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Variations in the concentration of magnesium stearate as a lubricant in the evaluation test results of paracetamol tablet preparations

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ABSTRACT

Tablets are an oral drug preparation that can be formulated with or without additional substances. This preparation has many advantages, one of which is that it is practical to use and can be produced on a large scale. Tablets are produced using 3 methods, namely dry granulation, wet granulation and direct compression. Each manufacturing method must be adapted to the tablet material to be printed. So it is necessary for formulators to know the characteristics of the materials to be used.Tablet production involves excipients or additional substances which have an important role. Excipients are one of the considerations in preformulation studies to determine the right characteristics and quantities to produce tablets that meet the requirements. One of the excipients in tablet formulation is a binder. So far tablet binders are divided into 2 types, namely natural polymer binders and synthetic polymer binders. Additional materials play 2 important roles in making tablets, one of which is the binder. The binder is intended to provide tablet compactness and durability so that the binder guarantees the integration of several powder particles into a granulate (Oktavia, 2011).

Granulation is a process of increasing the size of small powder particles that are bound together to become large ones that can flow freely. The purpose of granulation is to make the mass flow freely, compact the mixture of ingredients, create a uniform mixture that does not separate, improve the compressibility characteristics of the active substance, control the speed of release of the active substance from the dosage form, reduce dust and improve the appearance of the tablet (Lachman, 1994). Observation of the results of evaluating the physical quality of the preparation includes organoleptic tests, hardness test, brittleness test, disintegration time test and weight uniformity test. The results of this research based on the friability test, the F1 result was 0.74%, fulfilling the requirements of the tablet friability test, namely, no more than 0.8% loss of the total mass of the FI 3rd edition tablet. 4. The results of the tablet uniformity test show that there is not a single tablet whose weight deviates from column A, namely more than 5% and there is not a single tablet whose weight deviates from column B, namely more than 10% from the average weight in F1. All tablets in FI have a uniform tablet weight with no deviation so that FI complies with the specified range requirements.

Keywords : Granula, Magnesium Stearat, Paracetamol

INTRODUCTION

Granulation is a process of increasing the size of small powder particles that are bound together to become large ones that can flow freely. The purpose of granulation is to make the mass flow freely, compact the mixture of ingredients, create a uniform mixture that does not separate, improve the compressibility characteristics of the active substance, control the speed

of release of the active substance from the dosage form, reduce dust and improve the appearance of the tablet (Lachman, 1994).

Tablets are an oral drug preparation that can be formulated with or without additional substances. This preparation has many advantages, one of which is that it is practical to use and can be produced on a large scale. Tablets are produced using 3 methods, namely dry granulation, wet granulation and direct compression. Each manufacturing method must be adapted to the tablet material to be printed. So it is necessary for formulators to know the characteristics of the materials to be used.Tablet production involves excipients or additional substances which have an important role. Excipients are one of the considerations in preformulation studies to determine the right characteristics and quantities to produce tablets that meet the requirements. One of the excipients in tablet formulation is a binder. So far tablet binders are divided into 2 types, namely natural polymer binders and synthetic polymer binders. Additional materials play 2 important roles in making tablets, one of which is the binder. The binder is intended to provide tablet compactness and durability so that the binder guarantees the integration of several powder particles into a granulate (Oktavia, 2011).

Paracetamol preparations are drugs that can relieve and relieve fever and pain (Samar et al., 2013). In general, the materials used in making tablets, apart from the active substance, are fillers, binders, disintegrants and lubricants. Paracetamol is a material with poor compactibility characteristics and poor flow properties. To improve its flow properties and compactness, the active ingredient is made in tablet form using the wet granulation method. The wet granulation method requires a lubricant to prevent friction between particles. The wet granulation method is used for active ingredients that are resistant to heating, for example Paracetamol. Wet granulation is a formulation technology by mixing a powder or tablet mixture in the presence of a liquid as a binding agent which is mixed with dry powder.

METHODS

Prepare tools and materials, weigh 250 grams of paracetamol then grind it finely and set aside. Weigh out 6.5 grams of talcum then grind it, set aside. Weigh out Magnesium stearate F1: 6.5 grams, F2: 13 grams, F3: 19.5 grams, then put it in a crushed mortar, set aside. Weigh the lactose F1: 49 gr, F2: 42.5 gr, F3: 36 gr and k- 55.5 gr, then mix with paracetamol until smooth and homogeneous. Mix with CMC Na mucilage which has been given essence then stir until homogeneous. Then sifted using sieve number 12, then oven the granules at 50°C for 30 minutes. Sift again with a granule sieve. Add the glidant and lubricant to the granules that have been formed, then stir until homogeneous, next, granule testing was carried out.

RESULTS

Organoleptic testing or sensory testing is a testing method that uses human senses as the main tool for measuring product acceptability. The senses used in organoleptic tests are the sense of sight, sense of smell and sense of taste. This test includes observing the color, smell, shape and taste of the preparation. Based on the results of observations on the three granule formulas, they have a pink or pink color, namely from additional essence coloring substances. The shape is uniform granules, has a strawberry smell and a bitter taste due to the nature of the active substance Paracetamol.

Observation of the results of evaluating the physical quality of the preparation includes organoleptic tests, homogeneity, pH, stickiness tests, spreadability tests and emulsion type. The results of this research indicate that there is an influence of differences in the concentration of stearic acid and triethanolamine in that F1 has a denser form than F2 and F3, after storage for 3 weeks F2 and F3 experienced a color change to light brown. This shows that the formulation has the best properties for body scrub cream preparations, is stable and meets the requirements based on organoleptic tests, homogeneity tests, pH tests in accordance with the standard facial skin

pH in general, namely 4.5-7, while for the emulsion type test, and the stability test that was carried out on day 12 did not experience any changes or phase separation, namely F1 with a stearic acid concentration of 15% and triethanolamine 1%.

The pH test aims to determine the suitability of the pH of each paracetamol granule preparation formula in acidic or basic conditions. Checking the pH of paracetamol granule preparations was carried out using a pH meter. The results of examining the pH of paracetamol granules obtained results namely F1= 6.93, F2= 6.96 and F3= 7.12. pH measurements on paracetamol granulated preparations show that the three formulas do not comply with the paracetamol pH range, namely between 5.5 and 6.5 (Martindale ed 36). If the pH of paracetamol granulated preparations is too high, this can affect the stability and effectiveness of the drug.

Based on the pH results obtained in F1 and F2, the pH is close to neutral, namely 6.93 and 6.96, and F3 has a neutral pH, namely 7.12, this is due to the use of CMC Na and Talcum ingredients in each formula. CMC Na has a pH of 2-10 (HOPE ed 5 p. 120-121) which is alkaline and the pH of Talc has a pH of 6.5-10 (HOPE ed 5, p. 767) which is alkaline.

DISCUSSION

Apart from that, there is the influence of additional ingredients, namely Magnesium stearate, magnesium stearate is the magnesium salt of stearic acid which is used as a lubricating agent in the production of pharmaceutical tablets and food supplements. Magnesium stearate itself is relatively neutral, and in aqueous solution, has a pH of around 7 (HOPE ed 5 p 430). However, in practice, magnesium stearate is insoluble in water, so direct pH measurements of this compound are not applicable. When magnesium stearate is mixed with water, the magnesium stearate does not completely dissolve so the pH of the mixture reflects the pH of the water used rather than the pH of the magnesium stearate itself.

In the water content test in formulation 1 the result was 1.10%, in formulation 2 the result was 0.30% and in the third formulation the result was 2.29%. The water content values obtained by all formulations met the standards and did not exceed 3 - 5%, however in formulation 2 the water content was very small because the oven was too long so the granules were too dry. This water content test is carried out to determine the water content in the granules that have been made after drying. Drying aims to control that the granule mass is not easily overgrown by fungi and microbes. Water content testing is carried out using a moisture analyzer. Good granules have a humidity of 2-5%. The test results show that the three formulas meet the requirements.

Flow time is the time required for a number of granules to flow in a device. These flow properties can be used to assess the effectiveness of lubricants, where the presence of lubricants can improve the flow properties of a granule. The granule flow rate is expressed in grams/second and the granules flow for no more than 10 seconds. From this test, the results of the flow time test showed that the three formulations met the requirements set by the Indonesian Ministry of Health, 2018, namely having a flow time of less than 10 seconds. In FI the flow time obtained is 1.37 seconds, F2 the flow time obtained is 2.28 seconds, and F3 the flow time obtained is 2.53 seconds.

The test for the angle of repose of granules is an important granule test to carry out because it determines the flow properties of the granules. The powder will form a cone, the flatter the cone, the smaller the angle of repose (Voight, R, 1995). Based on the results of the granule angle of repose test, it can be seen that the three formulas that have been made have angles of repose that meet the requirements, namely with an average angle of repose for formula I granules of 26.5°, formula II 25.20°, and formula III 26.5°. where the requirement for the angle of repose value is $25° > \alpha < 40°$ (Rori et al, 2016). The smaller the angle of repose, the better the flow properties of the granules and the better the flow properties of the granules, the easier the granules will be to compress in making tablets.

The compressibility test aims to determine the ability of the compressed powder material to form a compact mass after a certain pressure is applied. a good compressibility range is <20% (Chandira R.M, 2012). Based on the results of the granule compressibility test, it can be seen that the granules from the three formulas that have been made have a percent compressibility index that meets the requirements of all formulas, namely less than 20%. The percentage of compressibility is influenced by the granule size and granule shape.

In the disintegration time test, testing was carried out using a Desintegration Tester tool. To test the disintegration time, each tube was filled with one tablet, then the basket was placed in a beaker filled with water, at a temperature of 37°C. In formulation 1, all the tablets tested could not be destroyed due to the combined influence of Magnesium stearate and Talcum as a greater lubricant and Magnesium stearate has the property of being insoluble in water while magnesium stearate has hydrophobic properties so it will inhibit the release of efficacious ingredients (Giang, T.P. 1987 .) so that the tablet has a longer disintegration time. In the disintegration time test carried out, it did not meet the requirements in the literature, where the time required to crush the tablet was no more than 15 minutes. Meanwhile, the results obtained were that the tablet experienced erosion at the 4th minute but at the 15th minute the tablet was not completely dissolved.

Friability is a parameter used to measure the resistance of the tablet surface to the friction it experiences during packaging and shipping. Fragility was measured with a friabilator for 4 minutes at 25 rpm. The friability test is related to weight loss due to erosion that occurs on the tablet surface. The greater the percentage of friability, the greater the tablet mass lost. High fragility will affect concentration/grade the active substance is still contained in the tablet. Tablets with a small concentration of active substance (tablets with a small weight), loss of mass due to brittleness will affect the level of active substance still contained in the tablet. From this test, the F1 result was 0.74%, meeting the requirements for the tablet friability test, namely, no more than 0.8% loss of the total tablet mass (FI Edition III).

In the tablet hardness test, the test was carried out on 10 tablets and each tablet was placed in an upright position on the hardness tester. Next, the pressing tool is rotated until the tablet breaks. Read the tool scale which shows the hardness of the tablet in Kg units. (Development of Pharmaceutical Preparations, Goeswin Agoes 1997). In tablet hardness testing, it was found that F1 did not meet the tablet hardness test requirements, namely 1.44 kg, while the requirements for oral tablets were 4-8 kg. This is due to the use of CMC-Na binder using a low concentration so that the tablets are easy to become brittle, The weight uniformity test aims to determine the magnitude of the deviation in weight per tablet and this deviation is related to the deviation in dose per tablet. So it is hoped that when the drug enters the body it is the same and in accordance with the therapeutic safety of the tablet preparation. The results of the tablet uniformity test show that there is not a single tablet whose weight deviates from column A, namely more than 5%, and there is not a single tablet whose weight deviates from column B, namely more than 10% from the average weight in F1. All tablets in FI have a uniform tablet weight with no deviation so that FI complies with the specified range requirements.

CONCLUSION

- In the organoleptic test, the results obtained from observations were that the three granule formulations had a pink or pink color, namely from the essence coloring additives. The shape is uniform granules, has a strawberry smell and a bitter taste due to the nature of the active substance Paracetamol.

- In the pH test, the results obtained for F1 and F2 had a pH close to neutral, namely 6.93 and 6.96, and F3 had a neutral pH, namely 7.12, this was due to the use of CMC Na and Talcum ingredients in each formula. CMC Na has a pH of 2-10 which is basic and the pH of Talc has a pH of 6.5-10 which is basic.
- In the water content test in formulation 1 the result was 1.10%, in formulation 2 the result was 0.30% and in the third formulation the result was 2.29%. The water content values obtained by all formulations met the standards and did not exceed 3 - 5%, however in formulation 2 the water content was very small because the oven was too long so the granules were too dry.
- In the test, the results of the flow time test showed that the three formulations met the requirements set by the Ministry of Health of the Republic of Indonesia, 2018, namely having a flow time of less than 10 seconds. In FI the flow time obtained is 1.37 seconds, F2 the flow time obtained is 2.28 seconds, and F3 the flow time obtained is 2.53 seconds.
- Based on the results of the granule angle of repose test, it can be seen that the three formulas that have been made have angles of repose that meet the requirements, namely with an average angle of repose for formula I granules of 30.9°, formula II 30°, and formula III 34.8°. where the requirement for the angle of repose value is 25°> α < 40° (Rori et al, 2016).
- Based on the results of the granule compressibility test, it can be seen that the granules from the three formulas that have been made have a percent compressibility index that meets the requirements of all formulas, namely less than 20%.
- 3. The disintegration time test carried out did not meet the requirements in the literature, where the time required to disintegrate the tablet was no more than 15 minutes. Meanwhile, the results obtained were that the tablet experienced erosion at the 4th minute but at the 15th minute the tablet was not completely dissolved.
- 4. The results of the tablet uniformity test show that there is not a single tablet whose weight deviates from column A, namely more than 5% and there is not a single tablet whose weight deviates from column B, namely more than 10% from the average weight in F1. All tablets in FI have a uniform tablet weight with no deviation so that FI complies with the specified range requirements.
- 5. Based on the fragility test, the F1 result was 0.74%, meeting the requirements for the tablet fragility test, namely, no more than 0.8% loss of the total mass of FI 3 edition tablets.

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