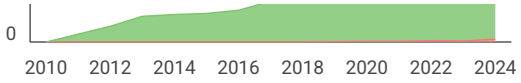

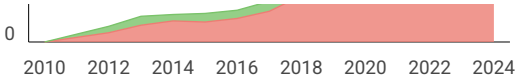

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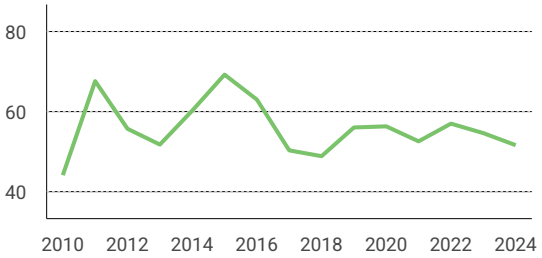
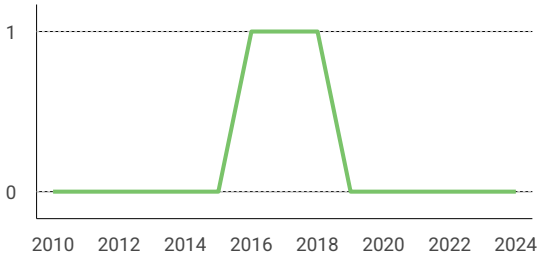


Documents cited by public policy (Overton)



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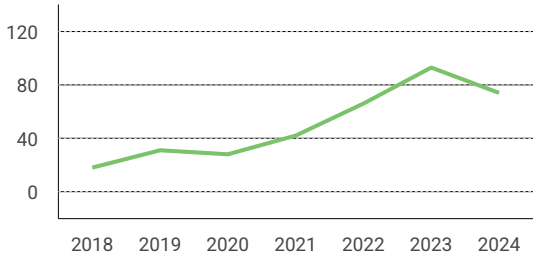

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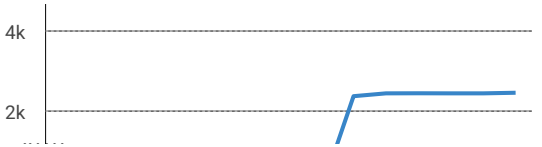

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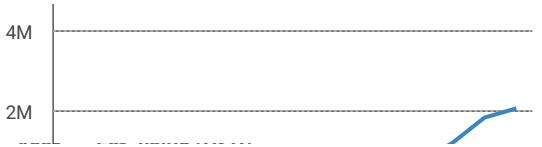

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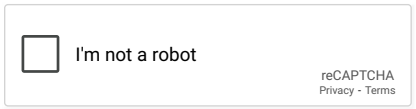

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