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EFFECT OF GELATIN AS A BINDER ON TURMERIC EXTRACT TABLET FORMULATION

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ABSTRACT
In line with the progress of the times in which all aspects of many products are made easy and comfortable for the wearer. The main components for tablet formulations are the fillers, binders, crushers, thinners and lubricants. Among these components, the binders play a key role on the powder cohesion properties during the formation of tablet granules. In this study, turmeric extract tablets were formulated using 15 g of turmeric extract, 35 g of aerosil, 12.8 g of lactose, 1% magnesium stearate, 200 ml of aquadest and gelatin as a binder. To evaluate the effect of gelatin on the tablet formulation, the gelatin was then prepared in different formulation namely 0.1 g (formulation A), 0.2 g (formulation B) and 0.5 g (formulation C), respectivley. Based on the tablet properties, the turmeric tablet with formulation C met the standard requirements of friability less than 1%, the hardness in the range of 4 -8 kg and disintegration time under 15 minutes.

Keywords: Gelatin; Turmeric extract tablets; Wet granulation

1. INTRODUCTION

In line with the progress of the times in which all aspects of many products are made easy and comfortable for the wearer. As well as the development of traditional and herbal medicines, one of them is made into tablet preparations. Tablets are solid preparations containing active substances with or without additives that can be made with various sizes, shapes and surface markings (Depkes, 2014). A binder is needed to fulfillment the standard of pharmaceutical, which is a tablet component that has an important role in the tablet disintegration process in the body. The type and concentration of the binder will determine the characteristics of the resulting tablet (Suci, Kartadarma, & Darusman, 2015). The use of binders such as agar flour, PVP, gelatin, starch, maltodextrin, durian seed starch and cempedak, tragacanth, goroho banana peel sap can be used as a binder (Putri & Husni, 2018).

Gelatin can generally be used to bind the main components for the tablet formation. Unfortunelty, the characteristic of produced tablets tends hard, consequently the disintegration time of tablet is quite long (Pratiwi, Murukmihadi, & Aisiyah, 2017). The nature of gelatin is responsible on the compactness and durability of the tablets. The effect of gelatin on the temu lawak extract tablets show the high hardness, low friability and, long disintegration time (Pratiwi et al., 2017). Theses fact mean that the use of binder increases the hardness, reduce the friability and extend the disintegration time. However, several studies were also shown the fluctuating

results of the effect of gelatin on the tablet properties as reported by Kurniawan, Yogatama, and Aryani (2013); (Suci et al., 2015; Suyono & Nurhaini, 2016) (see **Table 1**).

In this work, the gelatin was used as binder for prepareing the turmeric extract tablet (TET). The turmeric plant (*Curcuma longa L)* has many health benefits. The turmeric rhizome contains curcuminoid compounds about 10% of which 1-5% is curcumin (Shamsher & Puneet, 2017). The curcumin has biological activities such as antioxidant, neuroprotective, anti-inflammatory, antiaging and others. Due to the effect of gelatin on the tablet properties are positive significant, therefore, this work tries to evaluate the effect of gelatin in the different formulation on the turmeric extract tablets.

Table 1. Research Results on the Use of Various Types of Binding Materials Tablet Manufacturing

Types of binders and the levels	Extract Tablet Type	Effect of addition of binder on hardness, friability and disintegration time of tablets	References
Gelatin (1% - 9 %)	Ekinase extract lozenges	Increasing hardness Decreasing friability Disintegration time	(Safitri, Gusmayadi, & Muchlifah, 2014)
Pregelatinized corn starch (5 % - 20 %)	Vitamin E tablets	Increasing hardness Decreasing friability Disintegration time	(Apriani & Arisanti, 2015)
Polivinil Pirolidon (PVP) (2% - 4%)	Jackfruit leaf extract tablets	Increasing hardness Decreasing friability Disintegration time	(Mindarwanis & Hasanah, 2017)
Avicel PH 102 (35% - 45%)	Papaya leaf extract tablets	Increasing hardness Decreasing friability Disintegration time	(Novriyaldi, Suhardiana, & Juniarin, 2020)
CMC-Na (1% - 3%)	Ketepeng leaf lozenges	Increasing hardness Decreasing friability Disintegration time	(Nugraheni, Mundriyastutik, & Jaya, 2018)
Gelatin (5% - 15%)	roselle petals chewable tablets	Increasing hardness Decreasing friability	(Pratiwi et al., 2017)
Tepung agar (0,5% -2%)	Onion extract tablets	Increasing hardness Decreasing friability Disintegration time	(Kurniawan et al., 2013)
Gelatin (1% - 5%)	Turmeric extract tablets	Increasing hardness Increasing-decreasing friability	(Suyono & Nurhaini, 2016)
CMC-Na (1% - 3%)	Cangkring wood extract tablets	Increasing hardness Decreasing friability Disintegration time	(Suci et al., 2015)
HPMC-Na (2% - 4%)	Cangkring wood extract tablets	Increasing hardness Decreasing friability Disintegration time	(Suci et al., 2015)
Mucilago starch cempedak (6% - 10%)	Paracetamol tablets	Increasing hardness Increasing disintegration time	(Sapri, Setiawan, & Khairunnisa, 2012)

2. METHODS

2.1. Materials

Turmeric extract obtained from PT. Borobudur Semarang, aerosil, lactose, gelatin, magnesium stearate and aquadest were obtained from PT. Brataco Chemica Yogyakarta.

2.2. Tools

The tablet testing equipment used a hardness tester (hardness test equipment), friabilator tester (friability test equipment) and disintegration tester (disintegration time test equipment).

2.3. Procedure

Granules were made using the wet granulation method. Aquadest is poured into a beaker containing gelatin and then heated until the gelatin dissolves in the aquadest. Next, the gelatin solution was poured into a container containing turmeric extract, arosyl, and lactose. The mixture of these ingredients is stirred until evenly distributed then sieved through a 12-mesh sieve and then dried in an oven at 40oC for 24-30 hours. After drying, the mixture of ingredients that have become granules are removed from the oven and then sieved through a 14/30 mesh sieve. Furthermore, the granules retained in mesh 30 were added with magnesium stearate (Mg stearate) 1% of the weight of the granules and then printed with a tablet press machine (single punch). Then the physical properties of the tablets were tested which included hardness test, friability test and disintegration time test. Tablets that met the standard requirements for hardness, friability and disintegration time were then replicated 3 times. Then the results of the replication were analyzed statistically using SPSS version 22.

2.4. Determination of Tablet Standard Test

Tests for tablets that have been printed include tests for weight uniformity, size uniformity, hardness, friability and, disintegration time. The weight uniformity test of turmeric extract tablets was carried out by weighing 20 tablets using a digital scale and calculating the average weight ($\bar{y}$). Next, each tablet was weighed and the weight was recorded. The calculation of the deviation value (SD) of each tablet and the coefficient of variation (CV) are presented in equations 1 and 2. Weight uniformity is said to be good if the kV or CV value is less than 5% (Hadisoewignyo & Fudholi, 2013).

$$\text{Deviation Standard (SD)} = \sqrt{\frac{\sum(y-\bar{y})^2}{n-1}} \quad (1)$$

$$\text{CV} = \frac{SD}{\bar{y}}\ x\ 100\% \quad (2)$$

The size uniformity test was carried out by taking 10 tablets. Then measure the thickness and diameter of each tablet using a caliper. Then the average value ($\bar{y}$) of the thickness and diameter of the tablet was calculated. Standard thicknesses and diameters meet the ranges in equation 3 as decribed by (Depkes, 1979), as follows;

$$\frac{4}{3}\ x\ \text{thickness} \leq diameter \leq 3\ x\ \text{thickness} \quad (3)$$

Hardness test was carried out on 10 tablets of turmeric extract. Hardness is measured by Hardness tester so that the average value is obtained. The unit of average TET hardness is kg. The hardness of tablets that meet the standards is in the range of 4-8 kg.

The friability test was carried out by taking 20 turmeric extract tablets and then freeing them from dust, weighing them using a digital scale (**Table 2**). The weight of the 20 tablets is expressed as Wo. Then 20 tablets were put into the fribilator and rotated for 4 minutes at a speed of 25 revolutions per minute. After that, the tablets were dusted again and weighed. The weight of these 20 tablets is then expressed as Wt. The calculation of the amount of % brittleness is stated in the following equation 4. Maximum weight loss or % brittleness is not more than 1% (Allen, 2014).

$$\%\ \text{Friability} = \frac{(Wo-Wt)}{Wo}\ \text{x}\ 100\% \quad (4)$$

The disintegration time test was carried out by inserting 6 tablets of turmeric extract into the disintegration tester (a basket-shaped tube). Then run the tool in a vessel filled with about 600 ml of water at a temperature of 36 °C – 38 °C. The basket is lowered and raised regularly 30 times per minute. The tablet is declared crushed if no part of the tablet is left on the gauze, except for fragments from the coating substance. The time required to crush the six tablets is no more than 15 minutes (Depkes, 2020).

Table 2. Turmeric Extract Tablet Formulation

Composition	Material Weight		
	Formula A	Formula B	Formula C
Tumeric Extract	15 g	15 g	15 g
Aerosil	35 g	35 g	35 g
Lactose	12.8 g	12.8 g	12.8 g
Gelatin	0.1 g	0.2 g	0.5 g
Magnesium stearate	1 %	1 %	1 %
aquadest	q.s	q.s	q.s

The formulations that met the tablet standard requirements were then replicated three times to show that the formulations showed no different standard results (still complied with the tablet standards). Next, statistical analysis (normality, homogeneity, ANOVA and post Hoc LSD tests) was performed using SPSS version 22 software.

3. RESULTS AND DISCUSSION

3.1. Tablet Granule Formation

In a preliminary experiment, tablets were made using the direct compression method, but turmeric extract and fillers had not succeeded in forming tablets. The wet granulation method was chosen because the granules from turmeric extract and other excipients can be bonded by the addition of a gelatin solution. Gelatin (binder) functions to bind turmeric extract with additional ingredients so that good granules are obtained and the tablets become compact and not easily broken. The use of excessive binder solution will result in a mass that is too wet and granules that are too hard, so that the resulting table has a long disintegration time. While the use of too little will cause weak adhesion so that the resulting tablet will be brittle (Parrott, 1971).

In the process of wet granulation, with the liquid binder, the binder will wet the surface of the particles and form liquid bridges between the particles. The steps that occur when the binder is added are the formation of pendular, funicular, capillary and droplet (**Figure 1**). The process of granule formation begins with the pendular stage, which is the formation of a space between the particles which is filled by some of the binding agent and forms a liquid bridge between the particles. As the binding fluid content increases, the number of liquid bridges between the primary particles increases and the granules move from a pendular state to a funicular state. In the funicular stage there is an increase in surface tension of approximately 3 times that of the pendular stage. On increasing the binding fluid content, the liquid bridges coalesce into a continuous network leading to a capillary state. At this stage all the spaces between the particles are filled by the binding agent. Due to the capillary forces on the concave surface between the liquids on the surface of the granules, granule formation will occur. The next stage is the droplet stage where at this stage the particles are covered by liquid droplets. Bond strength is influenced by the surface force of the liquid used. The last stage is the possibility of trapped air in the granules. The liquid saturation at the surface may be < 100% as represented by the pseudo-droplet stage. The increase in pore fluid saturation as a function of the binder fluid content may vary during the granulation process, depending on the formulation and equipment variables, both of which affect the degree of granule consolidation (Hadisoewignyo & Fudholi, 2013; Narang & Badawy, 2019).

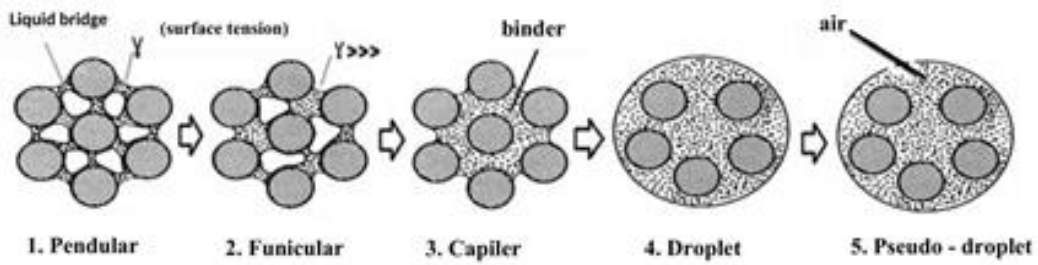

Figure 1. Mechanism of Granule Formation

3.2. Turmeric Tablet Properties

The results of the test can be seen in **Table 3**. The results of the hardness test of the three formulas showed that the use of 0.1 g gelatin (formula A) gave a hardness of 3.62 ± 0.41 kg. The same results with the use of 0.2 g gelatin (formula B) gave a hardness of 3.62 ± 0.34. While the use of 0.5 g gelatin showed an increase in the hardness of the tablet, namely 4.98 ± 0.2 kg. From these results, it can be seen that the addition of gelatin will increase the hardness of the tablet. The results of the friability test showed that the three formulas gave friability that met the standard of friability, however, formula B (gelatin 0.2 g) gave 0% friability, which means that no dust flakes or fragments of the tablet were found after the test. This shows that there is no linearity between the value of hardness and brittleness. The same thing happened to the results of the disintegration time test, where the fastest disintegration time of 10.78 minutes actually occurred in the formula with the largest gelatin. This explains that it is very possible that there is no linearity between the hardness value and the disintegration time which can be concluded in this study. The nonlinearity between hardness and disintegration time is that any increase in tablet hardness does not always increase tablet disintegration time. A logical explanation is possible because there are external factors that cause differences in conditions on the tablet, such as:

a. The difference in temperature when the granules are dried in the oven. Ovens that are used simultaneously with other materials that are often inserted and removed into the oven cause the room temperature to decrease in temperature. This affects the water content in the granules and tablets that are printed, so the size of the water content contained in the tablet will affect the hardness and brittleness of the tablet (Kusumawati, 2012).
b. The difference in temperature when the tablets were stored. The moisture content of a room can also affects the quality of the tablet. Research conducted by (Dwi, 2013), regarding the effect of storage on the physical quality of paracetamol tablets with a binder of polyvinyl pyrrolidone K30 made by wet granulation found significant differences in hardness and friability between tablets stored in room and air-conditioned conditions. However, there was no significant difference in the weight and disintegration time of the tablets. Changes in hardness and brittleness of tablets in an air-conditioned room were greater than those in room conditions. This indicates that there is an effect of temperature during tablet storage on the value of hardness and brittleness. Similar research conducted by (Arifah, 2014; Lestari, 2013) also showed the effect of room temperature on vitamin C on the parameters of brittleness, hardness and disintegration time.
c. The difference in drying time when the granules are dried in the oven. The results of research conducted by Jayanti 2013 that the duration of drying of the granules can reduce the moisture content of the granules and the hardness of the tablets but does not affect the friability of the tablets.
d. The difference in tablet storage time from printing to testing on tablets. This is if the humidity in the room is very high and the tablet is hygroscopic, the quality of the tablet will change with time.

Table 3. Results of Examination of Physical Properties of Tablets

No	Tablet Physical Properties	Standard Limit	Average and Deviation		
			Formula A	Formula B	Formula C
1.	Tablet weight (%, CV)	< 5	1.025	1.199	0.802
2.	Average tablet diameter (cm)	4/3 x tablet thickness ≤	D = 1.33	D = 1.33	D = 1.33
3.	Average tablet thickness (cm)	Diameter ≤ 3 x tablet thickness	t = 0.52 (fulfill)	t = 0.48 (fulfill)	t= 0.46 (Fulfill)
	Diameter (D), thickness (t)				
4.	Friability (%)	< 1	0.188	0	0.84
5.	Hardness(kg)	4 – 8	3.62 ± 0.41	3.62 ± 0.34	4.98 ± 0.2
6.	Disintegration time (minutes)	< 15	15.79	25.41	10.78

From **Table 2** formulas A and B do not meet the requirements for hardness and disintegration time. Only formula C satisfies all three requirements. Furthermore, formula C was replicated 3 times and the results were obtained as presented in **Table 4.** The results of replication showed that formula C met the specified requirements for hardness, friability and disintegration time.

Table 4. Formula C. Replication Results

No	Tablet Physical Properties	Standard Limit	Average and Deviation		
			1	2	3
1.	Tablet weight (%, CV)	< 5	0.617	0.619	0.518
2.	Average tablet diameter (cm)	4/3 x tablet thickness ≤	D = 1.33 t = 0.53	D = 1.34 t = 0.54	D = 1.34 t= 0.54
3.	Average tablet thickness (cm) Diameter (D), thickness (t)	Diameter ≤ 3 x tablet thickness	(fulfill)	(fulfill)	(fulfill)
4.	Friability (%)	< 1	0.16	0.0047	0.0877
5.	Hardness(kg)	4 – 8	4.46 ± 0,23	4.56 ± 0,24	4.54 ± 0.39
6.	Disintegration time (minutes)	< 15	3.66	14.04	11.34

Furthermore, the results of 3 times replication of turmeric extract tablet formulations that met the standards were tested statistically. This test includes the results of the disintegration time test (9.918 ± 4.386), the results of the friability test (0.065 ± 0.074), the result of hardness test (4.635 ± 0.234) and, the results of the weight uniformity test (0.616 ± 0.355). Statistical analysis using SPSS version 22 software were carried out show that 1. Normality Test, 2. Homogeneity Test, 3. ANOVA Test and 4 Post-Hoc Test – LSD. Meanwhile, the results of the size uniformity test and tablet hardness test were not tested because statistically, they had met the requirements. The results of statistical tests for 3 times replication showed that the data were normally distributed, homogeneous and there was no significant difference at the 95% confidence level. The limitation of this study lies in the limitations of the tools because they have to take turns in their use so it is very possible that there are differences in test results that are estimated from other factors.

4. CONCLUSIONS

The effect of the use of gelatin as a binder in the turmeric extract tablets has been successfully performed in this work. The tablets were made by using the wet granulation method. The main component of tablet consisted of the turmeric extract, aerosil, lactose, gelatin, and aquades. The formula C shows the good properties in which the friability less than 1%, the hardness in the range of 4 -8 kg and disintegration time under 15 minutes. These properties meet with the standard requirements of the tablets. It is recommended to further researchers to combine gelatin with other binders, and after all the requirements have been met, the test can be carried out preclinical and clinical.

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6. CONFLICT OF INTEREST

The author declares that there no competing conflicts of interest.

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