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Preparation of Single Garlic, Red Ginger, Lemon and Apple Vinegar Combination Tablets By Wet Granulation Method

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ABSTRACT

Garlic, red ginger, lemon, and apple cider vinegar are spices in Indonesia that can be useful for increasing the body's resistance and preventing degenerative diseases. Tablet preparations are preferred because they are practical, easy to use, and easy to carry anywhere. The aim of this research is to see the effect of differences in the concentration of internal and external disintegrants, binders, gliders, and lubricants in each formula. Tablets are made with the single active ingredients of garlic, red ginger, apple cider vinegar, and lemon. The wet granulation method was chosen because natural materials have poor flow properties, so by using the wet granulation method, the flow rate, compressibility, and binding capacity of the granules can be improved for the better so that they can be molded into tablet preparations. The research results showed that all tablet formulas met the tablet evaluation requirements. The concentration of external and internal disintegrants, binders, gliders, and anti-adherents does not make a difference in flow time or angle of repose but provides different water content values in formula 3.There is an influence of differences in the concentration of additional ingredients on the quality of the tablets produced. The greater the concentration, the better the weight uniformity, the harder the resulting tablet, and the longer the disintegration time. Tablet fragility on F2 is high than formula 1 and 3, but still meets tablet quality requirements.

Keywords: *Single garlic; ginger; lemon wet granulation; tablet combination*

INTRODUCTION

Indonesia has many spices, such as single garlic and red ginger, which are widely used as food flavorings as well as medicines. The use of a single garlic clove and red ginger can be combined with lemon, honey, and apple cider vinegar. People use this herb to maintain heart health, reduce high blood pressure, lower cholesterol levels, improve the immune system, repair and so on, for heart health, stroke, gout, diabetes, hepatitis, tumors, cancer, kidneys, gallstones, ulcers, osteoporosis, vertigo, obesity, blood thickness, lung infections, tingling in hands and feet, calcification, impotence, bronchitis, and asthma (Wiendarlina, 2022; Ulaen et al., 2023). Giving preparations of red ginger, garlic, apples, lemon, and honey can significantly reduce cholesterol levels in white mice (Ifora, 2016). The results of research conducted by Ulaen et al. (2023) on patients who were given a combination of single garlic juice, red ginger, apple vinegar, lime, and honey showed that there was an effect of giving single garlic juice before and after treatment on measurements of body weight and blood pressure. cholesterol, uric acid, and glucose levels in respondents.

Tablets are solid preparations that contain medicinal ingredients, with or without fillers. Based on how it is made, it can be classified into

printed tablets and felt tablets. In general, compressed tablets contain active substances and fillers, binders, disintegrants, and lubricants; they can also contain coloring materials and shellac (coloring materials adsorbed on insoluble aluminum hydroxide), which are permitted (DepKes RI, 2020). The additional materials used in this research were variations of corn stach as an internal disintegrant and binder, explotab as an external disintegrant, talc as a glidant, Mg sterate as a lubricant, and laxose as a filler. Starch is widely available and useful in tablet production because its inert nature, cheapness, and use as a filler, binder, disintegrant, and glidant. Starch has the advantage of being an excipient, namely that it can be mixed and has inert properties with most medicinal ingredients. (Adetunji et al. (2006); Priyanta et al. (2012) in Sakinah, 2018). Corn starch can function as a binder at a concentration of 5-25 % and a destroyer at a concentration of 3-5 % (Rowe, 2009). Corn starch has the ability to absorb water, which influences the starch development process and makes tablets easier to disintegrate (Yuniarsih, 2023). The advantage of explotab material as a disintegrating agent is its strength of capillary action, which will draw liquid into the tablet, so that in tablet formulation this material will expand and cause the tablet to break, disintegrate, and then dissolve (Lestari, 2022). Talc and magnesium stearate function as lubricants, which reduce friction during the tablet pressing process and also prevent the tablet mass from sticking to the mold. A good lubricant must have lubricating, non-stick, and lubricating properties. One ingredient that has lubricant and anti-stick properties that is often used is talc. This material is cheap and easy to obtain, but the lubricating properties of talc are not good. For this reason, it is necessary to add Mg Sterat, which has good lubricating properties, so that when the two are combined, they will complement each other. However, magnesium stearate has hydrophobic properties, so it can inhibit the release of nutritious ingredients (Sofyan 2015). Generally, formulas with lactose as a filler show good drug release rates. In addition, the price of lactose is cheaper than many other fillers (Setiani, 2018). Lactose can function as a binder and filler, and with corn starch, it can increase the ability to flow granules and crush tablets. (Rowe, 2009). Based on the description above, it is known that several ingredients have the same function, and the combination of ingredients used can affect the action of one ingredient over another, so in this study, variations in the concentration of additional ingredients were carried out in each formula.

In making tablet preparations, the active substance and other auxiliary ingredients are first changed from powder form into granular granules. There are 3 compression methods for making tablets, namely making using the wet granulation method, dry granulation method and direct compression method (Ansel, 2005). In natural material preparations, the wet granulation method is usually used. This is because natural materials have poor flow properties, so by using the wet granulation method, the flow rate, compressibility, and binding capacity of the granules can be improved (Suparman et al., 2021).

The research that will be carried out this time will make a tablet preparation using garlic herb with the removal of the honey ingredient used in previous research because honey causes the granule formula to become moist and difficult to dry. Apart from that, it is hoped that the tablet dosage form can cover the unpleasant taste and smell of single garlic when consumed. Each formula differentiates the concentration of corn starch, explotab, talc, magnesium stearate, and lactose.

METHODS

Equipments

The equipment used in this research includes standard laboratory glassware (Pyrex®), analytical scales (LabPRO), oven (Furnace), 30 mesh filter (PT Pharmeq), oven (memmert), moisture analyzer (AND MX®), dehumidifier, tapping density, tablet press (Rimek®), caliper (Brand Tricle), hardness tester (YD-3), friability tester, and disintegrator tester.

Materials

The materials used in this research include: single garlic (*Allium sativum* L.), red ginger (*Zingiber officinale* var., Rubrum Roscoe), and lemon family (*Citrus limon* (L.) Osbeck), apple vinegar (Tahesta®), Corn starch (Bratachem ®), explotab (Bratachem ®), talc (Bratachem ®), magnesium stearate (Bratachem ®), lactose (Bratachem ®), and aquadest.

Making a Single Garlic Powder And Red Ginger

The ingredients used in this research were single garlic, red ginger, and lemon obtained from PT. Parung fresh vegetable plantation. The samples were then identified at the Indonesian Institute of Sciences (LIPI), and the results obtained were that the samples or ingredients used were: single garlic (*Allium sativum* L.), belonging to the Amaryllidaceae family; red ginger (*Zingiber officinale* var., Rubrum Roscoe) of the Zingiberaceae family; and lemon family (*Citrus limon* (L.) Osbeck) of the Rutaceae. Making a single garlic powder and red ginger Each sample was wet-sorted by separating the sample from the skin. Next, they are washed thoroughly and chopped, then dried using a dehumifier at a temperature of 50 °C for ±24 hours. After that, the simplicia is ground in a grinder until it becomes simplicia powder, then sieved using sieve No. 40 and stored in a dry and clean container.

Tablet Manufacturing

This research uses an experimental type of research. Tablets are made with the single active ingredients of garlic, red ginger, apple cider vinegar, and lemon. The concentration of active substances used is based on research by Wiendarlina (2019) and tablet formula refers to research by Rackmah (2018). Each formula differentiates the concentration of corn starch, explotab, talc, magnesium stearate, and lactose. The formulation can be seen in Table 1. The weight of the tablets is 650 mg per tablet.

The active ingredients, corn starch, and lactose, were sieved using mesh No. 12, then mixed with corn starch, which has been developed previously with warm water. Then stir until a smooth consistency forms. After that, the mass is sieved through sieve No. 8 until it becomes a suitable granule. The granules were dried in the oven at a temperature of 40–60 °C overnight.

The dried granules are sieved through mesh No. 12, then the granules are placed in a container containing Explotab corn starch, talc, and magnesium stearate, sifted through mesh No. 30, and the mass is mixed for 5 minutes. Ready to be pressed.

Table 1. Formulation of Garlic Herb Tablet Preparations

Ingredient	Formulation (% w/w)			Function
	1	2	3	
Single garlic	4,64	4,64	4,64	Active ingredient
Red Ginger	2,28	2,28	2,28	Active ingredient
Apple vinegar	4,22	4,22	4,22	Active ingredient
Lemon	2,92	2,92	2,92	Active ingredient
Corn Starch	1	2	3	Disintegrant and
Corn Starch	5	10	15	Binder
Explotab	1	2	3	Disintegrant
Talc	1	2	3	Lubricant
Mg stearate	0,5	1	2	lubricant
Lactose ad	100	100	100	Filler

Granul Evaluation

Water Content

Each formula was weighed as 2 g of granules, then placed in a moisture balance (Hadisoewignyo and Fudholi, 2013).

Flowability Test

For each formula, 50 g of granules were weighed and put into a flow meter, and then the flow time was measured with a stopwatch (units g/second). Testing was carried out three times (Aulton, 2008).

Angle of Repose

50 g of granule is put into the flowmeter. The falling mass will form a cone, and then the diameter of the granule mass is measured. This experiment was carried out three times (Aulton, 2008).

Tablet Evaluation

Appearance Test

The appearance of the tablet was observed, such as uniformity of coloring, surface shape, broken or plain lines and markings, organoleptics, as well as other physical parameters of the tablet.

Size Variation Test

Measure the diameter and thickness using a caliper. According to the Indonesian Ministry of Health (2020), unless stated otherwise, the tablet diameter should not be more than 3 times.

Weight Variation Test

A total of 20 tablets/formulas were counted, weighed one by one, and the average weight of the tablets was determined. The requirement for weight uniformity is that no more than 2 tablets deviate more than column B, namely 10 % (DepKes RI, 2020).

Friability Test

The friability test (f) is carried out using a friabilator. Into the tool, 20 tablets or formulas that have been weighed previously (a) are inserted, and the tool is set at a rotation speed of 25 minutes. Then, in the 100th cycle, the tablet is removed, then cleaned of loose dust, after which it is weighed again (b). The results obtained are entered into equation 1. Based on Lachman (1994), the brittleness requirement is 0.8–1.0 %.

$$f = \frac{a-b}{a} \text{ x } 100\ \% \qquad (1)$$

Hardness test

Tablet hardness was determined using 20 tablets from each formula and tested with a hardness tester. According to Syukri (2018), a good tablet must have a hardness of 4 to 8 units kg/cm^2 or 4 - 8 kp.

Disintegration Test

Six tablets of each formula were put into the disintegrant tester basket containing ± 800 ml of water with a temperature of ± 37 °C, then raised and lowered 30 times/minute. All tablets must be destroyed. According to DepKes RI (2020), this test of uncoated tablets does not exceed 15 minutes.

Statistical Analysis

The tablet obtained from this preparation were tested statistically using ANOVA and if there were differences, the Duncan test was carried out.

RESULTS AND DISCUSSION

Drying garlic and red ginger powder, made using a dehumidifier at a temperature of 50 °C at RH 17 % Dehumidifiers have the advantage that the dried product is more hygienic, has good quality, and is easier to control the temperature and humidity of the air. The color and product produced are better compared to high-temperature dryers (Handayani et al., 2014). The resulting garlic powder has a strong taste, distinctive odor, and brownish-white color. The red ginger powder has a spicy taste, distinctive smell, and a light brown color.

Table 2. Evaluation of Granule Parameters

Granul evaluation ±SD	F1	F2	F3
Water content (%)	3,06 ± 0,35 [(a)]	3,5 ± 0,10 [(a)]	4,3 ± 0,20 [(b)]
Flowability test (g/s)	6,53 ± 0,59 [(a)]	6,38 ± 0,09 [(a)]	6,21 ± 0,58 [(a)]
Angle of repose (°)	29,83 ± 3,34 [(a)]	29,24 ± 3,10 [(a)]	29,69 ± 2,32 [(a)]

Results of Granule Evaluation

Granules consist of the active ingredient of garlic concoction with various concentrations of a binding agent, namely corn starch. The test results for water content, flow rate, and angle of repose can be seen in Table 2.

Water content requirement for granules is around 2–5 %; at this humidity, granules are more stable and store better (Widjayanti and Iwan, 2022). Based on the results of granule testing for water content in each formula, it meets the requirements; with excess water content in the granules, it will cause violations of the granule properties; and with low water content, the content of the granules and the water content will facilitate the compression process on tablets.

According to Aulton (2008), the granule flow rate should be 4–10 g/sec. The granule flow rate test results for the three formulations ranged from 6.21 to 6.53 in the light flow category. The faster the flow time, the better the granules produced. Corn starch binder influences the flow rate, which provides good flow properties. The greater the concentration of corn starch as a binder, the better the flow rate. Granule flow rate results vary because they are influenced by shape, size, surface condition, granule humidity, and the addition of pelican material Flow properties can be improved by adding lubricants to reduce friction between particles The lower the lubricant concentration, the more sticky the granules will be, resulting in the granules becoming larger in size and making it more difficult to flow (Supomo et al., 2015)., The smaller the concentration of the binder, the smaller the size, viscosity, and density, thereby increasing the cohesive force between granule or powder particles. High cohesion forces make it difficult for granules to flow freely. A small density means that the molecular weight is also small, causing a lack of influence of the gravitational force on the mass because the cohesive force is higher than the gravitational force, so the granules cannot flow freely (Elisabeth, 2018).

The angle of repose is a fixed angle at which an accumulation of cone-shaped granule mass in a horizontal shape occurs. The results of the angle of repose in the three formulas show that it is in the range 29.24–29.83 (°), so it meets the requirements, namely 20–30° in the good category (Aulton, 2008). The smaller the particle size, the higher the cohesive force. The higher the cohesive force, the more it can make it difficult for the granules to flow and result in the angle of repose formed becoming larger (Wijayanti and Iwan, 2022).

From the results of statistical tests, it can be concluded that the water content of formula 2 is in a different subset column. This is influenced by the amount of binder used. The higher the amount of binder used, the more moisture the granules will absorb (Yuniarsih, 2023).

Figure 1. Garlic Herb Tablets

Table 3. Evaluation of Tablet Parameters

Evaluation Tablet		F1	F2	F3
Univormity	t (cm)	0,355 ± 0,05[a]	0,3175 ± 0,0[b]	0,3345 ± 0,03[b]
	d (cm)	0,8432 ± 0,00[a]	0,851 ± 0,01[b]	0,845 ± 0,01[b]
	weight (mg)	632 ± 8,75 [a]	636,3 ± 7,68 [a]	645 ± 8,37 [b]
Friability (%)		0,169 ± 0,10[a]	0,236 ± 0,00[a]	0,226 ± 0,12[a]
Hardness (Kp)		4,75 ± 0,88[a]	5,82 ± 0,99[b]	6,28 ± 1,04[b]
disintegration time (minute)		6,10 ± 1,01[a]	11,12 ± 0,85 [b]	11,31 ± 0,06[b]

Tablet evaluation results

Appearance Test

Garlic herb tablets have a brownish white color, a round shape, no broken lines on the top or bottom surface, a distinctive garlic aroma, and a slightly bitter taste.

Size Variation Test

The results of this test show that the three formulations comply with the requirements, namely that the tablet diameter does not exceed three times and is not less than 1 1/3 of the tablet thickness (DepKes RI, 2020). Tablet size uniformity is related to the ease of use of the tablet; the shape and diameter of the tablet are determined by the shape of the tablet and also depend on the weight of the granules inserted into the tablet mold. The results of the size uniformity test can be seen in Table 3.

Weight Variation Test

The weight uniformity test is carried out to determine whether the tablets obtained have a uniform weight or not, so they are weighed. This test can affect the uniformity of the active ingredients contained in the tablet. According to Depkes RI (2020), the requirement for uniformity of tablet mass is that if the tablet has an average mass > 650 mg, there must not be 2 tablets whose mass deviates by more than 5 %, and the average mass is 1 tablet whose mass deviates by more than 10 %. Thus, all formulas can be formulated in such a way that they meet the requirements. uniformity of weights in formulas 1 and 2 are in the same subset, while in formula 3 they are in different subsets this is cause the addition binders and lubricants (glidant and antiadherent), where increasing the binder concentration will improve the size of the granules so that they flow easily, and increasing the lubricant concentration will make it easier for the granules to flow into the tablet printer (Supomo, 2015). A formula that has good flow characteristics will have a uniform ability to fill the compression space (Lestari, 2022). The results of the weight uniformity test can be seen in Table 3.

Friability Test

Tablet friability test results for the three formulations show that the index is in the range of 0.2 %. Based on Lachman (1994), the tablet friability requirement does not exceed 0.8 %, so it can be stated that the tablet friability test meets the requirements. The lower the friability value, the better the tablet produced. The results of statistical tests on tablet friability showed that there was no difference in tablet friability values for each formula. Good brittleness indicates good tablet hardness (Mariyani, 2012). However, formula 2 has a greater brittleness value than formulas 1 and 3, which could be due to the water temperature when making corn starch as a binder. In accordance with research conducted by Karisma sari (2012) increasing the temperature and amount of water will reduce the fragility of the tablet; conversely, at a low temperature and amount of water, it will increase the fragility of the tablet.

Hardness Test

Tablet hardness test results for the three formulations showed that they were in the range of 5.25–6.34 kp. Based on Syukri (2018), the requirements for this test are 4 to 8 kp. Thus, it can be said that the tablet hardness test meets the requirements. Tablets must have sufficient hardness to withstand the distribution process,

but the hardness of the tablet must meet the requirements so that it is easily broken and easily destroyed when the tablet is in the body. The results of statistical tests on tablet hardness showed that there was no difference in tablet hardness values in formulas 2 and 3, but gave different results in formula 1. Tablet hardness affects the disintegration time of the tablet, and if the tablet has high hardness, it will have strong binding capacity and high density. The higher the starch concentration,corn as a crusher, hence its hardness. more increasing. Tablet hardnessincreases because violence is influenced humidity, the higher the humiditywill cause a binding force between particles.the stronger the resulting tablet will get harder (Mariyani, 2012).

Disintegration Test

The disintegration time test results for the three formulations showed that they were in the range of 9.30–10.37 minutes, in accordance with the requirements. According to the DepKes RI (2020) uncoated tablets have a disintegration time of no more than 15 minutes. The results of the study showed that variations in binder and concentration influenced the tablet disintegration time. The results of statistical tests on tablet disintegration time showed that there was no difference in the value of tablet disintegration time in formulas 2 and 3, but gave different results in formula 1 The results showed that variations in binders and disintegrants influenced the tablet disintegration time. The tablet disintegration time obtained in formula 3 is longer, this is due to the high concentration of binder and external and internal disintegrating agents used in formula 3, so the tablet disintegration time is longer, and each binder has different characteristics so that the results obtained vary. Variations in the binder and concentration used affect the tablet disintegration time (Nurul, 2020) Corn starch can function as a binder at a concentration of 5-25 % and a destroyer at a concentration of 3-5 % (Rowe, 2009). Cornstarch has the ability to absorb water, thus affecting the starch development process and making tablets more easily crushed (Yuniarsih, 2023). The explotab material as a disintegrating agent is the strength of its capillary action which will draw liquid into the tablet, so that in the tablet formulation this material will expand and cause the tablet to break, disintegrate, and then dissolve (Lestari, 2022). (Nurul, 2020). Apart from that, the disintegration time is also influenced by the addition of lactose. The more lactose added in formula can increase the hardness of the tablet, increasing the hardness, friability and disintegration time of the tablet significantly (Tarigan, 2010). where there is more lactose in formulas 1 and 2 than in formula 3, thus providing a faster disintegration time than formula 3.

CONCLUSION

The concentration of external and internal disintegrants, binder, glidant, and anti-adherent has an effect on the granules of each formula produced. There is no difference in flow time or angle of repose in the granules produced, but it influences the water content of the granules.

The differences in the concentration of external and internal disintegrants, binders, glidants, and anti-adherents influence the quality of the tablets produced; the greater the concentration, the better the weight uniformity, the harder the tablets produced, and the longer the disintegration time. High tablet fragility in formula 2 but still meets tablet quality requirements.

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