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ORIGINAL ARTICLES

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Optimization of polyvinylpyrrolidone concentration as a binder in red ginger dry extract tablets in combination with zinc sulfate

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ABSTRACT

Introduction: Polivinilpirolidon (PVP) one of binders which can obtain the tablet standard criteria, i.e hardness 3-6 KgF and friability less than 1%. Aims of this research to find out the optimum concentration of PVP as binder on ginger extract plus zink tablets.

Methods: The tablets are made in 5 formulas with PVP concentrations as binders of 2.8%, 3.1%, 3.4%, 3.7%, and 3.9%, respectively. The data observed on the evaluation of flow time granules, stationary angles, and compressibility, while for hardness and brittleness tablets.

Results and discussion: Based on the granule test results, the granule flow time obtained for formula 1 to formula 5 is qualified, formula 1 has the highest value compared to formulas 2, 3, 4, and 5. The results of the tablet test based on statistical analysis showed that the hardness for formula 1 was significantly different from formula 4, while formulas 1, 3, and 5 did not differ significantly. Shows that the hardness of formula 4 is the best. On the fragility test formula 1 is not qualified because the brittleness value is more than 1%. Furthermore, based on statistical tests for formula 2 and formula 3, it does not differ significantly, but formula 4 and formula 5 differ significantly, while formula 4 and formula 5 do not differ significantly but with formula 2 and formula 3 differ significantly, and the smallest brittleness value is in formula 5.

Conclusion: From this study, it can be concluded that the tablets that provide the best physical quality are formula 5 tablets with a PVP content of 3.9%..

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Introduction

Ginger plants are many types, and are mostly used for traditional medicine (Shiming, et al., 2022) One of the many types of ginger that is often used as a medicinal plant is a type of red ginger that contains compounds including gingerol, shogaol, and paradol. Gingerol in long-term storage can turn into shogaol. Some types of ginger contain compounds such as quercetin, zingerone, gingerenone-A, and 6-dehydrogingerdione. There are also terpene compounds such as bisabolene, curcumene, zingiberene, farnesene, and sesquiphellandrene, which are the main components of ginger is essential oil. Sampled, there are also other compounds such as polysaccharides, lipids, organic acids, and crude fibers (Mao et al., 2019). Some of the pharmacological activities of ginger: anti-inflammatory, antioxidant, antiemetic, antibacterial, antidiabetic, and cytotoxic (Rini et al, 2018). Priyanto research, 2013 states that red ginger which is believed with zinc to provide antiatherosclerosis effects. The combination of Red Ginger Rhizome Extract (ERJM) with Zinc (Zn) as an antiateroma is synergistic at a combined dose of ERJM 50 mg / kg with Zn 6.67 mg / kg in rabbits given an atherogenic diet and hypercholesterolemia rabbits (Priyanto, 2013). In previous studies, polyvinylpyrrolidone was used as a binding agent in making tablets with concentrations used namely 0.5%, 1.6%, 2.8%, 3.9%, and 5.0%. From the results of the study, the best formula was obtained was a tablet that uses a PVP binder of 2.8% and 3.9% (Sholehah, 2019). The difference between the previous study and this study is in the type of tablet, in this study the tablets made were not tablets or Chewable tablets, but ordinary tablets or conventional tablets, which in the filling material did not mind the taste. Previous research on the manufacture of tablets has been obtained that Polyvinylpyrrolidone (PVP) levels of 2.8 and 3.9% are the best concentrations, then it will be seen whether in the form of conventional tablets, PVP with these levels will provide good tablet quality or not.

Materials

The main ingredients of dried extract of red ginger rhizomes produced by PT. Haldin Pacific Universe, and Zinc Sulfate with pharmaceutical grade quality. Additional ingredients used Polyvinylpyrrolidone, Amilum Pro Tablets, Lactose, Talk, and Mg stearate with pharmaceutical grade quality

Table 1. Tablet Formula Formula Tablet Extract Dried Red Ginger and Zinc Extract

Material	Concentration (%)				
	1	2	3	4	5
Dried Red Ginger Extract	30.08	30.08	30.08	30.08	30.08
Zink Sulfate	2.06	2.06	2.06	2.06	2.06
Sucrose	20	20	20	20	20
PVP	2.8	3.1	3.4	3.7	3.9
Magnesium Stearate	1	1	1	1	1
Talk	2	2	2	2	2
Mannitol ad	100	100	100	100	100

Methodology

Formula Drafting

The research begins with an examination of organoleptic and solubility of the extract. Furthermore, a tablet formula is made for each tablet weighing 500 mg with the content of active ingredients for half the dose. The full formula can be seen in Table 1.

Granule Manufacturing

The next stage is the manufacture of granules with the beginning of weighing the ingredients for each formula, then mixed until homogeneous. To the mixture was then added 54 mL of 96% ethanol, made long enough to be made into wet granules. The obtained wet granules are then oven-dried at 50oC for 24 hours.

Granule Evaluation

The next stage is granule evaluation which includes drying shrinkage test, flow time, stationary angle, compressibility test and granule particle size distribution evaluation.

Tablet Making

After the granules meet the requirements, the next manufacture of tablets is carried out using a mini rotary machine with 8 stations. The engine settings are intended for tablets weighing 500 mg hardness 4-6 KgF. All formulas are forged using the same machine settings.

Tablet Evaluation

The tablets obtained are further evaluated which include organoleptic examination, uniformity of size, uniformity of weight, hardness, and brittleness.

Data analysis

The data obtained were statistically analyzed in comparison using the one-way Anova test with the help of the SPSS program.

Results and Discussion

The characteristic results of dried red ginger extract can be seen in the appendix to table 2 and the granule evaluation results can be seen in appendix to table 3. From the results of the organoleptic evaluation of dry red ginger extract, an extract was obtained in the form of a brownish-yellow fine powder that has a characteristic ginger smell and a spicy taste. solubility of the extract. The result is 100mg of ginger extract dissolved in 1.90 mL of water. From the data it can be interpreted that one part of the extract dissolves in 19 parts of water. The results of the F1 to F5 granule drying shrinkage test meet the requirements of a good granule, namely 3-5% (Voight, 1995).

Table 2. Characteristics of Red Ginger Extract

No	Parameter	result
1.	Organoleptic	Color : Yelow Brownish Odour: Typical of Ginger Taste: Spicy Shape: Fine Powder
2.	Solubility	100 mg Deeply Soluble in 1,90 mL air

Shrinkage drying on the granules can affect the physical properties of the resulting tablets. The greater the shrinkage of drying in the granule, it is feared that the granule has a reduced ability to flow due to the presence of moisture also can occur the sticking of the granule on the punch during printing which can affect the weight and size of the resulting tablet due to the large content of compounds that evaporate including water in the granule, The result graph can be seen in the Figure 1. F1 stationary angle test results until. F5 meets requirements that range from 25º to 45º the result graph can be seen in the appendix to chart 2. The flow time test results obtained F1 to F5 results meet the flow time requirements with the highest value for flow time found in Formula 1 and the lowest in Formula 5. The results of the flow properties evaluation show that the addition of PVP concentration will increase the cohesiveness of the granules so that the particle size becomes uniform, and the particle size is large. So, it is expected to obtain a good uniformity of weight and uniformity of tablet size. A graph of the results can be seen in the appendix to chart 3. Compressibility test results obtained from the results of formula 1 to formula 5 research meet the requirements of a special flow category with a requirement of %compressibility of 5-15% (Siregar and Wikarsa, 2010). From these results, there is a decrease in the percentage of refractive index because the higher the PVP concentration causes the properties of molecules that attract each other, thereby reducing the cavity between particles. The result graph can be seen in Figure 4.

Table 3. *Average* Particle *Diameter*

Formula	Flow time (g/detik)	Angle of repose (º)	Compressibility (%)	LOD (%)	Granule size (µm)
F1	4,26 ± 0,08	33 ^{O}	9,02 ± 0,05	3,60%	563,5
F2	4,04 ± 0,11	32^{O}	8,72 ± 0,64	3,40%	568,1
F3	3,89 ± 0,16	32 ^{O}	7,98 ± 0,00	3,22%	593,1
F4	3,93 ± 0,07	31 ^{O}	6,43 ± 1,34	3,23%	569,8
F5	3,46 ± 0,04	30 ^{O}	5,66± 0,00	3,21 %	607,9
Requirement	100 g less than 10 second (Aulton 2002)	< 50º (Agoes 2012)	≤ 20% (Agoes 2012)	3 – 5% (Voigt 1995)	250 – 2000µm (Agoes 2012)

Table 4. Average Particle Diameter

	Formula 1	Formula 2	Formula 3	Formula 4	Formula 5
Diameter(µm)	563,5	568,1	593,1	569,8	607,9

Table 5. Tablet Organoleptic Test Results

Formula	Shape	Odour	Color	Taste
Formula 1	Round	Typical Ginger	Light Brown	Spicy sweet
Formula 2	Round	Typical Ginger	Light Brown	Spicy sweet
Formula 3	Round	Typical Ginger	Light Brown	Spicy sweet
Formula 4	Round	Typical Ginger	Light Brown	Spicy sweet
Formula 5	Round	Typical Ginger	Light Brown	Spicy sweet

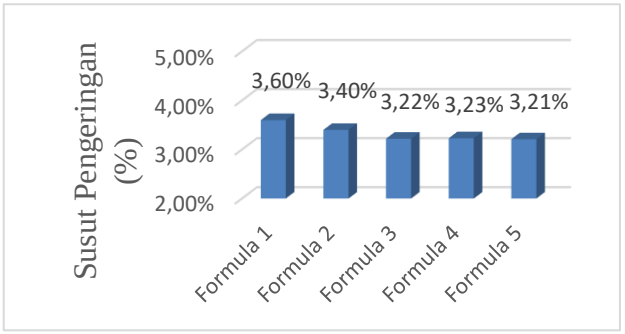

Figure 1. Graph of the Effect of Formula on Granule Drying Shrinkage

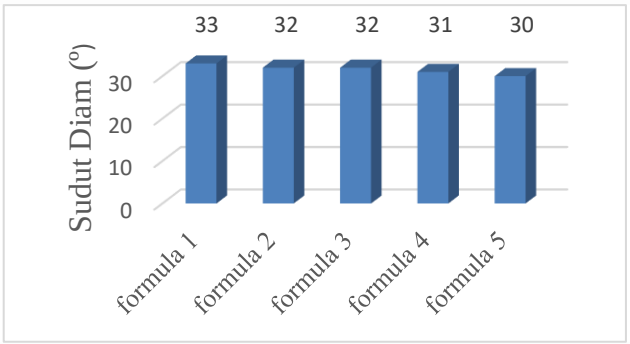

Figure 2. Graph of the Effect of the Formula on the Stationary Angle of the Granule

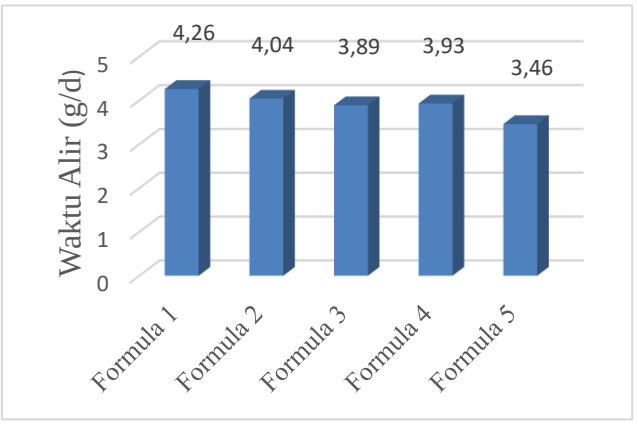

Figure 3. Graph of the Effect of Formula on Granule Flow Time

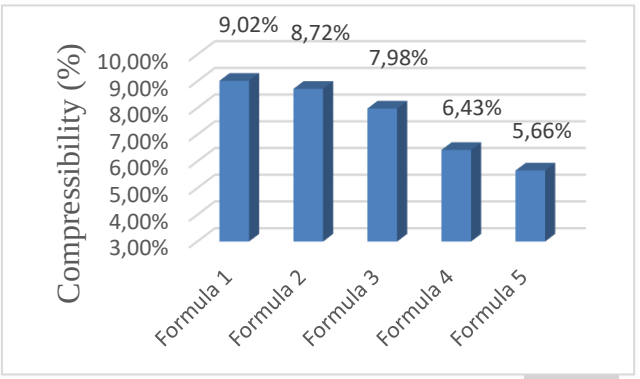

Figure 4. Graph of the Effect of Formula on Granule Compressibility

The granule particle size distribution test results of the five formulas were mostly held on sieve number 30. More distributed granules at a certain size means that the quality of the granules is quite good as a material for tablet processing (Lachman et al, 2008) On sieve number 30 the greatest number of left-behind granules is in formula 5 which means that PVP binding in formula 5 is the best. The result graph can be seen in Figure 5.

The results of measuring the particle size of the granule show that the formula 5 granule has the largest size of 607.9 µm while the formula 1 granule has the smallest granule size. All formulas meet the requirements. The results table can be seen in the appendix to table 4. Organoleptic test results include color, shape, aroma, and taste. The resulting tablets have a round shape, have a distinctive ginger flavor, and have an uneven light brown color due to the inhomogeneity between the extract colors that are different from other tablet excipients.

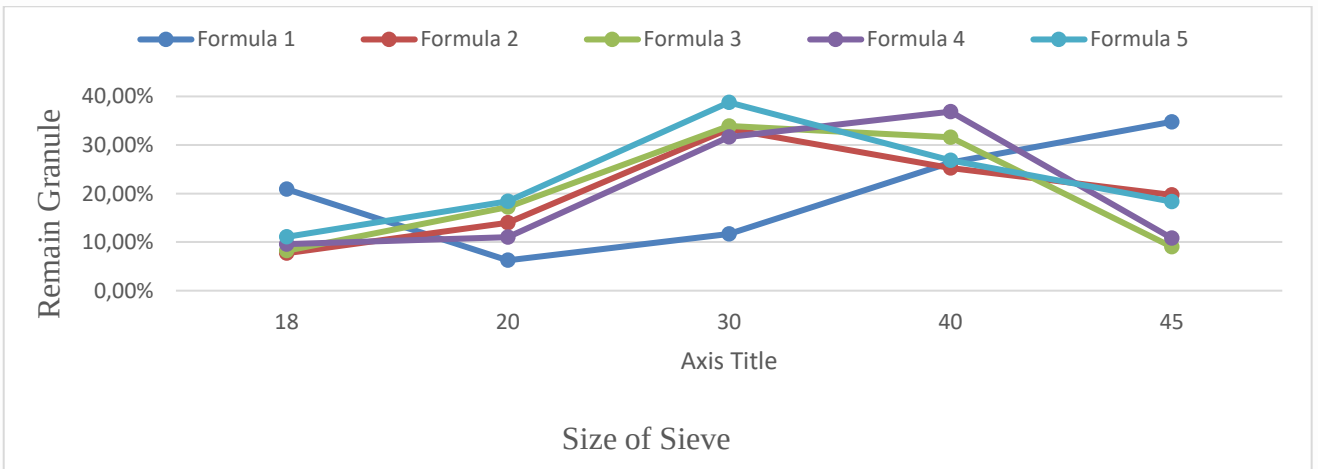

***Figure** 5*. **Graph of** *the* **Formula's Effect on the Granule Distribution**

Table 6. Size Uniformity Test Results

Formula	Thick (mm)
Formula 1	3,45
Formula 2	3,47
Formula 3	3,36
Formula 4	3,65
Formula 5	3,43

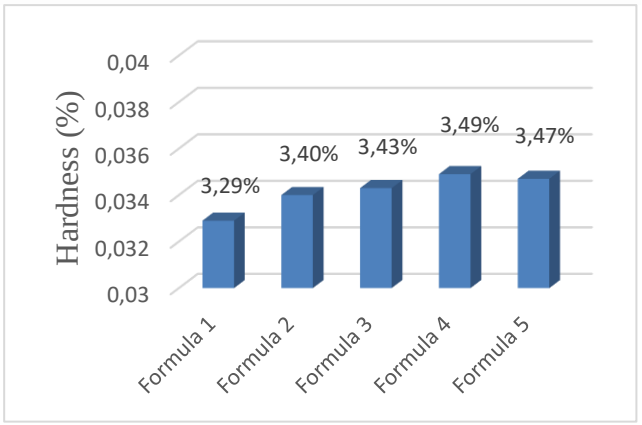

Figure 6. Graph of the Formula's Effect on the Hardness and Friability of Tablets

The results table can be seen in the appendix to table 5. The result of the uniformity test of the size of the diameter of the tablets of all formulas is 1.3 cm. The result of the thickness of the tablets is shown in table 6, namely the thinnest is Formula 3 and the thickest is Formula 4. This is due to the shape, size, and weight of a granule due to the difference in the number of binders in each formula so that when pressing occurs, the thickness of the tablet is determined by the density of the pressed granule. The results of the weight uniformity evaluation showed that no more than 2 tablets deviated more than 5% and none of the tablets deviated more than 10% of the average weight. The results table can be seen in the appendix to table 7.

Hardness test results from formula 1 to formula 5 are eligible. Formula 1 has the lowest hardness while formula 4 has the highest hardness. This is because there is a difference in the number of binders in each formula, the greater the concentration used, the greater the hardness produced. A graph of the results can be seen in the appendix of chart 6. The results of the variance analysis test on hardness data resulted in a sig value of 0.023 smaller than 0.05 meaning that there was a significant difference between the five formulas. Then continued the Tukey HSD test and the results showed that formula 1 is different from formula 4 and vice versa, but not formula 2, 3, and 5. The difference in binding concentration between formula 1 (2.8%) and formula 4 (3.7%) causes a significant difference.

The results of the fragility test conducted on the five formulas showed that Formula 2 to Formula 5 tablets were qualified, while Formula 1 tablets did not meet the requirements. This is due to the lower concentration of the binder used so that the resulting tablets are too fragile. A graph of the results can be seen in the appendix to chart 7. The results of the variance analysis test on fragility data resulted in a sig value of 0.000 smaller than 0.05 meaning that there was a significant difference between the five formulas. Followed by the Tukey HSD test and the results showed that there were significant differences between formulas. Formula 1 is not eligible because of the fragility value of more than 1%. For formula 2 and formula 3 are the same but not as formula 4 and formula 5. For formula 4 and formula 5 are the same but not as formula 2 and formula 3. The smallest percent value of fragility is formula 5. Thus, of the 5 formulas, the best level is in formula 5, namely with a PVP content of 3.9%

Tabel 7. Hasil Uji Keseragaman Bobot Tablet

No	Formula 1		Formula 2		Formula 3		Formula 4		Formula 5	
	Bobot	**%**	**Bobot**	**%**	**Bobot**	**%**	**Bobot**	**%**	**Bobot**	**%**
Rerata	0,514		0,511		0,513		0,523		0,507	
SD	0,013		0,004		0,009		0,010		0,003	
Max	6,420		1,565		3,313		4,206		1,577	
Ket	Memenuhi Syarat		Memenuhi Syarat		Memenuhi Syarat		Memenuhi Syarat		Memenuhi Syarat	

Coclusion

As the results of the study, for 5 formulas, only 4 formulas were obtained, namely formula 2 to formula 5, while for hardness, all formulas were qualified, but the better fragility was formula 5. Thus, the optimum concentration of polyvinylpyrrolidone (PVP) as a binder of red ginger extract tablets is in formula 5.

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