Ad-Dawaa' Journal of Pharmaceutical Sciences
ISSN: 2654-7392, E-ISSN: 2654-6973
Vol. 4, No. 2, December 2022, Hal. 15-20
DOI: https://doi.org/10.24252/djps.v4i2.25212

Modified Cassava Starch as A Tablet Binder in Direct Compression Method

Wira Noviana Suhery*, Anita Lukman, Afriyanti

Department of Pharmacy, Sekolah Tinggi Ilmu Farmasi Riau, Pekanbaru, Indonesia

*Corresponding author e-mail: wiranoviana@stifar-riau.ac.id

ABSTRACT

Research on the potential of modified cassava starch as a binder for the direct compression method has been carried out. The use of modified cassava starch as a binder using six formulas with the drug model ibuprofen. Variations in the concentration of modified cassava starch were modified cassava starch 48 and modified cassava starch 72 were 15%, 17.5%, and 20%, respectively. The formula with a modified starch 72 concentration (15%) is the best formula that produced optimal tablets. The value of hardness was 5.3 kg/cm2, friability of 0.90%, and disintegration time of 2.06 minutes which are the main parameters of the binder.

Keywords *: Binder, Direct Compression, Ibuprofen, Tablets.*

INTRODUCTION

There are two kinds of starch in the pharmaceutical industry, namely natural starch, and modified starch. Starch in its natural form (native starch) is starch produced from tubers and has not undergone changes in physical and chemical properties or processed chemically-physically. This starch is widely used in the food and pharmaceutical industries as a filler and binder in the manufacture of tablets, pills, and capsules (Ostertag, 2001).

Native starch causes several problems related to retrogradation, low stability, and low paste resistance. This is the reason for starch modification (Fortuna *et al*., 2001). Modification of starch is an attempt to change the chemical and physical properties of native starch. Modification of starch can be done by cutting the molecular structure, rearranging the molecular structure, oxidation, or substitution of chemical groups on the molecule. There are several modification methods, including chemical, physical, and hydrolysis modifications (Wurzburg, 1989).

In our previous studies, the manufacture and test of the physical properties of modified cassava starch and modified cassava flour (MOCAF) by fermentation using lactic acid bacteria (*Lactobacillus* sp). Modification of starch using fermentation is an enzymatic method that is considered safe and environmentally friendly (Oyeyinka *et al*, 2020). Based on the evaluation carried out, it was found that the modified cassava starch produced better flow and compressibility properties, as well as a change in the shape of

the surface of the starch granules with several large diameter shallow holes. Therefore, it can strengthen the bonds between grains so that it is potential as a binder in tablet formulations. The study used modified cassava starch as a filler, binder, and disintegrant in one formula. However, the resulting tablet has a high friability (Suhery *et al*., 2013).

The binder in the tablet formulation serves to increase the cohesiveness between the powder particles. A good binder can not only produce tablets with sufficient hardness but also have good disintegration time. The most appropriate parameter to evaluate the quality of a binder is HFR (Hardness-Friability-ratio) to estimate the mechanical strength of the tablet, being a ratio that compares strength. It has been stated that the higher the HFR value, the stronger the tablet (Ugoeze and Nwachukwu, 2020).

Therefore, this study aims to determine the potential of modified cassava starch as a binder in the direct compression method. The concentration of modified cassava starch was varied to find the best formula that gave the HFR value and disintegration time that met the requirements.

MATERIAL AND METHODS

Materials and Instrument

Modified cassava starch 48 and modified cassava starch 72 were prepared by the method developed by Suhery *et al*., 2013, ibuprofen, potassium dihydrogen phosphate, aquadest, sodium hydroxide (NaOH), avicel PH 101, magnesium stearate.

Analytical balance (Shimadzu®), spatula, mortar and pestle, single-punch tablet machine (TDP®), friability tester, calipers (Tricle brand®), Monsanto stokes, disintegration tester (Distek®), dissolution tester (Electrolab®), and UV spectrophotometer (Shimadzu®).

Formulation of ibuprofen tablet

Tablets ingredients were accurately weighed as mentioned in Table 1. Ibuprofen, modified cassava starch 48 or modified cassava starch 72, avicel PH 101 were mixed in a big mortar. Then, magnesium stearate was added and mixed for 3 minutes. The blend powder was compressed using a single punch tablet machine.

Evaluation of tablet properties

Weight uniformity

The average tablet weight was calculated using 20 tablets. The tablets are weighed individually, there may not be two tablets each of which deviates from the average weight by more than the value of 5%, and there may not be a single tablet that deviates from the average weight by more than the value of 10%.

Hardness determination

A total of 20 tablets were taken randomly and hardness was measured using a hardness tester. The mean value of tablet hardness and standard deviation was calculated.

Friability testing

A total of 20 tablets were taken randomly. The tablet samples were weighed accurately

Table 1. Formulation of ibuprofen tablet with modified cassava starch as a tablet binder

Materials	Formulas					
	FI	FII	FIII	FIV	FV	FVI
Ibuprofen (mg)	400	400	400	400	400	400
Modified cassava starch 48 (%)	15	17.5	20	-	-	-
Modifed cassava starch 72 (%)	-	-	-	15	17.5	20
Avicel PH 101 (%)	23.26	20.76	18.26	23.26	20.76	18.26
Mg stearat (%)	0.2	0.2	0.2	0.2	0.2	0.2
Quantity per tablet (mg)	650	650	650	650	650	650

and placed each in the friability tester, respectively. After a certain number of cycles (100 revolutions per 4 minute). Weight loss indicates the tablet's ability to withstand this type of wear. Percent friability is determined using the following formula:

$$\%\ friability \frac{(initial\ weight - final\ weight)}{initial\ weight} x\,100$$

Disintegration test

Disintegration time was measured for 6 tablets by inserting a disc into each tablet using 900 ml of purified water at 37±2ºC in disintegrating apparatus. The disintegration time of the tablets was recorded until the tablets disintegrated. The result of this measurement is no more than 15 minutes.

Dissolution test

The dissolution of ibuprofen tablets was measured using dissolution apparatus. Each tablet was put into a dissolution flask in 900 mL of phosphate buffer solution pH 7.2 at 37 ± 0.5˚C at 150 revolutions per minute. A total of 5 ml samples were taken at intervals of 5, 10, 15, 20, 25, and 30 minutes. Each sampling was replaced with 5 ml of dissolution medium. The concentration of ibuprofen from each sample (n=3) was determined using spectrophotometer UV-Vis at a maximum wavelength of 264.2 nm.

Measurement of tablet size uniformity

Measuring the thickness and diameter of the tablet using a caliper. A total of 20 tablets were taken randomly. Then the diameter and thickness of the tablets were measured respectively.

RESULTS AND DISCUSSION

In this study, modified cassava starch 48 and modified cassava starch 72 were used as a binder in the direct compression of ibuprofen tablets. Modified cassava starch 48 and modified cassava starch 72 are starch which is modified by fermentation with *lactobacillus* sp for 48 and 72 hours, respectively. Characterization of the physicochemical properties of modified cassava starch showed better properties compared to native starch. The results of the characterization of modified cassava starch have been reported by Suhery *et al*, 2013.

In this study, ibuprofen was used as the drug model. Ibuprofen is a BCS class 2 drug with low solubility and high permeability. Thus, the formulation factor is one of the factors that can increase the dissolution of ibuprofen. Avicel PH 101 is used as a filler as well as a disintegrant in the formula. Amount of Avicel for each formula is different because

Table 2. Evaluation of ibuprofen tablets

Parameters	F I	F II	F III	F IV	F V	F VI
Weight (g)	0.64	0.65	0.65	0.65	0.65	0.65
Tablet weight deviation (%)	0.01	0.01	0.01	0.01	0.01	0.01
Diameter (cm)	1.30	1.30	1.30	1.30	1.30	1.30
Thickness (cm)	0.47	0.46	0.46	0.46	0.46	0.45
Hardness (kg/cm²)	4.89	4.65	4.99	5.30	5.27	5.18
Friability (%)	2.47	2.39	1.42	0.90	1.32	2.51
Disintegration time (min)	3.13	1.21	1.00	2.06	0.80	0.69
HFR	1.98	1.94	3.51	5.89	3.99	2.06
Drug content (%)	102.79	101.64	102.03	104.90	104.32	105.09

Avicel se rves to suffice the tablet weight up to 650 mg per tablet. There are variations in the concentration of modified cassava starch as a binder, effect to concentration of Avicel different for each formula. Avicel PH 101 is MCC original quality, while PH 102 is available as a partially agglomerated product with a larger particle size distribution and slightly better fluidity. The two values do not show a significant difference in compressibility (Figure 1) (Chaerunisaa *et al*, 2019).

Evaluation of weight uniformity is one of the parameters to show the uniformity manufacturing tablet. The weight uniformity affects the homogeneity of drug content (Priyambodo, 2007). The weight uniformity of the tablet must show no more than two tablets whose weight deviated by 5% from the average weight, and there was not a single tablet whose weight deviated by 10% from the average weight. tablets (Departemen Republik Indonesia, 2020). The results showed that all formulas of ibuprofen tablets have weight uniformity based on Indonesian Pharmacopeia (Table 2).

Friability is influenced by less binding powder, too much fine powder, inappropriate use of binder materials, and too dry blend mass. The friability value of all formulas showed that the six formulas have different levels, ranging from 0.90 to 2.51%. Based on the results obtained, only FIV meets the value of friability requirements (<1%).

Disintegration time is the time required for a tablet to mechanical break up of a compressed tablet into small granules upon ingestion. Based on the result of the disintegration time showed that all formula meets the disintegration time requirement i.e no more than 15 minutes (Departemen Republik Indonesia, 2020). Modified cassava starch 72 FIV showed faster disintegration time than other formulas. This is due to water absorption capacity and swelling power.

Based on the HFR values obtained, FIV is the best formula for ibuprofen tablets. This value is obtained by comparing the hardness and friability of tablets. The greater of HFR values the better the mechanical strength of the tablets (Ugoeze and Nwachukwu, 2020).

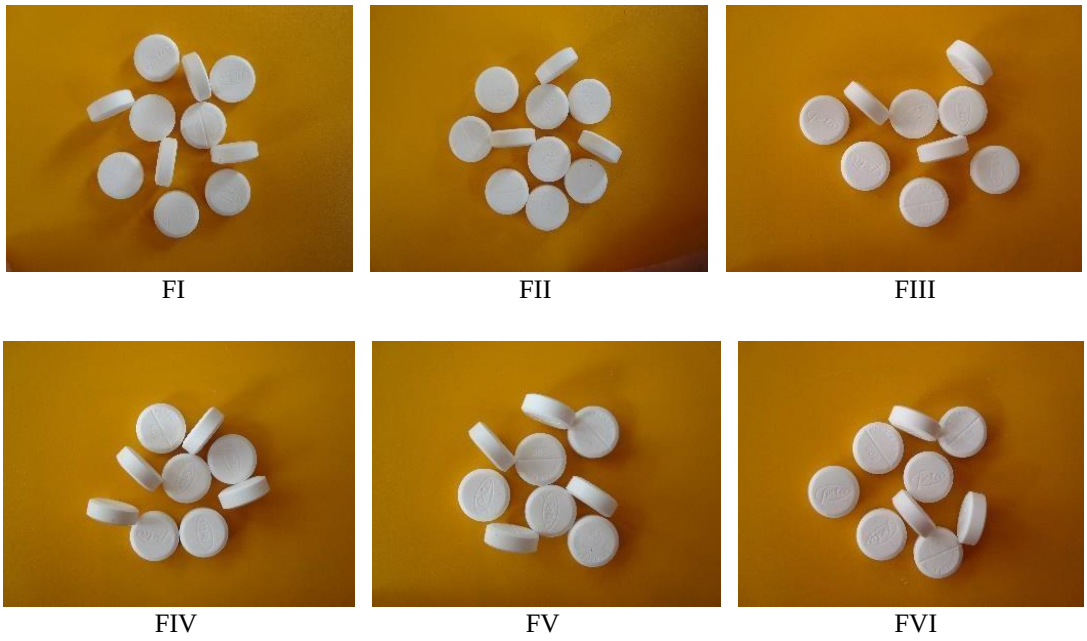

Figure 1. Ibuprofen tablets

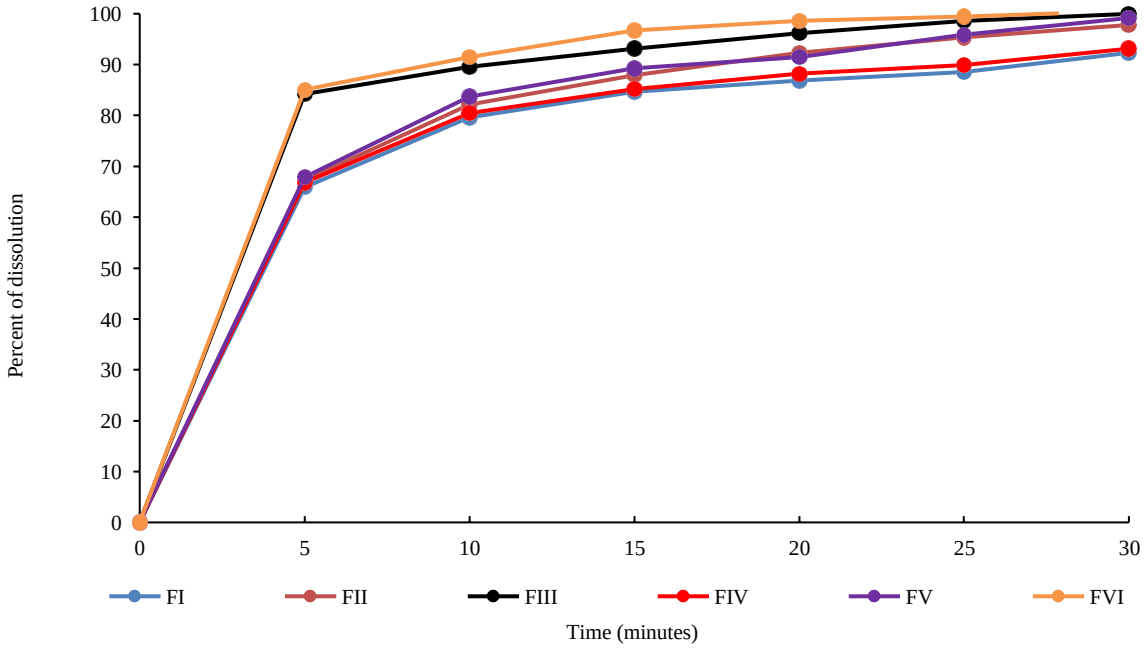

Figure 2. The dissolution profile of ibuprofen tablets

Based on the Indonesian Pharmacopoeia VI edition, the requirements for determining the concentration of the active substance Ibuprofen are 90 %-110%. From the results obtained, the formula meets the requirements, namely FI 102.79%, F II 101.64%, F III 102.03%, F IV 104.90%, FV 104.32%, F VI 105.09%. However, the results obtained are quite large, which is more than 100%. This is possible due to the homogeneity of the mixture during mixing and the variations during the compression process.

The results of the dissolution test of ibuprofen tablets in a phosphate buffer medium of pH 7.2 showed the dissolution level of the substance per unit time (Figure 2).

Percent dissolution of ibuprofen tablets within 30 minutes are FI (92.32%), F II (97.80%), F III (99.99%), F IV (93.14%), FV (99.16%), FVI (100.54%). These results indicated that the value obtained exceeds the value of Q, which is not less than 80% dissolved in 60 minutes (Indonesian pharmacopeia VI). Based on the evaluation results, the physical properties of the tablets showed that all formulas meet the specified requirements.

CONCLUSION

Modified cassava starch 72 has the potential as a binder tablet in the direct compression method with a concentration of 15%. The tablet characteristics have good mechanical strength, as well as disintegration times and dissolution that meet Indonesian pharmacopoeia requirements.

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