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Addition Of Various Concentrations Of Gadung Tuber Starch Which Is Determined As A Binder To The Physical Properties Of Mefanamic Acid Tablets By Wet Granulation

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ABSTRACT

In previous studies, the polysaccharide extract of gadung tuber has a hypoglycemic effect, wherein the plant contains a high glycemic index indicating that carbohydrates undergo rapid digestion and are absorbed in large quantities so that blood glucose levels suddenly experience a rapid rise in insulin which can lower cholesterol values. (Sumunar et al., 2015) This research method is an experiment in which this research was carried out, by making starch from gadung starch and making tablets by wet granulation. Based on the results of the research that has been done, it can be concluded that the use of gadung starch as a binder can produce mefanamic acid tablets that meet the requirements for uniformity of tablet weight, tablet hardness, tablet friability, and tablet disintegration time in the Indonesian Pharmacopoeia. The addition of gadung starch (Discorea Hispida Dennst.) as a binder to mefanamic acid tablets causes differences in the physical properties of the tablets, namely in greater tablet hardness, smaller tablet friability and longer tablet disintegration time. The significance value obtained was 0.00 <0.05, because there was a significant difference in the gadung formulation and the gadung formulation as a binder for mefanamic acid tablets

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INTRODUCTION

Preparation technology is a way of formulating or designing a drug into a dosage form using technology. Drug preparations are dosage forms that contain active substances that are ready to be used (consumed). Technology causes drugs to no longer be consumed in their pure substance form. There are many benefits that can be obtained by making active substances in dosage forms, including better patient acceptance so that people will no longer hesitate to take drugs (Dra. Murtini Gloria and Yetri Elisa, 2018).

Starch from various plants is reported to be used as a substitute for auxiliary materials in tablet formulation, one of which is durian seed starch. Durian seed starch is a polysaccharide containing amylose and amylopectin, with different compositions (Modified Starch from Local Roots, n.d.). Amylose is a straight-chain polysaccharide consisting of -1,4-glycosidic glucose molecules, starch consisting of 20% water-soluble parts (Kumalawati et al., 2018). Various sources of carbohydrates included in the tuber group include yam tubers (Discorea Hispida Denst) (Hida Kumalawati, et al, 2018). Pregeltinated gadung starch in tablet preformulation can be used as a binder for tablets, as a filler or as a tablet disintegrator, as a binder the use of starch in the form of natural polymers is still limited because natural polymer materials are easily contaminated with bacteria (stale), due to this the pharmaceutical industry still uses a lot of these ingredients. synthetic polymers as well. There are various types of starch used in Indonesia, starch which has the ability to bind tablets, one of which is yam tuber. Based on research (Hazrati et al., 2022) in isolation of gadung tuber starch, Dioscorea hispida Dennst has a low water content (9.45%) and starch content of (37.62%) compared to cassava starch and significantly contains hemicellulose (4.36%), cellulose (5.63%), and lignin (2.79%) (Hazrati et al., 2021). This is also evidenced by data from the Indonesian Ministry of Health (2014), every 100 grams of "Gadung" contains 20.9 grams of carbohydrates, 77.4 grams of water and 0.20 mg of copper. This shows that the content of carbohydrate, water and copper including high and quite high. Gadung tuber has bioactive compounds including water soluble polysaccharides, discorin and diosgenin which have an important role as a medicine. The low fat content in gadung is beneficial for obese people, the calcium which is quite high compared to rice can prevent osteoporosis.

Granules are agglomerates of smaller particles (powder), generally in an uneven or spherical shape and become like a single larger particle with the intention of increasing flowability. The purpose of making granules is to prevent segregation, improve powder flow, increase porosity, increase powder compressibility, avoid the formation of hard materials from powders, especially in hygroscopic powders (Setiawan, H, 2014).

Wet granulation is a method that is carried out by wetting the tablet mass using a binder solution until a certain degree of wettability is obtained, then granulating. The wet granulation method is suitable for active ingredients that are poorly soluble in water and for active ingredients that are heat and moisture resistant. In general, the wet granulation method is used for active substances that are difficult to print because they have poor flowability and compressibility. Producing tablets using the wet granulation method has several advantages, namely: preventing segregation of the powder mixture, improving the flow properties of the powder, improving the compactibility of the powder, by increasing the cohesiveness of the powder because there is the addition of a binder which can cause the formation of solid bridges, increasing the dissolution of hydrophobic drugs, maintain the distribution of drugs or dyes that are always evenly distributed in dry granules and can be used to hold small doses of drugs (Hadisoewignyo and Fudholi, 2013).

The granules to be printed must be able to flow regularly and easily into the tablet printer. Regularity and uniformity of flow are necessary to produce tablets of uniform weight. For this reason, measurements of the flow rate and angle of repose of the granules were carried out. A good granule flow rate if it is greater than 10 g/sec, with an angle of repose between 24 - 40° (Zaman, N,2020). Good granule requirements have a moisture content of 1-2% (Anief, M, 2015).

The fines content is one of the granule parameters that can affect the properties of the tablet mass, such as flow rate, compressibility index and others. Determination of the particle size distribution is to determine the amount of fines in the granule, fines are particles that have a size < 100 mesh (Anief, M, 2015), the requirement for the amount of fines in the granules should not be more than 20%. If the number of finnes is small, the angle of repose will be reduced. It also affects the flow properties and uniformity of tablet weight. excessive amount of finnes can make tablet capping at the time of printing (Ansel HC, 2014). Tablets are classified according to their route of use or function and form or production process. Tablet preparations contain active ingredients and other ingredients known as excipients. This material is neutral and each additional ingredient has a specific function (Edy, H. J, Mansauda, K. L. R, 2020).

1. Filling Material

Fillers are needed in solid preparations, especially tablets which function to increase or gain mass so that there is sufficient mass of the mixture so that it is easy to compress (Anwar, 2012). Fillers are needed especially for small doses of active substances. Fillers are generally added in the range of 5-10% (depending on the amount of active substance and desired tablet weight). Another function of fillers is to improve the compressibility and flow properties of the active ingredients. Good criteria for fillers are not reacting with active substances and other additives, not having physiological and pharmacological activities, having good physico-chemical stability, and not

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affecting the dissolution and bioavailability of tablet preparations (Hasisoewignyo and Fudholi, 2013). The fillers that can be used are lactose, dextrose, Microcrystalline cellulose, glucose, sucrose, starch, calcium carbonate, dicalcium phosphate, and magnesium carbonate (Ansel HC, 2014).

2. Binder

Binders provide adhesion to the powder mass during granulation and to tablet presses and add to the cohesion already present in the excipients. Binders can be added in dry form, but are more effective when added in solution. Common binders include gelatin, sucrose, povidone, methylcellulose, carboxymethylcellulose and hydrolyzed starch pastes. The most effective dry binding agent is microcrystalline cellulose, which is commonly used in making direct compressed tablets. (RI Ministry of Health, 2014).

3. Destroyers

A disintegrant, also known as a disintegrant, is a material that helps the tablet disintegrate after being swallowed. The disintegrant content, the method of addition and the degree of density play a role in the effectiveness of the disintegration of the tablet (DepKes RI, 2014).

4. Lubricant Material

Lubricants or lubricants reduce friction during the tablet compression process and are also useful for preventing tablet mass from adhering to the die. Stearic acid compounds with metals, stearic acid. In general, lubricants are hydrophobic, so they tend to reduce the speed of tablet disintegration and dissolution. Therefore excessive levels of lubricant must be avoided. Polyethylene glycol and some lauryl sulfate salts are used as soluble lubricants, but such lubricants generally do not provide optimal lubricating properties, and higher concentrations are required (DepKes RI, 2014).

METHOD

The method in this study was an experiment in which the research was carried out in the Solid dosage formulation laboratory, Pharmacy Study Program, University of North Sumatra, Medan and the testing of felt tablets was carried out in the Solid dosage formulation laboratory, Pharmacy Study Program, Imelda University, Medan. The duration of this research was carried out for 4 months from February - June 2023.

RESULTS AND DISCUSSION

Descriptive Result

Gadung starch was tested physically, organoleptic and qualitatively. The results show ordinary starch which is produced from durian fruit seeds in the form of very fine powder, cream color, odorless and tasteless. The gadung powder was examined under a microscope with a magnification of 400 times. These starch granules are concentric starch which is generally small round and oval in shape with a hilus in the middle as shown in the picture.

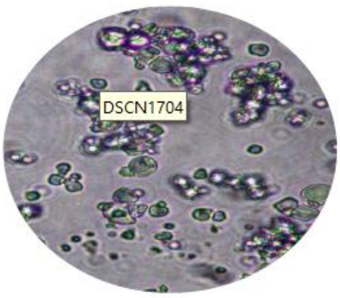

Figure 1. The gadung powder was examined under a microscope with a magnification of 400 times.

Table 1. Granule angle of repose

No	Formula	Flow time	granule angle of repose
1	F1	6,34	32,44
2	F2	5,30	31,42
3	F3	5,45	31,65

The data obtained shows that formula I, formula II, and formula III have angles of repose that meet the requirements, namely (32.44°), (31.42°), and (31.65°). If seen from the graphic data, it shows that the smallest angle of repose is formula II (31.42°) and formula I has the largest angle of repose (31.44°) from where the formula is. The results of the data show that the angles of repose for the four formulas meet the requirements. A good angle of repose is an illustration of the non-cohesive nature of the granules so that they provide good flow properties, spread out, and form low piles.

Based on the results of the one-way ANOVA statistical data, the p-value in the sig column was 0.000 <0.05 level of significance (α). This proves that there are differences between one formula and another. This is due to the difference in the concentration of Gadung starch as a binding agent for mefanamic acid

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Kompresibility OF Granulated

Table 2. Compresibility (%)

No	Formula	Compresibility %
1	F1	5,82
2	F2	5,87
3	F3	5,96

The results of the data show that the tap index is less than 20% and the lower the concentration of Gadung starch, the better the index value. Where the formula I, formula II, and formula III have a determination index of 5.82%, 5.87%, and 5.96%, the better compressibility index is formula III, this is shown when the granules are already more resistant to impact so there is less volume shrinkage. The results of the data from the one-way variant ANOVA statistics of formula I and formula II obtained a p-value in the sig column of 0.000 <0.05, which means that it shows a significant difference between formula I and other formulas. This is because the addition of Gadung starch concentration as a binder for mefanamic acid tablets greatly affects the flow time of the granules. Whereas formula I and formula III obtained p-values in the sig column 0.00 < 0.05 level of significant (α), this proves that there is a significant difference between formula I and formula III, due to the addition of Gadung starch to mefanamic acid tablets effect on the index setting

Tablet Evaluation

Based on the evaluation results of the examination of formula I to formula III tablets, the resulting tablets weighed 250 mg, had an average diameter of 1.06 cm and an average thickness of 0.78 cm.

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These tablets have a uniform shape and color, namely flat round tablets with a brownish white color, while the aroma has a distinctive odor with a bitter taste

Tablet Hardnest Test

Table 3. Compresibility (%)

No	The weight of Amlum Gadung	F1 (3%)	F2(6%)	F3(9%)
1	F1	0,649	0,649	0,650
2	F2	8,82	7,09	7,02
3	F3	1,35	1,09	1,07

From the results of the evaluation of weight uniformity in F1 to F3, the requirements were met, namely the tablet weight was not more than two tablets which deviated from the average tablet weight set in column A, which was 5% and not a single tablet deviated from column B, which was 10%.

Tablet Weight Uniformity Test

Table 4. Compresibility (%)

No	Tablet Weight Uniformity Test	F1 (3%)	F2(6%)	F3(9%)
1	Mean	7,19	6,2	5,3

Table hardness test is a test that describes the resistance of tablets against mechanical stress and shock. In the tablet hardness test that has been carried out, the results of the evaluation of tablet hardness are said to be good if they have a hardness of 4-8 kg (Parrot, 1971). In table 4, it can be seen that the evaluation results obtained from all formulations meet the requirements. It can be seen that the difference in concentration affects the hardness of the tablet. The higher the concentration of the starch binder formula, the lower the value obtained hardness. The hardness of tablets with gadung binder has met the requirements. This is because gadung has good compressibility (Agoes, 2006).

This test was carried out by one-way ANOVA testing. The significance value obtained is 0.00 <0.05 so that Ho is rejected, because there is a significant difference in the gadung formulation and the gadung formulation as a binding agent for mefan acid tablets.

CONCLUSION

Based on the results of the research that has been done, it can be concluded that the use of gadung starch as a binder can produce mefanamic acid tablets that meet the requirements for uniformity of tablet weight, tablet hardness, tablet friability, and tablet disintegration time in the Indonesian Pharmacopoeia. The addition of gadung starch (Discorea Hispida Dennst.) as a binder to mefanamic acid tablets causes differences in the physical properties of the tablets, namely in greater tablet hardness, smaller tablet friability and longer tablet disintegration time.

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