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Analysis of Flow Characteristics and Paracetamol Tablet Hardness Using 2D Double Mixer of Design Drum Type with Rotation and Mixing Time Variations

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Abstract – Font 11

One of the tablet manufacturing processes using the wet granulation method is the process of mixing the active ingredient granules, fillers, binders and pelicans. The parameters of the mixing process are important to study because they will affect the physical properties of the tablet. This study studied the effect of the variable duration and the size of the mixing cycle on the physical properties of paracetamol tablets using a 2D double mixer. The results of the analysis and testing showed that the variation of mixing time and the size of the rotation had a significant effect on the flow properties of the granules and the hardness of the tablets. In addition, the optimal parameter results to obtain optimal tablet hardness occurred at 15 minutes of mixing process and 50 rpm of rotation.

Keywords: *mixer-2D, drum, flow properties, tablet hardness, paracetamol*

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INTRODUCTION

Paracetamol is one of the most popular drugs in the society. Paracetamols is an analgesic-antipyretic drug which often produce and use due to its safety [1]. There are

only several people who use paracetamol to reduce fever (antipyretic) but most people use paracetamol as an analgetic to relieve mild to moderate pain [2].

Paracetamol has been used since 1893. The active substance of paracetamol had bad flow characteristic and compressibility, so, the appropriate method to make the tablet was using wet granulation [2].

One of paracetamol production process used wet granulation was paracetamol mixing process which was consisted of powder paracetamol as an active substance, amylum lactose as a filler, PVP K-30 as a binder, magnesium stearate as a lubricant, and aquadest as a wetting. Mixing process was conducted after oven and sifting process, so, the form of tablets' materials was granules.

Mixing process used mixer machine. There were several mixer tubes forms. In this study, the researchers studied mixer tube in the form of drum and cylinder. Few researchers studied about variations of mixing process duration and shaft tube mixer rotation to the physical characteristics of tablets. It needed deeper study to this research.

METHODS AND EXPERIMENTAL APPARATUS

This research used experiments method from 2D double mixer machine designed. The stages of research design were: Design and manufacture of 2D double mixers; preparation of paracetamol granules after it passed heating and sieve stages; process of granule weighing; process of testing flow characteristics; printing of paracetamol tablets; process of hardness testing; and analysis of test results.

In this study, the design and manufacture of 2D double mixer was carried out in the CNC ITATS laboratory. The material preparation of paracetamol tablet granule, flow characteristics test and tablet hardness were conducted in the *Mitra Sehat Mandiri* Pharmacy Academy laboratory in Sidoarjo.

There are variables in this study such as: independent variables (the amount of rotation and the lenght if mixing process); dependent variables (granule flow characteristics and the amount of tablet hardness); and control variables : mixer tube of drum type and granule mass.

Tools and Materials

There were some tools which was needed in this study as shown in Figure 1, such as 2D double mixer machine, mixer tube, digital scale, measuring cup, sieve shaker, measuring funnel, caliper, stop watch, tablet mold machine, and hardness tester.

a. Double mixer b. Digital Scale c. Measuring Cup

Figure 1. The tools of flow characteristics test

The materials were paracetamol (main material in the experimental), PVP K-30 (binder between the materials), lactose (diluent), talc (glidant), amylum manihot (crushing agent), magnesium stearate (flow lubricant), aquadest (binder of all materials).


a. Sieve shaker


b. Funnel flow


c. Tablet mold machine

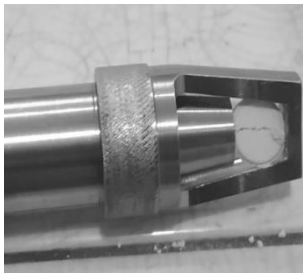
d. Hardness tester

Figure 2. The tools of flow characteristics test and hardness tables test

Flow characteristics test procedures in this study such as: measure the weight of granule according to the size of 100 grams; prepare a stopwatch to measure the time of granule flow characteristics; pour the granule into measuring funnel; and allow the granule to flow freely and take note of the time needed through the funnel.

Further, measurement procedure of repose angle includes: measure the weight of granule according to the size of 100 grams; pour the granule into measuring funnel; allow the granule to flow freely through the funnel; measure the height of granule powder which was formed by using a caliper; and measure the diameter of granule powder which was formed by using a caliper. Then, procedure of tablet hardness test, such as: measure the weight of granule according to the size of 100 grams; put the granule to the measure cup to compress the granule by tapping the measure cup; put the granule into tablet mold; put the granule tablet into MHT-20 type hardness tester equipment; turn the knob on the HT-20 type hardness tester equipment; stop turning the knob if there was cracked to the tablet; take note of medicine hardness as shown on the HT-20 type hardness tester equipment.

Tablet making with wet granulation method is the most common method for tablet making. In this method, physical characteristics of tablet will be tested such as flow characteristics, hardness, tensile, and disintegrate time [3], [4], [5], [6].

Several researchers have been carried out the study of granule mixer with tablet materials [7]. The researchers used v-shell mixer and the angle was 90^{o} with single blender tube and tumbling type which was used in many mixing fields like powder mixers. Space capacity of mixer tube was 60%, 15rpm, 30 rpm, and 45 rpm for rotation variations. Mixing rotation in the machine was controlled by DC motor power and motor speed controller of DC12V to DC40V. The conclusion was time and rotation affected to the mixing similarity. The purpose of V tube mixer developing was non-drug powder [8]. Vitamin B6 tablets which were made using wet granule method used physical characteristics test.

Paracetamol had bad flow characteristics and compatibility with its crystalline form. It necessary to make granule with granulation method [5]. It related to the powder mixing process of drug materials, the aim of mixing was to produce the mixing of drug supply in different drug types between two types or materials which could produce better homogeneity in the granule materials mixture become tablet. The process would be handled two particles, so that each particle unit, molecule, and etc from the materials could interact with others materials. Principally, drug materials mixing imitated to fluid mechanic principles because materials mixing would occur if there were movement or displacement of materials mixing and it would be mixed horizontally or vertically [9]. Flow characteristics was a critical factor in the production of solid preparation drugs because flow characteristics of powders affected to reproducibility increasing of

compression space filling to tablets and capsules production. It caused better heavy similarity and pharmacological effects [10].

Flow time definition was the time required to flow from several granules to the funnel hole and we must measure the amount of substance flowing in the certain time. Powder mixture flowing was very important to tablet making and we must make sure for efficient mixing. The flow speed of powder mixture related to flow characteristics of powder mixture and it affected to the filling both drugs and weight from tablets to the molding holes in the tablet machine and it gave facility to the material movements.

In tablet preparation could be made in three methods; wet granulation, dry granulation, and direct compression. Method chose of preparation tablet making was usually adjusted with active substance characteristics which would be made into tablets. It was to know resistant substance to heat, moisture, stability, dose, and other.

a. Wet Granulation is a mixture process of active substance particles and excipients into larger particles by adding the right amount of binder liquid, so that, a moist mass can be granulated. This method usually used if active resistance was resistance to moisture and heat. Generally, active substance was difficult to form directly due to bad flow and compressibility characteristics. The principle of wet granule method was making wet of mass tablet with a certain binder solvent until it obtained certain wet level. The final step was wet mass was granulated.
b. Dry Granulation was formed and the chunks needed to be filtered become granule. It necessary to be added outer phase and formed into tablet.
c. Direct_Compression was direct formed. it was made by compression method and we needed to apply high pressure to the powder/granule using a steel punch/mold.

Flow Characteristics

Flow characteristics are critical factors in the solid preparation tablet production because powder flow characteristics affected to the reproducibility level of compression filling space in the tablets and capsules. It made a better uniformity of preparation dosage and its pharmacological effects. Flow time is the time needed to flow from several granules through measured funnel hole. It was the amount of substance flowing in the certain time.

Flow Speed

The flow of powder mixture was very important in the tablet manufacturing to ensure efficient mixing. Flow speed of powder mixing related flow characteristics of powder mixing and it influenced the filling of both weight and drugs in the tablet inti molding holes of tablet machine. Besides the movement of tablet materials would be easier.

The use of binder-filler could repair flow characteristics, so, it had better flow speed of powder mixing. The greater we used binder filler; the better flow speed got. Speed of flow rate could be calculated using this formula (1):

$$Q = \frac{\text{Vol}}{\text{t}} \quad \ldots (1)$$

Where Q is debit, Vol is volume, and t is time. Table 1 shows the relation between flow rate and powder flow characteristics.

Table 1. Relation between flow rate and powder flow characteristics [13]

Flow Rate (g/second)	Flow Characteristics

>10	Free to Flow
4-10	Easy to Flow
1,6-4	Cohesive
<1.6	Very Cohesive

Parameter of flow characteristics was repose angle (sudut diam). We could use repose angle to compare the test of physical characteristics of granule or powder mixing by calculating cotangent from the height of the cone formed. Repose angle was a fixed angle which was occurred between heap of conical particles and horizontal field when a certain amount of powder was poured into the measuring device [11]. Repose angle was measured with this formula (2):

$$tg\ \alpha = r\ h \quad \ldots (2)$$

Where α is repose angle, h is cone height, and r is radius.

Hardness Test

Tablet hardness test could be defined as a tablet strength test which reflect overall tablet strength and it is measured by applying pressure to the tablet diameter. Tablet must have a certain strength and hardness and it could withstand from various mechanical shock during manufacture, packaging, and transportation and we needed hardness tester for the tools [2]. Hardness was a parameter which describes the tablet's resistance to resist mechanical emphasis like shock, abrasion and crack to the tablet during the stages of packaging, transportation, and use. The hardness was used to measure compression pressure. We can say tablet in a good condition if the tablet has 4 to 8 kg [12].

Tablet hardness test was a test which is conducted to know physical hardness of tablet preparation to the mechanical stress or friction. The aim was to know the resistance of tablet preparation in the face of pressure obtained several processes; packaging, distribution, and stored.

RESULTS AND DISCUSSIONS

Flow Characteristics Time Test

Table 2. The result of Flow Characteristics Time Test

Flow Time (second)		Rotation (rpm)		
		n_1 = 30	n_2=50	n_3=70
Duration (t = minute)	t_1 = 5 minute	16,542	13,756	17,224
	t_2 = 10 minute	13,692	12,446	16,082
	t_1 = 5 minute	12,72	11,944	15,382

The experiment was conducted with the mass of medicine powder 100 grams and the form of tube type was drum. The result of flow characteristics test was shown in Table 2 and Figure 3.

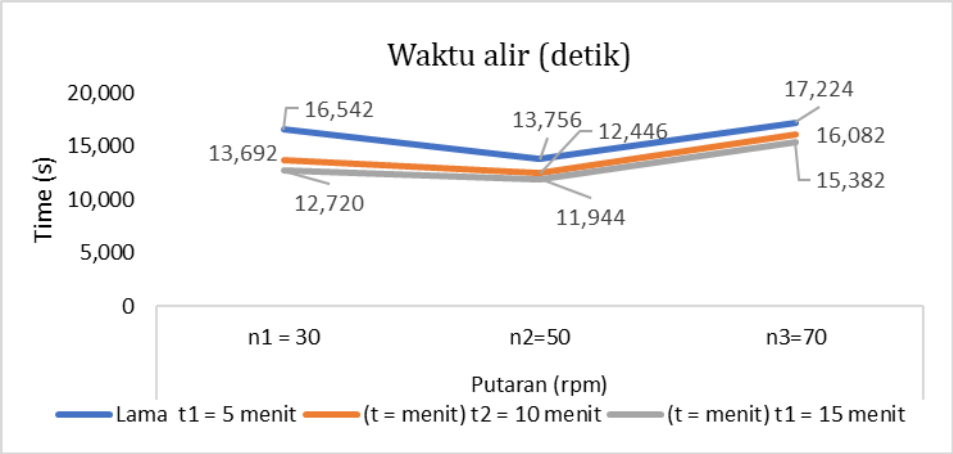

Figure 3. Test result diagram of mixer frum flow characteristic time

Flow Speed

The flow rate was calculated by comparing the weight of the powder per unit of flow time (gram/second) with the formula (3), then the result can be seen in Table 3 and Figure 4.

Flow Rate = Powder Weight (gram) / time(second) ..... (3)

Table 3. The results of flow rate test

Flow Rate (gram/second)		Rotation (rpm)		
		n_1 = 30	n_2=50	n_3=70
Duration (t = minute)	t_1 = 5 minute	6,045	7,269	5,805
	t_2 = 10 minute	7,303	8,034	6,218
	t_1 = 5 minute	7,861	8,372	6,501

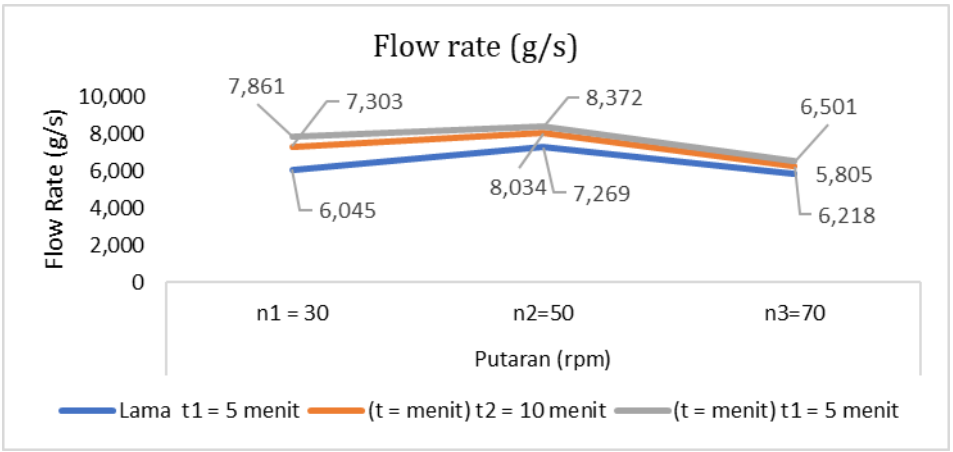

Figure 4. Rotation Effect and Mixing Time on powder flow rate

Table 4 and 5 shows the recapitulation of repose angle and index angle and the relation of rest angle and flow characteristics. The test result of repost angle value showed value range between 31^o-33^o, so that, the flow characteristics condition was in a good category.

Table 4. Recapitulation of repose angle and index angle

Sample	t (minute)	n (rpm)	D (cm)	H (cm)	α°	Index angle
1	5	30	12,482	3,792	31,257	good
	5	50	11,676	3,922	33,861	good
	5	70	11,906	3,772	32,333	good
2	10	30	12,074	3,852	32,537	good
	10	50	11,674	3,612	31,716	good
	10	70	11,76	4,002	34,215	good
3	15	30	11,646	3,73	32,619	good
	15	50	11,732	3,716	32,333	good
	15	70	11,846	3,988	33,940	good

Table 5. The relation of rest angle and flow characteristics

Rest Angle (°)	**Flow Characteristics**
25 – 30	Special
31 – 35	Good
36 - 40	Moderate
41 – 45	Good Enough
46 – 55	Bad
56 – 65	Very Bad
➢ 60	Too Bad

Source: Index table according to the relation between repost angle and flow characteristics (United States Pharmacopoeia : 32th.2009:643)

Tablet Hardness Test

Tablet hardness test was carried out after tablet mold process was finished and it obtained the data in table 5:

Table 5. The drug tablet hardness result of Mixer Drum

Drug Tablet Hardness (Kg)		Rotation (rpm)		
		n_1 = 30	n_2=50	n_3=70
Duration (t = m**in**u**te**)	t_1 = 5 minute	4,30	5,16	4,12
	t_2 = 10minute	5,20	5,66	4,46
	t_1 = 5 minute	5,56	5,92	4,66

The requirement which was appointed by Farmakope to hardness tablet was in the range of 4 to 8 kilograms (Health Department of Republic Indonesia, 2014). So that, the performance of tablet mixer machine was the best result using drum tube which had meet the requirements as shown in Figure 5.

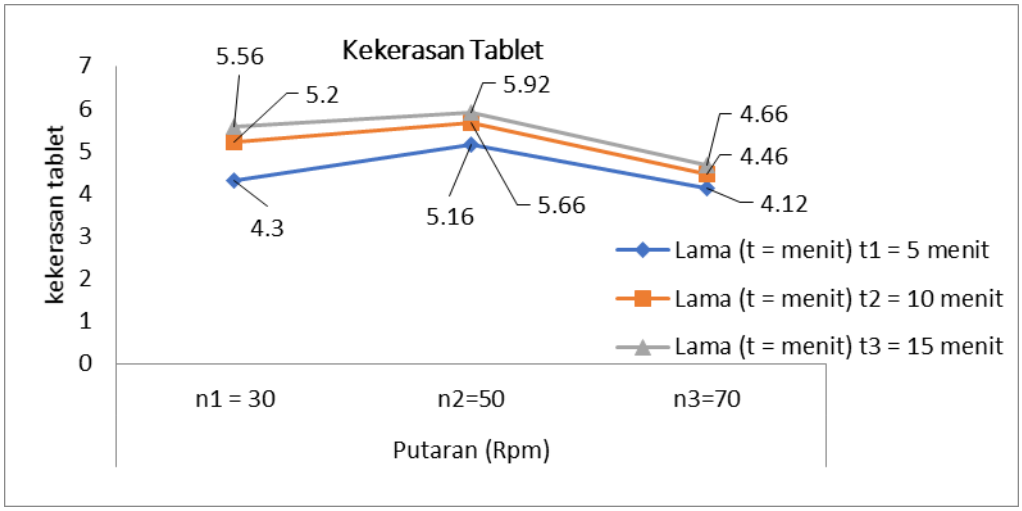

Figure 5. Graphic of drug tablet hardness result of Mixer Drum

Variance Analysis

The researchers must conduct old variance analysis to know the effect of the duration variation of mixing process and the size variation of the rotation both flow characteristics and tablet hardness. The researchers carried out variance analysis and it obtained the confidence level of 95%.

Hypothesis Testing:
1. Ho was accepted and H1 was rejected if F calculation < F table
2. Ho was rejected and H1 was accepted if F calculation > F table

The analysis results of flow characteristics variances were obtained :
1. For Variation of mixing cycle F count= 31.712 > F table = 6.94
2. For Variation of mixing duration F count = 112.565 > F table = 6.94

The result calculation of Fcount showed that the 95% confidence level of Ho was rejected and H1 was accepted. It could be concluded that rotation size variance and mixing process duration had a significant effect to the flow characteristics. Another analysis was variance analysis of tablet hardness with the variance size and the duration of the rotation to know significant differences. The analysis calculation results of tablet hardness variances were obtained

- ✓ For rotation variation of Fcount = 109.515 > F table = 6.94
- ✓ For variation in mixing time, Fcount = 34.0 > Ftable = 6.94

The variance analysis result of 95% confidence level showed that Ho was rejected and H1 was accepted. It could be said that the variance of rotation size and the duration of mixing process had a significant effect to the hardness tablet.

Mathematical Equation Model Approach of Flow Characteristics and Tablet Hardness

Mixing old variable and rotation size to the flow characteristics could be made using a mathematical model approach, as follow:

$$Y' = 12.461 - 0.039\ X1 + 0.047\ X2 \quad \text{..... (4)}$$

Where Y is Granule Flow Time, X1 is Mixing Time and X2 is Mixing Round. Determination coefficient from equation (4) above was R = 0.477, it means the accuracy of mathematical model approach was low. The result of mathematical model graph was described as a surface respond as shown in Figure 6.

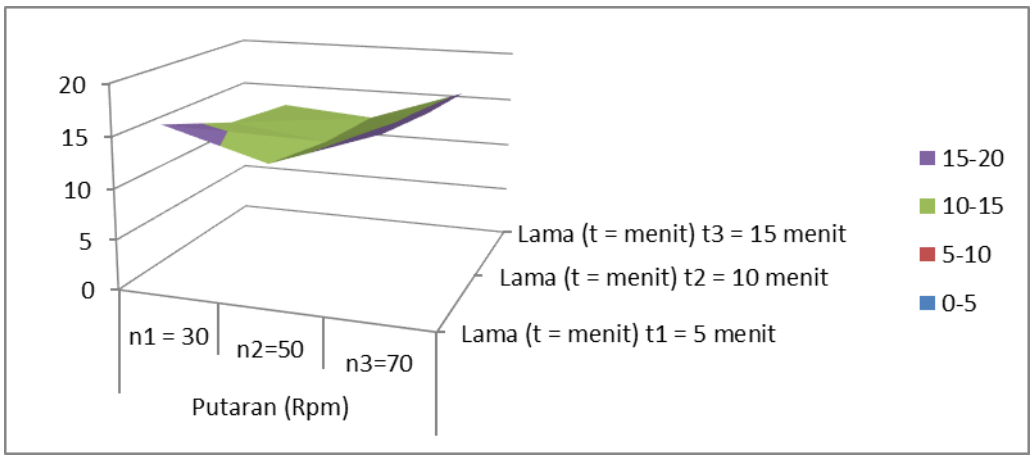

Figure 6. Flow Characteristics of Surface Graph

Mathematical equation model connected between the duration and the size of mixer ratation to the tablet hardness and it could see from this equation (3). Where Y is Hardness of tablets, X1 is Mixing Time and X2 is Mixing Round. Determination coefficient from equation (5) was R=0.461, It means that the accuracy of mathematical model approach was low.

$$Y' = 5.624 + 0.013\ X1 - 0.015\ X2 \quad .. (5)$$

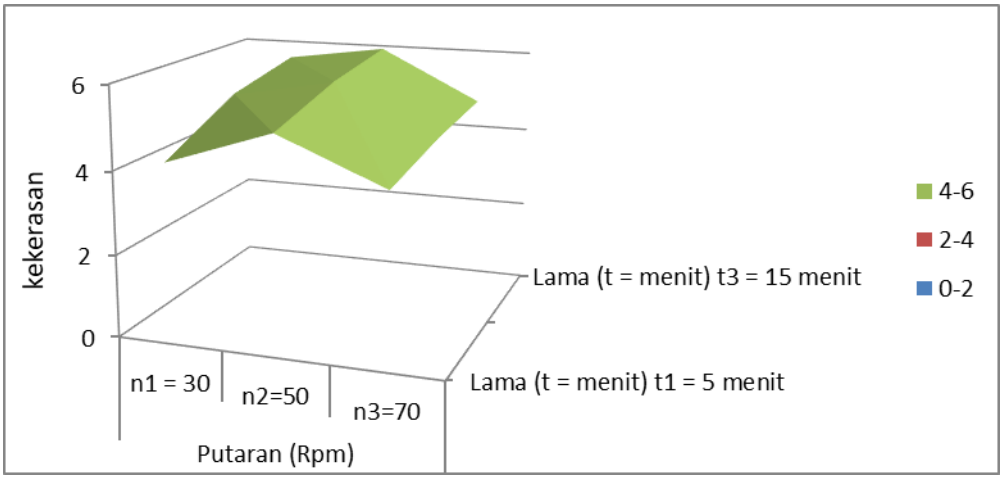

Figure 7. Surface graph of Tablet Hardness Test

CONCLUSIONS

Based on the result of the test and data analysis could be concluded that using 2D double mixer with drum type were:

1. The variation of mixing duration and rotation size in the granule mixing process for paracetamol tablet materials had a significant to the flow time.
2. The variation of mixing time and rotation size gave a significant effect to the paracetamol tablet hardness.

3. Mixing of paracetamol tablet materials used 2D double mixer machine with tube type and the drum form produced hardness tablet which met the standards set by farmakope.
4. The parameter of granule mixing producing the most optimal hardness tablet was occurred in 50 rpm rotation and the mixing duration was 15 minutes.

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DECLARATION OF CONFLICTING INTERESTS

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REFERENCES

[1] D. Sugiyono, "Formulasi Tablet Parasetamol Menggunakan Tepung Bonggol Pisang Kepok (Musa Paradisiaca CV. Kepok) Sebagai Bahan Pengikat," *Media Farm. Indones.*, vol. 12, no. 1, 2017.
[2] F. Y. Wong, C. M. Tan, B. Ponnusamy, S. B. S. Gima, and M. A. Adnan, "Design and Development of V-Blender Machine, Part," 2015, [Online]. Available: researchgate.net.
[3] N. N. Kusumo and S. R. Mita, "Pengaruh Natural Binder pada Hasil Granulasi Parasetamol," *Farmaka*, vol. 14, no. 1, pp. 228–235, 2016.
[4] N. Hidayati, N. Meilany, and S. D. Andasari, "Formulasi Tablet Kunyah Asetosal Dengan Variasi Konsentrasi PVP Sebagai Bahan Pengikat," *CERATA J. Ilmu Farm.*, vol. 11, no. 1, pp. 7–14, 2020.
[5] M. Hilaria, "Pengaruh Penambahan Amilum Gewang (Corypha Utan Lamarck) Secara Intragranular dan Ekstragranular Terhadap Sifat Fisik Tablet Paracetamol dengan Metode Granulasi Basah", Jurnal Ilmiah Manuntung, Vol. 6 No.1, Page. 110-121, 2020.
[6] E. Zulfa, M. P.-J. Pharmascience, and undefined 2019, "Formulasi Tablet Paracetamol dengan Bahan Pengikat Pati Umbi Gembili (Dioscorea esculenta L)," *ppjp.ulm.ac.id*, vol. 06, no. 02, pp. 55–64, 2019.
[7] I. N. Fadhilah and S. Dwi, "Formulasi dan Uji Stabilitas Fisik Sediaan Tablet Ekstrak Buah Pare (Momordica charantia L.) secara Granulasi Basah," *Smart Med. J.*, vol. 2, no. 1, pp. 25–31, 2019.
[8] T. Samudro, A. Pudji, and M. R. Mak'ruf, "V-Shaped Powder Mixer," 2020.
[9] H. Sumanti, I. Sudirman, and I. Hapsari, "Pengaruh Amilum Beras Ketan (Oryza Sativa Lf glutinosa Auct) Sebagai Bahan Penghancur Terhadap Sifat Fisis Tablet Vitamin B6," *Pharm. J. Farm. Indones. (Pharmaceutical J. Indones.*, vol. 6, no. 03, 2016.
[10] H. Sumanti, I. S.-… J. of Indonesia), and U. 2016, "Pengaruh Amilum Beras Ketan (Oryza Sativa Lf glutinosa Auct) Sebagai Bahan Penghancur Terhadap Sifat Fisis Tablet Vitamin B6," *jurnalnasional.ump.ac.id*, vol. 06, no. 03, 2009.
[11] L. Lachman, A. L. Herbert, and L. K. Joseph, *Teori dan Praktek Farmasi Industri*, III., vol. 658. 1994.

[12]E. L. Parrott, *Pharmaceutical technology: fundamental pharmaceutics*. Burgess Publishing Company, 1970.