

EVALUATION OF DISINTEGRATION AND DISSOLUTION TEST OF METOCLOPRAMIDE ORALLY DISINTEGRATING TABLET USING MALTODEXTRINS FROM BANANA STARCH (*MUSA PARADISIACA* L) AS SUPERDISINTEGRANT

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ABSTRACT

Objective: The objective of this study was to know maltodextrin can be used as a superdisintegrant and to know the dissolution time and to know disintegration and dissolution test of metoclopramide orally disintegrating tablet (ODT) better than conventional metoclopramide tablets.

Methods: The methods used in this study include the formulation of banana starch, formulation of maltodextrin, and then maltodextrin formulated into ODT with metoclopramide drug model, and evaluated the disintegration and dissolution test of ODT metoclopramide.

Results: The results of the evaluation of 5 ODT formulas studied, showed ODT with maltodextrin 15% (ODT 4) gave the fastest *in vitro* disintegration of 22.2 s, the *in vivo* disintegration averaged between 55.38 s and 75.72 s, and dissolution test results against ODT 4 and metoclopramide tablets (positive comparator) showed statistically significant differences ($p < 0.05$).

Conclusion: Maltodextrin can be formulated superdisintegrant on metoclopramide ODT by giving disintegration, and dissolution was better than the conventional tablets.

Keywords: Maltodextrin, Superdisintegrant, Orally disintegrating tablet.

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INTRODUCTION

Maltodextrin is one of the starch derivatives known as safe food [1]. Maltodextrins are produced from a partial hydrolysis process by an α -amylase enzyme having a dextrose equivalent (DE) value of <20. Maltodextrins have high solubility and are readily soluble in cold water, capable of forming films, low hygroscopicity, capable of dispersing auxiliaries, and capable of inhibiting crystallization and has a strong binding [2]. Maltodextrins are oligosaccharides belonging to prebiotics. Starches of this group provide more benefits in the food industry, even pharmaceuticals. In the pharmaceutical field, maltodextrin has also been used as a thin-film coating agent and as a drug carrier niosome [3].

Banana is one of the plants that contain the source of starch. However, not all types of bananas produce starch with good quality. The best result of starch is starch made from banana [4]. The banana has good physicochemical properties, so banana has great potential to be developed as food and other necessities, for example, as an additional material in the pharmaceutical field, either in the form of original starch or in the form of modified result.

Drug delivery systems are a means of strategy for product development and extending the product life cycle in the pharmaceutical market. To assist patients, several rapidly destroyed drug delivery systems have been developed [5]. One of them is an orally disintegrating tablet (ODT). According to the Food and Drugs Administration, USA, ODT is defined as a solid dosage form containing the active compound of the drug, which can be destroyed rapidly, usually in seconds, when placed on the tongue. The main criterion of ODT is rapidly destroyed in the oral cavity with the help of saliva in 15–60 s [6]. The desiccant (disintegrant/superdisintegrant) is used to meet the criteria by which the tablet is destroyed at a set time limit.

Based on the nature and usefulness of maltodextrin described above and to improve the use of maltodextrin, the authors are interested in

conducting research on the use of maltodextrin from banana starch as superdisintegrant in the ODT preparation with the metoclopramide drug model.

METHODS

Research design

The methods used in this study include the manufacture of banana starch and maltodextrin manufacture, then maltodextrin is formulated into ODT preparations. The ODT preparation will be evaluated for crushing time *in vitro*, *in vivo*, and dissolution.

Materials

The ingredients used in this study were raw bananas, distilled water, α -amylase enzymes (LIPI Bogor), commercial maltodextrin (Qinhuangdao Lihua Starch Co., Ltd.), metoclopramide tablets (Soho), and pro quality chemicals analysis (E Merck, Germany), namely: Sodium sulfite, sodium hydroxide, hydrochloric acid, magnesium stearate, talc, and mannitol.

Preparation of banana starch

The raw banana peel is peeled, washed, cut into pieces, then weighed with a total weight of 500 g, put in a blender and 500 ml of Sodium Sulfite solution, turned on a blender for 2 min at low speed, then covered with a cloth, squeezed, then the dregs are added with distilled water, scraped, and squeezed again until the water is clear. The combined filtrate was allowed to stand for 12 h, then discharged the solution and added distilled water, silenced again until the solution was clear. The solution was removed, and the resulting starch deposit was dried in an oven at 40°C for 48 h, then dried starch, crushed inside the mortar, and sieved with no sieve 60. The obtained banana starch is stored at room temperature in a sealed container [7].

Preparation of maltodextrin

60 g of banana starch is suspended with distilled water until the volume is 300 ml. The resulting suspension regulated its pH to 5.5 using pH

meter by adding 0.1 N NaOH. To the mixture was added 50 ml of α -amylase enzyme then incubated for 30 min at 60°C. Subsequently, the mixture was cooled by immersing the container in cold water to a temperature of 30–40°C, to stop enzyme activity by adding HCl 0.1 N to a pH of 3.5–4.5. After 30 min, the obtained solution was neutralized with 0.1 N NaOH to a pH of 7.0. The results obtained in the freeze dryer then determined DE. The obtained maltodextrin is stored at room temperature in a sealed container [8].

Preparation of ODT Metoclopramide

Tablets are made in direct print with 200 mg tablet weight and 9 mm cross-section. Maltodextrin was used as a disintegrant with concentrations of 0%, 5%, 10%, 15%, and 100% (ODT1-ODT5). Drugs used are metoclopramide HCl.

The composition of ODT Metoclopramide can be seen in Table 1.

Each material is weighed and then put into the mixture and mixed until homogeneous. The homogeneous mixture is then printed directly with the tablet press machine.

Evaluation of destroyed time *in vitro*

One tablet is inserted in each tube of the basket and used water temperature $37 \pm 2^\circ$ as a medium, then tool run. The crushed time of the tablet is recorded that since the basket containing the tablet is raised down until the tablet is destroyed. Tablets declared destroyed if no part of the tablet left behind Dikasa [9].

Evaluation of destroyed time *in vivo*

This test uses six volunteers before the test runs, each volunteer is required to wake his mouth, then attach one ODT tablet on top of their tongue and leave the tablet completely destroyed. The time it takes for the tablet to crumble without chewing is calculated, after which the tablet is immediately spit out. Repeat 3 times for each volunteer. The endpoint for the crushed time of the mouth is the time when the tablet wrapped in the tongue becomes crushed (the tablet is not intact anymore).

Evaluation of dissolution test

In vitro, drug release studies were performed using a Type 2 (paddle) dissolution tool with a dissolution medium of 900 ml of $37 \pm 0.5^\circ\text{C}$ with a spin speed of 50 rpm within 30 min. At intervals of 1 min, 2.5 min, 5 min, 10 min, 15 min, 20 min, 25 min, and 30 min, then 10 ml of the trailer was taken. The cupping takes place in the same position that is between the surface medium of dissolution and the upper part of the paddle no <1 cm from the container wall [10]. This sample solution is then measured uptake using an ultraviolet spectrophotometer at a wavelength of 272 nm. Furthermore, the cumulative percentage of drug release is obtained. The dissolution test was performed on ODT and metoclopramide tablets.

Data obtained from drug release profiles from ODT and metoclopramide tablet preparations were compared *in vitro*. Data were compared using t-test with significance 0.05 ($p=0.05$). Statistical analysis was performed using SPSS 16.0 program.

RESULTS

Results of banana starch examination

The source of starch used in this study is banana raw. The process of insulating starch is done using as many as 2000 g of raw banana. The yield of the isolation process is 875 g (43.75%) of banana starch. This shows that the starch content in the raw banana fruit has not been hydrolyzed. The characterization of banana starch can be seen in Table 2.

Result of maltodextrin examination

In this study used banana kepok starch as a source of raw materials for the manufacture of maltodextrin. The maltodextrin hydrolysis process of the banana starch is enzymatically enriched as follows: 60 g banana

Table 1: Formulation of ODT metoclopramide

Materials (mg)	Formulation code				
	ODT1	ODT2	ODT3	ODT4	ODT5
Metoclopramide	10	10	10	10	10
Maltodextrin	-	10	20	30	182.5
Magnesium stearate	5	5	5	5	5
Talc	2.5	2.5	2.5	2.5	2.5
Mannitol	182.5	172.5	162.5	152.5	-
Total	200	200	200	200	200

Metoclopramide=Drug, Maltodextrin=Disintegrant, Magnesium stearate=lubricant, Talc=Lubricant, Mannitol=Filler. ODT: Orally disintegrating tablet

Table 2: Result characterization banana starch

Examination	Result
Microscopic	Single items. Oval shape or round oval grains. Hilus is a point on a narrow end with a clear concentric lamella
Organoleptic	
Shape	Smooth powder
Color	White
Smell	No smell
Taste	No taste
Identification	
a. Suspension in water with heating	The white viscous solution is not transparent
b. Iodine test	Dark blue, when heated the blue color disappears and reappears when cooled
c. Litmus paper	Do not change the color of red litmus paper
d. pH meters	4.7
Water content	11.23%
Ash content	0.29%
Solubility	4.3%
Swelling power	8.6%

starch is suspended with distilled water up to 300 ml, so the total weight of the suspense is 300 g.

Result of destroyed time *in vitro*

In this study, the crushed time criterion of the ODT preparation is expected to be <30 s. To be able to meet the criteria of disintegration time required a disintegrant. Disintegrant is a material or combination of ingredients to expand and destroy the tablet after contact with water or disintegration medium so that the absorption of a nutritious substance works well. In this study used maltodextrin as a disintegrant. Use of maltodextrin as a good disintegrant is generally 5–15%. Excessive use of maltodextrin will actually decrease the destruction time of tablets. The crushed time *in vitro* tablet meets the expected criteria except on ODT1 and ODT5. ODT1 gives a break time of 80.5 s; this is due to the composition of the formula in ODT1 in the absence of maltodextrin as a disintegrant. The result of tablet to ODT1-ODT5 can be seen in Table 4.

Crusher added to facilitate rupture or destruction of tablets when in contact with liquids, may also serve to pull water into the tablet, inflate and cause the tablet to rupture [11]. While on ODT5 gives the destruction time of 83 s. The high time destroyed tablets in ODT5 is due to the use of maltodextrins in large quantities (excessive). Known maltodextrins have the ability to add cohesion between the particles so that the density of the granules will be higher, causing the longer disintegration time.

Table 3 also shows that ODT4 has the fastest *in vitro* breakdown time of 22.2 s, compared to ODT3 (27.5 s), ODT2 (36.5 s), ODT1 (80.5 s), and ODT5 (83, 8 s). ODT4 is a formula using 15% maltodextrin as disintegrant and mannitol as filler. This ODT4 shows the fastest *in vitro*

Table 3: Condition manufacture of maltodextrin from banana starch

Temperature (°C)	Enzyme volume (ml)	Time (menit)	Fehling test	DE
72	15	15	-	-
72	30	15	-	-
60	15	15	-	-
60	15	30	+	5
60	30	30	+	11
60	50	30	+	17, 18

DE: Dextrose equivalent

Table 4: Result of tablet to ODT1-ODT5

Formulation code	Time destroyed* <i>in vitro</i> (detik)
ODT1	80.5±2.9313
ODT2	36.5±1.0393
ODT3	27.5±0.8830
ODT4	22.2±1.0756
ODT5	83.0±1.7895
Criteria	<30 detik

*6 repetition treatments. ODT: Orally disintegrating tablet

destroy time. Based on the above description, the researchers chose the ODT4 formula untu evaluated further.

Result of destroyed time *in vivo*

Destroyed time *in vivo* is the time it takes to break down in the mouth. The endpoint for time devastated in the mouth is the time when the tablets are placed on the tongue, crushed until there is no complete clump. The results of the destroyed *in vivo* ODT4 time test can be seen in Appendix 38 which shows that all the formula meets the expected criteria as ODT in this study since the *in vivo* crushed time of the tablet's average is about 55.38±0.296 s–75.72±1.5856 s (<60 s).

In the mouth, the fastest *in vivo* destroyed time was about 55.38±0.296 s, indicated by the 5th volunteer; this corresponds to the expected ODT criterion of <60 s. This indicates that the tablet will be destroyed when contact with saliva in the mouth. A low salivary amount (about 2 ml) in the mouth. Results *in vivo* degradation time longer than wetting time.

Result of dissolution test

The dissolution test was performed using a rowing method with a speed of 50 rpm, a distilled water medium, which within 30 min of dissolved metoclopramide was not <75% of the amount indicated on the label.

In this study expected dissolution criteria of ODT metoclopramide gave the release of an active ingredient not more than 30% at min 1 and not <85% at min 15. Dissolution tests were performed on ODT4 and metoclopramide tablets. The cumulative average of the dissolution test results can be seen in Table 5:

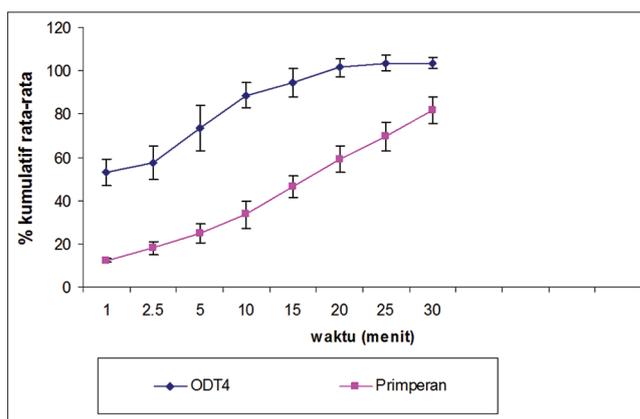
The average cumulative% graphic image of the dissolution test results of the ODT4 and metoclopramide tablets can be seen in Fig. 1.

From Table 5 and Fig. 1, it can be seen that cumulative percent dissolved in the 1st min, 15th min, and 30th min for ODT4 53.17%, 94.70%, and 103.64% while for tablet metoclopramide of 12.40%, 46.37%, and 81.69%. Drug release from ODT4 does not meet the expected criteria, although ODT4 provides drug release about 2–4 times faster than metoclopramide tablets. This suggests that maltodextrin as a disintegrant may increase the rate of drug release. The rate of drug release is the stage that most determines the speed of drug bioavailability [8].

Table 5: Result of dissolution test average ODT4 metoclopramide

Tablet name	Time (min)	% cumulative average	Deviation standard*
ODT4	1	53.1722	6.2626
	2.5	57.6299	7.8990
	5	73.4161	10.589
	10	88.7379	5.5794
	15	94.6993	6.5228
	20	101.599	4.2240
Metoclopramide tablet	25	103.489	3.6289
	30	103.635	2.5148
	1	12.4042	0.6071
	2.5	17.9895	2.9031
	5	24.851	4.6533
	10	33.4791	6.2200
	15	46.3697	4.8675
	20	59.06	6.1405
	25	69.4786	6.7129
	30	81.6883	6.0193

*6 repetition treatments. ODT: Orally disintegrating tablet

**Fig. 1: The average cumulative cumulative graph of the dissolution test results of the orally desintegrating Tablet 4 and metoclopramide tablets in the distilled water distillation medium**

CONCLUSION

Based on the observations made and the discussion can be concluded that maltodextrin derived from the process of hydrolysis of banana starch with the α -amylase enzyme can be used as a superdisintegrant in the manufacture of ODT. Viewed from the crash time, and drug release profile that meets ODT criteria. The dissolution of ODTs is better than the dissolution of metoclopramide tablets because ODT4 provides faster drug release than metoclopramide tablets and shows statistically significant differences ($p < 0.05$).

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