

FORMULATION OF GRANULES AND TABLETS ACTIVE INGREDIENT PARACETAMOL IBUPROFEN AND ITS EVALUATION RESULTS

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ABSTRACT

Granulation is a process of increasing the powder size where a powder mixture that has a small cohesive force is changed into a larger particle size. Granulation begins with mixing the required active ingredients, so that a form of active ingredient is achieved through a mixing process (Musnamar, 2005). Dry granulation (slugging) is processing active ingredient and excipient particles by pressing the dry mixture into a solid mass. After it becomes a solid mass, it is then broken down again to produce particles that are larger than the original powder (granule). Dry granulation is used for active ingredients that have an effective dose that is too high to be directly compressed, active ingredients that are sensitive to heating and humidity, active ingredients that are difficult to flow (Chaerunnisa et al, 2009). Ibu profen is a derivative of propionic acid which has strong analgesic, antipyretic and not too strong anti-inflammatory properties. Ibuprofen has a dose-dependent duration of around 9-8 hours which is longer than the half-life.

Testing the angle of repose F1 before compression is 24°, after compression is 25°. At F2 before compression it is 25°, at F3 before compression it is 30°. The test results of all formulations met a good angle of repose range of 25 - 30°, but did not match the formula design. In flow time testing. According to the Indonesian Ministry of Health, 2018 stated that the flow speed is good if the granules flow <10 seconds. In F1, the flow time before they become granules is 50 seconds and after they become granules it is 6.39 seconds, where these results meet the literature. Meanwhile, for F2, F3, and K-, no results were obtained after becoming granules because the formulation could not go through the slugging process.

Keywords : granulation, ibuprofen, paracetamol

INTRODUCTION

The aim of combining the active ingredient paracetamol with ibuprofen is to control pain more effectively. Extends the half-life of the drug in the body.

Disintegrants or crushing agents are one of the important components in making tablet preparations. The function of a disintegrant is to break down the tablet so that the active ingredients can be released. The disintegrant used in this formulation is Amylum Manihot, this formulation is made by varying the concentration of Amylum Manihot, namely 3% (F1); 10% (F2); and 20% (F3) which is intended to observe the disintegration time for each formulation.

Dry granulation (slugging) is processing active ingredient and excipient particles by pressing the dry mixture into a solid mass. After it becomes a solid mass, it is then broken down again to produce particles that are larger than the original powder (granule). Dry granulation is used for active ingredients that have an effective dose that is too high to be directly compressed, active ingredients that are sensitive to heating and humidity, active ingredients that are difficult to flow (Chaerunnisa et al, 2009).

The dry granulation method is a tablet manufacturing method that is used if the active substance in the formulation is thermolabile or sensitive to moisture and heat, and has relatively poor flow properties and compressibility.

The dry granulation method, also called slugging, is a method of making tablets by pressing a mixture of dry ingredients (active substance particles and excipients) into a solid mass which is then

broken down again to produce larger sized particles (granule) than the original powder. The principle of this method is to make granules mechanically, without the help of binders and solvents, the bond is achieved through force (Kloe, 2010).

In this process the tablet components are compacted using a tablet printing machine then pressed into a die and compacted with a punch to obtain a mass called slug, the process is called slugging, in the next process the slug is then sieved and stirred to obtain granules that have better flowability than the mixture. beginning. If the slug obtained is not satisfactory then the above process can be repeated (Kloe, 2010).

Dry granulation is also called slugging, which is processing particles of active substances and excipients by pressing a mixture of dry ingredients into a solid mass which is then broken down again to produce particles that are larger than the original powder (granule). The principle of this method is to make granules mechanically, without with the help of binders and solvents, the bond is achieved through force. This technique is quite good, used for active substances that have an effective dose that is too high to be directly compressed or active substances that are sensitive to heating and humidity (Andayana, 2009).

Dry granulation aims to improve the flow properties and/or compressibility of the printed tablet mass. The dry granulation method is carried out by pressing the powder mass at high pressure so that it becomes large sized tablets (slugs) that are not well shaped, then ground and sifted until granules with the desired particle size are obtained (Sirisha, et al. 2018).

METHODS

Prepare tools and materials, Weighing 175 grams of Acetaminophen, 100 grams of Ibuprofen, 7.3 grams of Manihot Starch (F1= 10.95 g, F2= 36.5 g, F3= 73 g), 7.3 grams of PVP, and (F1= 0, 13985 g, F2= 0.08875 g, F3=0.00845 g), mix ad homogeneously (inner phase), The resulting internal phase mixture is inserted into the die on a tablet press, until slugs are formed, with each weighing more than 500 mg. Put the slugging results into the mortar then grind slowly until granules are formed, Sift the granules with a no 12 mesh sieve,.

Weighing 1.825 grams of Magnesium Stearate and 3.65 grams of Talcum, and mixing with the inner phase which has been sieved until homogeneous (outer phase). After the granule mixing process, granule evaluation tests are carried out including tests for water content, pH, flow time, angle of repose, organilepticity, homogeneity, partic

le size distribution, compressibility, stability.

Compress the tablets using a tablet molding machine, and carry out tablet evaluation tests including disintegration time tests, hardness tests, friability tests, weight uniformity tests, active substance concentration tests and dissolution tests.

Table 1. Formulation granul

Material	F1	F2	F3
Paracetamol	350 mg	350 mg	350 mg
Ibuprofen	200 mg	200 mg	200 mg
Amylum Manihot	3%	10%	20%
Magnesium Stearat	0,5%	0,5%	0,5 %
Talkum	1%	1%	1%
PVP	2%	2%	2%
Laktosa	Ad 100%	Ad 100%	Ad 100%

RESULTS

Organoleptic tests are carried out to determine the physical appearance of the preparation. Organoleptic tests are carried out visually, to see color, shape, smell and taste (Julianti et al., 2022). From the results of the organoleptic evaluation test, the results showed that F1 was odorless, white, granular and had a bitter taste. Meanwhile, slugging cannot be carried out for F2 and F3, because at a concentration of 5-10% Manihot Amylum can function as a binder. Where in F2 the concentration of Amylum Manihot is 10% and F3 the concentration of Amylum Manihot is 20%, both formulations also use a binder, namely PVP, at 2%, resulting in the amount of binder being too high and resulting in slugging not being possible.

The pH test is a test of the degree of acidity of a substance that is made into a solution. The purpose of pH testing on preparations is to determine the quality of the preparations. The results of the pH evaluation test on the formulation showed that F1 has an acidic pH, this is because the active substances Acetaminophen and Ibuprofen are acidic substances, the other ingredients are acidic and there is a lack of alkaline ingredients, resulting in the preparation being acidic.

Compressibility test is the ability of granules to form tablets with a certain pressure. Compressibility is also usually called the car index which can be used to determine flow properties. The greater the compressibility value indicates that the granule has poor flow properties. In testing granule compressibility using the dry granulation method for F1, the results were 8.616%, so it can be said to be good, because according to Aulton, 2002, the compressibility test requirements are declared good if it is below 20%, the smaller the compressibility value indicates the granule has good flow properties. In granule size and granule shape which are influenced by compressibility, the smaller the bulk density obtained, the better the flow properties (Alfenjuni & Gusmayandi, 2012). Meanwhile, for F2, F3, and K-, no results were obtained after becoming granules because the formulation could not go through the slugging process.

Water content testing is carried out to determine the amount of water content contained in the granules. Water content measurements are carried out using a moisture balance tool. The way moisture balance works is to read the water content automatically, by inserting a sample of ± 2 grams into an aluminum cup, then cover it and wait until the % LOD number appears on the tool screen (Sudarsono et al., 2021). From the results of the F1 granule water content test, it was found that the granules met the water content requirements because they had a percent value of less than 5%, which was 2.55% in F1. Meanwhile, water content has not been obtained for F2, F3 and K-, because the slugging process cannot be carried out.

Testing the angle of repose of granules is carried out by inserting 50g of granules into the funnel of the flow tester. Open the cover at the bottom of the funnel. The height of the cone and the radius of the cone formed are measured. (Cheiya, 2023). The angle of repose test is important for the granule angle. This is a granule test that is carried out to determine the flow properties of the granule. The powder will form a cone, the flatter the cone produced, the smaller the angle of repose. The results of the F1 angle of repose test before compression were 24°, after compression 25°. At F2 before compression it is 25°, at F3 before compression it is 30°. The test results of all formulations met a good angle of repose range of 25 - 30°, but did not match the formula design.

DISCUSSION

The flow time test was carried out to determine the flow properties of the granules. The flow rate is determined by measuring the speed at which the powder flows from the tool. The powder is placed on top of the funnel and then flowed and the time it takes for the granules to flow from the funnel to the bottom is recorded. The flow rate is good if the granules flow <10 seconds. In F1, the flow time before becoming granules was 50 seconds and after becoming granules it was 6.39 seconds, where these results meet the literature. Meanwhile, for F2, F3, and K-, no results were obtained after becoming granules because the formulation could not go through the slugging process.

The tablet hardness test is carried out to determine the strength of the tablet so that it is resistant to shock, friction during the manufacturing, packaging and distribution processes. The hardness of a

tablet greatly influences the dissolution test. The hardness requirement for non-coated tablets is 4-8 kg (Fadhilah et al, 2019).

In the results of formulation 1, the tablet hardness was found to be 2.4 kg, where this result did not meet the requirements because tablet hardness was influenced by several factors, including the pressing force and time used during pressing, the properties of the raw material, and the type of adhesive used. Tablet hardness is generally related to the type and purpose of use. The greater the pressure applied when tableting will increase the hardness of the tablet. (Ansar et al., 2009).

The disintegration time test was carried out using a disintegrator tester. The hardness of a drug is usually influenced by the binder used (Garnadi et al, 2019). According to the Indonesian Pharmacopoeia Edition V, the disintegration time test is carried out by placing 6 tablets into the basket one by one, using distilled water at a temperature of 37°C as a medium. The basket will be raised and lowered until the tablets run out and there are no remaining tablet fragments on the gauze. The disintegration time for uncoated tablets should be less than 15 minutes (Fadhilah et al, 2019). Formula 1 shows results that meet the requirements, namely 4 minutes, where the results take no more than 15 minutes.

The tablets being tested are cleaned first, then weighed carefully. A total of 20 tablets were put into the friabilator and the tool was run for 1 minute 40 seconds at a speed of 25 rpm. Once finished, the tablet is then cleaned of dust and weighed again carefully. The percentage of tablet weight lost was calculated. Next, the average value of the three tests that were carried out was determined. In the tablet friability test, the fragility result was 7.782%. Based on the results above, it can be seen that the tablet has a high percentage of fragility so that it exceeds the range of fragility of a good tablet and does not meet the requirements. Tablet friability can be influenced by the uniformity of the powder size of each material and the amount of fines (Voigth et al., 1995). An increasing number of fines will increase the fragility of the tablet.

The weight uniformity test can affect the accuracy of the dosage of the active substance contained in each tablet. Weight uniformity aims to control the quality of tablets to determine the uniformity of active substance levels. Uniformity is based on research that has been carried out with reference to the tablet weight requirements which state that no more than 2 tablets have a deviation of more than 5% for column A, and not a single tablet has a deviation of more than 10% for column B. Tablet weight uniformity is obtained for formulation I does not meet the tablet weight requirements because there are 5 more tablets than column A (5%). The factors that influence weight uniformity are lack of careful practice during compounding, separation of the mixture of ingredients during the manufacturing process, lack of homogeneity of a medicinal preparation so that the content of a preparation is not uniform, which can cause deviations in the form of dosages that are not uniform.

CONCLUSION

Organoleptic test, the granule preparation has a white color obtained from the color of the active additive. It is odorless and is in granular form.

In pH testing, it was found that F1 has an acidic pH, this is because the active substances Acetaminophen and Ibuprofen are acidic substances, the other ingredients are acidic and there is a lack of alkaline ingredients, resulting in the preparation being acidic.

In testing granule compressibility using the dry granulation method for formulation 1, the result was 8.616%, so it can be said to be good, because according to Aulton, 2002, the compressibility test requirements are declared good if it is below 20%, the smaller the compressibility value indicates the granule has good flow properties.

In testing the water content of F1 granules, it was found that the granules met the water content requirements because they had a percent value of less than 5%, which was 2.55% in F1. Meanwhile, water content has not yet been obtained for F2, F3 and K-, because the slugging process cannot be carried out.

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